Constituents of *Annona coriacea*. The Structure of a New Diterpenoid

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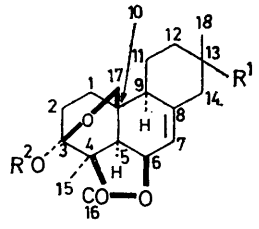
A new diterpenoid, 3,17-epoxy-3α-hydroxy-13-hydroxyacetyl-13-methylpodocarp-7-en-16,6β-olactone (1), has been isolated from *Annona coriacea*; the structural assignment is based on chemical and spectral evidence and is confirmed by conversion of the diterpenoid (1) into (−)-13,13-dimethylpodocarp-7-ene. This correlation indicates the absolute stereochemistry of (I) except for the configuration at C-13 which remains undefined.

WE have previously described[1] two new diterpenoids with a clerodane skeleton isolated from the acetone extract of bulbs of *Annona coriacea*. In an extension of this work we have examined a third new diterpenoid, $C_{20}H_{26}O_6$, m.p. 261—263°, $[\alpha]_D$ −174°, to which the structure (1) can be assigned.[2]

The presence of an α-ketol group in the side chain of (1) was suggested by a singlet at δ 4·75 (2H) in the n.m.r. spectrum ascribable to the hydroxymethyl group adjacent to the carbonyl group. This signal was moved downfield to δ 5·12 on formation of the acetate (2). Confirmatory evidence for the presence of a $CO{\cdot}CH_2{\cdot}OH$ group was obtained from oxidation of (1) with periodic acid which gave the nor-acid (3). A prominent peak at *m/e* 303 (M − $CO{\cdot}CH_2OH$), in the mass spectrum of (1), agrees with the presence of an α-ketol group in the side chain.

A tertiary hydroxy-group is also present in (1), and a diacetate (4) was obtained on refluxing (1) with acetic anhydride and anhydrous sodium acetate: its n.m.r. spectrum differs from that of monoacetate (2) only in the presence of another tertiary methyl signal as a singlet at δ 2·0; the i.r. spectrum of (4) exhibits carbonyl bands at 1775, 1750, and 1730 cm^{-1}.



(1) $R^1 = CO{\cdot}CH_2OH$, $R^2 = H$
(2) $R^1 = CO{\cdot}CH_2OAc$, $R^2 = H$
(3) $R^1 = CO_2H$, $R^2 = H$
(4) $R^1 = CO{\cdot}CH_2OAc$, $R^2 = Ac$
(5) $R^1 = CO_2Me$, $R^2 = H$
(6) $R^1 = CO_2Me$, $R^2 = Ms$

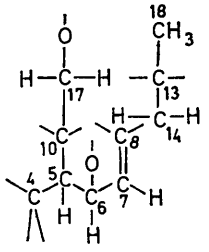
The n.m.r. spectrum of the acid (3) is of particular interest: † the chemical shifts and the various couplings (verified by double resonance experiments) indicate the presence of the part-structure (3a) in (3). The proton at C-7 appears at δ 5·72, as a broad doublet coupled (*J*

† We thank Dr. Z. Samek of the Czechoslovak Academy of Science for recording and discussing this spectrum.

[1] M. Ferrari, F. Pelizzoni, and G. Ferrari, *Phytochemistry*, 1972, **10**, 3267.

[2] F. Pelizzoni, presented in part at the VIIIth International Symposium on the Chemistry of Natural Products, New Delhi, February 1972.

5 Hz) with the proton at C-6. The latter proton is also coupled with the 5α-proton (J 6·5 Hz) and thus gives rise to a doublet of doublets centred at δ 4·95. In addition to the coupling with the proton at C-6, the



(3a)

5α-H shows a pronounced long range coupling (^4J 2·2 Hz) with one of the C-17 methylene protons and thus it forms, at δ 2·21, a doublet of doublets. The C-17 methylene protons give rise to a pair of doublets centred at δ 3·56 and 4·04 (J_{gem} 9 Hz); the upfield doublet is further split by the long range coupling with 5α-H. The pair of doublets centred at δ 2·23 (partly overlapped) and at δ 2·50 can be attributed to the two nonequivalent protons at C-14 (J_{gem} 12·5 Hz). The doublet at δ 2·50 is broadened and exhibits unresolved small couplings with both proton at C-6 and C-7 and with the methyl protons at C-13, which form a broad singlet at δ 1·05.

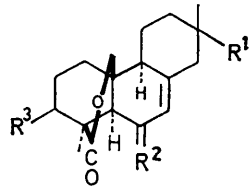
In view of the presence of the above fragment (3a) as well as the α-ketol chain and a second tertiary methyl group (sharp singlet at δ 1·39) the pimarane (or isopimarane) [3] skeleton of the diterpenoid (1) seems acceptable. The tricarbocyclic structure was confirmed by dehydrogenation with selenium of the methyl ester (5) which gave a mixture from which 1,7-dimethylphenanthrene was isolated.

Important stereochemical information can be obtained from the n.m.r. spectrum of (3), in particular, from the pronounced long-range single path coupling, $^4J_{5,17}$ 2·2 Hz; the strict requirement of a W-conformation for the intervening bonds is well realised in the proposed stereochemical arrangement of the A and B ring disregarding the centre C-9. The reason for locating the hemiacetal group at C-3 is discussed below. Furthermore the coupling constant $J_{5,6}$ corresponds well to the data reported [4] for the γ-lactone formed between C-4 and C-6 (as opposed to C-10 and C-6) in a 1,3-diaxial arrangement. The value of $J_{6,7}$ supports the quasi-equatorial nature of the proton attached at C-7.[4]

The configuration of C-13 cannot be simply derived from the n.m.r. spectrum of (3). The observed long-range couplings $^4J_{14,18} \neq 0$ and $^4J_{14',18} = 0$ indicate a more suitable coupling path for the low-field C(14)-proton with the protons at C(18) and suggested a quasi-*anti*-periplanar conformation of C(14)–H and C(13)–CH_3 bonds. This leads further to the assumption of a quasi-axial conformation of C(14)–H bond which seems to be in agreement with the lack of σ–π-enhancement of the geminal coupling $^2J_{14,14'}$ 12·5 Hz, as well as with the finding of detectable allylic and homoallylic couplings even between H(14) and H(6) and H(7). However, these couplings are not well pronounced which may presumably be explained by the presence of an electronegative substituent at C-6. This assignment of the allylic C(14)-protons at lower field, is in contradiction to the assignment which can be made on the basis of the anisotropy of the double bond and which suggests that the axial-proton signal is at the higher field. The agreement between both assignments may be achieved by assuming that the sign of the internal shift of the C(14)-protons is determined by shielding effects of the CO·R group at C-13. This leads to a quasi-*syn*-periplanar position of the CO·R and H(14) in accordance with the quasi-*anti*-periplanar position of H(14) and H(18) previously assigned on the basis of the long-range couplings. Thus the final assignment of the configuration at C-13 depends on the determination of the conformation of the c-ring.

In agreement with the location of the tertiary hydroxy-group on the bridgehead carbon atom, the ester (5) was readily converted into the mesylate (6) which was unchanged even after prolonged reflux in collidine. The n.m.r. spectrum of the mesylate (6) differs from that of the ester (5) only in the presence of the methyl group on a sulphur atom at δ 3·18.

The formation of the diols (7) and (8) respectively, on reduction with sodium borohydride of the nor-acid (3) and its methyl ester (5) strongly suggests the presence



(7) $R^1 = CO_2H$, R^2 = H, β-OH, R^3 = β-OH
(8) $R^1 = CO_2Me$, R^2 = H, β-OH, R^3 = β-OH
(9) $R^1 = CO_2Me$, R^2 = H, β-OH, R^3 = β-OAc
(10) $R^1 = CO_2Me$, R^2 = H, β-OAc, R^3 = β-OAc
(11) $R^1 = CO_2Me$, R^2 = O, R^3 = β-OAc
(13) $R^1 = CO_2Me$, R^2 = H, H, R^3 = H
(14) $R^1 = CO_2H$, R^2 = H, H, R^3 = H
(23) R^1 = CHO, R^2 = H, H, R^3 = H

of a hemiacetal group at C-3 and agrees with the 1,3-diaxial arrangement of the hydroxymethyl group at C-10 with the lactonic carbonyl group as suggested by the n.m.r. spectrum of the nor-acid (3), discussed above. The reduction of the hemiacetal group occurs together with the transformation of the γ-lactone into the more stable δ-lactone function and consequently the two resulting secondary hydroxy-groups were located at C-6 and at C-3. The protons attached to C-6 and C-3 give rise, after exchange with D_2O, to triplets at 4·52 (J 5 Hz) and 3·8 (J 8 Hz). The former proton is coupled with the protons at C-5 and C-7 while the latter

[3] J. W. Rowe, 'The Common and Systematic Nomenclature of Cyclic Diterpenes,' 2nd edn., Madison, Wisconsin, 1968.

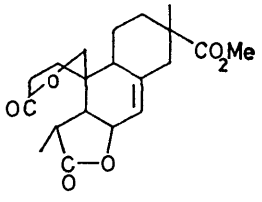
[4] G. A. Ellestad, R. H. Evans, jun., and M. P. Kunstmann, *J. Amer. Chem. Soc.*, 1969, **91**, 2134.

does not exhibit any coupling to any proton whose signal appears at lower field than δ 3. On acetylation, ester (8) yields the monoacetate (9) and the diacetate (10). In the n.m.r. spectrum of (9) the resonance due to the proton at C-3 moved downfield to δ 5·10, and in (10) the resonances due to the protons at C-3 and C-6 moved downfield to δ 5·06 and 5·53.

The β-configuration of the hydroxy-group at C-3 follows from analogy with the reduction of methyl lantanolate with sodium borohydride [5] which gave as major product (90%) the 3β-OH epimer. On the other hand, as ring A is conformationally mobile we cannot exclude the α-configuration for the 3-hydroxy-group on the basis of the coupling constants of the signal due to the proton at C-3. The α-configuration could be explained by the attack of the hydride ion from the β-face of the molecule, if the BH_4^- ion is co-ordinated to the ethereal oxygen atom.

The presence of a free hydroxy-function at C-6 in the monoacetate (9) was confirmed by treatment with Jones reagent yielding a conjugated ketone (11), $\lambda_{max.}$ 240 nm (ε 10,311),[6] $\nu_{max.}$ 1740, 1680, and 1650 cm^{-1}; [7] the n.m.r. spectrum showed two singlets at δ 5·96 and 3·04 due to the olefinic proton and to the proton attached at C-5. The diacetate (10) as well as the nor-ester (5) were unaffected by Jones reagent.

The relative positions of the hemiacetal and the lactonic carbonyl group were also confirmed by the retro-aldol rupture of the C_3–C_4 bond caused by alkaline treatment of the nor-ester (5); after acidification and esterification with diazomethane we obtained the com-

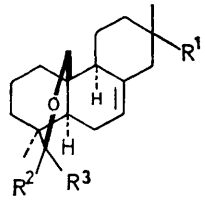


(12)

pound (12) which is isomeric with the starting material. The most important feature of the isomerised product is the absence of hydroxylic functions ($\nu_{max.}$ 1765 and 1730 cm^{-1}) and the transformation of a tertiary methyl group into a secondary one [doublet at δ 1·35 (3H) (*J* 7 Hz)].

By treatment with ethanedithiol and boron trifluoride–ether followed by desulphurisation with Raney nickel, the nor-ester (5) yielded the δ-lactone (13). The reduction of the keto group at C-3 was accompanied with the γ ⟶ δ rearrangement of the lactone system and with the reductive elimination of the allylic hydroxy-group at C-6.[8] The i.r. spectrum of (13) does not exhibit any absorption which could be ascribed to the hydroxy-groups and shows the band due to ester and lactone at 1725 cm^{-1}. The n.m.r. spectrum presents the olefinic proton resonance as a multiplet at δ 5·26, shifted upfield in comparison with the derivatives with the oxygen function at C-6. Saponification of the ester (13) yielded the acid (14), whose i.r. spectrum contains an acidic band at 1705 cm^{-1} in chloroform, moved to 1630 and 1380 cm^{-1} (as carboxylate ion) after addition of a few drops of diethylamine; the absorption of the δ-lactone is at 1725 cm^{-1}, unaffected by diethylamine.

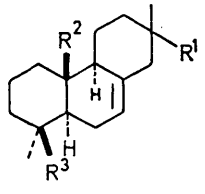
The functional groups present in the compound (13) were further confirmed by reduction of (13) with di-isobutyl(hydrido)aluminium which gave a mixture of the two epimeric aldehydes (15) and (16) (ratio 7 : 3) ($\nu_{max.}$ 3600, 3400, 2715, and 1725 cm^{-1}). In the n.m.r. spectrum both epimers show the aldehydic proton



(15) and (16) R^1 = CHO, R^2 = OH or H, R^3 = H or OH
(17) and (18) R^1 = CH_2OH, R^2 = OH or H, R^3 = H or OH
(26) R^1 = CH_2OH, R^2 = R^3 = H
(27) R^1 = Me, R^2 = R^3 = H

as a singlet at δ 9·45; the C-16 proton resonance is at δ 5·0 as singlet in the more abundant epimer and at δ 4·8 as singlet in the less abundant one. In this reaction the two epimeric alcohols (17) and (18) were formed as by-products ($\nu_{max.}$ 3640, 3500, and 3400 cm^{-1}); δ 3·3 [2H, C(13)–CH_2OH].

Reduction of the ester (13) with sodium borohydride gave the triol (19) ($\nu_{max.}$ 3300 cm^{-1}); in addition to the singlet at δ 3·5 (2H) due to the CH_2OH protons at C-13, the n.m.r. spectrum of the triol (19) contained two AB quartets [δ 3·87 and 4·07 (*J* 10 Hz), δ 3·7 and 4·18 (*J* 11 Hz)] arising from the hydroxymethyl groups axially oriented at C-4 and at C-10. In the corresponding triacetate (20) ($\nu_{max.}$ 1730 cm^{-1}), the C(13)–CH_2OAc, C-16 and C-17 protons moved downfield by *ca.* 0·4 p.p.m.



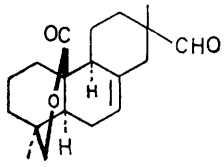
(19) R^1 = R^2 = R^3 = CH_2OH
(20) R^1 = R^2 = R^3 = CH_2OAc
(21) R^1 = R^2 = R^3 = Me
(22) R^1 = R^2 = R^3 = CHO
(25) R^1 = R^2 = R^3 = CH_2OMs

The proposed structure (1) was confirmed in all respects but the configuration at C-13, by transformation

[5] A. K. Barua, P. Chakrabarti, S. P. Dutta, D. K. Mukherjee, and B. C. Das, *Tetrahedron*, 1971, **27**, 1141.
[6] T. G. Halsall and M. Moyle, *J. Chem. Soc.*, 1960, 1324.
[7] L. Mangoni and M. Belardini, *Gazzetta*, 1962, **92**, 983.
[8] L. F. Fieser, Ching Yuan, and T. Goto, *J. Amer. Chem. Soc.*, 1960, **82**, 1996.

of the triol (19) into (—)-13,13-dimethylpodocarp-7-ene (21).[9]

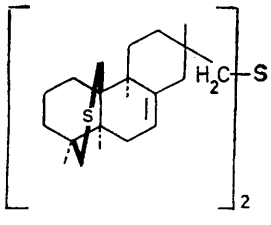
In a first attempt to remove the hydroxy-groups, the triol (19) was oxidised according to Fetizon in order to obtain the trialdehyde (22) which could be a suitable compound for a subsequent reduction to the hydrocarbon (21). Unfortunately, but not unexpectedly, a mixture of the lactones (23) and (24) was obtained instead of the desired compound. This result could be perhaps explained by an intramolecular Cannizzaro condensation involving the axially oriented aldehyde groups at C-10 and at C-4 which are first formed. The lactones (23) and (24) with sodium borohydride were smoothly reconverted into the starting triol (19).



(24)

Similarly, an attempt to prepare the hydrocarbon (21) on $LiAlH_4$ reduction of the triol-trimesylate (25) was unsuccessful: only the two ethers (26) and (27) were obtained.

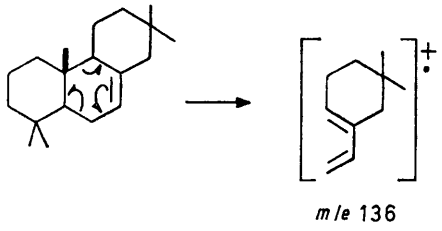
The mesylate (25) was eventually transformed into the hydrocarbon (21) by taking advantage of the easy formation of a cyclic structure between the positions 16 and 17. On treatment with sodium sulphide in dimethyl sulphoxide, (25) gave the compound (28) which without isolation was desulphurised to (21) by refluxing with Raney nickel. The n.m.r. spectrum of the hydrocarbon (21) in [$^2H_6$]benzene showed five tertiary methyl resonances and a multiplet centred at δ 5·36 due to the C-7 olefinic proton.[10] The position of the double bond can be determined from the mass spectrum: the base peak, at *m/e* 136, corresponds to the fragment formed by the easy retro-Diels–Alder fission as shown in Scheme 1. The rotatory dispersion curve of (21) is a plain negative curve with $[\Phi]_{250}$



(28)

—2600.[11] The data reported above and the i.r. spectrum allow us to assign to the hydrocarbon (21) the structure of (—)-13,13-dimethylpodocarp-7-ene.

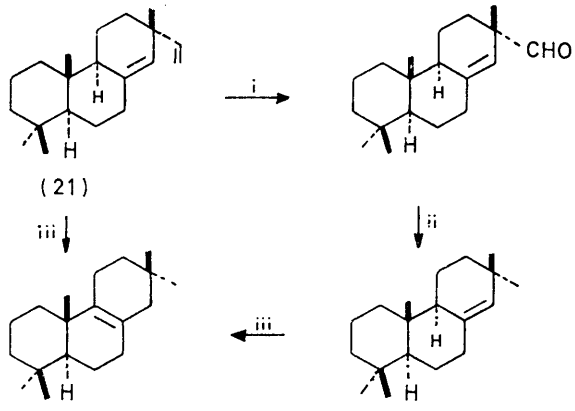
In order to gain definitive proof of its structure the hydrocarbon (21) was converted by acidic treatment into the 8(9)-isomer which was identified as (+)-13,13-dimethylpodocarp-8(9)-ene by direct comparison with



SCHEME 1

an authentic sample. The latter one was available by acidic treatment of (—)-13,13-dimethylpodocarp-8(14)-ene[12] obtained from (—)-isopimara-8(14),15-diene by the same sequence used to prepare 13,13-dimethylpodocarp-7-ene from isopimara-7,15-diene[13] (see Scheme 2).

(+)-13,13-Dimethylpodocarp-8(9)-ene, which we have obtained from the hydrocarbon (21) and from (—)-isopimara-8(14),15-diene, had $[\alpha]_D$ +44°, and its n.m.r. spectrum does not show any olefinic proton and the



SCHEME 2 Reagents: i, OsO_4, then HIO_4 in dioxan; ii, NH_2-$CONHNH_2$, then KOH in diethylene glycol, 200°, N_2; iii, dry HCl in $CHCl_3$

resonances due to the tertiary methyls are at δ 0·89, 0·92 (6H), 0·95, and 1·02. The position of the double bond is confirmed by the mass spectrum: the base peak is at *m/e* 245 ($M^+ - CH_3$) and other significant fragments are at *m/e* 260 (M^+), 175 ($M^+ - 85$), 163 ($M^+ - 97$), 149 ($M^+ - 111$), and 69 in agreement with the fragmentation reported[14] for pimara-8(9)-diene.

A study of the configuration of C-13 is in progress.

EXPERIMENTAL

For general experimental details, see our previous paper.[1]

Extraction.—The diterpenoid 3,17-*epoxy*-3α-*hydroxy*-13-*hydroxyacetyl*-13-*methylpodocarp*-7-*en*-16,6β-*olactone* (1) was isolated by filtration from the concentrated acetone

[9] R. E. Ireland and J. Newbould, *J. Org. Chem.*, 1962, **27**, 1931.

[10] C. R. Enzell and B. R. Thomas, *Acta Chem. Scand.*, 1965, 1875.

[11] C. R. Enzell and S. R. Wallis, *Tetrahedron Letters*, 1966, 243.

[12] A. Diara, C. Asselineau, and E. Lederer, *Bull. Soc. chim. France*, 1960, 2171.

[13] R. E. Ireland and J. Newbould, *J. Org. Chem.*, 1963, **28**, 23.

[14] G. R. Waller, ' Biochemical Applications of Mass Spectrometry,' Wiley-Interscience, New York, 1972, p. 367.

extract of dry bulbs of *Annona coriacea* and was recrystallised from acetone as prisms, m.p. 261—263°, $[\alpha]_D$ −174° (*c* 1 in pyridine), $\nu_{max.}$ (Nujol) 3400, 1740, 1700, and 1660 cm^{-1}, δ (C_5D_5N) 5·72 [d, $J_{6,7}$ 5 Hz, C(7)-H], 4·98 [dd, $J_{5,6}$ 5·5 and $J_{6,7}$ 5 Hz C(6)-H], 4·75 (s, CH_2OH), 4·22 and 3·62 (ABq, J_{AB} 10 Hz, the upfield part of the quartet had ^4J 2·2 Hz, CH_2O), and 1·0 and 1·54 (tertiary methyls) (Found: C, 66·1; H, 7·15. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·25%), $\lambda_{max.}$ (MeOH) 205 nm (ε 5000), *m/e* 362 (M^+, 28%), 344 (41), 303 (69), 285 (100), 271 (57), 257 (73), and 211 (70).

Acetylation of the Diterpenoid (1).—The diterpenoid (1) (150 mg) was acetylated under normal conditions. The crude product was purified by chromatography on silica gel using gradually increasing quantities of methanol in chloroform to afford 13-acetoxyacetyl-3,17-epoxy-3α-hydroxy-13-methylpodocarp-7-en-16,6β-olactone (2), m.p. 205° (from ethyl acetate–light petroleum), $\nu_{max.}$ ($CHCl_3$) 3500, 1750, 1730, and 1665 cm^{-1}, δ (C_5D_5N) 5·75 [d, $J_{6,7}$ 5 Hz, C(7)–H], 5·12 (s, CH_2OAc), 5·0 [dd, C(6)–H, partially superimposed on the previous signal], 4·25 and 3·65 (ABq, J_{AB} 10 Hz, the upfield part of the quartet had ^4J 2·2 Hz, CH_2O), 2·1 (AcO), and 1·55 and 1·10 (tertiary methyls) (Found: C, 65·5; H, 7·1. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%), *m/e* 404 (M^+, 13%), 386 (31), 344 (16), 303 (73), 285 (100), 271 (37), 257 (66), and 211 (57%).

The monoacetate (2) on refluxing with acetic anhydride and anhydrous sodium acetate for 5 h, and crystallisation of the crude product from ethyl acetate–light petroleum yielded the *diacetate* (4) (90 mg), m.p. 233—235° $\nu_{max.}$ ($CHCl_3$) 1775, 1750, 1730, and 1675 cm^{-1}, δ (C_5D_5N) 5·68 [d, $J_{6,7}$ 5 Hz, C(7)–H], 5·06 (s, CH_2OAc), 4·86 [t, $J_{5,6}$ = $J_{6,7}$ 5 Hz, C(6)–H], 3·67 and 4·15 (ABq, J_{AB} 10 Hz, the upfield part of the quartet showed ^4J 2·2 Hz, CH_2O), 2·08 and 2·0 (2 × AcO), and 1·05 and 1·51 (tertiary methyls) (Found: C, 64·45; H, 6·9. $C_{24}H_{30}O_8$ requires C, 64·55; H, 6·75%), *m/e* 446 (M^+, 3%), 404 (23), 386 (100), 303 (32), 285 (98), 271 (16), 257 (30), and 211 (28).

Oxidation of Diterpenoid (1).—The compound (1) (6 g) dissolved in purified dioxan (2·6 l) and 0·1M-periodic acid (200 ml) was left at room temperature for 48 h. The solution was evaporated *in vacuo*, diluted with water, and extracted several times with ethyl acetate; the crude product was crystallised from acetone to yield 13-*carboxy*-3,17-*epoxy*-3α-*hydroxy*-13-*methylpodocarp*-7-*en*-16,6β-*olactone* (3) (4·25 g), m.p. 265—266°, $[\alpha]_D$ −158° (*c* 1 in pyridine), $\nu_{max.}$ (Nujol) 3500, 3100, 1730, 1710, and 1660 cm^{-1}.

The acid (3) (97 mg) afforded with diazomethane 3,17-*epoxy*-3α-*hydroxy*-13-*methoxycarbonyl*-13-*methylpodocarp*-7-*en*-16,-6β-*olactone* (5) which crystallised from ethyl acetate–light petroleum as needles (84 mg), m.p. 245—247°, $\nu_{max.}$ ($CHCl_3$) 3500, 1760, 1730, and 1670 cm^{-1}, δ (C_5D_5N), 5·72 [d, *J* 5 Hz, C(7)–H], 4·98 [dd, $J_{6,7}$ 5, $J_{5,6}$ 6 Hz, C(6)–H], 4·22 and 3·62 (ABq, J_{AB} 10 Hz, the upfield part of the quartet is superimposed to the singlet at δ 3·64, CH_2O), 3·64 (s, CO_2Me), and 1·08 and 1·5 (tertiary methyls) (Found: C, 66·2; H, 7·4. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·25%), *m/e* 362 (M^+, 21%), 344 (46), 316 (21), 303 (53), 284 (68), 271 (46), 257 (41), 229 (76), and 211 (100).

Dehydrogenation of the Ester (5).—Methyl ester (5) (300 mg) was heated at 300—320° with selenium (600 mg) for 50 h. Usual work-up was followed by chromatography on alumina. Elution with benzene–hexane (3 : 7) gave 1,7-dimethylphenanthrene identical with authentic material.

Mesylate of the Ester (5).—The methyl ester (5) (150 mg) was treated with methanesulphonyl chloride (0·5 ml) in dry pyridine (2 ml) at 0° for 66 h. The crude mesylate was purified on silica gel by elution with chloroform; it did not crystallise, although homogeneous by t.l.c. (2% MeOH in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 1770, 1725, 1675, 1360, and 1150 cm^{-1}, *m/e* 381 (M^+ − 59), 361 (M^+ − $MeSO_2$), 344 (M^+ − MsOH), and 79 ($MeSO_2$).

The mesylate was recovered unchanged after refluxing in collidine for 20 h.

Reduction of the Ester (5) *and the Acid* (3).—The methyl ester (5) (500 mg) in methanol (100 ml) was reduced with $NaBH_4$ (500 mg). After stirring for 1 h at room temperature, another 500 mg of $NaBH_4$ were added and the mixture was stirred for an additional 24 h. The crude product was chromatographed on silica gel, elution by chloroform and crystallisation from acetone giving 3β,6β-*dihydroxy*-13-*methoxycarbonyl*-13-*methylpodocarp*-7-*en*-16,17-*olactone* (8) (350 mg), m.p. 167—169°, $\nu_{max.}$ (Nujol) 3420, 3370, 1720, and 1730 cm^{-1} (shoulder), δ (C_5D_5N) 5·85 [d, $J_{6,7}$ 5 Hz, C(7)–H], 4·83 and 4·02 (ABq, J_{AB} 10 Hz, the upfield part of the quartet showed ^4J 2·2 Hz, CH_2O), 4·55 [t after D_2O exchange, $J_{5,6}$ = $J_{6,7}$ 5 Hz, C(6)–H], 3·66 (s, CO_2Me), 3·6 [C(3)–H, obscured by CO_2Me], and 1·98 and 1·18 (tertiary methyls) (Found: C, 65·6; H, 8·0. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·75%). Reduction with $NaBH_4$ of the acid (3) (143 mg) was carried out under the same condition but in EtOH and gave the 13-acid (7) (132 mg), almost pure. The n.m.r. spectrum of the acid (7) showed the signal of the proton at C-3 as a triplet at δ 3·80 ($J_{obs.}$ 8 Hz). The acid (7) gave with diazomethane the methyl ester (8).

Acetylation of the Ester (8).—The compound (8) (321 mg) was acetylated under the usual conditions. On chromatography over silica gel by elution with increasing quantities of methanol in chloroform the 3β-acetate (9) (163 mg) and the 3β,6β-diacetate (10) (35 mg) were obtained. The monoacetate crystallised from acetone as needles, m.p. 199—200°, $\nu_{max.}$ ($CHCl_3$) 3600, 3450, and 1730 cm^{-1}, δ (C_5D_5N) 5·78 [d, $J_{6,7}$ 6 Hz, C(7)–H], 5·1 [t, J_{obs} 8 Hz, C(3)–H], 4·48 [t after D_2O exchange, $J_{5,6}$ = $J_{6,7}$ 6 Hz, C(6)–H], 4·77 and 4·01 (ABq, J_{AB} 10 Hz, the upfield part of the quartet showed ^4J 2 Hz, CH_2O), 3·66 (s, CO_2Me), 2·06 (s, AcO), and 1·68 and 1·2 (tertiary methyls), *m/e* 388 (M^+ − H_2O, 26%), 328 (20), 298 (100), and 211 (48).

The diacetate (10) showed $\nu_{max.}$ ($CHCl_3$) 1730 cm^{-1}, δ (C_5D_5N) 5·8 [d, $J_{6,7}$ 6 Hz, C(7)–H], 5·53 [t, $J_{6,7}$ = $J_{5,6}$ 6 Hz, C(6)–H], 5·06 [t, J_{obs} 8 Hz, C(3)–H], and 4·47 and 4·09 (ABq, J_{AB} 10 Hz, the upfield part of the quartet had ^4J 2 Hz, CH_2O), *m/e* 388 (M^+ − AcOH, 34%), 328 (30), 298 (100), and 211 (64).

Oxidation of the Monoacetate (9).—The monoacetate 9) (100 mg) in acetone was treated with Jones reagent (15 drops) at room temperature for 30 min. The crude product was purified on silica gel by elution with increasing quantities of methanol in chloroform and by crystallisation from acetone to afford 3β-*acetoxy*-13-*methoxycarbonyl*-13-*methyl*-6-*oxopodocarp*-7-*en*-16,17-*olactone* (11) (69 mg), m.p. 199°, $\nu_{max.}$ ($CHCl_3$) 1740, 1680, and 1650 cm^{-1}, $\lambda_{max.}$ (MeOH) 240 nm (ε 10,311), δ (C_5D_5N) 5·96 (s, olefinic proton), 5·2 [m, C(3)–H], 4·26 (ABq, J_{AB} 12 Hz, CH_2O), 3·68 (s, CO_2Me), 3·04 [s, C(5)–H], 2·06 (AcO), and 1·88 and 1·18 (tertiary methyls) (Found: C, 65·2; H, 7·05. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%), *m/e* 404 (M^+, 12%), 362 (75), 344 (38), 289 (100), 271 (50), 254 (62), and 211 (62).

Treatment of Ester (5) *with Base*.—The ester (5) (360 mg) was stirred in N-NaOH (10 ml) under nitrogen at room temperature for 70 h. After acidification the crude acid was isolated and esterified with diazomethane and the ester was subjected to chromatography over silica gel giving 13-methoxycarbonyl-13-methyl-3,4-secopodocarp-7-ene-16,6β;3,17-diolactone (12) (150 mg), $\nu_{max.}$ ($CHCl_3$) 1765 and 1730 cm^{-1}, δ ($CDCl_3$) 5·60 [d, $J_{6.7}$ 8 Hz, C(7)–H], 5·0 [m, C(6)–H], 4·40 and 4·12 (ABq, J_{AB} 12 Hz, CH_2O), 3·67 (s, CO_2Me), 1·10 (s, tertiary methyl), and 1·35 (d, J 7 Hz, *Me*CH), *m/e* 362 (M^+, 5%), 344 (10), 316 (5), 303 (100), 257 (58), 229 (52), and 141 (64).

Conversion of the Ester (5) *into the δ-Lactone* (13).—A solution of the methyl ester (5) (360 mg) in ethanedithiol (15 ml) was treated with 12 drops of boron trifluoride–ether and left at 0° for 4 days. After chromatography on silica gel to remove unchanged ester (eluant; 0·5% MeOH in $CHCl_3$) the product was desulphurised by refluxing with Raney-Ni in EtOH (40 ml). 13-*Methoxycarbonyl*-13-*methylpodecarp*-7-*en*-16,17-*olactone* (13) was separated by chromatography over silica gel using 0·5% MeOH in $CHCl_3$ and crystallised from ethyl acetate–light petroleum as needles (250 mg), m.p. 172—174°, $\nu_{max.}$ ($CHCl_3$) 1725 cm^{-1}, δ (C_5D_5N) 5·26 (m, olefinic proton), 4·20 and 3·85 (ABq, J_{AB} 10 Hz, CH_2O–), 3·60 (s, CO_2Me), and 1·16 and 1·08 (tertiary methyls) (Found: C, 72·3; H, 8·25. $C_{20}H_{28}O_4$ requires C, 72·25; H, 8·5%), *m/e* 332 (M^+, 25%), 302 (11), 274 (100), and 213 (44).

The δ-lactone (13) (30 mg) was refluxed in diethylene glycol (10 ml) with 0·1N-NaOH (5 ml) for 3 h. After acidification the acid (14) was extracted with chloroform, $\nu_{max.}$ ($CHCl_3$) 1725 and 1705 cm^{-1} (after treatment of the chloroform solution with a few drops of diethylamine, $\nu_{max.}$ 1725, 1630, and 1380 cm^{-1}).

The acid (14) was esterified with an ethereal solution of diazomethane to give the ester (13).

Reduction of the Lactone (13) *with Di-isobutyl(hydrido)-aluminium*.—The lactone (13) (50 mg) was treated with di-isobutyl(hydrido)aluminium (0·5 ml; 20% solution in toluene) in anhydrous toluene (6 ml) at −70° for 1 h under nitrogen. The crude product was subjected to preparative t.l.c. (eluant: 2% MeOH in $CHCl_3$) to yield two epimeric aldehydes (15) and (16) (18 mg) and two epimeric alcohols (17) and (18) (14 mg). The mixture of the aldehydes had $\nu_{max.}$ ($CHCl_3$) 3600, 3400, 2715, and 1725 cm.$^{-1}$ The resonance of the aldehydic proton was at δ 9·45, as a singlet, in both the epimers; the resonance of the proton at C-16 was at δ 5·0 in the more abundant epimer and at δ 4·8 in the other (br s in $CDCl_3$ after D_2O exchange), *m/e* 304 (M^+).

The mixture of the alcohols [(17) and (18)] had $\nu_{max.}$ ($CHCl_3$) 3640, 3500, and 3400 cm.$^{-1}$ The resonance of the hydroxymethyl group at C-13 was a singlet at δ 3·30 in both epimers; the resonance of the proton at C-16 was at δ 5·0 in the more abundant epimer and at δ 4·78 in the other (br s in $CDCl_3$, after D_2O exchange), *m/e* 306 (M^+).

Reduction of the Lactone (13) *to the Triol* (19).—The lactone (13) (50 mg) was refluxed for 4 h in 50% aqueous ethanol with $NaBH_4$ (100 mg). The product was purified by chromatography on silica gel (eluant: 5% MeOH in $CHCl_3$) and crystallised from methanol to yield 13-*hydroxymethyl*-13-*methylpodocarp*-7-*ene*-16,17-*diol* (19) (35 mg), m.p. 204—206°, $\nu_{max.}$ (KBr) 3300 cm^{-1}, δ (C_5D_5N) 5·48 (m, olefinic proton), 3·87 and 4·07 (ABq, J_{AB} 10 Hz, CH_2OH), 3·70 and 4·18 (ABq, J_{AB} 11 Hz, CH_2OH), 3·50 (s, CH_2OH at C-13), and 1·25 and 1·02 (tertiary methyls) (Found: C, 74·2; H, 10·45. $C_{19}H_{32}O_3$ requires C, 74·0; H, 10·5%), *m/e* 290 ($M^+ - H_2O$), 277 (100), 259 (48), 247 (57), 241 (21), 229 (18), and 213 (9%).

Acetylation of the Triol (19).—The triol (19) (10 mg) was acetylated under the usual conditions to give the triacetate (20) purified by preparative t.l.c. (eluant: 2% MeOH in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 1730 cm^{-1}, δ (C_5D_5N) 5·38 (m, olefinic proton), 4·39 and 4·09 (ABq, J_{AB} 10 Hz, CH_2OAc), 4·59 and 4·09 (ABq, J_{AB} 11 Hz, CH_2OAc), 3·86 (s, CH_2OAc at C-13), 2·0 (6H, s, 2 × AcO), 2·03 (s, AcO), and 0·98 and 0·84 (tertiary methyls).

Oxidation of the Triol (19) *by Fetizon's Method*.—A mixture of the triol (19) (15 mg) and of an excess of Ag_2CO_3 on Celite in toluene was dried by azeotropic distillation and refluxed for 4 h under nitrogen. P.l.c. of the crude product (eluant: ethyl acetate–light petroleum) separated the lactones (23) and (24). Their i.r. spectra had bands ($CHCl_3$) at 2710 and 1720 cm^{-1}. Their n.m.r. spectra ($CDCl_3$) showed the resonance of the lactonic methylene as an AB quartet at δ 4·25 and 4·0 (J_{AB} 12 Hz) and at 4·23 and 3·89 (J_{AB} 11 Hz); the resonance of the aldehydic proton was at δ 9·4 as singlet for both compounds. Mass spectra of both compounds showed a molecular ion at *m/e* 302 and the base peak at *m/e* 274.

Trimesylate of the Triol (19).—The triol (19) (35 mg) was treated with mesyl chloride (0·5 ml) in dry pyridine (3 ml) at −20° overnight. The crude product was purified on silica gel by elution with 0·5% MeOH in chloroform to afford an amorphous sample (30 mg) of the trimesylate (25), $\nu_{max.}$ ($CHCl_3$) 1340 and 1170 cm^{-1}, δ ($CDCl_3$) 5·45 (m, olefinic proton), 4·41 and 4·01 (ABq, J_{AB} 10 Hz, CH_2OMs), 4·16br (s, CH_2OMs), 3·91 (s, CH_2OMs at C-13), 3·0 (9H, s, 3 × MeS), and 1·06 and 0·88 (tertiary methyls), *m/e* 350 ($M^+ - 2\ MeSO_3H$, 100%), 337 ($M^+ - MeSO_3H - CH_2OSO_2Me$, 22), 245 ($M^+ - 3\ MeSO_3H$, 28), 241 ($M^+ - 2\ MeSO_3H - CH_2OSO_2Me$, 33), and 211 (16).

Reduction of the Trimesylate (25).—The trimesylate (25) (15 mg) was refluxed with an excess of $LiAlH_4$ in tetrahydrofuran (5 ml) under nitrogen for 10 h. The crude mixture was subjected to preparative t.l.c. (eluant: 1% MeOH in $CHCl_3$) to give a trace of the triol (19), the hydroxy-ether (26), and in lower yield the ether (27). The hydroxy-ether (26) had $\nu_{max.}$ ($CHCl_3$) 3500 cm^{-1}, *m/e* 290 (M^+, 68%), 259 (44), 243 (22), 229 (18), and 192 (100). On acetylation the compound (26) gave a monoacetate, *m/e* 332 (M^+, 43%), 301 (20), 272 (47), 259 (100), and 241 (65). The mass spectrum of the ether (27) had *m/e* 274 (M^+, 100%), 259 (20), 243 (37), 231 (45), and 213 (18).

(−)-13,13-*Dimethylpodocarp*-7-*ene from Trimesylate* (25).—The trimesylate (25) (100 mg) was heated with Na_2S,-$9H_2O$ (150 mg) in dimethyl sulphoxide (10 ml) at 60—80° for 50 h under nitrogen. The solution was diluted with water, and extracted with chloroform. Desulphurisation of the crude sulphide was achieved by refluxing with an excess of Raney-Ni in EtOH for 5 h. Usual work-up followed by chromatography on alumina (activity I, eluant: hexane) afforded the hydrocarbon (21) (10 mg) as an oil. This material contained 90% of a single component (by g.l.c.) and did not crystallise, δ (C_6D_6) 5·36 (m, olefinic proton), 1·02, 0·93, 0·91, 0·89, and 0·85 (tertiary methyls), *m/e* 260 (M^+, 20%), 245 (30), 136 (100), o.r.d. $[\phi]_{620}$ −12°, $[\phi]_{589}$ −34°, $[\phi]_{300}$ −439°, $[\phi]_{270}$ −740°, and $[\phi]_{250}$ −1000° (*c* 0·1 in hexane, at 25°).

(+)-13,13-*Dimethylpodocarp*-8(9)-*ene from the Hydrocarbon* (21).—Dry hydrogen chloride was passed through an ice-cold solution of hydrocaron (21) (8 mg) in dry chloroform (4 ml) for 4 h. The crude product was purified on alumina (activity I) by elution with hexane to give (+)-13,13-dimethylpodocarp-8(9)-ene (4 mg) as an oil. The material contained *ca.* 90% of a single component (by g.l.c.), $[\alpha]_D$ +44° (the small quantity of the material did not allow us to determine the accuracy of this value), *m/e* 260 (M^+, 30%), 245 (100), 175 (M^+ −85, 42), 163 (M^+ −97, 22), 149 (M^+ − 111, 70), and 69 (53).

Rearrangement of (−)-13,13-*Dimethylpodocarp*-8(14)-*ene*.—Dry hydrogen chloride was passed for 4 h through an ice-cold solution of (−)-13,13-dimethylpodocarp-8(14)-ene (6 mg) {$[\alpha]_D$ −18° (lit.,[12] −15 ± 5°)}, obtained by Wolff–Kishner reduction of 13β-methylpodocarp-8(14)-ene-13α-carbaldehyde semicarbazone [m.p. 226—229° (lit.,[15] 226—228°)]. The crude product was purified on alumina by elution with hexane to give (+)-13,13-dimethylpodocarp-8(9)-ene as an oil (4 mg) identical with the sample obtained by acidic rearrangement of hydrocarbon (21).

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