Tetrahedron. Vol. 29, pp. 2575 to 2583. Pergamon Press 1973. Printed in Great Britain

THE CHEMISTRY OF *DODONAEA* SPP—IV†
DITERPENE AND FLAVONOID COMPONENTS OF *D. ATTENUATA*

T. G. PAYNE and P. R. JEFFERIES*
School of Chemistry, University of Western Australia, Nedlands, Western Australia, 6009

(*Received in the UK* 19 *February* 1973; *Accepted for publication* 29 *March* 1973)

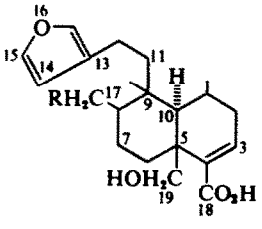
Abstract—Further details are given for the assignment of absolute stereochemistry to the acetoxy-hydroxy-acid (**1**) from *D. attenuata* and the lactone (**6**) from the var. *linearis*. The latter also provided a diene-acid shown to have structure **28**. Reductive cyclisation of the tosylate of the latter gives a cyclopropane derivative (**31**). A flavone from the var. *linearis* is shown to be 5,7-dihydroxy-3,4',6-trimethoxyflavone (**32**).

In 1967 we published a brief paper[1] assigning structure and absolute stereochemistry to the acetoxy-hydroxy-acid (**1**) from *Dodonaea attenuata* A. Cunn. In addition, the var. *linearis* Benth. gave a lactone (**6**) which was inter-related with **1** and which we considered to be the lactone from hautriwaic acid which had been reported[2] from *D. viscosa* in 1936. This view has since been confirmed by direct comparison[3] of samples. In the last few years the structures of several other diterpenes have been assigned in this[4] and other laboratories[5,6] by inter-relation with **1** and **6** and we now wish to describe the isolation and structure assignment to some minor components. We also take this opportunity to present further details associated with the earlier article.

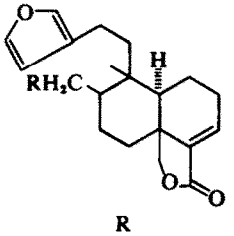
The hydroxy-acid (**1**, **2**, **3**) and lactone series (**4**, **5**, **6**) were inter-related by cyclisation of the former with NN'-dicyclohexylcarbodi-imide or alkaline hydrolysis of the latter, preferably in t-butyl alcohol, in view of the tendency of the lactones to undergo Michael-type additions. Easy manipulation of the functional groups in **1** required differentiation of the unsaturated A ring system from the furan and this was achieved by reduction with Na-EtOH which gave the lactone (**10**) and the dihydroxy acid (**7**). The latter was epimerised and cyclised to **10** via the methyl ester (**8**). At a later stage we found that di-imide reduction of the unsaturated acids gave good yields of the lactone (**10**) retaining the furan ring; a process which has been used by others.[7] The reduced lactone now provided a suitable base for the degradation sequences which were used to establish the structures. These were detailed in the short communication and are given in Schemes 1 and 2. The stereochemical arguments are also adequately detailed in the earlier note and are not repeated here.

Hydrolysis of esters of the hydroxy-acid or the lactones resulted in a proportion of β-addition to the conjugated system and this became the dominant reaction when the ester of **1** was treated with sodium methoxide in methanol. After saponification the methoxy-lactone (**25**) was obtained in good yield. The configuration of the methoxyl group follows from the NMR spectrum which shows the 4-H resonance (2·04 δ, *J* 9 Hz) expected for diaxial coupling.

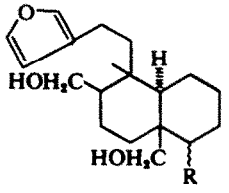
The NMR spectra of the lactones normally revealed the C 19-H_2 as a broad singlet. However, in the unsaturated hydroxy-lactone (**4**) and the nitrile (**27**) obtained by dehydration of the oxime



R
1: OAc
2: OH
3: H

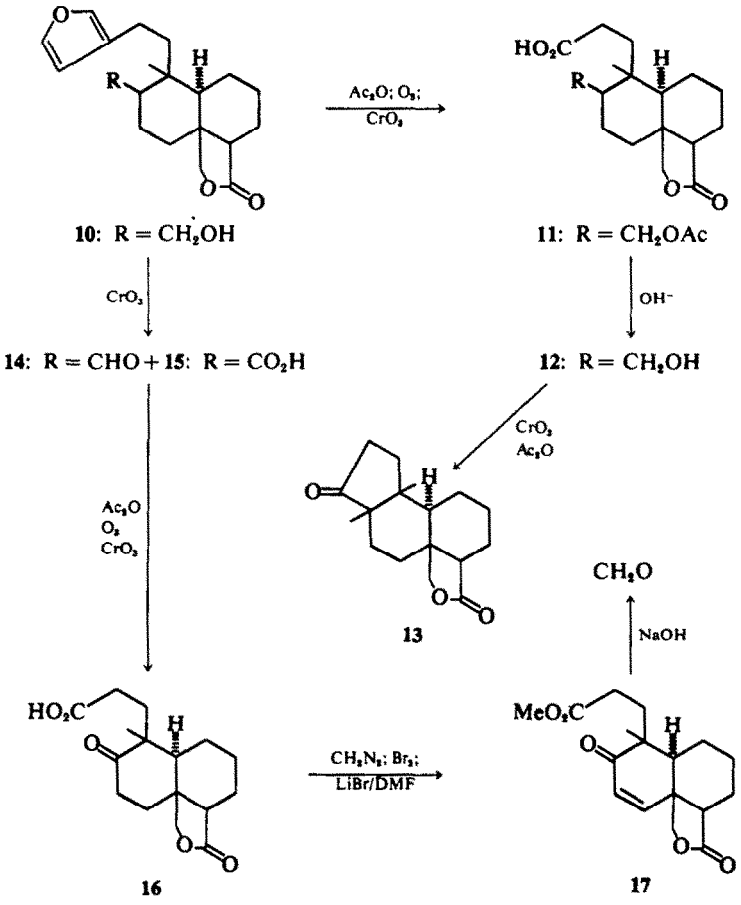


R
4: OH
5: OAc
6: H



R
7: αCO_2H
8: αCO_2Me
9: βCH_2OH

†Part III see Ref. 1. The papers *Tetrahedron Letters*, 1964, 3475 and *Aust. J. Chem.*, 1966, **19**, 2133 are regarded as Parts I and II, respectively.

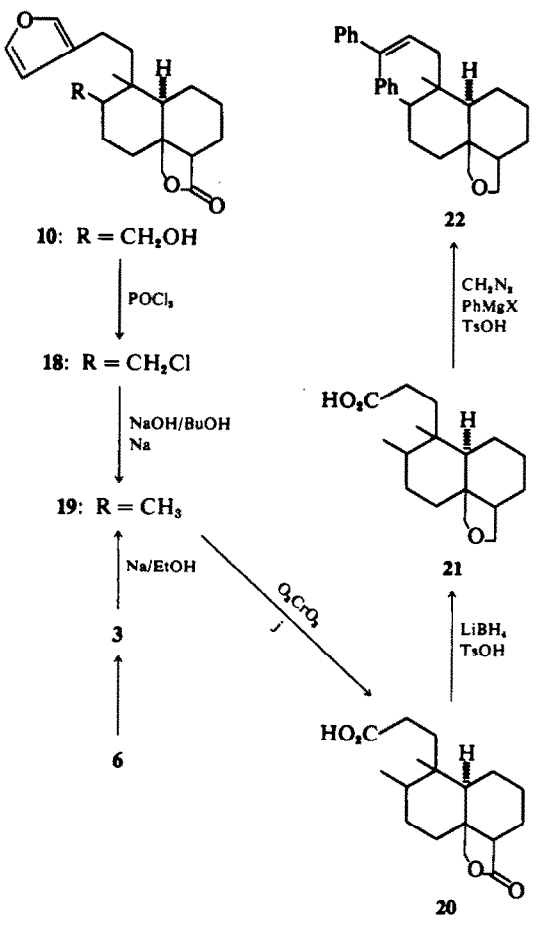


SCHEME 1

derived from the aldehyde (**14**) the signals were well separated, clearly revealing a long range coupling to one of the protons. Although W pathways are possible for the 4α-H or 6α-H in the nitrile (**27**) only the latter is acceptable for the lactone (**4**). In support of this there is no long range coupling evident in the spectrum of the Δ^6-lactone (**17**).

In addition to the lactone (**6**) the var. *linearis* also provided the hydroxy-diene-acid (**28**), separated from the lactone (**6**) as its methyl ester (**29**). Basic hydrolysis of the latter in t-butyl alcohol then gave the diene-acid (**28**). The spectral data for the lactone (**6**) strongly suggested its structure and this was confirmed by hydrolysis to the hydroxy acid (**3**) which could be reduced to the lactone (**19**) with di-imide or Na-EtOH. The lactone (**19**) had been derived before from **1** by way of the chlorolactone (**18**).

The NMR spectrum of the hydroxy-diene-ester (**29**) showed signals at 7·25 and 7·10 for the two α protons of a β-substituted furan, a triplet at 6·77 ($J \sim 3$ Hz) due to a vinyl proton β to carbonyl and a broad singlet at 6·14 δ due to two equivalent vinyl protons and the β proton of the furan ring. Singlets at 3·73 and 3·59 were assigned to $CO_2\underline{Me}$ and $\underline{CH_2}OH$ groups respectively. A singlet at 2·55 was assigned to the 10 H and signals at 0·86 δ arose from the secondary and tertiary methyl groups. The ester showed IR maximum at 3470 cm^{-1} for hydrogen bonded OH similar to that for the methyl ester of **3**. Bands at 3045 cm^{-1} and 1695 cm^{-1} corresponded to a disubstituted double bond and conjugated ester carbonyl respectively. The skeleton and disposition of oxygenated functions were established by reduction of the ester (**29**) with diimide which gave the lactone (**19**). The UV absorption shown by the acid (**28**) (λ_{max} 286, ε 9,200) can only be accommodated in the skeleton (**19**) as a doubly conjugated ester in the A-ring. The triplet nature of the C 3-H signal is evidently due to virtual coupling with the C 1-H which is magnetically equivalent to the C 2-H. In pyridine solution the C 1-H and C 2-H remain equivalent but are well separated from the furan β-H resonance and appear as a doublet (6·15 δ,

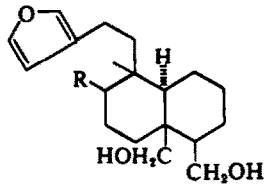


SCHEME 2

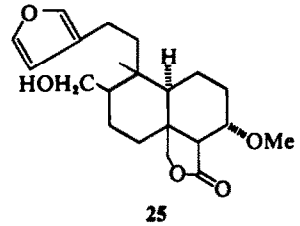
J 3 Hz). Coupling between the C-1 and C-10 protons is expected to be small since the associated dihedral angle is near 90°.

The ester tosylate (**30**) when reduced with $LiAlH_4$ gave an alcohol (**31**) characterised as its *p*-nitrobenzoate. The NMR spectrum of **31** showed a doublet at 0·14 δ (*J* 4·5 Hz) characteristic of a methylene proton of cyclopropane. Signals from the C-18 methylene group appeared as an AB pattern suggesting a hydroxymethyl group attached to a quarternary carbon; a signal (2H) at 5·59 δ ($W_{1/2}$ 4·5 Hz) conforms with the protons for an isolated double bond. The product (**31**) presumably arises by addition of hydride β to carbonyl followed by nucleophilic displacement of tosylate (see **30**). The alternative hydride addition to C-1 is discounted since the inductive effect of carbonyl favours hydride addition to C-3 rather than C-1 and the product had UV absorption (λ_{max} 209 mμ ε 8,200) expected for the furan without contribution from a vinyl cyclopropane chromophore.[8,9] Addition of hydride at C-1 should result in a 2-ene conjugated with cyclopropane.

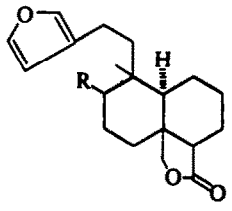
From a weakly acidic fraction of the var. *linearis* extract a pigment was isolated and this has been proved to be 5,7-dihydroxy-3,4',6-trimethoxyflavone (**32**). The NMR spectrum of the diacetate (**33**) showed methoxyl resonances at 3·89 (6H) and 3·79 (3H) from the three methoxyl groups, at 2·53 for the 5-OAc and at 2·38 (OAc). The aromatic proton signals 7·25 (8-H), 8·04 and 7·01 (B ring) were expected for the oxygenation pattern which was confirmed by diazomethane methylation to give the known 5-hydroxy-3,4',6,7-tetramethoxyflavone. Ethylation of (**32**) and alkaline degradation of the diethyl ether (**34**) gave p-methoxy-



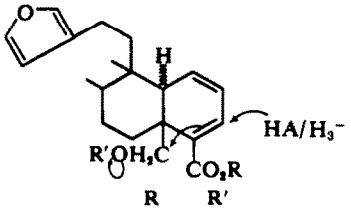
23: R = CH_2OH
24: R = CH_3



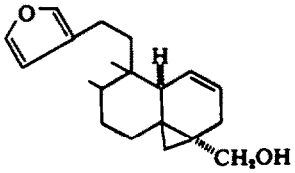
25



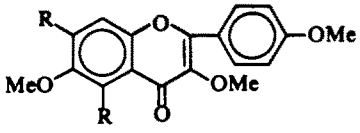
R
26: CH_2OTs
27: CN



	R	R'
28:	H	H
29:	CH_3	H
30:	CH_3	Ts



31



32: OH
33: OAc
34: OEt

benzoic acid and 2,4-diethoxy-6-hydroxy-ω,3-dimethoxyacetophenone.

EXPERIMENTAL

General experimental details are as described previously.[10] MS were recorded with a Varian MAT CH7 Spectrometer at 70 eV. NMR spectra were recorded on a Varian A60 Spectrometer for $CHCl_3$ or $CDCl_3$ solutions, unless otherwise stated and a Bruker Spectrospin High Resolution NMR Spectrometer (90 MHz).

Extraction of D. attenuata. Leaves and terminal branches of *D. attenuata* (9·0 kg), collected in August 1964 along the gorges of the Murchison River below the area designated as the Ross Graham Lookout, were air dried, milled and exhaustively extracted with ether. The combined extracts were washed with 8% $NaHCO_3$ and the acids recovered from the washings with 10% HCl to give a resin which partially crystallized. Washing with a little ether gave ent-17-*acetoxy*-15,16-*epoxy*-19-*hydroxy*-3,13(16),14-*clerodatrien*-18-*oic acid* (**1**). Recrystallization from MeOH or EtOAc gave prisms, m.p. 160–162°, $[\alpha]_D$ −109° (*c*, 2·2). (Found: C, 67·6; H, 7·6; Acetyl, calc as $COCH_3$, 10·6. $C_{22}H_{30}O_6$ requires: C, 67·7; H, 7·7; Acetyl, calc as $COCH_3$, 11·0%). λ_{max} 210 nm (ϵ = 10,200). NMR: s, 0·82, 2·03 (tertiary Me, OAc); t, 6·74 (*J* 3 Hz, C 3-H); t, 7·35 m, 7·23 and q, 6·29 (furan H_3); br m, 4·50 to 3·52 (C 17-H_2. C 19-H_2).

The mother liquors were filtered through activated charcoal (300 g) in ether. Early fractions gave a resin (25 g) which was chromatographed on silicic acid (800 g). Elution with $CHCl_3$-MeOH (50:1) gave ent-15,16-*Epoxy*-17,19-*dihydroxy*-3,13(16),14-*clerodatrien*-18-*oic acid* **18** → **19** *lactone* (**4**, 5 g) which crystallized from acetone-light petroleum as plates, m.p. 180–181°, $[\alpha]_D$ −154° (*c*, 1·3 in EtOH). (Found: C, 72·9; H, 7·9. $C_{20}H_{26}O_4$ requires: C, 72·7; H, 7·9%). ν_{max} (nujol) 3550, 1760 cm^{-1} (OH, γ-lactone). NMR: s, 0·65 (tertiary methyl); AB portion of an ABX spectrum, δ_A, 3·85; δ_B, 3·38; J_{AB} 10·5, J_{AX}3, J_{BX}7 (C 17-H_2); AB δ_A, 4·33 δ_B, 3·92; *J* 8 Hz (C 19-H_2); q, 6·74, $W_{1/2}$ 11 Hz (C 3-H); t, 7·34; m, 7·22 and q, 6·27 (furan H_3).

Later fractions were chromatographed on alumina. Elution with benzene gave ent-17-*acetoxy*-15,16-*epoxy*-19-*hydroxy*-3,13(16)14-*clerodatrien*-18-*oic acid* **18** → **19** *lactone* (**5**, 1·5 g) which crystallized from MeOH as plates, m.p. 97–98°, $[\alpha]_D$ −137° (*c*, 1·6). (Found: C, 70·6; H, 7·5. $C_{22}H_{28}O_5$ requires: C, 70·9; H, 7·6%. ν_{max} 1775, 1740 cm^{-1} (γ-lactone, acetate). NMR: s, 0·70, 2·03 (tertiary Me, OAc). AB, δ_A, 4·32; δ_B, 3·93; *J* 8 Hz (C 19-H_2); AB part of ABX δ_A, 4·29; δ_B, 3·80; J_{AB}11, J_{AX}4, J_{BX}7·5 Hz; q, 6·75, $W_{1/2}$ = 10 Hz (C 3-H); 7·35, 7·23 and 6·29τ (furan H_3). Elution with benzene-ether (10:1) gave a further 1·5 g of the hydroxy-lactone (**4**).

ent-15,16-*Epoxy*-17,19-*dihydroxy*-3,13(16),14-*clerodatrien*-18-*oic acid* (**2**). (i). The acetoxy-hydroxy-acid **1** (720 mg) in diglyme (30 ml) was heated at 100° for 3 hr with $LiBH_4$ (from 0·5 g $NaBH_4$ and 0·6 g LiCl). After addition of H_2O the product was isolated with ether to give the dihydroxy-acid (**2**, 635 mg). Recrystallization from EtOH-benzene gave prisms, m.p. 174–176°, $[\alpha]_D$ −107° (*c*, 1·2 in EtOH). (Found: C, 68·6; H, 8·2. $C_{20}H_{28}O_5$ requires: C, 68·9; H, 8·1%).

(ii) The acetoxy-hydroxy-acid (**1**) (392 mg) in MeOH (50 ml) was heated under reflux with KOH (2·5 g) for 2 h. The mixture was poured into water and extracted with ether. Crystallization of the product from acetone-benzene gave the dihydroxy-acid (**2**).

Lactonization of the dihydroxy-acid (**2**). The dihydroxy-acid (**2**, 291 mg) in pyridine (10 ml) was heated with N,N′-dicyclohexylcarbodi-imide (174 mg) at 100° under N_2 for 2 hr. The filtrate was diluted with $CHCl_3$ (250 ml), which was washed with 2N HCl and water. The neutral product in benzene was chromatographed on Al_2O_3 (10 g). Elution with benzene-$CHCl_3$ (9:1 and 4:1) gave the hydroxy-lactone (**4**, 202 mg). Recrystallization from acetone-light petroleum gave plates, m.p. and mixed m.p. 179–180°. ent-17-*Acetoxy*-15,16-*epoxy*-19-*hydroxy*-3,13(16),14-*clerodatrien*-18-*oic acid* **18** → **19**-*lactone* (**5**). (i). Acetylation of the hydroxy-lactone (**4**) with acetic anhydride and pyridine at room temperature overnight and crystallization of the product from MeOH gave the acetoxy-lactone (**5**) m.p. and mixed m.p. 97–98°. (ii). The acetoxy-hydroxy-acid (**1**) (406 mg) was heated with the carbodi-imide in pyridine (15 ml) as for (**2**) to give the acetoxy lactone (**5**) (267 mg).

Reduction of the acetoxy-hydroxy-acid (**1**) *with* Na/EtOH. To the acetoxy-hydroxy-acid (**1**, 4·0 g) in boiling ethanol (600 ml), sodium (54 g) was added in small pieces and the mixture heated under reflux until all the metal had dissolved. The solution was cooled, diluted with water, concentrated under reduced pressure and extracted with ether to give a neutral fraction which was discarded. The aqueous layer was acidified and extracted with ether, the extract then being washed with 8% $NaHCO_3$ solution and water. Removal of the solvent gave ent-15,16-*epoxy*-17,19-*dihydroxy*-13(16),14-*clerodadien*-18-*oic acid* **18** → **19**-*lactone* (**10**, 1·84 g) which crystallized from acetone-light petroleum as needles, m.p. 151–153°, $[\alpha]_D$ −21° (*c*, 2·8). (Found: C, 71·9; H, 8·3. $C_{20}H_{28}O_4$ requires: C, 72·3; H, 8·5%. ν_{max} 3625, 1785 cm^{-1} (OH, γ-lactone). NMR: s, 0·61 (tertiary Me); AB, δ_A 4·31, δ_B 4·25, *J* 10 Hz (C 19-H_2); AB of ABX, δ_A 3·83, δ_B 3·32. J_{AB} 10·5, J_{AX} 2·5, J_{BX} 7 Hz (C 17-H_2); 7·36, 7·23, 6·28 (furan H_3). Recovery of the acids from the $NaHCO_3$ with ether gave the diol-acid (**7**, 1·56 g) which crystallized from EtOAc-light petroleum as prisms, m.p. 169–170°, $[\alpha]_D$ −3° (*c*, 1·1 in EtOH). (Found: C, 68·3; H, 8·8. $C_{20}H_{30}O_5$ requires: C, 68·5; H, 8·6%). The diol acid could not be lactonised by treatment with NN′-dicyclohexylcarbodi-imide.

ent-15,16-*Epoxy*-17,19-*dihydroxy*-13(16),14-*clerodadien*-18-*oic acid* **18** → **19**-*lactone* (**10**). Methylation of the dihydroxy-acid (**7**) with diazomethane in ether-methanol gave the dihydroxy-ester (**8**), which crystallized from aqueous MeOH as solvated needles, m.p. 62–64° $[\alpha]_D$ +6° (*c*, 2·1). (Found: C, 66·2; H, 8·7. $C_{21}H_{32}O_5H_2O$ requires: C, 65·9; H, 9·0%). ν_{max} 3640, 1730 cm^{-1} (OH, ester carbonyl). NMR: s, 0·68, 3·64 (tertiary Me, CO_2Me); m, 3·02 $W_{1/2}$ 8 Hz (C 4-H); br s, 3·84 (C 19-H_2); m, 4·0–3·1 (C 17-H_2); 7·31, 7·21, 6·26 (furan H_3).

The methyl ester (**8**, 139 mg) in dry MeOH (50 ml) was heated under reflux with sodium methoxide (from 200 mg Na) for 44 h. Sodium hydroxide (1·5 g) was then added and reflux continued for a further 4 h. The solution was concentrated, poured into water, acidified and extracted with ether to give the lactone-alcohol (**10**, 95 mg) which crystallized from acetone-light petroleum as prisms, m.p. and mixed m.p. 151–153°.

ent-17-*Acetoxy*-19-*hydroxy*-14,15,16-*trisnor*-*clerodane*-13,18-*dioic acid* **18** → **19**-*lactone* (**11**). Acetylation of the lactone-alcohol (**10**) with Ac_2O and pyridine at room temperature overnight gave the lactone-acetate which crystallized from acetone-light petroleum as plates, m.p. 97–98° $[\alpha]_D$ −24° (*c*, 1·1). (Found: C, 70·3; H, 8·2.

$C_{22}H_{30}O_5$ requires: C, 70·6; H, 8·1%). ν_{max} 1785, 1740 cm^{-1} (γ-lactone, acetate). NMR: s, 0·68, 2·04 (tertiary Me, OAc); AB, δ_A 4·33, δ_B 4·24, J 10 Hz (C 19-H_2); AB of ABX, δ_A 4·30, δ_B 3·78 J_{AB} 11, J_{AX} 4·5, J_{BX} 7·5 Hz (C 17-H_2); 7·35, 7·24 and 6·30 (furan H_3). The above acetoxy-lactone (1·20 g) in EtOAc was cooled to −70° and saturated with ozone. Removal of the solvent under reduced pressure gave the crude ozonide which was taken up in acetone (50 ml) and oxidized with excess Jones reagent for 1·5 h. The acidic product was isolated with ether and chromatographed on silicic acid (20 g). Elution with $CHCl_3$ gave the *trisnor-acetoxy-lactone-acid* (**11**, 808 mg) which crystallized from benzene-light petroleum as prisms, m.p. 116–117°, $[\alpha]_D$ −23° (*c*, 1·5). (Found: C, 64·4, H, 8·0. $C_{19}H_{28}O_6$ requires: C, 64·75; H, 8·0%). ν_{max} 1785, 1740, 1705 cm^{-1} (γ-lactone, acetate, carboxylic acid). NMR: s, 0·70, 2·07 (tertiary Me, OAc); AB, δ_A 4·33, δ_B 4·27 J 9·5 Hz; AB of ABX, δ_A 4·24, δ_B 3·80, J_{AB} 10·5, J_{AX} 4·5, J_{BX} 7·5 Hz (C 17-H_2).

ent-8,13-*Cyclo*-19-*hydroxy*-13-*oxo*-14,15,16,17-*tetranor*-*clerodane*-18-*oic acid* **18** → **19** *lactone* (**13**). The acetoxy-lactone-acid (**11**, 512 mg) was saponified with 5% NaOH aq (50 ml) for 2 h at 100°. The mixture was poured into 10% Na_2SO_4 solution, acidified and extracted with $CHCl_3$ to give the hydroxy-lactone-acid (**12**, 483 mg) which crystallized from acetone-light petroleum as prisms, m.p. 175–176°, $[\alpha]_D$ −18° (*c*, 1·7 in EtOH). (Found: C, 65·7; H, 8·5. $C_{17}H_{26}O_5$ requires: C, 65·8; H, 8·4%). The compound did not give a colour with tetranitromethane. The hydroxy-lactone-acid (**12**, 980 mg) in acetone (70 ml) was oxidized with a slight excess of Jones reagent at room temperature for 1·5 h. The crude product in acetic anhydride (10 ml) was heated under reflux for 40 min and the solvent removed under reduced pressure. The residue was heated at 280° for 40 min at 20 mm taken up in $CHCl_3$ and filtered through charcoal. The filtrate was washed with $NaHCO_3$ solution, dried and evaporated to give a resin (249 mg). Chromatography on Al_2O_3 (10 g) and elution with benzene gave the *keto-lactone* (**13**, 122 mg). Recrystallization from n-heptane gave needles m.p. 151–153° changing to prisms m.p. 157–9°. (Found: C, 73·3; H, 8·5. $C_{16}H_{22}O_3$ requires: C, 73·3; H, 8·5%). ν_{max} 1785, 1740, 1413 cm^{-1} (γ-lactone, cyclopentanone and methylene adjacent to a carbonyl). RD (*c*, 0·12 in MeOH $[\Phi]_{620}$ +301°; $[\Phi]_{589}$ +336°; $[\Phi]_{321}$ +6455°; $[\Phi]_{318}$ +6350°; $[\Phi]_{312}$ +6640°; $[\Phi]_{302}$ +3010° (inflection); $[\Phi]_{277}$ −4750°; $[\Phi]_{245}$ −1255°. NMR: s, 1·02 (tertiary Me); s, 4·31 (C 19-H_2).

Oxidation of the hydroxy-lactone (**10**). To the hydroxy-lactone (**10**, 1·09 g) in pyridine (20 ml) was added a solution of CrO_3 (1·1 g) in pyridine (20 ml) and the mixture set aside for 2·3 h. The mixture was poured into 5% aq K_2CO_3 and extracted with ether. The lactone-aldehyde (**14**, 791 mg) crystallized from EtOAc-light petroleum as plates, m.p. 132–133° (cap), $[\alpha]_D$ −16°, (*c*, 2·2). (Found: C, 72·4; H, 8·0. $C_{20}H_{26}O_4$ requires C, 72·7, H, 7·9%). NMR: s, 0·84 (tertiary Me); AB, δ_A 3·36, δ_B 3·30, J 10 Hz (C 19-H_2) 7·36, 7·25, 6·29 (furan H_3); d, 9·72, J 3 Hz (CHO).

Recovery of the acids from the K_2CO_3 solution with 5% HCl into ether, washing with 5% HCl, water, and removal of the solvent gave ent-15,16-*epoxy*-19-*hydroxy*-13(16)14-*clerodadiene*-17,18-*dioic acid* **18** → **19** *lactone* (**15**, 180 mg).

Recrystallization from EtOAc-light petroleum gave prisms m.p. 194–204°, $[\alpha]_D$ −32° (*c*, 1·2). (Found: C, 69·0; H, 7·6. $C_{20}H_{26}O_5$ requires: C, 69·3; H, 7·6%). NMR: s, 0·82 (tertiary Me); br. s, 4·32 (C 19-H_2); 7·33, 7·21 and 6·27 (furan H_3).

The lactone-aldehyde (**14**, 791 mg) in Ac_2O (30 ml) with NaOAc (1·2 g) was boiled for 10 hr. The mixture was cooled, diluted with ether and stirred with 8% aq $NaHCO_3$ for 2 hr. Isolation with ether and filtration in benzene through alumina (20 g) gave the enol-acetate as an oil (769 mg), ν_{max} 1785, 1755 cm^{-1} (γ-lactone, and acetate). This product in acetone (100 ml) was ozonised at −70°, then oxidized with an excess of Jones reagent for 10 h at room temperature. MeOH and H_2O were added, the solution concentrated under reduced pressure and extracted with $CHCl_3$ to give a gum (585 mg) which was methylated with CH_2N_2 in ether-MeOH. The product in EtOH (15 ml) and HOAc (1·0 ml) was boiled for 2 h with Girard "T" reagent (1·2 g). NaOAc (10 g) was added, the solution diluted with water and extracted with ether. The aqueous layer was acidified with 10% HCl, heated at 100° for 1 h, cooled and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $NaHCO_3$ solution and the acids recovered from the aqueous layer with dilute HCl into $CHCl_3$. Removal of the solvent gave the keto-lactone-acid (**16**, 150 mg) which crystallized from acetone-light petroleum as needles, m.p. 158–159°, $[\alpha]_D$ +20° (*c*, 1·1). (Found: C, 65·1; H, 7·4. $C_{18}H_{22}O_5$ requires: C, 65·3; H, 7·5%). The addition of *m*-dinitrobenzene to a solution of the keto-lactone-acid (**16**) in ethanolic KOH gave a purple colour. ν_{max} (Nujol) 1775 cm^{-1} (γ-lactone); 1700 cm^{-1} (ketone and carboxylic acid). NMR: s, 0·93 (tertiary Me). AB δ_A, 4·49, δ_B, 4·41; J 10 Hz (C 19-H_2).

Methylation of the keto-lactone-acid (**16**) with diazomethane gave the *methyl ester* which crystallized from acetone-light petroleum as rectangular prisms, m.p. 85–86°. (Found: C, 66·4; H, 7·8. $C_{17}H_{24}O_5$ requires: C, 66·2; H, 7·8%). ν_{max} 1785, 1735, 1710 cm^{-1} (γ-lactone, $-CO_2Me$, cyclohexanone). NMR: s, 0·92 and 3·65 (tertiary Me, CO_2Me); AB δ_A, 4·48; δ_B 4·40. J 9·5 Hz (C 19-H_2). For a benzene solution the C-19 and C-20 protons gave rise to singlets at 4·80 and 0·40τ respectively. RD (*c*, 0·094 in MeOH); $[\Phi]_{340}$ +137°; $[\Phi]_{320}$ +1815°; $[\Phi]_{273}$ −1283°; $[\Phi]_{245}$ −791°.

The oxime, prepared from the keto-lactone-ester with hydroxylamine hydrochloride in pyridine, crystallized from methanol as needles, m.p. 237–239° (decomp.). (Found: N, 4·3%. $C_{17}H_{25}O_5N$ requires: N, 4·3%).

Bromination and dehydrobromination of the methyl ester of the keto-lactone-acid (**16**). The methyl ester of **16** (235 mg) in HOAc (10 ml) was treated dropwise with Br_2 (121 mg) in ether (2·5 ml) at room temperature. Dilution with water, and isolation with ether, gave the bromoketone as an oil (290 mg). NMR: s, 1·03, 3·65 (tertiary Me, CO_2Me); q, 5·19 $W_{1/2}$ 20 Hz (C 7-H); br s, 4·74 (C 19-H_2). The crude bromoketone (290 mg) in DMF (15 ml) was heated at 100° with LiBr (0·8 g) and Li_2CO_3 (0·5 g) for 16 h under N_2. The mixture was poured into water and extracted with ether to give the Δ^6-*keto-lactone-ester* (**17**, 158 mg) which crystallized from THF-light petroleum as plates m.p. 115–117°. (Found: C, 66·0; H, 7·1. $C_{17}H_{22}O_5$ requires: C, 66·6; H, 7·2). ν_{max} 1785, 1740, 1675 cm^{-1} (γ-lactone, ester, αβ-unsaturated ketone). λ_{max} 225 nm (ε, 7,000). NMR: s, 0·95, 3·65 (tertiary Me, CO_2Me); AB, δ_A 4·70; δ_B 4·27, J 9 Hz (C 19-H_2); AB, δ_A 6·91; δ_B 6·05, J 10 Hz (C 6-H, C 7-H).

Treatment of the Δ^6-*keto-lactone-ester* (**17**) *with* NaOH.

The method used for the isolation and estimation of the formaldehyde liberated by the base-catalysed retro-aldol fission is essentially that used by Barton and de Mayo.[11] The Δ^6-keto-lactone-ester (**17**, 1·95 mg) in EtOH (0·2 ml) was treated with a solution of NaOH (0·08 g) in 50% aq EtOH (0·8 ml) and allowed to stand at room temperature for 12 h. 15% H_2SO_4 (0·8 ml) was then added and the solution extracted with $CHCl_3$ (2 × 2·0 ml) and the whole aqueous layer used in the chromotropic acid test for formaldehyde which was carried out as described by Bricker and Johnson,[12] and indicated 28 μg (15% theoretical) HCHO had been liberated. A parallel reaction on the methyl ester of **16** with NaOH (0·1 g) in aq EtOH (1·5 ml) at room temperature for 20 h gave no colour with the chromotropic acid reagent under the conditions given above. The parent acid (**16**, 4 mg) was recovered.

ent-15,16-*Epoxy*-19-*hydroxy*-13(16),14-*clerodadien*-18-*oic acid* **18** → **19** *lactone* (**19**). The hydroxy-lactone (**10**, 384 mg) in pyridine (12 ml) was treated with $POCl_3$ (1·0 ml) at 20° for 15 h and then at 100° for 30 min. Isolation with ether gave the chlorolactone (**18**, 370 mg) as plates (MeOH), m.p. 139–140°, $[\alpha]_D$ −24° (*c*, 1·4). (Found: C, 68·1; H, 7·9; Cl, 10·4. $C_{20}H_{27}O_3Cl$ requires: C, 68·5; H, 7·8; Cl, 10·1%). ν_{max} 1785 cm^{-1} (γ-lactone). NMR: s, 0·64 (tertiary Me); AB, δ_A 4·30, δ_B 4·20, *J* 9·5 Hz (C 19-H_2); AB of ABX, δ_A 3·77. δ_B 3·20, J_{AB} 11, J_{AX} 2·5, J_{BX} 8·5 Hz (C 17-H_2); 7·39, 7·26, 6·30 (furan H_3).

The chlorolactone (**18**, 324 mg) in n-butanol (50 ml) was boiled with NaOH (1·0 g) for 2·5 h under N_2. Na (6 g) was added during 15 min and reflux continued for 40 min. After steam distillation the involatile residue was acidified and the products isolated with ether. Chromatography on alumina (14 g) and elution with benzene-light petroleum (1:4) gave the *lactone* (**19**, 155 mg) which crystallized from MeOH as prisms, m.p. 96–97°, $[\alpha]_D$ −13° (*c*, 1·9). (Found: C, 75·9; H, 8·9; $C_{20}H_{28}O_3$ requires: C, 75·9; H, 8·9%). NMR: s, 0·59 (tertiary Me); d, 0·85, *J* 5·5 Hz (sec Me); AB δ_A 4·31, δ_B 4·21, *J* 9·5 Hz (C 19-H_2); 7·33, 7·21, 6·26 (furan H_3).

ent-19-*Hydroxy*-14,15,16-*trisnorclerodan*-13,18-*dioic acid* **18** → **19** *lactone* (**20**). The lactone (**19**, 1·74 g) in acetone (70 ml) was ozonised at −70°. The solution at 15° was then oxidised with Jones reagent for 11 h. MeOH (1 ml) was added, and the acidic product isolated with ether to give the *lactone-acid* (**20**, 1·19 g) which crystallized from benzene-light petroleum as needles, m.p. 156–158° $[\alpha]_D$ −7° (*c*, 1·6). (Found: C, 69·1; H, 8·8. $C_{17}H_{26}O_4$ requires: C, 69·4; H, 8·9%). ν_{max} 1785, 1705 cm^{-1} (γ-lactone, carboxylic acid). NMR: s, 0·62 (tertiary Me, d, 0·84 (sec. Me); AB, δ_A 4·30, δ_B 4·20, *J* 9·5 Hz (C 19-H_2).

Methylation of the lactone-acid (**20**) with diazomethane in ether gave the lactone-ester which crystallized from light petroleum as solvated needles, m.p. 78–79° and 84–87°, $[\alpha]_D$ −5° (*c*, 1·2). ν_{max} 1785, 1735 cm^{-1} (γ-lactone, ester). NMR: s, 0·61, 3·67 (tertiary Me, CO_2Me); d, 0·83, *J* 5·5 Hz (sec Me); AB, δ_A 4·32, δ_B 4·20, *J* 9·5 Hz (C 19-H_2). In C_6H_6: s, 3·86 (C 19-H_2); s, 0·25 (tertiary Me).

ent-18,19-*Epoxy*-14,15,16-*trisnorclerodane*-13-*oic acid* (**21**). The lactone acid (**20**, 577 mg) in diglyme (50 ml) containing LiCl (2·0 g) and $NaBH_4$ (2·0 g) was heated at 100° for 2 days. The acidic fraction was isolated with ether to give a resin (438 mg) which was taken up in dry benzene (70 ml), toluene-p-sulphonic acid (600 mg) added, concentrated to 40 ml and then azeotroped with benzene (50 ml) for 3·5 h, washed with water, dried and evaporated to give ent-18,19-*epoxy*-14,15,16-*trisnorclerodan*-13-*oic acid* (**21**, 419 mg) which crystallized from benzene-light petroleum as needles, m.p. 126–127° (cap), $[\alpha]_D$ + 6° (*c*, 1·6). (Found: C, 72·6; H, 10·0. $C_{17}H_{28}O_3$ requires: C, 72·8; H, 10·1%). ν_{max} 1745, 1705 cm^{-1} (carboxylic acid). NMR: s, 0·56 (tertiary Me); d, 0·80 (sec Me); s, 3·76 (C 19-H_2); AB of ABX, δ_A 3·88, δ_B 3·41, J_{AB} 8, J_{AX} 3·5, J_{BX} 0 Hz (C 18-H_2).

ent-13,13-*Diphenyl*-18,19-*epoxy*-14,15,16-*trisnorclerod*-12-*ene* (**22**). The ether-acid (**21**) was methylated with diazomethane in ether to give the methyl ester as a mobile oil. NMR: s, 0·55, 3·67 (tertiary Me, CO_2Me); d, 0·81 (sec Me); s, 3·83 (C 19-H_2); AB of ABX δ_A 3·87, δ_B 3·36, J_{AB} 8, J_{AX} 3·5, J_{BX} 0 Hz (C 18-H_2). The ether-ester (422 mg) in ether (20 ml) was added to PhMgBr, from Mg (1·6 g) and bromo-benzene (6·0 g) in ether (25 ml), and the solution boiled for 3·5 h. After steam distillation the involatile part was isolated with ether. The product (561 mg) in benzene-light petroleum (1:9) was chromatographed on alumina (15 g). Benzene-light petroleum (1:4) gave the *diphenylcarbinol* (537 mg) which crystallized from MeOH as needles, m.p. 181–182° $[\alpha]_D$ 0° (*c*, 1·0). (Found: C, 82·9; H, 9·4. $C_{29}H_{38}O_2$ requires: C, 83·2; H, 9·2%). ν_{max} 3590 cm^{-1} (OH); 3020, 3055, 3080 cm^{-1} (aromatic C-H); λ_{max} 258 nm (ε, 500). NMR: s, 0·40 (tertiary Me); d, 0·63, *J* 5·5 Hz (sec Me); s, 3·61 (C 19-H_2); AB of ABX, δ_A 3·81, δ_B 3·28, J_{AB} 8, J_{AX} 3·5, J_{BX} OHz (C 18-H_2); m, 7·3 (phenyl H_{10}). To the diphenylcarbinol (73 mg) in dry benzene (80 ml) was added toluene-p-sulphonic acid (302 mg) and the solution concentrated to 50 ml. Additional benzene (100 ml) was added dropwise and the mixture distilled, maintaining the volume at 50 ml. After 2 h reflux, the product in benzene-light petroleum was filtered through alumina (3 g) to give the diphenylethylene (**22**, 66 mg). Recrystallization from EtOH gave plates, m.p. 103–104°, $[\alpha]_D$ + 49° (*c*, 1·10). (Found: C, 87·4; H, 9·1. $C_{29}H_{36}O$ requires: C, 87·0; H, 9·1%). λ_{max} 252 nm (ε, 30,000). NMR (CCl_4): s, 0·45 (tertiary Me); d, 0·60, *J* 6 Hz (sec Me); d, 2·15, *J* 7·5 Hz (C 11-H_2); s, 3·56 (C 19-H_2); AB of ABX, δ_A 3·75, δ_B 3·23, J_{AB} 8, J_{AX} 3·5, J_{BX} 0 Hz (C 18-H_2); t, 5·99, $W_{1/2}$ 15 Hz (C 12-H); m, 7·16 (phenyl H_{10}).

Selenium dehydrogenation of the lactone (**19**). The lactone (**19**, 597 mg) was heated with Se (1·0 g) at 310° under N_2 for 11 h. The residue was broken up and washed with ether which was washed with 2% NaOH. The residue, when filtered through alumina (30 g) gave an oil (120 mg). This product in EtOH was treated with 1,3,5-trinitrobenzene (130 mg) to give 1,2-dimethylnapthalene 1,3,5-trinitrobenzene adduct (145 mg, 21%) as yellow needles, m.p. and mixed m.p. with authentic material 147–148° (cap). The adduct in benzene-light petroleum (1:9) was filtered through alumina (25 g). The eluate was treated with picric acid in ethanol to give 1,2-dimethylnaphthalene picrate as orange needles, m.p. and mixed m.p. with authentic material 129–130° (cap).

ent-15,16-*Epoxy*-13(16),14-*clerodadiene*-17,18,19-*triol* (**23**). (i). Methylation of the lactone acid (**15**) with diazomethane in ether-methanol gave the methyl ester as a resin. ν_{max} 1785, 1735 cm^{-1} (γ-lactone, ester C=O). NMR: s, 0·78 (tertiary Me); s, 3·70 (CO_2Me). AB, δ_A 4·38; δ_B 4·32, *J* 9·5 Hz, (C 19-H_2). The lactone-ester (117 mg) in dry MeOH (25 ml) was boiled with NaOMe (from 1·0 g Na) for 48 h. Isolation with ether and methylation (CH_2N_2) gave a resin (106 mg) whose IR

and NMR spectra were identical with those of the ester of **15**. The product in THF (20 ml) was boiled with $LiAlH_4$ (0·15 g) for 2 h. Isolation with ether gave the triol (**23**, 75 mg) which separated from THF-light petroleum as plates, m.p. 182–185° varying with the rate of heating, $[\alpha]_D$ −31° (*c*, 1·2 in EtOH). (Found: C, 71·3; H, 9·5. $C_{20}H_{32}O_4$ requires: C, 71·4; H, 9·6%). (ii). The hydroxy-lactone (**10**, 187 mg) in THF (50 ml) was boiled with $LiAlH_4$ (180 mg) for 3·5 h. The product (180 mg), isolated in the usual way with ether, crystallized from THF-light petroleum as plates, m.p. and mixed m.p. 183–185°.

ent-15,16-*Epoxy*-19-*hydroxy*-13(16),14-*clerodadiene*-17-*nitrile*-18-*oic acid* **18** → **19** *lactone* (**27**). The *oxime*, prepared from the lactone-aldehyde **14** with hydroxylamine hydrochloride in pyridine at room temperature overnight crystallized from aqueous MeOH as needles, m.p. 216–218° (decomp), (Found: N, 3·9. $C_{20}H_{27}O_4N$ requires: N, 4·1%). The oxime (360 mg) was boiled in Ac_2O (15 ml) for 5·5 h. Isolation with ether and crystallization from MeOH (charcoal) gave the *lactone-nitrile* (**27**) as prisms, m.p. 173–175°, $[\alpha]_D$ −18° (*c*, 1·2). (Found: N, 4·2. $C_{20}H_{25}O_3N$ requires: N, 4·3%). ν_{max} 2230, 1785 cm^{-1} (C≡N, γ-lactone). NMR: s, 0·92 (tertiary Me); AB δ_A, 4·36, δ_B 4·21, *J* 9·5 Hz (C 19-H_2); 7·37, 7·26, 6·30 (furan H_3).

ent-17,19-*Dihydroxy*-15,16-*epoxy*-3α-*methoxy*-13(16),14-*clerodadien*-18-*oic acid* **18** → **19**-*lactone* (**25**). The acetoxy-hydroxy-acid (**1**) in MeOH was methylated (CH_2N_2), to give the methyl ester as a resin. ν_{max} 3450, 1740, 1700 cm^{-1} (OH, acetate. CO_2Me). NMR: t, 6·75, *J* 3 Hz (C 3-H); s, 0·88 (tertiary Me); s, 2·01 (OAc); s, 3·73 (CO_2Me); m, 7·35, 7·22, 6·29 (furan H_3); AB δ_A 4·09, δ_B 3·75, *J* 11 Hz (C 19-H_2); m 4·45–3·40 (C 17-H_2).

The methyl ester (2·10 g) in MeOH (70 ml) was heated under reflux with NaOMe (from 5·5 g Na) for 34 h under N_2. Water 5 ml) was added and the solution was heated under reflux for a further 2·5 h. The mixture was poured into water, acidified and extracted with ether. The ether extract was washed with $NaHCO_3$ solution, 5% aq K_2CO_3, water, and the solvent removed to give the *hydroxy-methoxy-lactone* (**25**, 1·18 g) which crystallized from acetone-light petroleum as prisms, m.p. 157–159°, $[\alpha]_D$ +7° (*c*, 2·1). Found: C, 70·0; H, 8·5. $C_{21}H_{30}O_5$ requires: C, 69·6; H, 8·3%). ν_{max} 3620, 1775 cm^{-1} (OH, γ-lactone). NMR: s, 0·64 (tertiary Me); s, 3·36 (OMe); d, 2·04, *J* 9 Hz (C 4-H); s, 4·18 (C 19-H_2); m, 7·33, 7·20, 6·27 (furan H_3).

Tosylation of the lactone-alcohol (**10**). Tosyl chloride (0·77 g) was added to the hydroxy-lactone (**10**, 293 mg) in pyridine (10 ml) at 0°. After 4 days the product was isolated with ether and chromatographed on alumina (10 g). Elution with benzene-light petroleum (1 : 1) and benzene gave the *lactone tosylate* **26** (380 mg). Recrystallization from acetone-light petroleum gave needles, m.p. 121–123°, $[\alpha]_D$ −25° (*c*, 1·5). (Found: C, 66·5; H, 7·2; S, 7·0. $C_{27}H_{34}O_6S$ requires: C, 66·6; H, 7·0; S, 6·6%). NMR: s, 0·59 (tertiary Me); s, 2·45 (ArMe); AB, δ_A 4·25, δ_B 4·15, *J* 9·5 Hz (C 19-H_2); AB of ABX, δ_A 4·15, δ_B 3·75 J_{AB} 10, J_{AX} 4, J_{BX} 7 Hz (C 17-H_2); m, 7·31, 7·11, 6·18 (furan H_3); A_2B_2, δ_A 7·72, δ_B 7·28 (phenyl H_4).

ent-15,16-*Epoxy*-13(16),14-*clerodadiene*-18,19-*diol* (**24**). The lactone tosylate (26, 660 mg) in THF (50 ml) was heated under reflux with $LiAlH_4$ (1·0 g) for 26 h. The diol (**24**, 421 mg), isolated with ether, crystallized from ethyl acetate-light petroleum as plates, m.p. 141–143°, $[\alpha]_D$ −9° (*c*, 5·3). (Found: C, 75·4; H, 9·8. $C_{20}H_{32}O_3$ requires: C, 75·0; H, 10·1%). ν_{max} 3625, 3450. NMR: s, 0·75 (tertiary Me); d, 0·84, *J* 5·5 Hz (sec Me) s, 3·85 (C 19-H_2); AB of ABX, δ_A 3·93, δ_B 3·39 J_{AB} 11·5, J_{AX} ~ 1, J_{BX} 3·5 Hz (C 18-H_2); m, 7·36, 7·22, 6·27 (furan H_3).

Extraction of Dodonaea attenuata *var.* linearis. Leaves and terminal branches of *D. attenuata* var. *linearis* (7·6 kg), collected 8 miles south of Coolgardie, W.A. in October 1963, were dried, milled, and exhaustively extracted with cold ether. The combined ether extracts were washed with 8% aq $NaHCO_3$ and then 5% aq NaOH. Recovery into ether of the acids from the $NaHCO_3$ solution gave a resin. After washing with a little ether and filtration, 58 g of a crystalline solid was obtained, part (5·5 g) of which was methylated (CH_2N_2) and the product (5·2 g) chromatographed on acid washed Al_2O_3 (150 g). Elution with benzene-light petroleum (1 : 1) and benzene gave ent-15,16-*epoxy*-19-*hydroxy*-3,13(16),14-*clerodatrien*-18-*oic acid* **18** → **19**-*lactone* (**6**, 2·25 g). Recrystallization from EtOH gave plates m.p. 119–120°, $[\alpha]_D$ −156° (*c*, 1·3). (Found: C, 76·6; H, 8·4. $C_{20}H_{26}O_3$ requires: C, 76·4; H, 8·3%). ν_{max} 1775 cm^{-1}. NMR: s, 0·61 (tertiary Me); d, 0·87, *J* 6 Hz (sec Me); AB, δ_A 4·30, δ_B 3·92, *J* 8 Hz (C 19-H_2); q, 6·74 $W_{1/2}$ 11 Hz (C 3-H); m, 7·35. 7·22, 6·26 (furan H_3). Elution with benzene-ether gave *methyl* ent-15,16-*epoxy*-19-*hydroxy*-1,3,13(16),14-*clerodatetraen*-18-*oate* (**29**, 2·3 g). Recrystallization from aqueous MeOH gave plates, m.p. 96–97°, $[\alpha]_D$ −233° (*c*, 1·4). (Found: C, 72·9; H, 8·1. $C_{21}H_{28}O_4$ requires: C, 73·2; H, 8·2%). ν_{max} 3470, 3045, 1695 cm^{-1} (OH, —CH=CH—, ester carbonyl NMR: s, 0·85 (tertiary Me); d, 0·86, *J* 5·5 Hz (sec Me); s, 2·60 (C 10-H); s, 3·77 (CO_2Me and C 19-H_2); d 6·17, *J* 3 Hz (C 1-H), C 2-H); t, 6·85, *J* 3 Hz (C 3-H); m, 7·31, 7·17, 6·21 (furan H_3).

The 5% NaOH soluble part of the original ether extract was recovered into ether which was washed successively with 8% aq $NaHCO_3$, 5% aq Na_2CO_3, and 5% aq NaOH. Recovery of the acids from the Na_2CO_3 solution with 10% HCl and ether gave a resin which partially crystallized on standing. Washing with a little ether and recrystallization of the residue from EtOH gave 5,7-*dihydroxy*-3,4',6-*trimethoxyflavone* (**32**, 7 g) as yellow needles, m.p. 164–165°. (Found: C, 62·4; H, 4·7. $C_{18}H_{16}O_7$ requires: C, 62·8; H, 4·7%). The flavone gave a green colour with ferric chloride and a red colour on reduction with Mg/HCl. λ_{max}^{EtOH} 273 nm, log ε 4·31; 341 nm, log ε 4·29. $\lambda_{max}^{EtOH/NaOH}$ 276 nm, log ε 4·46; 296 nm (sh), log ε 4·34; 378 nm, log ε 4·12.

ent-15,16-*Epoxy*-19-*hydroxy*-3,13(16),14-*clerodatrien*-18-*oic* (**3**). The lactone (**6**, 5·79 g) in t-butanol (70 ml) was boiled with NaOH (5 g) in water (20 ml) for 8 h. After distillation the acidified residue was extracted with $CHCl_3$ to give the hydroxy-acid (**3**, 5·3 g). Recrystallization from EtOH gave needles, m.p. 183–184° $[\alpha]_D$ −105° (*c*. 1·4). (lit.[2] for hautriwaic acid, m.p. 182–184°, $[\alpha]_D$ −104°). (Found: C, 72·1; H, 8·5%. $C_{20}H_{28}O_4$ requires: C, 72·3; H, 8·5%.). NMR: (C_5H_5N) s, 0·83 (tertiary Me); d, 0·79 (sec Me); AB, δ_A 4·44, δ_B 4·07, *J* 10·5 Hz (C 19-H_2); m, 6·46 (C 14-H).

Reduction of the hydroxy-acid (**3**) *with sodium in ethanol.* The hydroxy-acid (**3**, 2 g) in boiling EtOH was reduced by dissolution of Na (50 g). The product (40 g) was chromatographed on acid washed alumina (100 g) and elution with benzene-light petroleum (1 : 1) and benzene gave ent-15,16-epoxy-19-hydroxy-13(16),14-

clerodadien-18-oic acid 18 → 19-lactone (19, 1·71 g) which crystallized from MeOH as needles m.p. and mixed m.p. 96–97°. Elution with ether gave a crystalline acid (1·5 g) m.p. 165–170 which could not be purified.

Di-imide reduction of the lactone (6). The lactone (6, 222 mg) in diglyme (20 ml) was boiled with tosyl hydrazide (1·8 g) and NaOAc (2·0 g) for 1 h. Isolation with ether and crystallization from aq MeOH gave the dihydro-lactone (19, 161 mg) as needles m.p. and mixed m.p. 96–97°.

ent-15,16-*Epoxy*-19-*hydroxy*-1,3,13(16),14-*clerodatetraen*-18-*oic acid* (28). The hydroxy-ester (29, 1·25 g), t-butanol (40 ml), NaOH (1·6 g), in water (5 ml) were heated at 100° for 4·5 h. The solution was concentrated under reduced pressure, and extracted with ether. Acidification of the aqueous layer and ether extraction gave the hydroxy-acid (28, 1·2 g). Recrystallization from EtOAc-light petroleum gave needles, m.p. 161–163°, $[\alpha]_D - 153°$ (*c*, 1·5). (Found: C, 72·25; H, 8·1. $C_{20}H_{28}O_4$ requires: C, 72·7; H, 7·9%). λ_{max} 286 nm, (ϵ 9200). NMR: (C_5H_5N): s, 0·82 (tertiary Me); d, 0·79 (sec Me); s, 4·11 (C 19-H_2) d, 6·15, *J* 3 Hz (C 1-H, C 2-H); s, 2·69 (C 10-H); m, 6·42 (C 14-H).

Tosylation of the hydroxy-ester (29). The hydroxy-ester (29, 946 mg) was treated with $TsCl/C_5H_5N$ for 2 days. The neutral product (30, 1·26 g), isolated with ether crystallized from MeOH as needles, m.p. 108–109° (decomp.) λ_{max} 290 nm, (ϵ 5500). ν_{max} 3045, 1720 cm^{-1} (—CH=CH—, ester carbonyl). NMR: (CCl_4); s, 0·79 (C 8-Me, C 9-Me); s, 2·40. (Ar-CH_3); s, 3·55 (CO_2Me; s, 2·50 (C 10-H) s, 4·13 (C 19-H_2); m, 6·08 (C 1-H, C 2-H, C 14-H); m, 7·09, 7·25 (furan H_3); A_2B_2 δ_A 7·62; δ_B, 7·25 (phenyl H_4).

$LiAlH_4$ *reduction of the ester-tosylate* (30). The ester-tosylate (30, 936 mg) in THF (50 ml) was treated with $LiAlH_4$ (0·4 g) under reflux for 18 h. Chromatography of the product on alumina (15 g) and elution with benzene-light petroleum (1:1) gave the alcohol (31) as a resin (487 mg). λ_{max} 209 nm (ϵ 8200). ν_{max} 3630, 3055, 3030 cm^{-1} (OH, cyclopropyl C—H, —CH=CH—). NMR: (CCl_4); s, 0·73 (tertiary Me); d, 0·86, *J* 5 Hz (sec Me); d, 0·14, *J* 4·5 Hz (C 19-H); AB, δ_A 3·61, δ_B 3·52, *J* 11·5 Hz (C 18-H_2); m, 5·59 $W_{1/2}$ 4·5 Hz (C 1-H, C 2-H); m, 7·25, 7·13, 6·16 (furan H_3).

The *p-nitrobenzoate*, prepared with *p*-nitrobenzoyl chloride in pyridine, crystallized from ether-methanol as cream needles, m.p. 152–155°, $[\alpha]_D + 15°$ (*c*, 1·3). (Found: C, 71·8; H, 7·0; N, 3·0. $C_{27}H_{31}O_5N$ requires: C, 72·1; H, 7·0; N, 3·1%). ν_{max} 3040, 1730 cm^{-1} (—CH=CH—, ester carbonyl). NMR: (CCl_4); s, 0·75 (tertiary Me); d, 0·88, *J* 5 Hz (sec Me); d, 0·38, *J* 5 Hz (C 19-H); AB, δ_A 4·51; δ_B 4·28, *J* 12 Hz (C 18-H_2); m, 7·25, 7·13, 6·17 (furan H_3); br s, 8·19 (ArH_4).

Di-imide reduction of the hydroxy-ester (29). The hydroxy-ester (29, 265 mg) in diglyme (20 ml) was heated under reflux with tosyl hydrazide (2·0 g) and anhydrous NaOAc (3·0 g) for 1·5 h. The solution was cooled, poured into water and extracted with ether. The ether extract was washed thoroughly with water and the solvent removed to give an oil (260 mg) which was filtered through alumina (20 g) in benzene to give the *lactone* (19, 216 mg). Recrystallization from benzene-light petroleum gave plates, m.p. and mixed m.p. 95–96°.

Acetylation of 5,7-*dihydroxy*-3,4′,6-*trimethoxyflavone* (32). The flavone (32, 251 mg) was acetylated with acetic anhydride (5 ml) and perchloric acid (2 drops) at room temperature for 2 h. The solution was poured into ice water and the product isolated with ether to give 5,7-*diacetoxy*-3,4′,6-*trimethoxyflavone* (33) which crystallized from EtOH as needles, m.p. 170–171°. (Found: C, 61·7; H, 5·0. $C_{22}H_{20}O_9$ requires: C, 61·7; H, 4·7%). NMR: s, 3·89, 3·89, 3·79 (3 × OMe); s, 2·53, 2·38 (2 × OAc); s, 7·25 (C 8-H); A_2B_2, δ_A 8·04; δ_B 7·01 (phenyl H_4).

Partial methylation of 5,7-*dihydroxy*-3,4′,6-*trimethoxyflavone* (32). The flavone (32, 250 mg) in MeOH (30 ml) was treated with CH_2N_2 in ether at 0° for 2 h. The solvent was removed, the residue taken up into $CHCl_3$ the solution repeatedly washed with 1% NaOH and then water. The $CHCl_3$ extract was dried and evaporated to give 5-hydroxy-3,4′,6,7-tetramethoxyflavone (96 mg) which crystallized from ethanol as yellow plates, m.p. and mixed m.p. with authentic material from *Dodonaea lobulata*,[13] 172–173° (lit.[13] m.p. 173–174°).

Ethylation of 5,7-*dihydroxy*-3,4′,6-*trimethoxyflavone* (32). The flavone (32, 1·35 g) in acetone (100 ml) was heated under reflux with anhydrous K_2CO_3 (10 g) and diethyl sulphate (6 ml) for 5 days. Acetic acid (3 ml) was then added dropwise and reflux continued for a further 4 h. The solution was concentrated, poured into water and extracted with $CHCl_3$. Removal of the solvent gave a semicrystalline residue (1·4 g) which was taken up in ether and filtered through alumina (40 g). The eluate (1·1 g) crystallized from benzene-light petroleum to give 5,7-*diethoxy*-3,4′,6-*trimethoxyflavone* (34) as needles, m.p. 123–124°. (Found: C, 66·4: H, 6·5. $C_{22}H_{24}O_7$ requires: C, 66·0; H, 6·05%). NMR: t, 1·53 (6 × H) and q 4·20 (4 × H) *J*, 7 Hz (2 × OEt); s, 3·91, 3·88, 3·85 (3 × OMe); s, 6·72 (C 8-H). A_2B_2, δ_A 8·06, δ_B 7·01 (phenyl H_4).

Alkaline degradation of 5,7-*diethoxy*-3,4′,6-*trimethoxyflavone* (34). The diethyl ether (34, 562 mg) in ethanol (25 ml) was heated under reflux with NaOH (5 g) and water (5 ml) for 20 h under N_2. The product was poured into water and the solution acidified, saturated with NH_4Cl and extracted with ether. The ether extract was washed with 8% $NaHCO_3$ solution, water, and the solvent was removed to give a fraction (0·3 g) which was taken up in light petroleum and chromatographed on alumina. Elution with light petroleum and benzene gave 2,4-diethoxy-6-hydroxy-ω,3-dimethoxyacetophenone (282 mg) which crystallized from light petroleum as prisms m.p. and mixed m.p. with authentic material,[14] 65–66°. This compound was also obtained as needles m.p. 56–57° changing to prisms m.p. 65–66°. (lit.[14] m.p. 60–62°). Recovery of the acids from the $NaHCO_3$ extract gave *p*-methoxybenzoic acid (194 mg), m.p. and mixed m.p. 183–184°.

Acknowledgements—Grateful acknowledgement is made to General Motors Holden for a postgraduate scholarship and to the Western Australian Herbarium for identification of the plant material.

REFERENCES

[1]P. R. Jefferies and T. G. Payne, *Tetrahedron Letters* 4777 (1967)
[2]M. Kotake and K. Kuwata, *J. Chem. Soc. Japan* **57**, 837 (1936)
[3]H.-Y. Hsu, Y. P. Chen and H. Kakisawa, *Phytochemistry* **10**, 2813 (1971)
[4]B. Scaf, Ph.D. Thesis University of Western Australia, 1972

[5]M. Ferrari, F. Pelizzoni and G. Ferrari, *Phytochemistry* **10**, 3267 (1971)
[6]J. T. Pinhey, R. F. Simpson and I. L. Batey, *Aust. J. Chem.* **24**, 2621 (1971)
[7]J. S. Scarpa, M. Ribi and C. H. Eugster, *Helv. Chim. Acta* **49**, 858 (1966)
[8]C. Djerassi, F. W. Donovan, S. Burstein and R. Mauli, *J. Am. Chem. Soc.* **80**, 1972 (1958)
[9]W. G. Dauben and L. E. Friedrich, *Tetrahedron Letters* 1735 (1967)
[10]H. J. Bakker, E. L. Ghisalberti and P. R. Jefferies, *Phytochemistry* **11**, 2221 (1972)
[11]D. H. R. Barton and P. de Mayo, *J. Chem. Soc.* 887 (1954)
[12]C. E. Bricker and H. R. Johnson, *Ind. Eng. Chem. Analyt* **17**, 400 (1945)
[13]R. M. Dawson, M. W. Jarvis, P. R. Jefferies, T. G. Payne and R. S. Rosich, *Aust. J. Chem.* **19**, 2133 (1966)
[14]R. M. Dawson, C. A. Henrick, P. R. Jefferies and E. J. Middleton, *Aust. J. Chem.* **18**, 1871 (1965)