Constituents of *Erythroxylon monogynum* Roxb. Part VI.[1] Unusual Oxidation Reactions

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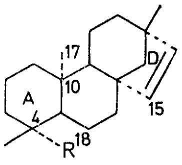
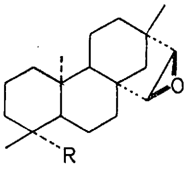
A study has been made of the products from oxidation of eight diterpenoid primary and secondary alcohols. The influence of long-range steric factors on an unusual oxidative cleavage process, and the spectral characteristics of some ketones and their epoxides, are described.

WE recently found [2] that oxidation of erythroxylol A[3] (1) gave rise to a variety of compounds, including the expected aldehyde [3] (2) and the corresponding epoxide (10). The remainder were two C_{19} tertiary alcohols (3) and (17), an epoxy-alcohol (18), and three C_{19} dienes (20), all of which are formed by rupture of the $C{-}CH_2{\cdot}OH$ bond. The fission products are formally derived from a C-4 carbonium ion and were considered to arise because of the resulting relief of 1,3-diaxial interaction of the C-4 hydroxymethyl and C-10 methyl groups.

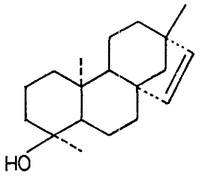
In an attempt to acquire more information on the steric requirements for the cleavage reaction, three secondary alcohols [(4)—(6)] † were prepared by reaction of the appropriate Grignard reagent with the aldehyde (2). These alcohols, on oxidation with chromium trioxide in aqueous acetic acid, gave the corresponding ketones (7)—(9) as major products, together with the ketone epoxides (11)—(13), but in each case the expected cleavage products (3), (17), and (20) were detected in only minor amounts (Table 1).



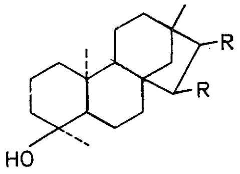
(1) $R = CH_2{\cdot}OH$
(2) $R = CHO$
(3) $R = OH$
(4) $R = CHMe{\cdot}OH$
(5) $R = CHEt{\cdot}OH$
(6) $R = CHPh{\cdot}OH$
(7) $R = Ac$
(8) $R = COEt$
(9) $R = Bz$



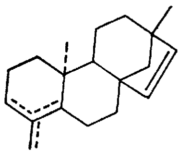
(10) $R = CHO$
(11) $R = Ac$
(12) $R = COEt$
(13) $R = Bz$
(14) $R = CH_2{\cdot}OH$
(15) $R = OH$
(16) $R = CHMe{\cdot}OH$



(17)

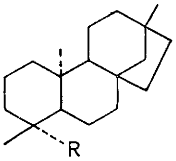


(18) $RR = O$
(19) $R = H$

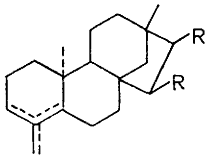


(20) Δ^3, Δ^4, $\Delta^{4(18)}$ isomers

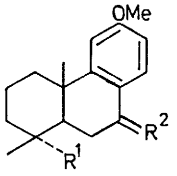
To determine the generality of cleavage of axial primary alcohols in the beyerane series, the oxidations of erythroxylol A epoxide [2] (14) and dihydroerythroxylol A[3] (21) were investigated. The primary alcohol (14) gave, after chromatographic separation, the known [2] aldehyde (10) as major product (34%). The least polar fraction, giving one spot on t.l.c., but three peaks on g.l.c., showed analytical and spectral data in accord with the molecular formula $C_{19}H_{28}O$ and almost certainly contained the isomeric olefin epoxides (27). The remaining fractions were further separated by t.l.c. and afforded three isomeric C_{19} epoxy-alcohols. The most polar and also the most abundant of these cleavage products was identified as the 4β-(equatorial) alcohol [2] (18). The alcohol of intermediate mobility was shown to be the 4α-epimer (15) by its synthesis from the naturally occurring [2] axial alcohol (3). The remaining epoxy-alcohol also contains a tertiary hydroxy-group and is tentatively formulated as (29), since it shows in its n.m.r. spectrum one secondary (τ 8·99, J 5 Hz) and



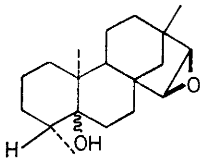
(21) $R = CH_2{\cdot}OH$
(22) $R = CO_2Me$
(23) $R = CHO$
(24) $R = OH$
(25) $R = CHMe{\cdot}OH$
(26) $R = Ac$



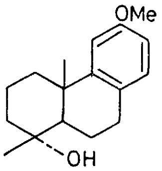
(27) $RR = O$
(28) $R = H$
Δ^3, Δ^4, $\Delta^{4(18)}$ isomers



(30) $R^1 = CH_2{\cdot}OH$, $R^2 = H_2$
(31) $R^1 = CHO$, $R^2 = H_2$
(32) $R^1 = CHO$, $R^2 = O$



(29)



(33)

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† The secondary alcohols (4),[2] m.p. 40—57°, (5), and (6), in view of their m.p.s, must be assumed to be pairs of diastereoisomers. It has not been possible to obtain confirmatory evidence of this since each pair appears as a single spot on t.l.c. and the n.m.r. spectra of the crude mixtures from the Grignard reactions appear to be those of single compounds in each case.

[1] Part V, J. C. Fairlie, R. McCrindle, and R. D. H. Murray, *J. Chem. Soc.* (*C*), 1969, 2115.

[2] A. Martin and R. D. H. Murray, *J. Chem. Soc.* (*C*), 1968, 2529.

[3] R. McCrindle, A. Martin, and R. D. H. Murray, *J. Chem. Soc.* (*C*), 1968, 2349.

two tertiary methyl resonances (τ 9·09 and 9·01). Moreover the chemical shift values of the epoxide protons (τ 7·14 and 6·77, J 3 Hz) imply [2] that the 15α-proton (at lower field) is interacting with a methyl group at C-10.* Alcohol (29) can be visualised as arising from a 1,2-hydride shift from C-5 to the β-face of a carbonium ion at C-4 and capture of solvent at C-5, possibly from the less hindered β-face.

Dihydroerythroxylol A (21) on oxidation gave isostevic acid,[4] isolated as its methyl ester (22). The expected aldehyde (23) isolated in much smaller amounts was extremely unstable, giving rise to several, as yet unidentified, polar compounds. The C_{19} tertiary alcohols (19) and (24) were also isolated; their structures were confirmed by synthesis from the known [2] naturally occurring alcohols (3) and (17). Since epoxidation or saturation of the double bond in ring D of erythroxylol A prior to oxidation greatly affected the degree of cleavage of the axial hydroxymethyl group in (14) and (21) (see Table 1), oxidations of the corresponding secondary alcohols (16) and (25) were performed. In each case the expected methyl ketones (11) and (26) were the major products, together with surprisingly small amounts of cleavage products.

TABLE 1

Products isolated from oxidations; substrate–chromium trioxide ratio 1 : 1·1

		Normal oxidation			Oxidative cleavage		
Substrate		Ketone (aldehyde) (%)	Oxo-epoxide (%)	Total (%)	Norolefins (%)	Noralcohols (%)	Total (%)
Erythroxylol A	(1)	(2) 35·5	(10) 4·5	40·0	(20) 2·0	(3), (17) 6·5	8·5
Methyl carbinol	(4)	(7) 71·0	(11) 5·5	76·5	(20) 2·5	(3), (17) 4·0	6·5
Ethyl carbinol	(5)	(8) 77·5	(12) 10·0	87·5	(20) 2·0	(3), (17) 4·0	6·0
Phenyl carbinol	(6)	(9) 72·0	(13) 7·0	79·0	(20) 4·0	(3), (17) 2·0	6·0
Erythroxylol A epoxide	(14)		(10) 34·0	34·0	(27) 4·5	(15), (18) 15·5	20·0
Epoxy-methyl carbinol	(16)		(11) 87·5	87·5	(27) 0·5	(15), (18) 4·0	4·5
Dihydroerythroxylol A methyl carbinol	(25)		(26) 82·0	82·0	(28) 1·0	(19), (24) 5·0	6·0
Dihydroerythroxylol A	(21)	(23) 13·5	(22) 28·0	41·5	(28) 9·5	(19), (24) 27·5	37·0
O-Methylpodocarpinol	(30)	(31) 80·5	(32) 3·0	83·5	0·5	(33) 1·0	1·5

The chromium trioxide–acetic acid oxidation of *O*-methylpodocarpinol (30), which also contains an axial hydroxymethyl substituent, gave the aldehyde [5] (31) as the major product (80·5%). That benzylic oxidation [6] was a competing process was shown by the isolation of the keto-aldehyde (32), $\nu_{max.}$ 2725 and 1725 (·CHO) and 1683 cm.$^{-1}$ (C:O), $\lambda_{max.}$ 281 nm. (ε 17,000). In accord with the presence of a keto-group at C-7, the n.m.r. signal for the *peri* C-14 aromatic proton in (32) has moved downfield to τ 2·03 (J 8 Hz) from τ 3·16 in the aldehyde (31). Only one tertiary alcohol was isolated (1%) and by analogy with results in the beyerane series it is likely to be the equatorial alcohol (33).

DISCUSSION

The chromium trioxide–aqueous acetic acid medium could oxidise the alcohols studied (Table 1) in three distinct ways; these comprise the normal oxidation [7] of the primary and secondary alcohols, epoxidation [8] of the Δ^{15}-double bond, and cleavage of the C(4)–C(18) bond.

The cleavage reaction, previously unknown for primary alcohols, has been reported [9-11] to take place in systems with a quaternary carbon atom adjacent to that carrying a hydroxy-group. Mechanistic studies [10] suggest that bond rupture is induced by a chromium(V) ester [10,12] and that the cleavage mechanism may involve carbonium ion intermediates.[11] In the present study, the origin of the norditerpenoids isolated can best be explained as arising from esterification of the alcohol, presumably with Cr^{V}, followed by heterolytic rupture of the C(4)–C(18) bond. The carbonium ion thus formed (at C-4) could then give rise to the three noralkenes by deprotonation at any of the adjacent carbon atoms. Alternatively, solvent capture at the electron-deficient centre, predominantly from the less hindered side (equatorial approach), would yield both epimeric noralcohols.

The results obtained (Table 1) show that the cleavage reaction depends on steric factors in rather a surprising fashion and is associated mainly with the primary alcohols. The five secondary alcohols underwent normal oxidation to the corresponding ketones, with attendant epoxidation [8] of the double bond when present, fission

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* In this department, the chemical shift of the *endo*-hydrogen at C-15 in 15- and/or 16-oxygenated beyeranes and norphyllocladanes has proved useful in giving the position of oxygenation and also the stereochemistry with an oxygen substituent at C-15.

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[5] W. P. Campbell and D. Todd, *J. Amer. Chem. Soc.*, 1942, **64**, 928.

[6] C. R. Bennett and R. C. Cambie, *Tetrahedron*, 1966, **22**, 2845.

[7] K. B. Wiberg, 'Oxidation in Organic Chemistry,' Academic Press, New York, 1965.

[8] O. Wintersteiner and M. Moore, *J. Amer. Chem. Soc.*, 1943, **65**, 1507; J. Iriarte, J. N. Shoolery and C. Djerassi, *J. Org. Chem.*, 1962, **27**, 1139; D. C. Kleinfelter, R. W. Aaron, W. E. Wilde, T. B. Bennett, H. Wei, and J. E. Weichert, *Tetrahedron Letters*, 1969, 903; A. K. Aswathy and J. Rocek, *J. Amer. Chem. Soc.*, 1969, **91**, 991.

[9] W. A. Mosher and F. C. Whitmore, *J. Amer. Chem. Soc.*, 1948, **70**, 2544; W. A. Mosher and E. O. Langerak, *ibid.*, 1949, **71**, 286.

[10] J. Hampton, A. Leo, and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 306.

[11] P. T. Lansbury, V. A. Pattison, and J. W. Diehl, *Chem. and Ind.*, 1962, 653.

[12] K. B. Wiberg and H. Schafer, *J. Amer. Chem. Soc.*, 1969, **91**, 933.

being a relatively unimportant process (*ca.* 6%). However, whereas erythroxylol A (1) suffered oxidative fission to the extent of 8%, much larger proportions of cleavage products were obtained from the epoxy-alcohol (14) (20%) and the dihydro-alcohol (21) (37%). Here only the functionality in ring D has changed yet there is a marked effect on the degree of cleavage. Models show that in the sequence etheno-bridge (1), epoxide (14), ethano-bridge (21), the C-15 (or 15α-) proton interacts successively more severely with the angular C-10 methyl group. This presumably results in increasing compression[13] between the C-10 methyl group and the 4α-hydroxymethyl group, which is relieved by cleavage of the C(4)–C(18) bond. In support of this theory, removal of the 1,3-diaxial interaction across ring B led to a marked decrease in the yields of cleavage products, to 1·5% for *O*-methylpodocarpinol (30).

There are two important competing processes for the alcohols under consideration, namely normal oxidation to the ketone or aldehyde, and the cleavage reaction. The rates of these will differ and will be affected differently by structural factors. For normal oxidation, the secondary alcohols should react faster than the primary alcohols. This is a consequence of the increase in non-bonded interactions across the α-face of ring A, which results from replacement of one of the hydrogen atoms of the axial C-4 hydroxymethyl group by a methyl, ethyl, or phenyl substituent. The secondary alcohols will have the higher ground state energies and hence require less activation energies for oxidation to the ketones than in the case of the corresponding conversions of the primary alcohols into the aldehydes. For the secondary alcohols, oxidation to the ketone is found to be the predominant process. Thus the structural features which have a bearing on the fission reaction are not manifested in the proportion of cleavage products, only about 6% from the secondary alcohols, since the rate of normal oxidation is much greater than the rate of cleavage.

However, for the primary alcohols, since oxidation to the aldehyde is relatively slower, the rate of the cleavage reaction becomes more important and the effects of conformational buttressing on the alternative oxidative reaction of bond fission are reflected in the greater abundance of cleavage products.

The carbinols, ketones, and keto-epoxides show some interesting spectroscopic properties. The i.r. solution spectra of the methyl ketone (7), the ethyl ketone (8), and the corresponding epoxides (11) and (12) in carbon tetrachloride each show a split carbonyl band (Table 2) whereas the phenyl ketone (9) and its epoxide (13) each show only one maximum. In chloroform solution however the doublets collapse to one broad absorbance at slightly lower wave-number. These bands may represent discrete ring conformational or rotational (ring A chair) isomers, or may possibly be due to Fermi resonance.

TABLE 2

I.r. solution spectra (ν_{CO} in cm.$^{-1}$)

		In CCl$_4$	In CHCl$_3$
Methyl ketone	(7)	1703, 1696	1692 *
Methyl ketone epoxide	(11)	1705, 1698	1691 *
Ethyl ketone	(8)	1704, 1694	1689 *
Ethyl ketone epoxide	(12)	1705, 1695	
Phenyl ketone	(9)	1683 *	
Phenyl ketone epoxide	(13)	1685 *	

* Band showing several shoulders.

The n.m.r. spectra of the various carbinols, ketones, and keto-epoxides allow assignments of signals to the tertiary methyl groups (Table 3). The signal from the C-13 methyl group does not alter appreciably, remaining at τ 9·01 ± 0·02 throughout. The methyl signal at highest field in the carbinol system is attributed to that at C-10, shielded by the double bond.[14] This is confirmed by the further shielding observed on conversion of the carbinol into the ketone. Epoxidation of the double bond produces a downfield shift of this signal as anticipated.[2] The magnetic anisotropy of the carbonyl group which causes the shielding[15] of the C-10 methyl group deshields the C-4 methyl group. In addition, the phenyl group deshields the C-4 methyl group even in the carbinol, and on oxidation further deshielding results in the very low field signal at τ 8·59. Since the C-10 methyl signals in each case appear at such high field, this suggests that ring A is in a chair conformation, and if, as suggested by the i.r. spectra, more than one conformation is present, these are presumably rotameric[16] in nature.

TABLE 3

N.m.r. *C*-methyl signals (τ values; solvent CCl$_4$)

		10-Me	4-Me	13-Me
Methyl carbinol	(4)	9·18	9·14	9·03
Methyl ketone	(7)	9·47	8·94	9·01
Methyl ketone epoxide	(11)	9·27	8·90	9·00
Ethyl carbinol	(5)	9·18	9·12	9·01
Ethyl ketone	(8)	9·51	8·97	9·02
Ethyl ketone epoxide	(12)	9·31	8·93	9·02
Phenyl carbinol	(6)	9·17	9·02	9·02
Phenyl ketone	(9)	9·35	8·59	9·01
Phenyl ketone epoxide	(13)	9·17	8·57	9·01

In an attempt to freeze out the conformational isomers, the n.m.r. spectrum of the methyl ketone (7) was recorded at different temperatures. The spectrum is temperature dependent[17] (Table 4); the signals

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[15] C. R. Narayanan and N. R. Bhadane, *Tetrahedron Letters*, 1968, 1565.

[16] S. Bory, M. Fetizon and J. Rens, *Bull. Soc. chim. France*, 1966, 2011; N. L. Allinger, P. Crabbé, and G. Perez, *Tetrahedron*, 1966, **22**, 1615.

[17] K. Hirao, S. Mitsubayashi, J. Uzawa, A. Tahara, N. Mitomo, and S. Hayashi, *Tetrahedron Letters*, 1969, 29; M. Fetizon, G. Moreau and N. Moreau, *Bull. Soc. chim. France*, 1968, 3295; J. A. Pople, W. G. Schneider and H. J. Bernstein, 'High Resolution Nuclear Magnetic Resonance,' McGraw-Hill, New York, 1959, pp. 377—385.

TABLE 4

Methyl n.m.r. signals for ketone (7) in dichloromethane

Temp.	Ac	10-Me	4-Me	13-Me
+34°	7·91	9·45	8·93	9·02
−70	7·86	9·49	8·92	9·02
−91	7·85	9·49	8·92	9·02

assigned to the C-4 and C-13 methyl groups were unaffected by temperature decrease whereas the C-10 methyl resonance moved upfield by 0·04 p.p.m. and the acetyl signal moved to lower field by 0·06 p.p.m. The two temperature-dependent signals are those which would be expected to move if rotation about the C(4)–C(18) bond is being influenced by change in temperature.[17] Thus the magnetic field seen, as a time average, by the methyl groups at −91° is different from that observed at +34°. This evidence, though not conclusive, suggests that rotameric isomers are present.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra refer to solutions in carbon tetrachloride and were recorded by Mrs. F. Lawrie, Glasgow (Unicam SP 100 mark II and Perkin-Elmer 257 spectrophotometers). Microanalyses were performed by Mr. J. M. L. Cameron and his staff. N.m.r. spectra were obtained by Mrs. S. Hamilton and Mr. J. Gall with Perkin-Elmer R10 and Varian Associates HA-100 spectrometers for *ca.* 0·3M-solutions in carbon tetrachloride, with tetramethylsilane as internal standard. Mass spectra were recorded by Mr. A. Ritchie with an A.E.I.-G.E.C. MS12 spectrometer. G.l.c. was performed with a Perkin-Elmer F 11 chromatograph. Unless otherwise stated, Merck grade H alumina was used for chromatography and Kieselgel G (Merck) for both analytical and preparative t.l.c. Light petroleum refers to the fraction b.p. 40—60°. Aqueous acetic acid refers to glacial acetic acid–water (19 : 1). The oxidations were carried out with a stock solution of chromium trioxide (7·6 g.) in aqueous acetic acid (250 ml.), with a substrate–trioxide ratio of 1 : 1·1 unless otherwise stated.

Conversion of the Aldehyde (2) *into the Secondary Carbinols* (5) *and* (6).—(*a*) The aldehyde (370 mg.) in dry ether (20 ml.) was added to ethylmagnesium bromide [from magnesium (90 mg.) and ethyl bromide (1·5 ml.)] in ether (20 ml.) and the mixture was kept at reflux for 30 min. Work-up with ether and preparative t.l.c. [ethyl acetate–light petroleum (1 : 6)] afforded the ethyl carbinol (5) (385 mg.), m.p. 55—85° (prisms from methanol), $\nu_{max.}$ 3623 cm.$^{-1}$.

(*b*) The aldehyde (265 mg.) in dry ether (15 ml.) was added to phenylmagnesium bromide [from magnesium (50 mg.) and bromobenzene (1 ml.)] in ether (15 ml.) and the mixture was kept at reflux for 30 min. Work-up and isolation by t.l.c. [ethyl acetate–light petroleum (1 : 9)] gave the phenyl carbinol (6) (233 mg.), m.p. 140—172° (prisms from methanol), $\nu_{max.}$ 3628 cm.$^{-1}$; τ 4·30 and 4·50 (2H, ABq, *J* 5·5 Hz), and 4·80 (1H, s, C*H*Ph·OH).

Oxidation of the Carbinols.—(*a*) The methyl carbinol[2] (4) (172 mg.) in aqueous acetic acid (7 ml.) was kept with the chromium trioxide solution (1·8 ml.) for 1 hr. Methanol (5 ml.) was added and after 5 min. the bulk of the solvent was removed under reduced pressure. The residue was neutralised with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extracts were washed with water, dried, and evaporated to give a solid (167 mg.). Preparative t.l.c. [ethyl acetate–light petroleum (1 : 5)] gave, in order of decreasing mobility (i) a hydrocarbon fraction (3·8 mg.) containing a mixture of the isomeric dienes (20) identical (i.r. spectrum, g.l.c., and t.l.c. on silver nitrate-impregnated silica) with those previously isolated;[2] (ii) the methyl ketone[2] (7) (117 mg.), m.p. 67—69°; (iii) a mixture (7 mg.) containing the original methyl carbinol (4) and traces of 4α-hydroxy-18-norhibaene[2] (3), the latter being identified solely by t.l.c.;[2] (iv) the methyl ketone epoxide[2] (11) (10 mg.), m.p. 150—152°; and (v) 4β-hydroxy-18-norhibaene[2] (17) (6 mg.).

(*b*) The ethyl carbinol (5) (108 mg.) in aqueous acetic acid (7 ml.) was kept with the chromium trioxide solution (1·1 ml.) for 1 hr. Work-up gave an oil (104 mg.), separation of which by t.l.c. gave (i) a similar hydrocarbon fraction (20) (1·5 mg.); (ii) the *ethyl ketone* (8) (67 mg.), m.p. 38—41° after sublimation at 70—75°/0·03 mm. (Found: C, 84·3; H, 10·9. $C_{22}H_{34}O$ requires C, 84·0; H, 10·9%); (iii) the original carbinol (21 mg.); (iv) the *ethyl ketone epoxide* (12) (9 mg.), m.p. 133—136° after sublimation at 140°/0·05 mm. [Found: *M*, 330 (mass spectrometry). $C_{22}H_{34}O_2$ requires *M*, 330]; and (v) 4β-hydroxy-18-norhibaene (17) (3 mg.).

(*c*) The phenyl carbinol (6) (179 mg.) in aqueous acetic acid (7 ml.) and the chromium trioxide solution (1·6 ml.) were kept for 1·5 hr. Work-up gave a solid (179 mg.) which was separated by t.l.c. [ethyl acetate–light petroleum (1 : 19)] giving (i) the hydrocarbon mixture (20) (4 mg.); (ii) the *phenyl ketone* (9) (107 mg.), m.p. 155—156·5° (plates from ether) (Found: C, 86·25; H, 9·45. $C_{26}H_{34}O$ requires C, 86·15; H, 9·45%); (iii) the original carbinol (30 mg.); (iv) the *phenyl ketone epoxide* (13) (11 mg.), m.p. 206—208° (prisms from ether) (Found: *M*, 378. $C_{26}H_{34}O_2$ requires *M*, 378); and (v) a mixture from which 4β-hydroxy-18-norhibaene (17) (2·5 mg.) was isolated after further preparative t.l.c. [ethyl acetate–light petroleum (1 : 5)].

(*d*) Erythroxylol A epoxide[2] (14) (1·46 g.) in aqueous acetic acid (23 ml.) was kept with the chromium trioxide solution (15·4 ml.) for 1 hr. Work-up gave an oil (1·36 g.) which was adsorbed on alumina (60 g.) from light petroleum. Elution with light petroleum afforded a mixture (56 mg.) of the three isomeric epoxy-olefins (27) (Found: C, 83·65; H, 10·6. $C_{19}H_{28}O$ requires C, 83·75; H, 10·35%) together with an unidentified compound, present in minor amounts, which could be separated by g.l.c. (2·5% SE 30, 220°; retention times 24, 26, 27, and 15 min., respectively). Subsequent elution with ether–light petroleum (1 : 4) gave the aldehyde epoxide[2] (10) (468 mg.), m.p. 104—107° (from light petroleum). Elution with ether–light petroleum (1 : 1) gave a series of fractions containing mixtures which could be further separated by preparative t.l.c. [ethyl acetate–light petroleum (2 : 3)]. These mixtures afforded the following (in order of decreasing mobility): (i) a rearranged noralcohol epoxide, tentatively formulated as (29) (10 mg.), m.p. 156·5—158° (prisms from ether–light petroleum) (Found: *M*, 290. Calc. for $C_{19}H_{30}O_2$: *M*, 290); (ii) 4α-*hydroxy*-18-*norhibaene epoxide* (15) (25 mg.), m.p. 112—114° after sublimation at 115—120°/0·04 mm. (Found: C, 78·3; H, 10·35. $C_{19}H_{30}O_2$ requires C, 78·55; H, 10·4%) [this compound (7 mg.) was readily obtained by treatment of 4α-hydroxy-18-norhibaene[2] (3) (7 mg.) with *m*-chloroperbenzoic acid (12 mg.) in chloroform (1 ml.) at room temperature for 20 min.]; (iii) 4β-hydroxy-18-norhibaene epoxide[2] (18) (158 mg.); and (iv) the original alcohol (14) (29 mg.).

(*e*) Dihydroerythroxylol A[3] (21) (243 mg.) in aqueous acetic acid (7 ml.) was kept with the chromium trioxide solution (2·8 ml.) for 1 hr. Work-up gave an oil (236 mg.). Separation by t.l.c. [ethyl acetate–light petroleum (1 : 9)] afforded (i) a hydrocarbon mixture (28) (21 mg.) after distillation at 70—75°/0·02 mm. (Found: *M*, 258. $C_{19}H_{30}$ requires *M*, 258); (ii) the aldehyde (23) (33 mg.), m.p. 69—71° after sublimation at 55—60°/0·02 mm. (lit.,[4] m.p. 68—70°); (iv) a more polar fraction which was treated with diazomethane and subjected to further preparative t.l.c. [ethyl acetate–light petroleum (1 : 9)] giving the methyl ester (22) (74 mg.), m.p. 140—143° (from methanol) (lit.,[4] 143—144°); (v) 4α-*hydroxy*-18-*norhibane* (24) (12 mg.), m.p. 79·5—83° after sublimation at 80—85°/0·02 mm. (Found: C, 82·5; H, 11·6. $C_{19}H_{32}O$ requires C, 82·55; H, 11·65%), readily synthesised from 4α-hydroxy-18-norhibaene[2] (3) by catalytic hydrogenation; and (vi) 4β-*hydroxy*-18-*norhibane* (19) (52 mg.), m.p. 121—123·5° [needles from light petroleum (b.p. 60—80°)] (Found: C, 82·4; H, 11·6%), which was identical (i.r. and n.m.r. spectra, m.p. and t.l.c.) with the product obtained by hydrogenation of (17).[2]

(*f*) The carbinol (25) (280 mg.), m.p. 98—102°, $\nu_{max.}$ 3637 and 3618 cm.$^{-1}$, [readily derived from catalytic hydrogenation of (4)[2]], in aqueous acetic acid (7 ml.) was treated with the chromium trioxide solution (3·4 ml.) and kept for 1 hr. Work-up gave an oil (259 mg.) which on t.l.c. [ethyl acetate–light petroleum (1 : 9)] gave (i) a hydrocarbon mixture (28) (3 mg.); (ii) the *methyl ketone* (26) (227 mg.), m.p. 124—126° (needles from light petroleum) (Found: C, 83·75; H, 11·4. $C_{21}H_{34}O$ requires C, 83·4; H, 11·35%), $\nu_{max.}$ 1703 and 1697 cm.$^{-1}$; (iii) the 4α-tertiary alcohol (24) (2 mg.); and (iv) the 4β-tertiary alcohol (19) (11 mg.).

(*g*) The epoxy-carbinol (16) (160 mg.), m.p. 165—168° (rods from ether), $\nu_{max.}$ 3634 and 3600 cm.$^{-1}$, in aqueous acetic acid (5 ml.) was kept with chromium trioxide solution (1·8 ml.) for 1 hr. Work-up gave a solid (147 mg.) which was separated by t.l.c. [ethyl acetate–light petroleum (3 : 7)] to give (i) the epoxy-olefin mixture (27) (1 mg.); (ii) the epoxy-methyl ketone[2] (11) (138 mg.), m.p. 149—152°; and (iii) 4β-hydroxy-18-norhibaene epoxide (18) (5 mg.).

Oxidation of O-*Methylpodocarpinol*. *O*-Methylpodocarpinol (30) (673 mg.) in aqueous acetic acid (20 ml.) was kept with the chromium trioxide solution (8·5 ml.) for 2 hr. Work-up gave an oil (587 mg.) which was adsorbed on alumina (90 g.) from light petroleum. Elution with that solvent gave a fraction[18] (3 mg.), b.p. 90—95°/0·03 mm. which showed two peaks on g.l.c. (2·5% SE 30, 230°; retention times 13 and 14 min., respectively) (Found: *M*, 242. Calc. for $C_{17}H_{22}O$: *M*, 242). Elution with ether–light petroleum (1 : 4) gave the aldehyde (31) (456 mg.), m.p. 133—135° (rods from light petroleum) (lit.,[5] 133—135°). Subsequent elution with ethyl acetate gave a complex mixture which was acetylated with acetic anhydride–pyridine to facilitate its separation. Preparative t.l.c. (chloroform) of the acetylated material gave (i) *O*-methylpodocarpinol acetate (119 mg.), m.p. 75—76° (plates from methanol); (ii) the *formyl ketone* (32) (17 mg.), m.p. 97—99° after sublimation at 105—110°/0·02 mm. (Found: *M*, 286. $C_{18}H_{22}O_3$ requires *M*, 286); and (iii) probably 4α-hydroxy-12-methoxy-15-norpodocarpane (33) (6 mg.), b.p. 85—88°/0·03 mm. (lit.,[18] m.p. 107—109°) which shows a parent ion in the mass spectrum at *m*/*e* 260 ($C_{17}H_{24}O_2$).

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