Tetrahedron Vol. 24, pp. 3113 to 3125. Pergamon Press 1968. Printed in Great Britain

DITERPENOID TOTAL SYNTHESIS—IX*

LACTONES OF PODOCARPANE AND KAURANE SERIES

K. MORI, M. MATSUI and (in part) N. FUJISAWA

Department of Agricultural Chemistry, The University of Tokyo, Bunkyo-ku, Tokyo, Japan

(*Received in Japan* 30 *September* 1967; *accepted for publication* 24 *October* 1967)

Abstract Preparation of some lactones from tricyclic or tetracyclic resin acid analogs is described.

RECENT discoveries of lactonic diterpenoids such as gibberellin A_{15} (I),[1] 7β-hydroxykaurenolide (II),[2] sciadinone (III)[3] and marrubiin (IV)[4] prompted us to study the transformation of resin acids into lactones. Employing compounds with an axial carboxyl group at C-4, both photolytic and non-photolytic methods were investigated to obtain several 19 → 20 and 19 → 6 lactones. This paper describes in detail the synthesis of lactones, a part of which had been the subject of a preliminary communication.[5]

Photolytic approach

Photochemical lactonization reaction devised independently by Barton *et al.*[6] and by Petterson *et al.*[7] is the only method now available for converting saturated acids directly into lactones. At the outset of this work, however, there was no report on the application of this interesting reaction among diterpenoids,† although applications of other photolytic reactions for functionalization at C-20 had been published.[9-11]

The starting materials employed were (±)-desoxypodocarpic acid (Va),[12] (±)-14-hydroxypodocarpa-8,11,13-trien-19-oic acid (Vb),[13] podocarpic acid (Vd),[14] (±)-14α-hydroxypodocarpan-19-oic acid (XIa) prepared from the corresponding ester (X)[13] by treatment with lithium–ammonia and (±)-16ξ-hydroxy-17-norkauran-19-oic acid (XVa).[13] Firstly, the OH groups of the acids (Vb, Vd, XIa and XVa) were protected as acetates to give acetoxy acids (Vc, Ve, XIb and XVb). These were then treated with thionyl chloride to give acyl chlorides (VIa, VIb, VIc, XII and XVI). The corresponding amides (VIIa, VIIb, VIIc, XIII and XVII) were obtained in good yields from the acyl chlorides.

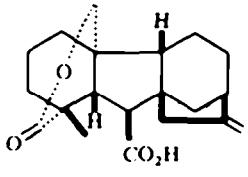
The amides in dry benzene with lead tetraacetate-iodine reagent was irradiated by an 8W low pressure mercury lamp for 7–12 hr‡ and the products were processed as

* Part VIII, K. Mori and M. Matsui, *Tetrahedron* **24**, 3095 (1968). The numbering system employed in this paper is that of R. McCrindle and K. H. Overton, *Adv. Org. Chem.* **5**, 53 (1965). Although the formulas depicted represent only one enantiomer, they are taken to mean a racemate with the exception of derivatives of podocarpic acid.

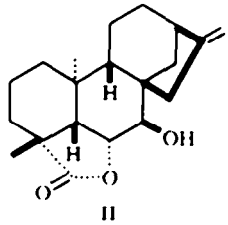
† After the submission of our preliminary communication, Professor P. R. Jefferies kindly informed us (K.M.) that his group had applied the same reaction to some kaurane derivatives.[8]

‡ A longer reaction period described in the preliminary communication was found to be unnecessary. We are indebted to Professor Petterson for his suggestion.

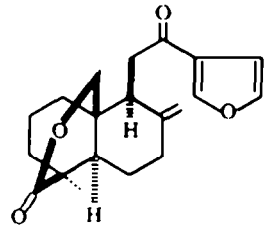
described by Barton *et al.*[6] The lactone fraction thus obtained from (±)-desoxypodocarpamide (VIIa) was found to be an oil and was chromatographed on alumina to give expected lactones VIIIa and IX in 2 3 and 8 12% yields, respectively. The assigned structures were confirmed by comparisons of their spectra with those of optically active authentic samples prepared from abietic acid through an entirely different route by Tahara *et al.*[9] Recrystallization of the lactone fractions obtained from the amides VIIb and VIIc gave lactones VIIIb and VIIIc in 12 and 5% yields, respectively. In these cases no γ-lactones were obtained. Jones oxidation[15] of the lactone fractions obtained from the amides XIII and XVII gave keto lactones XIV and XVIII in 3 and 20% yields, respectively. Here, too, no γ-lactones were obtained contrary to the observation with the simplest amide VIIa. Jefferies *et al.*[8] obtained an optically active lactone (XVIII) and converted it to a compound (XIX) with gibberellin-like activity.



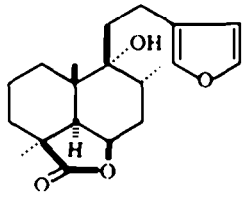
I



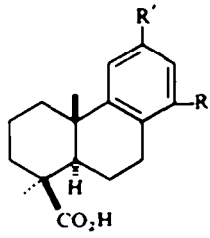
II



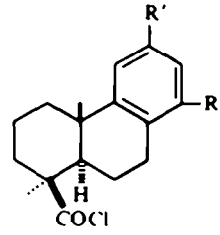
III



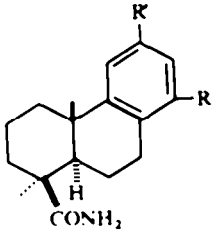
IV



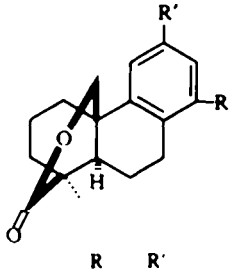
	R	R'
Va:	H	H
b:	OH	H
c:	OAc	H
d:	H	OH
e:	H	OAc



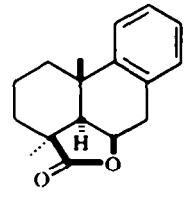
	R	R'
VIa:	H	H
b:	OAc	H
c:	H	OAc



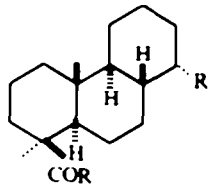
	R	R'
VIIa:	H	H
b:	OAc	H
c:	H	OAc



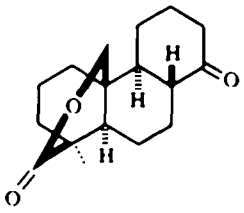
	R	R'
VIIIa:	H	H
b:	OH	H
c:	H	OH



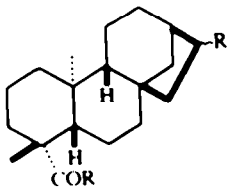
IX



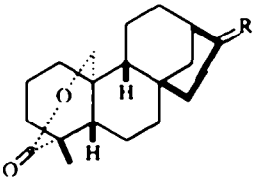
	R	R'
X:	OMe	OH
XIa:	OH	OH
b:	OH	OAc
XII:	Cl	OAc
XIII:	NH_2	OAc



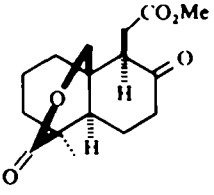
XIV



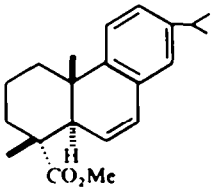
	R	R'
XVa:	OH	OH
b:	OH	OAc
XVI:	Cl	OAc
XVII:	NH_2	OAc



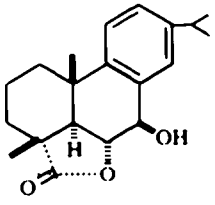
	R
XVIII:	O
XIX:	CH_2



XX



XXI



XXII

Several speculations are possible to account for the observed difference between the reaction of (±)-desoxypodocarpamide (VIIa) and these of other amides (VIIb, VIIc, XIII and XVII). Steric factors in cases of the amides (VIIb, XIII and XVII) or energy barriers to the required transition states in cases of the amides (XIII and XVIII) may prevent the formation of γ-lactones.* No conclusive explanation, however, can be given at present.

The IR and NMR spectral properties of the lactones are listed in Table 1. The NMR spectra of the δ-lactones can be classified into two types. Those with aromatic C ring show singlet (VIIIa) or slightly split doublet (J = 1·5 c/s, VIIIb and VIIIc) for the C-20 methylene protons, while those with saturated C ring show quartets where the downfield half of each quartet exhibits long range coupling of J = 1·5 c/s through 4σ bonds. Analogous quartets for the angular methylene protons of kaurane derivatives and sciadinone derivatives were observed by Jefferies *et al.*[8] and by Sumimoto

* Inspection of a molecular model suggests that a conformation with boat-boat A/B rings seems to be the most stable one among the possible conformations of the lactone IX.

and Kondo.[16] The latter authors also found that the angular methylene protons of a keto ester (XX) shows a two-proton singlet.[16]

Photolysis with t-butyl hypochlorite as a halogenating agent[6] gave a poor result and no further attempt was made to improve the yield.

TABLE 1. IR AND NMR DATA OF THE δ-LACTONES

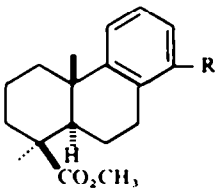
Compd	ν_{max} (cm^{-1}) of lactone C=O		δ(ppm from TMS, 100 Mc, $CDCl_3$) of C-20 CH_2			
	Nujol	$CHCl_3$ soln.	H_A		H_B	J_{AB}
VIIIa	1734	1732	4·36 (2H, s)			0
VIIIb	1700	1730	4·32 (2H, d, J = 1·5 c/s)			
VIIIc	1710	1730	4·24 (2H, d, J = 1·5 c/s)			
XIV	1724	1730	4·59	($J_{1\alpha,A}$ 2·0 c/s)	4·15	12
XVIII	1730	1738	5·16	($J_{1\alpha,A}$ 2·0 c/s)	4·14	12

Non-photolytic approach

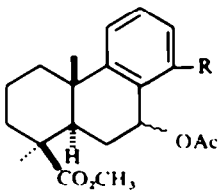
Since the photolytic method was proved to be unsuitable for the preparation of 19 → 6 lactones, another route to the desired γ-lactones was investigated starting from esters (XXIIIa and XXIIIb) with aromatic C ring. Recent successful conversion[17] of methyl $\Delta^{6,7}$-dehydrodehydroabietate (XXI) to a lactone (XXII) was encouraging for our study.

Methyl (±)-desoxypodocarpate (XXIIIa) in acetic acid was heated with lead tetra-acetate to give an acetoxy ester (XXIVa) contaminated with the starting material. This crude mixture dissolved in acetic acid was heated under reflux to effect elimination of the acetoxyl group. The desired unsaturated ester (XXVa) crystallized. Perbenzoic acid oxidation of the olefin (XXVa) gave crude crystalline epoxide (XXVI) which, without further purification, was hydrogenolyzed over Adams' platinum oxide. The resulting crude hydroxy ester (XXVIIa) was heated for 2·5 hr with methanolic potash to give crystalline hydroxy acid (XXVIIb). Under these conditions only the hydroxy ester could be hydrolysed[9] and the contaminating ester (XXIIIa) could be removed as neutral fraction. Since the hydroxy acid (XXVIIb) showed no tendency to lactonize spontaneously, the OH group was considered to be α and equatorial and accordingly the epoxide ring of the epoxy ester (XXVI) was considered to be α. This is in accord with the known inaccessibility on the β-face of the podocarpanoid diterpenes. Treatment of the hydroxy acid (XXVIIb) with methanolic hydrochloric acid as described by Tahara *et al.*[9] gave the desired γ-lactone (IX).

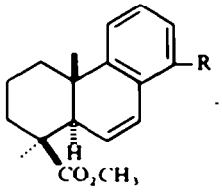
The transformation of the methoxy ester (XXIIIb) to 19 → 6 lactone was attempted in the same manner as described above. Lactones such as XXXIII and XXXVI were thought to be promising intermediates for the synthesis of kaurenolides. Acetoxylation of the ester (XXIIIb) gave an acetoxy ester (XXIVb) as crystals, which was heated to eliminate the acetoxyl group affording an unsaturated ester (XXVb). This was oxidized with perbenzoic acid to give a mixture of two diastereomers of the diol monobenzoate (XXVIIIa and XXVIIIb) in 16 and 15% yields, respectively. Defaye-Duchateau also



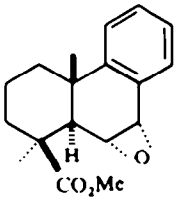
XXIIIa: R = H
b: OMe



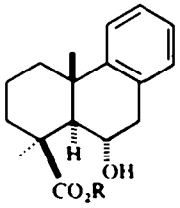
XXIVa: R = H
b: OMe



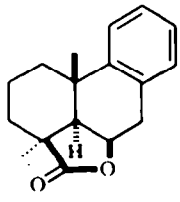
XXVa: R = H
b: OMe



XXVI

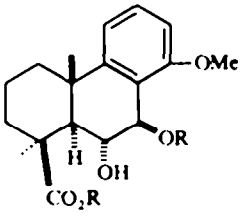


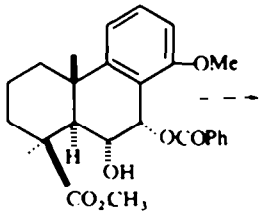
XXVIIa: R = Me
b: H



IX

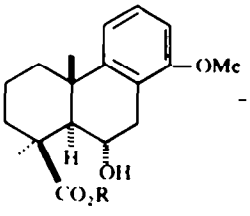
XXVb



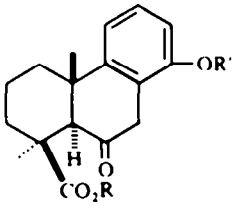


	R	R'
XXVIIIa:	Me	COPh
XXXIV:	H	H

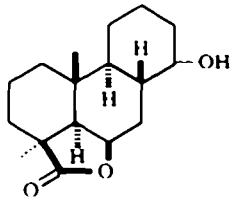
XXVIIIb



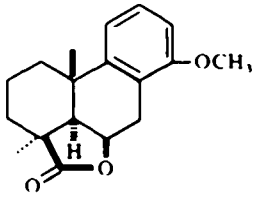
XXIX: R = Me
XXXV: H



	R	R'
XXX	Me	Me
XXXI	H	H
XXXII	Me	H
XXXVII	H	Me



XXXIII

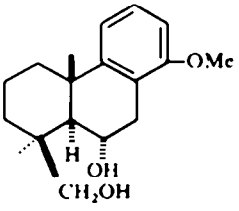


XXXVI

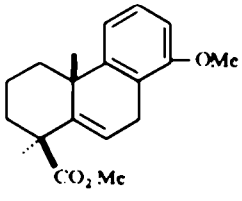
observed the formation of diol monobenzoates from the unsaturated ester (XXI). They were obviously derived from an intermediary 6,7-epoxide. The stereoformulas tentatively assigned to the two benzoates are based on the following facts. (i) Both of them gave the same hydroxy ester (XXIX) upon hydrogenolysis over Pd–C. (ii) Since the hydroxy acid (XXXV) derived from the benzoates (XXVIIIa and XXVIIIb) showed no tendency to lactonize spontaneously, the C-6 OH group was α and equatorial. (iii) The epimer (XXVIIIb) with a quasiaxial benzoxyl group was more easily eluted from alumina than the quasi-equatorial epimer (XXVIIIa). (iv) Comparison of the IR spectra of the epimers XXVIIIa (3600 (OH), 1720 ($OCOC_6H_5$) cm^{-1}) and XXVIIIb (3500, 1700 cm^{-1}) indicates the existence of intramolecular hydrogen bonding in the latter. NMR measurements did not afford clear-cut evidence for the assigned configurations, although a small high-field shift (0·11 ppm) of the angular Me resonance was observed in the case of XXVIIIa compared with that of XXVIIIb.

The hydroxy ester (XXIX) was oxidized with chromic acid to give the corresponding keto ester (XXX) which was demethylated with hydriodic acid in acetic acid. The resulting phenolic acid (XXXI) was esterified with diazomethane to give a phenolic ester (XXXII). This was hydrogenated over Raney nickel T-1[18] in hope of obtaining a dihydroxy ester with saturated C ring or a hydroxy lactone (XXXIII). Unfortunately, extensive hydrogenolysis of the C-6 OH group took place to give the known hydroxy acid (XI) as the major product (74% yield).* The minor oily neutral product (8%) absorbed at 1780 cm^{-1} in the CO region of the IR spectrum which was probably due to the desired lactone (XXXIII). No further attempt was made to isolate the lactone (XXXIII) in pure state in view of the disappointing yield.

Finally, efforts were directed to the preparation of the lactone (XXXVI). As reported by Tahara *et al.*[9] the C-4 axial ester, which is usually resistant to hydrolysis, can readily be hydrolysed when there exists a OH group at C-6. So the benzoxy ester (XXVIIIa) was converted to a dihydroxy acid (XXXIV). This, upon Birch reduction, gave a hydroxy acid (XXXV) which was also obtained from the hydroxy ester (XXIX) by alkaline hydrolysis. This acid was correlated to the keto ester (XXX) via a keto acid (XXXVII). Lactonization of the hydroxy acid (XXXV) under acidic condition was unsuccessful, although it worked well for the hydroxy acid (XXVIIb) without C-14 OMe group. The only product was a resinous acid instead of the expected lactone (XXXVI). This suggests that the C-6 OH group of the methoxy acid (XXXV) suffers β-elimination far more easily than that of the acid (XXVIIb).†



i



ii

* Hydrolysis of the axial ester group during the hydrogenolysis suggests the participation of the C-6 OH group generated by the reduction of the C-6 CO group.

† We could not convert a diol (i) obtained from previously described unsaturated ester (ii) by hydroboration-oxidation, to this keto acid (XXXVII).

EXPERIMENTAL

All m.ps are uncorrected.

(±)-14-*Acetoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (Vc)

The acid Vb (5 g) dissolved in pyridine (120 ml) was mixed with Ac_2O (100 ml). The mixture was heated on a boiling water bath for 2 hr and concentrated *in vacuo*. The residue was dissolved in THF (60 ml), mixed with sat $NaHCO_3$ aq (80 ml) and stirred and heated under reflux for 20 min. Then the mixture was acidified with dil HCl and extracted with EtOAc. The extract was washed with water and sat brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 5 g (90%) which recrystallized from EtOAc as small prisms, m.p. 210–212°; ν_{max} (Nujol) ~3200–~2400, 1775, 1740 (sh), 1710, 1610, 1574, 1198, 1188, 727 cm^{-1}. (Found: C, 71·80; H, 7·67. $C_{19}H_{24}O_4$ requires: C, 72·12; H, 7·65%).

O-*Acetylpodocarpic acid* (Ve)

This was prepared in the manner described for Vc in 85% yield. Recrystallization from EtOAc–petrol gave rosettes of needles, m.p. 180–182°; ν_{max} (Nujol) ~3200–~2400, 1770, 1700, 1612, 1585, 1216, 1202, 1170 cm^{-1}. (Found: C, 72·01; H, 7·50. $C_{19}H_{24}O_4$ requires: C, 72·12; H, 7·65%).

(±)-*Desoxypodocarpamide* (VIIa)

Thionyl chloride (20 ml) was added to a soln of Va (12 g) in purified $CHCl_3$ (350 ml). The mixture was heated under reflux for 30 min, left to stand for 4 hr at room temp and concentrated *in vacuo*. The residual oily crude VIa was dissolved in dry benzene (100 ml) and added dropwise to stirred and ice-cooled ether (350 ml) previously saturated with dry ammonia at 0–5° under a slow stream of dry ammonia during 30 min. After the addition, the mixture was stirred for 30 min at 0–5° and left overnight at room temp. It was then washed with water, dil NaOH aq and sat brine, dried (K_2CO_3) and concentrated *in vacuo* to give 11·8 g (99%) which recrystallized from THF–n hexane as prisms, m.p. 175–176°; ν_{max} (Nujol) 3510, 3340, 3290, 3160, 1680, 1612, 763, 733 cm^{-1} δ (ppm from TMS at 100 Mc, $CDCl_3$) 1·21 (3H, s), 1·31 (3H, s) ca. 2·90 (2H, m) ca. 5·85 (2H, broad) 7·17–7·26 (4H). (Found: C, 78·87; H, 8·66; N, 5·11. $C_{19}H_{23}ON$ requires: C, 79·33; H, 9·01; N, 5·44%).

(±)-14-*Acetoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid amide* (VIIb)

The acid Vc (4·5 g) in $CHCl_3$ (100 ml) was treated with $SOCl_2$ (20 ml). The mixture was left at room temp for 2 days and concentrated *in vacuo*. To a stirred soln of the residual oily acyl chloride in benzene (160 ml) dry ammonia was passed at 5–10° for 1·5 hr with stirring. The mixture was poured into HCl–NH_4Cl buffer and extracted with EtOAc. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 3·4 g (75%) which recrystallized from EtOAc as prisms, m.p. 196–197°; ν_{max} (Nujol) 3490, 3180, 1770, 1672, 1610, 1580, 1210, 1200, 1162 cm^{-1}. (Found: C, 71·62; H, 7·80; N, 4·57. $C_{19}H_{25}O_3N$ requires: C, 72·35; H, 7·99; N, 4·44%).

O-*Acetylpodocarpamide* (VIIc)

This was prepared in the manner described for VIIb in 76% yield and recrystallized from EtOAc–petrol as needles, m.p. 108–110°; ν_{max} (Nujol) 3480, 3380, 3300, 3220, 1762, 1670, 1612, 1580, 1218, 1170, 1030, 895 cm^{-1}. (Found: C, 71·89; H, 7·85; N, 4·19. $C_{19}H_{25}O_3N$ requires: C, 72·35; H, 7·99; N, 4·44%).

(±)-20-*Hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* 19 → 20 *lactone* (VIIIa) *and* (±)-6β-*hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* 19 → 6 *lactone* (IX)

A soln of VIIa (1 g), I_2 (3 g) and lead tetraacetate (5 g) in dry benzene (140 ml) was irradiated with an 8-W low press Hg lamp for 48 hr. (The lamp was immersed in the soln.) The mixture was filtered and the filtrate washed with water, $NaHSO_3$ aq and water, dried ($MgSO_4$) and concentrated *in vacuo*. The residual gum was dissolved in 95% EtOH (40 ml), mixed with KOH (2·5 g) in water (10 ml) and heated under reflux for 2 hr. The soln was concentrated *in vacuo*, diluted with water and extracted with ether to remove the neutral fraction. The aqueous layer was acidified with HCl and heated on a boiling water bath for 2 hr. After cooling, it was extracted with ether. The extract was washed with water, $NaHCO_3$ aq and sat brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual oil was chromatographed on alumina (1·5 × 15·5 cm) in petrol and the following fractions of 200 ml were collected. Fraction No. 1 (petrol:ether = 9:1) was an oil (62 mg). Fraction No. 2 (same eluant) was also an oil (21 mg). Fraction No. 3 (same eluant) was the crystalline γ-lactone IX (80 mg). Fraction No. 4 (petrol:ether = 1:1) was the crystalline δ-lactone VIIIa (11 mg).

Fraction No. 5 (ether) was also the δ-lactone VIIIa (8 mg). Fractions 6–8 (ether) were gums. Fraction No. 9 (EtOAc) was the δ-lactone VIIIa (5 mg). The experiment was repeated for 7 times. The average yields of the lactones were 8·12% for IX and 2·3% for VIIIa. The δ-lactone (VIIIa) crystallized from EtOAc–ether as needles, m.p. 149–150°; ν_{max} (Nujol) 1734, 1164, 1143, 1135, 1120, 1040, 758, 742; ($CHCl_3$) 1732 (1724 sh), 1165, 1160, 1145, 1138, 1125, 1045 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·35 (3H, s), 2·96 (2H, m), 4·36 (2H, s) 7·20, 7·28 (4H). The solution IR was identical with that of an authentic optically active sample. (Found: C, 79·49; H, 7·38. $C_{17}H_{20}O_2$ requires: C, 79·65; H, 7·86%). The γ-lactone (IX) crystallized from EtOAc–petrol as elongated prisms, m.p. 138–139°; ν_{max} (Nujol) 1768, 1195, 1178, 1114, 1040, 1005, 765, 735; ($CHCl_3$) 1772, 1184, 1118, 1044, 1006 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·16 (3H, s), 1·32 (3H, s), 3·12–3·65 (2H, m) 5·13 (1H, m) 7·21 (4H). The NMR spectrum was superimposable to that of an authentic sample. (Found: C, 79·65; H, 7·43. $C_{17}H_{20}O_2$ requires: C, 79·65; H, 7·86%).

(±)-14,20-*Dihydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* 19 → 20 *lactone* (VIIIb)

A soln of VIIb (1 g), I_2 (3 g) and lead tetraacetate (5 g) in dry benzene (160 ml) was irradiated with an 8-W low press Hg lamp for 12 hr. The mixture was filtered and the filtrate was washed with water, $NaHSO_3$ aq *bisulfite* and water, dried ($MgSO_4$) and concentrated *in vacuo*. The residual gum was dissolved in 95% EtOH (50 ml), mixed with KOH (3 g) in water (15 ml) and heated under reflux for 2 hr. Then the soln was saturated with CO_2 and extracted with ether to remove weak acid fraction. The aqueous layer was acidified with HCl and heated on a boiling water bath for 30 min. After cooling, it was extracted with ether. The extract was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated *in vacuo* to give 117 mg (12%) which recrystallized from EtOAc–petrol as prisms, m.p. >240°; ν_{max} (Nujol) 3360, 1700, 1588, 1276, 1174, 1035; ($CHCl_3$) ca. 3650, 1730, 1588, 1276, 1160, 1138, 1122, 1035 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln.) 1·34 (3H, s), 4·32 (2H, doubled doublet). (Found: C, 74·45; H, 7·28. $C_{17}H_{20}O_3$ requires: C, 74·97; H, 7·40%).

20-Hydroxypodocarpic acid 19 → 20 *lactone* (VIIIc)

This was prepared in the manner described for VIIIb in 5% yield. Recrystallization from EtOAc gave prisms, m.p. 228–230°; ν_{max} (Nujol) 3310, 1710, 1622, 1585, 1168, 1132, 1028; ($CHCl_3$) ca. 3650, ~3360, 1730, 1612, 1590, 1162, 1130, 1034 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·30 (3H, s), 4·24 (2H, d, J = 1·5 c/s). (Found: C, 74·46; H, 7·32. $C_{17}H_{20}O_3$ requires: C, 74·97; H, 7·40%).

(±)-14α-*Hydroxy*-5α,8β,9α,10β-*podocarpan*-19-*oic acid* (XIa)

A soln of X (4·8 g) in THF (50 ml) and t-BuOH (50 ml) was added to liquid ammonia (140 ml). Na (2·8 g) was added to the stirred soln cooled in a dry ice acetone bath. After 1 hr Li (0·5 g) was added and the stirring was continued for a further 2 hr. Then abs EtOH (20 ml) was added to destroy the excess metal and the mixture was left overnight at room temp to remove ammonia. The solvents were removed *in vacuo* and the neutral fraction was extracted with ether. The starting ester X (2·7 g) was recovered from the ether extract. The alkaline aqueous layer was acidified with HCl and extracted with EtOAc. The extract was washed with sat brine, dried (Na_2SO_4) and evaporated *in vacuo* to give XIa (1·7 g, 39%). This was recrystallized from MeOH–EtOAc as prisms, m.p. 278–280°; ν_{max} (Nujol) 3340, ~2600, 1694, 1052, 920, 743 cm^{-1}. (Found: C, 72·74; H, 9·96. $C_{17}H_{28}O_3$ requires: C, 72·82; H, 10·06%).

(+)-14α-*Acetoxy*-5α,8β,9α,10β-*podocarpan*-19-*oic* acid (XIb)

This was prepared in the manner described for the preparation of Vc in 57% yield. Recrystallization from MeOH–EtOAc gave prisms, m.p. 253–254°; ν_{max} (Nujol) ~2600, 1734, 1692, 1238, 1050, 1025, 968 cm^{-1}. (Found: C, 70·99; H, 9·31. $C_{19}H_{30}O_4$ requires: C, 70·77; H, 9·38%).

(±)-14α-*Acetoxy*-5α,8β,9α,10β-*podocarpan*-19-*oic acid amide* (XIII)

This was prepared in the manner described for the preparation of VIIb in 76% yield and recrystallized from EtOAc as leaflets, m.p. 242–244°; ν_{max} (Nujol) 3440, 3120, 1716, 1670, 1610, 1250, 1048, 1026, 965 cm^{-1}. (Found: C, 71·50; H, 9·83; N, 4·22. $C_{19}H_{31}O_3N$ requires: C, 70·99; H, 9·72; N, 4·36%).

(±)-14-*Oxo*-20-*hydroxy*-5α,8β,9α,10β-*podocarpan*-19-*oic acid* 19 → 20 *lactone* (XIV)

A soln of XIII (688 mg), I_2 (3 g) and lead tetraacetate (5 g) in dry benzene (160 ml) was irradiated with an 8-W low press Hg lamp for 7 hr. The mixture was filtered and the filtrate was washed with water, sat $NaHSO_3$ aq and sat brine. The residue obtained after removal of benzene was dissolved in 95% EtOH

(50 ml) and mixed with KOH (3·5 g) in water (10 ml). The soln was refluxed for 1·5 hr and then concentrated *in vacuo*. The residue was diluted with water and extracted with ether to remove the neutral fraction. The aqueous layer was acidified with HCl and heated on a boiling water bath for 30 min. After cooling, it was extracted with ether. The extract was washed with $NaHCO_3$aq and concentrated. The residue in acetone (30 ml) was oxidized with the Jones reagent (0·3 ml) at room temp for 10 min. MeOH was added to the mixture to destroy excess oxidant. The reaction mixture was diluted with water and extracted with ether. The extract was washed with $NaHCO_3$aq, dried ($MgSO_4$) and concentrated to give 20 mg (3%) which crystallized from EtOAc–petrol as prisms, m.p. 163–164°; ν_{max} (Nujol) 1724, 1706, 1142 cm^{-1}. δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·19 (3H, s), 4·15 (1H, d, J ~ 12), 4·59 (1H, d, J ~ 12 c/s). (Found: C, 73·52; H, 8·58. $C_{19}H_{24}O_3$ requires: C, 73·98; H, 8·75%).

(+)-16ξ-*Acetoxy*-17-*norkauran*-19-*oic acid* (XVb)

The acid XVa (880 mg) dissolved in dry pyridine (30 ml) was mixed with Ac_2O (30 ml). The mixture was left at room temp for 2 days and concentrated *in vacuo*. The residual oil (acetylated mixed anhydride) in THF (20 ml) was stirred with sat $NaHCO_3$aq (30 ml) at room temp for 3 hr. The mixture was acidified with HCl and extracted with EtOAc. The extract was washed with water and brine, dried ($MgSO_4$) and evaporated *in vacuo* to give 1·009 g (99%) of the acetate which crystallized from EtOAc–petrol as elongated prisms, m.p. 226–228°; ν_{max} (Nujol) 3300 ~ 2400, 1738, 1700, 1268, 1030 cm^{-1}. (Found: C, 72·44; H, 8·97. $C_{21}H_{30}O_4$ requires: C, 72·80; H, 8·73%).

(±)-16ξ-*Acetoxy*-17-*norkauran*-19-*oic acid amide* (XVII)

The acid XVb (950 mg) dissolved in purified $CHCl_3$ (20 ml) was mixed with $SOCl_2$ (12 ml) and left overnight at room temp and then concentrated *in vacuo* to give crystalline XVI; ν_{max} (Nujol) 1798, 1736, 1265, 1030, 835 cm^{-1}. This was dissolved in dry benzene (100 ml) and dry NH_3 was passed into the stirred soln for 1·5 hr at room temp. The benzene soln was washed with NH_4Claq and sat brine, dried ($MgSO_4$) and evaporated to give 832 mg (87%) of the amide which crystallized from EtOAc–petrol as prisms, m.p. 215–216°; ν_{max} (Nujol) 3470, 3360, 3195, 1740, 1650, 1606, 1252, 1035 cm^{-1}. (Found: C, 72·61; H, 9·08; N, 3·99. $C_{21}H_{31}O_3N$ requires: C, 73·00; H, 9·05; N, 4·05%).

(±)-16-*Oxo*-20-*hydroxy*-17-*norkauran*-19-*oic acid* 19 → 20 *lactone* (XVIII)

The amide XVII (800 mg), I_2 (3 g) and lead tetraacetate (5 g) were dissolved in dry benzene (160 ml) and irradiated with an 8-W low press Hg lamp for 48 hr. Subsequent treatment as described in the preparation of XIV gave 139 mg (20%) of XVIII. Recrystallization from EtOAc–petrol afforded prisms, m.p. 201–202°; ν_{max} (Nujol) 1742, 1730, 1145, 1038; ($CHCl_3$) 1738 (broad), 1148, 1040 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·20 (3H, s), 1·98 (2H, d, J = 2 c/s, C-15 methylene), 4·17 (1H, d, J_{AB} = 12 c/s), 5·18 (1H doubled d, $J_{HA\,H1\beta}$ 1·5 c/s, J_{AB} ~ 12 c/s). (Found: C, 75·33; H, 8·74. $C_{19}H_{26}O_3$ requires: C, 75·46; H, 8·67%).

Methyl (±)-7ξ-*Acetoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXIVa)

Compound XXIIIa (5 g) and lead tetraacetate (9·7 g) were dissolved in AcOH (28 ml). The soln was stirred and heated on a boiling water bath for 2 hr under N_2 atm. After cooling, the mixture was diluted with water and extracted with EtOAc. The extract was washed with water, $NaHCO_3$aq and brine, dried ($MgSO_4$) and concentrated to give an oil (5·7 g, 93·8%). This was triturated with MeOH to give crystalline powder. Recrystallized sample melted at 102–103°; ν_{max} (Nujol) 1700, 1230, 1175, 1140, 1020, 760 cm^{-1}. (Found: C, 76·46; H, 8·21. $C_{20}H_{26}O_4$ requires: C, 72·70; H, 7·93%). This powder was a mixture of the desired acetate and the starting material.

Methyl (±)-5α,10β-*podocarpa*-6,8,11,13-*tetraen*-19-*oate* (XXVa)

A soln of the crude XXIVa (5 g) in AcOH (120 ml) was heated under reflux for 15 hr. The solvent was removed *in vacuo* and the residue was triturated with MeOH to give a crystalline product. One recrystallization from MeOH virtually eliminated the contaminating impurity and pure unsaturated XXVa (2·3 g, 63%) was obtained. An analytical sample melted at 93·5–94°; ν_{max} (Nujol) 1725, 1220, 1200, 1150, 760 cm^{-1}; λ_{max} (EtOH) 263 mμ (ε 8400). (Found: C, 79·99; H, 8·19. $C_{18}H_{22}O_2$ requires: C, 79·96; H, 8·20%).

Methyl (±)-6α,7α-*oxido*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXVI)

To a soln of XXVa (4·65 g) in $CHCl_3$ (160 ml) perbenzoic acid (9 g) was added at 0–5°. The mixture was

left in a refrigerator for 4 days. The reaction mixture was washed thoroughly with K_2CO_3 aq carbonate, dried ($MgSO_4$) and evaporated to give an oil. This was triturated with MeOH to give crude epoxide contaminated with the starting material (2·85 g, 53·2%). A recrystallized sample melted at 90·5 91·5°; ν_{max} (Nujol) 1725, 1230, 1193, 1155, 985, 805, 770, 753 cm^{-1}; λ_{max} (EtOH) 266 mμ (ε 2600).

Methyl (±)-6α-*hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXVIIa)

The crude XXVI (1·6 g) dissolved in THF (25 ml) and MeOH (25 ml) was hydrogenolysed over Adams' PtO_2 (100 mg). The H_2 absorption (152 ml) ceased after 5 hr. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to give 500 mg of crystals and 700 mg of an oil. The crystalline material was shown to be XXIIIa generated by the saturation of the 6(7) double bond of the unsaturated ester XXVa contaminated in the starting material. The oil could not be induced to crystallize even after chromatography on alumina and employed for the next step without further purification.

(±)-6α-*Hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (XXVIIb)

The crude XXVIIa (600 mg) and KOH (2·4 g) were dissolved in MeOH (40 ml). The soln was heated under reflux for 2·5 hr, and then concentrated *in vacuo*. The residue was diluted with water and extracted with ether to remove neutral material. The ether extract contained 80 mg of XXIIIa contained in the starting material as a contaminant. The alkaline aqueous layer was acidified with HCl and extracted with ether. The ether extract was washed with water and sat brine, dried ($MgSO_4$) and concentrated to give 370 mg (63%) of crystalline acid. A sample recrystallized from MeOH melted at 183–184°; ν_{max} (Nujol) 3570, ~2600, 1690, 1675, 1283, 1250, 1072, 1056, 970, 760, 738 cm^{-1}. (Found: C, 74·75; H, 8·37. $C_{17}H_{22}O_3$ requires: C, 74·42; H, 8·08%).

(±)-6β-*Hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* 19 → 6 *lactone* (IX)

To a soln of XXVIIb (450 mg) in MeOH (228 ml), 15% HCl (98 ml) was added. The mixture was heated under reflux for 1 hr. Then MeOH was removed *in vacuo* and the aqueous layer extracted with ether. The ether extract was washed with $NaHCO_3$ aq and brine, dried ($MgSO_4$) and concentrated to give 170 mg (45%) of the crystalline lactone, m.p. 128–129° (crude), identified with an authentic sample prepared by the photochemical method by comparison of IR and NMR spectra.

Methyl (±)-7ξ-*acetoxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXIVb)

To a suspension of pure XXIIIb (4·2 g) in AcOH (30 ml) lead tetraacetate (7·0 g) was added. The mixture was stirred and heated on a boiling water bath for 30 min under N_2 atm. During this period the ester dissolved completely. After cooling, water was added to the soln. The crude ppt (4·1 g, 82%) was collected on a filter and recrystallized from EtOAc–MeOH as elongated prisms, m.p. 165–166°; ν_{max} (Nujol) 1736, 1725 (sh), 1600, 1582, 1240 cm^{-1}. (Found: C, 70·19; H, 7·75. $C_{21}H_{28}O_5$ requires: C, 69·97; H, 7·83%).

Methyl (±)-14-*methoxy*-5α,10β-*podocarpa*-6,8,11,13-*tetraen*-19-*oate* (XXVb)

A soln of XXIVb (3·7 g) in AcOH (100 ml) was heated under reflux for 16 hr. The solvent was removed *in vacuo* and the residue was dissolved in EtOAc. The EtOAc soln was washed with $NaHCO_3$ aq and brine, dried ($MgSO_4$), decolorized with charcoal and concentrated to give 3·0 g (99%) which recrystallized from MeOH as needles, m.p. 89–90°; ν_{max} (Nujol) 1732, 1634, 1590, 1262, 1220, 1143, 1055, 764 cm^{-1}; λ_{max} (EtOH) mμ (ε) 267 (7300), 298 (3900), 309 (3600); δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 0·85 (3H, s, C—10-$C\underline{H}_3$), 1·28 (3H, s, C 4C$\underline{H}_3$), 2·32 (1H, d, J = 3 C—5H), 3·64 (3H, s, $CO_2C\underline{H}_3$), 3·78 (3H, s, $OC\underline{H}_3$), 6·40, 6·50 (1H, doubled d. C 6 H $J_{5,6}$ = 3 c/s, $J_{6,7}$ = 10 c/s), 6·65–7·15 (4H, arom. H + C 7H). (Found: C, 76·20; H, 7·87. $C_{19}H_{24}O_3$ requires: C, 75·97; H, 8·05%).

Methyl (±)-6α-*hydroxy*-7β-*benzoyloxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXVIIIa) *and its* 7α-*isomer* (XXVIIIb)

To a soln of XXVb (3·0 g) in $CHCl_3$ (90 ml) at 0° perbenzoic acid (2·5 g) and benzoic acid (1·5 g) was added. The soln was left for 4 days in a refrigerator, then washed with K_2CO_3 aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue, when triturated with MeOH, gave 730 mg (16%) of XXVIIIa. This was recrystallized from EtOAc–petrol as prisms, m.p. 201–202° (dec); ν_{max} (Nujol) 3600 (no chelation), 1730, 1720, 1600, 1590, 1276, 1056, 718, 710 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·09 (3H, s, C-10 $C\underline{H}_3$), 1·45 (3H, s, C-4 $C\underline{H}_3$), 3·69 (3H, s), 3·74 (3H, s), 4·62 (1H, q, $J_{HH'}$ = 10 c/s, J_{HOH} = 5 c/s). (Found: C, 73·92; H, 7·02. $C_{26}H_{30}O_6$ requires: C, 73·91; H, 7·16%). The mother liquor was concentrated to give 2·5 g

of an oil. The above experiment was repeated 6 times. The oil (15 g) was chromatographed on silicic acid (5 × 26 cm) in benzene and the following fractions of 500 ml were collected. Fractions 1 and 2 (benzene) gave an oil (2·5 g) plus a small amount of XXIIIb. Fractions 3, 4 and 5 (5% ether in benzene) gave the 7α (axial)-ixomer (XXVIIIb, 4·0 g of crystals) plus an oil (2·5 g). Fractions 6 and 7 gave 0·4 g of the 7β (eq.)-isomer XXVIIIa. The yield of the 7α-isomer from the starting material was 15%. The 7α-isomer crystallized from EtOAc petrol as elongated prisms, m.p. 126–127° (dec); ν_{max} (Nujol) 3500 (chelation), 1728, 1700, 1600, 1590, 1285, 1055, 724, 715 cm^{-1}, δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 1·20 (3H, s, C-10 CH_3) 1·51 (3H, s, C-4·CH_3), 3·58 (3H, s), 3·63 (3H, s), 4·80 (1H, q, $J_{HH'}$ = 10 c/s, $J_{HH''}$ = 6 c/s). (Found: C, 73·42; H, 6·77. $C_{26}H_{30}O_6$ requires: C, 73·91; H, 7·16%).

Methyl (±)-6α-*hydroxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXIX)

The benzoate XXVIIIa (1·593 g) in EtOAc (80 ml) was shaken under H_2 atm with 10% Pd-C (500 mg) for 9 hr at room temp. The catalyst was filtered off and the filtrate was washed with sat $NaHCO_3$ aq. The EtOAc soln was dried ($MgSO_4$) and concentrated to give 1·052 g (93%) of the product. In the same manner 1·00 g of XXVIIIb gave 650 mg of the product. The hydroxy ester crystallized from EtOAc–petrol as needles, m.p. 132–133°; ν_{max} (Nujol) 3565, 1715, 1600, 1582, 1252, 1240, 1055 cm^{-1}. (Found: C, 71·45; H, 7·89. $C_{19}H_{26}O_4$ requires: C, 71·67; H, 8·23%).

Methyl (±)-6-*oxo*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXX)

a. *Oxidation of* XXIX. The ester XXIX (40 mg) dissolved in acetone (10 ml) was treated with the Jones chromic acid reagent (0·4 ml) at room temp for 3 min. The excess oxidant was destroyed by the addition of MeOH. The mixture was concentrated *in vacuo*, diluted with water and extracted with ether. The ether extract was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and concentrated to give an oil (35 mg, 88%); ν_{max} (film) 1720, 1580, 1240, 1110, 1015, 790 cm^{-1}. This was employed for the next step without further purification.

b. *Pyrolysis of* XXVIIIa. The benzoate XXVIIIa (20 mg) was heated at 240° for 10 min. After cooling, the reaction products were dissolved in ether. The ether soln was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and concentrated to give an oil which showed an identical IR spectrum with that of the authentic XXX.

(±)-6-*Oxo*-14-*hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (XXXI)

A soln of XXX (1 g) in AcOH (15 ml) containing 48% HBr (10 ml) and 60% HI (1·5 ml) was heated under reflux for 8 hr under N_2 atm, then concentrated *in vacuo* and extracted with ether. The ether soln was washed with water, dried ($MgSO_4$) and concentrated to give 600 mg (64%) of the acid as crystals. Recrystallization from EtOAc afforded prisms, m.p. 195–200° (dec); ν_{max} (Nujol) 3360, 3200–2600, 1718, 1590, 1240, 1125, 785, 729 cm^{-1}. (Found: C, 69·93; H, 6·78. $C_{17}H_{20}O_4$ requires: C, 70·81; H, 6·99%). This phenol is unstable and the colour of its solution rapidly turned to green-black.

Methyl (±)-6-*oxo*-14-*hydroxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oate* (XXXII)

A suspension of XXXI (0·7 g) in EtOAc (20 ml) was treated with an excess diazomethane in ether. Subsequent treatments in a usual manner afforded the product (0·7 g). This crystallized from EtOAc petrol as rods, m.p. 191–192°; ν_{max} (Nujol) 3365, 1738, 1695, 1610, 1590, 1280, 1240, 1194, 1175, 1120, 786, 730 cm^{-1}; δ (ppm from TMS at 100 Mc, $CDCl_3$ soln) 0·62 (3H, s, C-10 CH_3), 1·13 (3H, s, C-4 CH_3), 2·81 (1H, s, C-5H); an AB quartet, 8-H centered at 3·34 ($J_{88'}$ = 22 c/s), 8'-H at 3·80 (J = 22 c/s), 3·68 (3H, s, CO_2CH_3), 5·82 (1H, s, ArOH), 6·65–7·13 (3H, arom. H). (Found: C, 71·16; H, 7·43. $C_{18}H_{22}O_4$ requires: C, 71·50; H, 7·33%).

Catalytic hydrogenation of the oxo ester XXXII

The ester XXXII (0·5 g) in 99% EtOH (80 ml) was hydrogenated at 180° and an initial press of 100 kg/cm^2 for 1·3 hr over Raney Ni T-1 (5 g). After conventional work-up, an oily product in MeOH (30 ml) was mixed with KOH (3 g) in water (2 ml). The soln was heated under reflux for 1·5 hr, concentrated *in vacuo* and extracted with ether to remove neutral fraction. The aqueous layer (30 ml) was acidified (Congo red) with HCl. MeOH (50 ml) was added to the acidified soln heated under reflux for 30 min. After removal of MeOH *in vacuo*, the mixture was extracted with ether. The organic product was separated into acidic and neutral fractions. The acidic fraction (368 mg of crystals) was identified as XIa by IR comparison. The neutral fraction (40 mg of a gum) absorbed at 1780 cm^{-1}.

(±)-6α,7β-*Dihydroxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (XXXIV)

A soln of XXVIIIa (1·5 g) in MeOH (100 ml) containing KOH (3 g) was heated under reflux for 2·5 hr. MeOH was removed *in vacuo*. The residue was acidified with dil HCl. The ppt was collected on a filter and washed with a small amount of ether to give 1·1 g (99%) which crystallized from EtOH as prisms, m.p. 232–234° (dec); ν_{max} (Nujol) 3440, 3240, ~2600, 1700, 1600, 1585, 1260, 1242, 1092, 1060 cm^{-1}. (Found: C, 68·05; H, 7·71. $C_{18}H_{24}O_5$ requires: C, 67·48; H, 7·55%).

(±)-6α-*Hydroxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (XXXV)

a. *Birch reduction of* XXXIV. A suspension of XXXIV (500 mg) in abs EtOH (60 ml) was added to liquid NH_3 (160 ml) cooled in a Dry Ice–acetone bath. Li (8 g) was added portionwise to a stirred and cooled suspension during 2 hr. Then abs EtOH (10 ml) was added and the mixture was left overnight at room temp. The residue was diluted with water, concentrated *in vacuo* and acidified with HCl to give 350 mg (75%) which recrystallized from EtOH as small prisms, m.p. 212–213° (dec); ν_{max} (Nujol) 3650, ~3200–~2600, 1603, 1584, 1252, 1062, 1055, ~930, 784, 728 cm^{-1}. (Found: C, 70·64; H, 7·99. $C_{18}H_{24}O_4$ requires: C, 71·02; H, 7·95%).

b. *Hydrolysis of* XXIX. The ester XXIX (600 mg) in MeOH (30 ml) containing KOH (2 g) was heated under reflux for 3·5 hr. Subsequent work-up gave 550 mg (95%) of the acid identified by IR comparison.

(±)-6-*Oxo*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*trien*-19-*oic acid* (XXXVII)

The acid XXXV (500 mg) in acetone (100 ml) was treated with Jones chromic acid reagent (1 ml) for 5 min at room temp. Subsequent treatments in a usual manner gave a crystalline oxo acid (450 mg, 90%). This crystallized from EtOAc–petrol as rods, m.p. 189–190° (dec); ν_{max} (Nujol) ~2760, 1732, 1670, 1600, 1588, 1260, 1066, 900, 780, 712 cm^{-1}. (Found: C, 71·16; H, 7·35. $C_{18}H_{22}O_4$ requires: C, 71·50; H, 7·33%).

(±)-6α,19-*Dihydroxy*-14-*methoxy*-5α,10β-*podocarpa*-8,11,13-*triene* (i)

Sodium borohydride (1·7 g) was suspended in a soln of methyl (±)-14-methoxy-10β-podocarpa-5,8,11,13-tetraen-19-oate (11·2 g) in THF (70 ml). To the stirred and cooled (0–10°) suspension $BF_3 \cdot Et_2O$ (7·6 ml) in THF (10 ml) was added. The stirring was continued for 2 hr at 0–10°. Water was added to destroy the excess diborane, then 12% NaOH aq (16 ml) and 30% H_2O_2 (16 ml) were added to the stirred soln. The temp of the mixture was raised to 50° and then the mixture was left at room temp for 30 min and poured into brine. The mixture was extracted with ether. The ether soln was washed with sat brine, dried ($MgSO_4$) and concentrated to give 1·5 g (78%) which crystallized from EtOAc as needles, m.p. 173–174°; ν_{max} (Nujol) 3350, 1600, 1580, 1250, 1060, 1010, 784, 725 cm^{-1}. (Found: C, 74·12; H, 8·87. $C_{18}H_{26}O_3$ requires: C, 74·44; H, 9·03%).

Acknowledgements We are indebted to Professors P. R. Jefferies (University of Western Australia) and R. C. Petterson (Loyola University, Louisiana) for discussions. Our thanks are due to Drs. A. Tahara and K. Hirao for spectral comparisons. A donation of a bottle of podocarpic acid from Prof. Petterson is gratefully acknowledged.

REFERENCES

[1] J. R. Hanson, *Tetrahedron* **23**, 733 (1967).
[2] B. E. Cross, R. H. B. Galt and J. R. Hanson, *J. Chem. Soc.* 2944 (1963).
[3] C. Kaneko, T. Tsuchiya and M. Ishikawa, *Chem. Pharm. Bull., Tokyo* **11**, 271, 1346 (1963).
[4] J. W. B. Fulke and R. McCrindle, *Chem. & Ind.* 647 (1965).
[5] K. Mori and M. Matsui, *Tetrahedron Letters* 1633 (1966).
[6] D. H. R. Barton, A. L. J. Beckwith and A. Goosen, *J. Chem. Soc.* 181 (1965); *Proc. Chem. Soc.* 335 (1963).
[7] R. C. Petterson and A. Wambsgans, *J. Am. Chem. Soc.* **86**, 1648 (1964).
[8] E. L. Ghisalberti, P. R. Jefferies and W. A. Mincham, *Tetrahedron* **23**, 4463 (1967).
[9] A. Tahara, K. Hirao and Y. Hamazaki, *Tetrahedron* **21**, 2133 (1965).
[10] E. Wenkert and B. L. Mylari, *J. Am. Chem. Soc.* **89**, 174 (1967).
[11] J. W. ApSimon and O. E. Edwards, *Canad. J. Chem.* **40**, 896 (1962).
[12] K. Mori and M. Matsui, *Tetrahedron* **22**, 879 (1966).
[13] K. Mori and M. Matsui, *Tetrahedron Letters* 175 (1966); *Tetrahedron* **24** (1968).
[14] Kindly supplied by Professor R. C. Petterson.
[15] A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lewis, *J. Chem. Soc.* 2548 (1953).

[16] M. Sumimoto and T. Kondo, *10th Symposium on the Chemistry of Natural Products*, p. 208. Tokyo, Symposium Papers (1966).
[17] G. Defaye-Duchateau, *Bull. Soc. Chim. Fr* 1469 (1964).
[18] X. A. Dominguez, I. C. Lopez and R. Franco, *J. Org. Chem.* **26**, 1625 (1961).