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Ozonolysis of Derivatives of Labda-8(17),14-dien-13-ol (Manool) and Their Conversion into Large Ring Unsaturated Lactones

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Abstract

Dehydration of the unstable hydroperoxy ethers (4) and (6) formed on ozonolysis of the manool derivatives (2) and (5) resulted in the formation of the ten-membered unsaturated lactones (11) and (12) in good yield. The results of an investigation into the nature of the hydroxyl group and its spatial relationship to the exocyclic double bond in lactone formation are reported for other manool derivatives.

The keto alcohol (1), an intermediate in a projected synthesis, was obtained by ozonolysis of the unsaturated alcohol (2) derived from manool (3) but in low yield. The major ozonolysis product was identified as the relatively unstable hydroperoxy ether (4), $C_{18}H_{32}O_3$, showing an unusually sharp hydroxyl absorption (3490 cm^{-1}) and extensive C–O absorptions. The non-equivalence of the C 13 *gem*-dimethyl signals (δ_H 1·18, 1·40) confirmed a cyclic structure with an ether linkage between C 8 and C 13. The C 8 stereochemistry was ambiguous as both C 8 stereoisomers possess oxygen functions which are diaxial to the 10β-methyl and to one of the C 13 methyls and would result in deshielding of both these methyl signals. In the corresponding hydroperoxy ether (6), isolated from the ozonolysis of dihydromanool (5), the C 13 methyl signal appeared at δ 1·34. Since the 13*S* stereochemistry of dihydromanool results in a 13β-methyl in the hydroperoxy ether (6), its deshielded C 13 methyl established an 8β-hydroperoxy function. This configuration is also supported on mechanistic grounds (Scheme 1), with intramolecular nucleophilic attack on the developing C 8 carbocation by the C 13 hydroxyl from the less hindered α-face. The 13β-methyl (axial) signal of 8,13-epoxylabdane[1] which lacks a diaxial oxygen interaction is at δ 1·18.

The hydroperoxy ether (4), stable at low temperatures, was isolated in high yield by immediate low-temperature removal of the ozonolysis solvent (methanol). On standing, some decomposition to the enol ether (7) occurred. Similarly the enol ether (8) was obtained as a minor product of the ozonolysis of dihydromanool (5). Lithium aluminium hydride reduction of the hydroperoxy ether (4) gave the diol (9), the axial 8β orientation of the hydroxyl group being established by the low-field 10β methyl signal (δ 1·02) and the narrow band width ($W_{h/2}$ 6 Hz) of the C 8 carbinol proton (δ 3·97). Acetic anhydride/pyridine treatment of the diol (9) gave the hydroxy

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[1] Munro, M. H. G., Ph.D. Thesis, University of Otago, 1965, p. 224.

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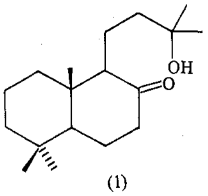
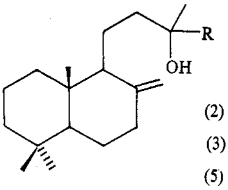
acetate (10) in which the typical downfield shift of the secondary carbinol proton on acetylation (δ 5·15) was observed.

Dehydration[2] of the hydroperoxy ether (4) gave the ten-membered unsaturated lactone (11), $C_{18}H_{30}O_2$, the result of a β-fragmentation reaction. Spectral data showed the presence of a disubstituted double bond [δ_H 5·18 (m); δ_C 148·2 (d), 120·6 (d)] and a lactone [1730, 1250, 1220 cm^{-1}; δ_C 173·9 (s)] function and so the product was bicyclic. The non-equivalence of the C 13 methyl signals was even more marked (δ_H 1·28, 1·61). Off-resonance ^{13}C n.m.r. showed five methyl, six methylene, three methine (including the double bond) and four quaternary (including the lactone) carbons, thus confirming that extensive transformation of the hydroperoxy ether (4) had occurred. A mechanism for the formation of the unsaturated lactone (Scheme 1) shows the anticoplanarity of the participating groups.

Similarly dehydration of the hydroperoxy ether (6) gave the unsaturated lactone (12). The *trans* nature of the $\Delta^{9(11)}$ double bond was established from a 270-MHz ^{1}H n.m.r. spectrum of lactone (12) in which the C 9, C 11 and C 12 protons appeared as an



(1)



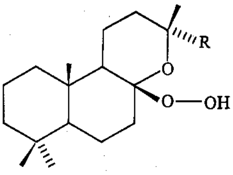
(2) R = Me

(3) R = $CH{=}CH_2$

(5) R = CH_2Me

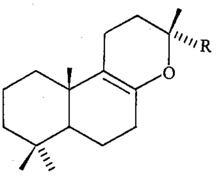
(19) R = $\underset{\text{O}}{\text{CH—CH}_2}$

(36) R = $\underset{\text{OH}}{\text{CH}}\text{Me}$



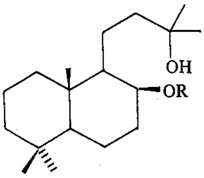
(4) R = Me

(6) R = CH_2Me



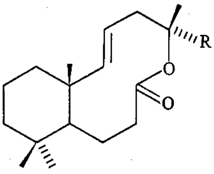
(7) R = Me

(8) R = CH_2Me



(9) R = H

(10) R = Ac

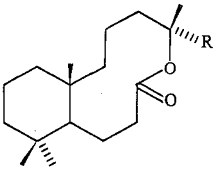


(11) R = Me

(12) R = CH_2Me

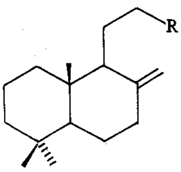
(20) R = $\underset{\text{O}}{\text{CH—CH}_2}$

(37) R = $\underset{\text{OH}}{\text{CH}}\text{Me}$



(13) R = Me

(14) R = CH_2Me

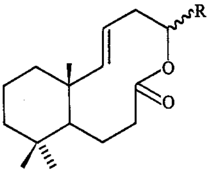


(15) R = CH_2OH

(17) R = $\underset{\text{OH}}{\text{CH}}\text{Me}$

(34) R = COOH

(48) R = $\underset{\underset{\text{O}}{\|}}{\text{C}}\text{Me}$



(16) R = H

(18) R = Me

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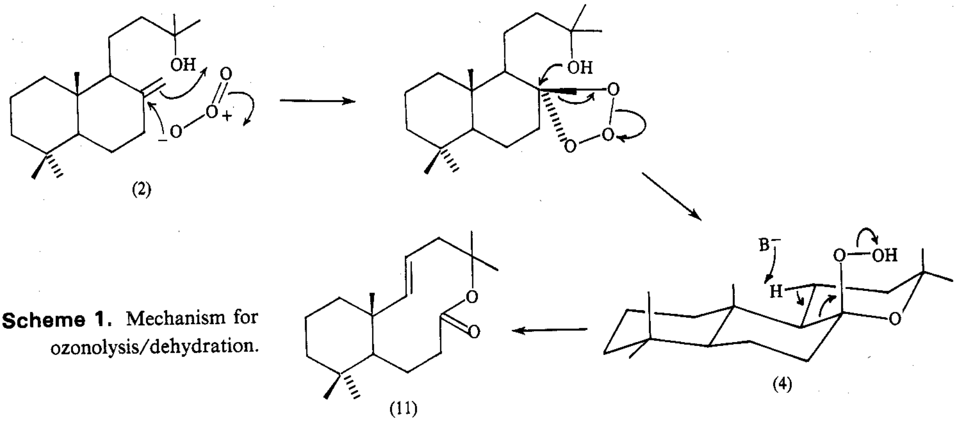
[2] Hazen, G. G., and Rosenburg, D. W., *J. Org. Chem.*, 1964, **29**, 1930.

ABMX system ($J_{9,11}$ 16 Hz, $J_{11,12\alpha}$ 10 Hz, $J_{11,12\beta}$ 3 Hz, $J_{12\alpha,12\beta}$ 13 Hz). Decoupling irradiation of each of these protons in turn confirmed the assignments.

The assignment of the allylic protons is based on a preferred conformation in which the 10β-methyl is nearly coplanar with the $\Delta^{9(11)}$ double bond since hydrogenation of the double bond in the unsaturated lactones (11) and (12) results in an upfield shift (approx. 0·09 ppm) of this signal. The vicinal coupling constants are consistent with those predicted from the dihedral angles ($\phi_{11,12\alpha} \approx 10°$; $\phi_{11,12\beta} \approx 120°$) measured from a Dreiding model.



Scheme 1. Mechanism for ozonolysis/dehydration.

The compounds (11) and (12) as obtained from the dehydration reaction were inhomogeneous, being accompanied by a small amount (approx. 7%) of the saturated lactones (13) and (14). This is attributed to the free-radical decomposition of the hydroperoxy ethers. The metal-ion-catalysed free-radical decomposition[3] of the hydroperoxy ether (12) increased the proportion of the saturated lactone (approx. 60%). Catalytic hydrogenation of the unsaturated lactones (11) and (12) gave the saturated lactones (13) and (14), respectively.

By using the readily available dihydromanool (5) to optimize reaction conditions it was shown that ozonolysis followed by *in situ* dehydration[2] (mesyl chloride/sulfur dioxide) provided an efficient one-pot synthesis (60%) of the ten-membered unsaturated lactone (12). The potential of this method as a synthesis of large ring unsaturated lactones was then investigated in terms of (*a*) the primary, secondary and tertiary nature of the hydroxyl group, and (*b*) the spatial relationship between the exocyclic double bond and the hydroxyl group. The substrates used were synthesized by standard methods which are described in the latter part of the Experimental.

Ozonolysis/dehydration of the primary alcohol (15), the (13*RS*)-secondary alcohol (17) and the epoxy tertiary alcohol (19) gave good yields of the corresponding unsaturated lactones (16), (18) and (20), respectively. This established that lactone formation was independent of the nature of the hydroxyl group and confirmed the generality of the synthesis from '5-en-1-ol' substrates.

Ozonolysis/dehydration of the '6-en-1-ol' (21) gave two products, the minor one being the eleven-membered unsaturated lactone (22). The major product was the keto mesylate (23), with derivatization occurring under the conditions of *in situ*

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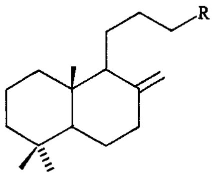
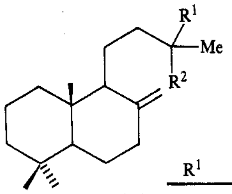
[3] Schreiber, S. L., *J. Am. Chem. Soc.*, 1980, **102**, 6136.

dehydration. The mesylate (23) showed ketone [1705 cm^{-1}; δ_C 211·8, s] and mesylate [1350, 1175 cm^{-1}; δ_H 2·93; δ_C 37·3, q] absorptions and a typically shielded (δ_H 0·68) 10β-methyl group. Similarly, the (13*RS*)-alcohol (24) and the (13*RS*)-fluoro alcohol (27) gave the lactones (26) and (29) and the keto alcohol mesylates (25) and (28) as the minor and major products respectively. It was possible to isolate the epimeric fluoro lactones (29). The fluorinated compounds (27), (28) and (29) showed characteristic $^1J_{C,F}$, $^2J_{C,F}$, and $^3J_{C,F}$ coupling in the ^{13}C n.m.r. The low lactone yields could be attributed to two factors—the failure of the seven-membered ether ring either to form (due to the increased distance between the hydroxy group and the C 8 carbocation) or to provide the anticoplanarity required for the rearrangement.

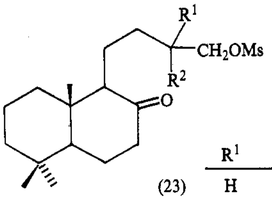
Ozonolysis/dehydration of the '7-en-1-ol' systems (30) and (32) gave only the corresponding keto mesylates (31) and (33). The diol system in (32) increases the



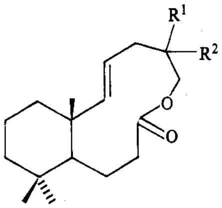
(21) R = $\mathrm{CH_2OH}$
(49) R = OMs
(50) R = CN
(51) R = COOH
(55) R = I



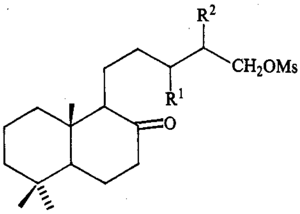
	R^1	R^2
(24)	H	$\mathrm{CH_2OH}$
(27)	F	$\mathrm{CH_2OH}$
(53)	H	CHO
(54)	F	$\mathrm{CH_2OAc}$



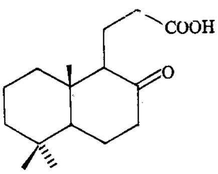
	R^1	R^2
(23)	H	H
(25)	H	Me
(28)	F	Me



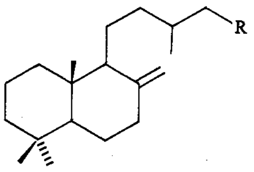
	R^1	R^2
(22)	H	H
(26)	H	Me
(29a)	Me	F
(29b)	Me	F



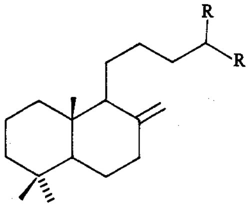
	R^1	R^2
(31)	Me	H
(33)	H	$\mathrm{CH_2OMs}$



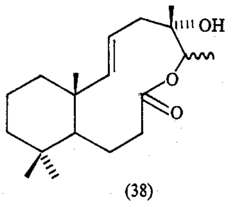
(35)



(30) R = $\mathrm{CH_2OH}$
(58) R = CHO



(32) R = $\mathrm{CH_2OH}$
(56) R = COOEt

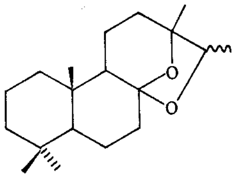


(38)

possibility of intramolecular participation but failure to do so is attributed to the distance between the reacting functions.

Ozonolysis/dehydration of the carboxylic acid (34) gave only the keto acid (35) showing carbonyl [1700 cm^{-1}; δ_C 212·1, s] and carboxylic [3200–2800, 1700 cm^{-1}; δ_C 179·5, s] absorptions together with the typical high-field 10β-methyl signal (δ_H 0·70). The failure to form any anhydride product is attributed to the reduced nucleophilic character of the carboxylic hydroxyl group.

The '6-ene-1,2-diol' system (36) provided competing intramolecular nucleophiles and thus the possibility of forming the ten- (37) and eleven- (38) membered unsaturated lactones. Ozonolysis/dehydration of (36) gave both the lactones (the relative yields varying with the concentration of the ozonized solution) together with a third product. The lactones were assigned on the basis of the chemical shift of the C 14 proton. In (38) this proton is part of an ester system and thus appeared at lower field (δ 4·91, q) than in (37) where it is part of a secondary alcohol system (δ 4·17, q). The third product isolated was the intramolecular acetal (39) which arose through the intermediacy of the 8-keto diol. It showed only C–O absorptions in the i.r. spectrum and a typical acetal carbon (δ 107·6) in the ^{13}C n.m.r. spectrum.



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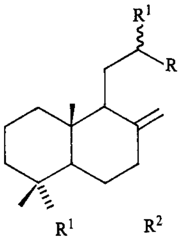
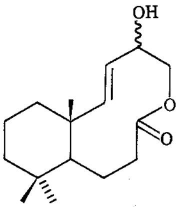
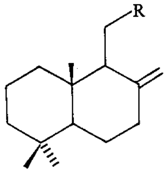


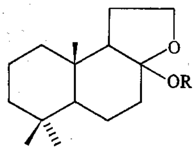
	R^1	R^2
(40)	OH	CH_2OH
(59)	OH	COOH
(61)	H	COOMe
(62)	OH	COOMe
(63)	SPh	COOH



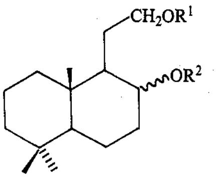
(41)



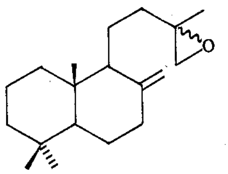
(42) R = CH_2OH
(60) R = CHO



(43) R = OH
(44) R = H



	R^1	R^2
(45)	H	α,βOH
(46)	Ac	αOAc
(47)	Ac	βOH



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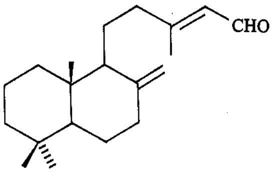

(57)

The only product isolated from ozonolysis/dehydration of the 12,13-diol (40) was the ten-membered unsaturated lactone (41), no corresponding acetal being detected. The alternative nine-membered unsaturated lactone was not considered as a possible structure in view of the failure of the '4-en-1-ol' system to produce any lactone.

No identifiable product could be isolated from ozonolysis/dehydration of the '4-en-1-ol' (42), despite repeated attempts. The 'ozonolysis product' obtained by low-temperature solvent removal showed spectral data consistent with some hydroperoxy ether formation—hydroxyl (3310 cm^{-1}) and extensive C–O absorptions in the i.r., a broad carbinol type signal at $\delta_{\rm H}$ 3·90 and four acetal carbon signals around $\delta_{\rm C}$ 110. From this spectral data and its behaviour towards lithium aluminium hydride the 'ozonolysis product' is formulated as a mixture of the hydroperoxy ether (43) (*m/z* 254) and the hemiacetal (44) (*m/z* 238), both epimeric at C 8. Hydride reduction of the 'ozonolysis product' gave the (8*RS*)-diol (45) which, because of its insolubility and the difficulty in handling, was acetylated with acetic anhydride/pyridine. Two products were isolated. The diacetate (46) showed only acetate absorptions [1725, 1250, 1045 cm^{-1}; $\delta_{\rm H}$ 1·98, 2·00; $\delta_{\rm C}$ 171·3(s), 170·0(s)]. The equatorial nature of the C 8 hydroxyl was established by the large band width ($W_{h/2}$ 10 Hz) of the C 8 carbinol multiplet (δ 5·07). The second product, the hydroxy acetate (47), showed hydroxyl (3490 cm^{-1}) and acetate (1710, 1240 cm^{-1}; $\delta_{\rm H}$ 2·02) absorptions. The low-field 10β-methyl signal ($\delta_{\rm H}$ 1·00) and the narrow band width ($W_{h/2}$ 6 Hz) of the C 8 carbinol multiplet (δ 3·97) established the axial orientation of the C 8 hydroxy group.

Dehydration of the 'ozonolysis product' produced a large number of products, none of which could be identified. Failure of the 4-en-1-ol system to yield a lactone is attributed to the inability of the five-membered hydroperoxy ether to satisfy the anticoplanar requirements.

Experimental

For general experimental details see ref. 4.

Ozonolysis of 15-Norlabd-8(17)-en-13-ol (2)

The hydroxy olefin (2) (0·71 g) in dry dichloromethane (20 ml) and dry pyridine (5 ml) was cooled to −78° and dry ozone bubbled through the solution until the blue coloration persisted. Dry nitrogen was passed through the solution to eliminate excess ozone. Removal of the solvent under vacuum at room temperature and p.l.c. (25% ether/hexane) gave:

(A) At highest $R_{\rm F}$: *8,13-epoxy-15,17-dinorlabd-8-ene* (7) (0·1 g, 12%) as an oil,[5] b.p. 84°/0·01 mm (Found: C, 82·6; H, 11·5. $C_{18}H_{30}O$ requires C, 82·4; H, 11·5%). $\nu_{\rm max}$: 1665, 1155, 1120 cm^{-1} (C=C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·88, 0·96, 1·10, 1·18. *m/z* 262 (M).

(B) *8α,13-Epoxy-8β-hydroperoxy-15,17-dinorlabdane* (4) (0·43 g, 50%), m.p. 110–112°, sublimed 70°/0·02 mm (Found: C, 72·9; H, 10·8. $C_{18}H_{32}O_3$ requires C, 72·9; H, 10·8%). $\nu_{\rm max}$ 3490 (OH), 1180–1030 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·82, 0·85, 0·92, 1·18, 1·40; 7·41, s, OH. ^{13}C n.m.r.: 39·2, t, C 1; 19·0, t, C 2; 42·3, t, C 3; 33·3, s, C 4; 56·5, d, C 5; 19·0, t, C 6; 38·3, t, C 7; 105·3, s, C 8; 56·8, d, C 9; 37·3, s, C 10; 14·9, t, C 11; 37·3, t, C 12; 72·5, s, C 13; 32·5, q, C 14; 27·2, q, C 16; 33·5, q, C 18; 21·6, q, C 19; 15·3, q, C 20. *m/z* 296 (M).

(C) At lowest $R_{\rm F}$: *13-hydroxy-15,17-dinorlabdan-8-one* (1) (50 mg, 6%) m.p. 58–59°,[6] b.p. 84°/0·08 mm (Found: C, 77·0; H, 11·4. $C_{18}H_{32}O_2$ requires C, 77·0; H, 11·5%). $\nu_{\rm max}$ 3460 (OH); 1705 cm^{-1} (C=O). ^{1}H n.m.r.: methyls at δ 0·72, 0·85, 0·97, 1·18, 1·18. *m/z* 280 (M). The yield of keto alcohol (1) varied with ozonolysis as it was unstable, undergoing hemiacetal formation and elimination to give the enol ether (7).

Ozonolysis of Labd-8(17)-en-13-ol (5)

Dihydromanool (5) (1 g) in dry dichloromethane (20 ml) and dry pyridine (5 ml) was ozonized as previously described. P.l.c. (15% ether/hexane) gave:

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[4] Grant, P. K., and Rowan, D. D., *Aust. J. Chem.*, 1981, **34**, 1959.

[5] Francis, M. J., Ph.D. Thesis, University of Otago, 1975, p. 222.

[6] Francis, M. J., Ph.D. Thesis, University of Otago, 1975, p. 219.

(A) At higher R_F: 8,13-epoxy-17-norlabd-8-ene (8) (0·1 g, 10%) as an oil, b.p. 68°/0·01 mm, identical by ^{1}H n.m.r. and i.r. with an authentic sample.[7] ^{13}C n.m.r.: 37·3, t, C 1; 18·7, t, C 2; 41·9, t, C 3; 33·2, s, C 4; 51·8, d, C 5; 19·1, t, C 6; 29·4, t, C 7; 143·3, s, C 8; 113·2, s, C 9; 36·6, s, C 10; 16·5, t, C 11; 30·5, t, C 12; 74·1, s, C 13; 29·0, t, C 14; 8·1, q, C 15; 24·9, q, C 16; 33·3, q, C 18; 21·6, q, C 19; 19·8, q, C 20.

(B) At lower R_F: *8α,13-epoxy-8β-hydroperoxy-17-norlabdane* (6) (0·64 g, 60%) as an oil, b.p. 70°/0·02 mm (Found: C, 73·4; H, 10·9. $C_{19}H_{34}O_3$ requires C, 73·5; H, 11·0%). ν_{max} 3440 (OH), 1170–1050 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·80, 0·80, 0·83, 0·83 (t, J 6 Hz), 1·34. ^{13}C n.m.r.: 39·1, t, C 1; 18·8, t, C 2; 42·1, t, C 3; 33·2, s, C 4; 56·5, d, C 5; 18·8, t, C 6; 37·0, t, C 7; 105·2, s, C 8; 57·0, d, C 9; 37·3, s, C 10; 14·4, t, C 11; 34·8, t, C 12; 74·5, s, C 13; 34·9, t, C 14; 7·7, q, C 15; 25·0, q, C 16; 33·5, q, C 18; 21·4, q, C 19; 15·7, q, C 20. m/z 310 (M).

Lithium Aluminium Hydride Reduction of Hydroperoxy Ether (4)

To the hydroperoxy ether (4) (0·4 g) in dry ether (20 ml) was added lithium aluminium hydride (0·2 g) and the mixture refluxed for $\frac{1}{2}$ h. Excess lithium aluminium hydride was destroyed by the careful addition of water and the ether solution washed with dilute sulfuric acid (10%) and then water. Removal of the solvent and p.l.c. (80% ether/hexane) gave *15,17-dinorlabdane-8β,13-diol* (9) (0·3 g), m.p. 126–127°, sublimed 65°/0·004 mm (Found: C, 76·3; H, 12·1. $C_{18}H_{34}O_2$ requires C, 76·5; H, 12·1%). ν_{max} 3450 (OH); 1110, 1050 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·85, 0·85, 1·02, 1·22, 1·22; 3·97, m, $W_{h/2}$ 6 Hz, CHOH. m/z 282 (M).

Acetylation of Diol (9)

Diol (9) (50 mg) was stirred with acetic anhydride (3 ml) and pyridine (3 ml) at room temperature for 18 h. Usual workup and p.l.c. (70% ether/hexane) gave *8β-acetoxy-15,17-dinorlabdan-13-ol* (10) (40 mg), m.p. 52–53°, b.p. 65°/0·004 mm (Found: C, 74·3; H, 11·3. $C_{20}H_{36}O_3$ requires C, 74·0; H, 11·2%). ν_{max} 1740 (C=O); 1235, 1170, 1040 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·87, 0·87, 0·98, 1·17, 1·17, 2·03 (OAc); 5·5, m, $W_{h/2}$ 6 Hz, CHOAc. m/z 324 (M).

Dehydration of Hydroperoxy Ether (4)

Mesyl chloride/sulfur dioxide[2] (0·8 ml) was added to a stirred solution of hydroperoxy ether (4) (0·6 g) in dry collidine (1·6 ml) and dry dimethylformamide (8 ml) at 10° and stirring continued for a further $\frac{1}{2}$ h. Usual workup and p.l.c. (15% ether/hexane) gave (E)-*15,17-dinor-8,9-secolabd-9(11)-en-8,13-olide* (11) (0·37 g, 65%), m.p. 130–131°, b.p. 45°/0·005 mm (Found: C, 77·9; H, 10·8. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·9%). ν_{max} 1730 (C=O); 1250, 1220, 1160, 1120 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·85, 0·97, 1·28, 1·61; 2·32, m, W 30 Hz, CH_2CO, $CH_2C{=}C$; 5·18, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 39·6, t, C 1; 18·4, t, C 2; 41·8, t, C 3; 34·8, s, C 4; 53·2, d, C 5; 23·7, t, C 6; 39·6, t, C 7; 173·9, s, C 8; 148·2, d, C 9; 40·4, s, C 10; 120·6, d, C 11; 42·2, t, C 12; 81·9, s, C 13; 27·2, q, C 14; 28·7, q, C 16; 32·8, q, C 18; 21·1, q, C 19; 17·1, q, C 20. m/z 278 (M).

Dehydration of Hydroperoxy Ether (6)

Mesyl chloride/sulfur dioxide dehydration of hydroperoxy ether (6) (0·7 g) as above gave, after p.l.c. (20% ether/hexane), (E)-*17-nor-8,9-secolabd-9(11)-en-8,13-olide* (12) (0·46 g, 70%), m.p. 116–117°, sublimed 60°/0·01 mm (Found: C, 77·9; H, 11·1. $C_{19}H_{32}O_2$ requires C, 78·0; H, 11·0%). ν_{max} 1730 (C=O); 1250, 1222, 1172, 1150, 1120 cm^{-1} (C–O). ^{1}H n.m.r. (270 MHz): methyls at δ 0·83, 0·86, 0·89 (t, J 6·5 Hz), 0·97, 1·24; 2·13 (dd, J 3, 13 Hz, H 12); 2·37 (m, W 63 Hz, CH_2CO); 2·77 (br dd, J 13, 10 Hz, H 12); 5·16 (d, J 16 Hz, H 9); 5·29 (oct, J 16, 12, 3 Hz, H 11). ^{13}C n.m.r.: 39·6, t, C 1; 18·3, t, C 2; 41·8, t, C 3; 34·7, s, C 4; 53·0, d, C 5; 23·5, t, C 6; 39·6, t, C 7; 173·7, s, C 8; 148·2, d, C 9; 40·2, s, C 10; 120·4, d, C 11; 41·6, t, C 12; 84·9, s, C 13; 32·2, t, C 14; 8·2, q, C 15; 24·5, q, C 16; 32·7, q, C 18; 21·0, q, C 19; 17·0, q, C 20. m/z 292 (M).

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[7] Grant, P. K., and Weavers, R. T., *Tetrahedron*, 1973, **29**, 2376.

Hydrogenation of Lactone (11)

The lactone (11) (0·35 g) in ethyl acetate (20 ml) was hydrogenated in the presence of prereduced Adams catalyst (0·05 g). After the absorption of 1 mol. equiv. of hydrogen (32 ml) the platinum was filtered off over Celite and the solvent evaporated. P.l.c. (20% ether/hexane) gave *15,17-dinor-8,9-secolabdan-8,13-olide* (13) (0·3 g) as an oil, b.p. 65°/0·003 mm (Found: C, 77·1; H, 11·5. $C_{18}H_{32}O_2$ requires C, 77·0; H, 11·5%). ν_{max} 1730 (C=O); 1260, 1230, 1165, 1120 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·80, 0·90, 0·90, 1·32, 1·57. ^{13}C n.m.r.: 38·7, t, C 1; 18·7, t, C 2; 42·6, t, C 3; 35·3, s, C 4; 47·2, d, C 5; 23·5, t, C 6; 36·6, t, C 7; 174·4, s, C 8; 38·0, t, C 9; 37·4, s, C 10; 17·3, t, C 11; 43·1, t, C 12; 83·1, s, C 13; 28·0, q, C 14; 27·6, q, C 16; 34·0, q, C 18; 22·0, q, C 19; 23·8, q, C 20. *m/z* 280 (M).

Hydrogenation of Lactone (12)

The lactone (12) (0·5 g) in ethyl acetate (20 ml) was hydrogenated in the presence of prereduced Adams catalyst. Workup as before and p.l.c. (20% ether/hexane) gave *17-nor-8,9-secolabdan-8,13-olide* (14) (0·4 g) as an oil, b.p. 83°/0·03 mm (Found: C, 77·4; H, 11·6. $C_{19}H_{34}O_2$ requires C, 77·5; H, 11·6%). ν_{max} 1730 (C=O); 1250, 1192, 1160, 1145, 1040 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·77, 0·87, 0·87, 0·87 (t, J 6 Hz), 1·52. ^{13}C n.m.r.: 39·0, t, C 1; 18·8, t, C 2; 42·5, t, C 3; 35·4, s, C 4; 47·5, d, C 5; 23·8, t, C 6; 36·6, t, C 7; 175·0, s, C 8; 35·4, t, C 9; 37·4, s, C 10; 16·9, t, C 11; 42·9, t, C 12; 85·7, s, C 13; 32·8, t, C 14; 8·3, q, C 15; 24·0, q, C 16; 33·8, q, C 18; 22·1, q, C 19; 23·8, q, C 20. *m/z* 294 (M).

*Ozonolysis/*in situ *Dehydration*

General procedure.—Optimal conditions for lactone formation (60%) were determined by ozonizing varying concentrations (2·5–15%) of dihydromanool (5) in dry dichloromethane or dry methanol followed by *in situ* dehydration by using mesyl chloride/sulfur dioxide^2 or the ferrous sulfate procedure. Solvent removal under vacuum in the cold before dehydration gave a decreased lactone yield. The following procedure was used for all ozonolysis/*in situ* dehydration reactions. Ozone was bubbled through a solution (2·5–5%) of the substrate in dry methanol at −78° until the blue colour persisted. Dry nitrogen was purged through the solution to remove excess ozone. The reaction solution was poured into a stirred solution of dry dimethylformamide (20 ml) and dry collidine (6 ml) and mesyl chloride (2 ml) saturated with sulfur dioxide added dropwise. After stirring for a further $\frac{1}{2}$ h, workup gave the crude product.

(i) 14,15,16-Trinorlabd-8(17)-en-13-ol (15) (0·8 g) gave, after p.l.c. (15% ether/hexane), (E)-*14,15,16,17-tetranor-8,9-secolabd-9(11)-en-8,13-olide* (16) (0·4 g) as an oil, b.p. 70°/0·05 mm (Found: C, 76·9; H, 10·4. $C_{16}H_{26}O_2$ requires C, 76·8; H, 10·5%). ν_{max} 1730 (C=O); 1250, 1193, 1160, 1145, 1130, 1040 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·87, 0·89, 1·00; 4·23, m, $W_{h/2}$ 16 Hz, CH_2O; 5·10, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 40·6, t, C 1; 18·6, t, C 2; 42·2, t, C 3; 34·9, s, C 4; 55·3, d, C 5; 23·3, t, C 6; 38·3, t, C 7; 175·0, s, C 8; 148·3, d, C 9; 40·3, s, C 10; 121·2, d, C 11; 32·6, t, C 12; 63·4, t, C 13; 33·4, q, C 18; 21·6, q, C 19; 17·1, q, C 20. *m/z* 250 (M).

(ii) (13*RS*)-14,15-Dinorlabd-8(17)-en-13-ol (17) (1 g) gave, after p.l.c. (15% ether/hexane), (E)(*13*RS)-*14,15,17-trinor-8,9-secolabd-9(11)-en-8,13-olide* (18) (0·35 g) as an oil, b.p. 50°/0·005 mm (Found: C, 77·1; H, 10·8. $C_{17}H_{28}O_2$ requires C, 77·2; H, 10·7%). ν_{max} 1725 (C=O); 1252, 1238, 1135, 1050 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·88, 0·98, 1·27 (d, J 6 Hz); 4·90, m, $W_{h/2}$ 10 Hz, CHO; 5·10, m, $W_{h/2}$ 12 Hz CH=CH. ^{13}C n.m.r.: 41·4, t, C 1; 18·7, t, C 2; 42·2, t, C 3; 34·7, s, C 4; 57·5, d, C 5; 22·7, t, C 6; 37·8, t, C 7; 175·9, s, C 8; 148·1, d, C 9; 39·6, s, C 10, 122·9, d, C 11; 42·5, t, C 12; 71·7, d, C 13; 19·8, q, C 16; 34·0, q, C 18; 21·8, q, C 19; 16·9, q, C 20. *m/z* 264 (M).

(iii) (14*RS*)-14,15-Epoxylabd-8(17)-en-13-ol (19) (0·7 g) gave, after p.l.c. (20% ether/hexane), (E)(*14*RS)-*14,15-epoxy-17-nor-8,9-secolabd-9(11)-en-8,13-olide* (20) (0·39 g), m.p. 140–141°, sublimed 80°/0·02 mm (Found: C, 74·3; H, 10·1. $C_{19}H_{30}O_3$ requires C, 74·5; H, 9·9%). ν_{max} 1730 (C=O); 1250, 1220, 1120, 1100, 1080, 1050 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·87, 0·98, 1·16; 2·67, m, CH_2C=C and CH_2CO; 3·60, t, J 3 Hz, CH–O; 5·18, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 39·3, t, C 1; 18·3, t, C 2; 41·7, t, C 3; 34·8, s, C 4; 53·1, d, C 5; 23·5, t, C 6; 39·3, t, C 7; 173·7, s, C 8; 149·3, d, C 9; 40·5, s, C 10; 119·3, d, C 11; 39·3, t, C 12; 82·4, s, C 13; 55·9, d, C 14; 44·2, t, C 15; 20·8, q, C 16; 32·8, q, C 18; 21·1, q, C 19; 17·1, q, C 20. *m*/*z* 306 (M).

(iv) 15,16-Dinorlabd-8(17)-en-14-ol (21) (0·54 g) gave, after p.l.c. (15% ether/hexane):

(A) At higher R_F: (E)-*15,16,17-trinor-8,9-secolabd-9(11)-en-8,14-olide* (22) (75 mg) as an oil, b.p. 90°/0·02 mm (Found: C, 77·1; H, 10·7. $C_{17}H_{28}O_2$ requires C, 77·2; H, 10·7%). ν_{max} 1725 (C=O); 1250, 1225, 1060, 1045 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·87, 0·87, 0·90; 3·70, d of t, ^2J 12 Hz, ^3J 4 Hz, ^3J 3 Hz, 14-H; 4·83, quintet, ^2J 12 Hz, ^3J 6 Hz, ^3J 6 Hz, 14-H; 5·10, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 40·3, t, C 1; 18·4, t, C 2; 41·9, t, C 3; 34·7, s, C 4; 51·8, d, C 5; 21·9, t, C 6; 37·9, t, C 7; 173·1, s, C 8; 142·7, d, C 9; 39·7, s, C 10; 127·2, d, C 11; 27·7, t, C 12; 32·6, t, C 13; 64·8, t, C 14; 33·2, q, C 18; 21·5, q, C 19; 17·9, q, C 20. *m*/*z* 264 (M).

(B) At lower R_F: a product which was replated (70% ether/hexane) to give *14-mesyloxy-15,16,17-trinorlabdan-8-one* (23) (0·18 g) as an oil, b.p. 97°/0·02 mm (Found: C, 62·7; H, 9·4; S, 9·6. $C_{18}H_{32}O_4S$ requires C, 62·8; H, 9·3; S, 9·3%). ν_{max} 1705 (C=O); 1175, 1100 cm^{-1} (SO_2O). ^{1}H n.m.r.: methyls at δ 0·68, 0·83, 0·95, 2·93 (Ms); 4·17, t, *J* 6 Hz, CH_2OMs. ^{13}C n.m.r.: 39·3, t, C 1; 19·0, t, C 2; 42·0, t, C 3; 33·7, s, C 4; 54·3, d, C 5; 24·0, t, C 6; 42·6, t, C 7; 211·8, s, C 8; 64·2, d, C 9; 42·6, s, C 10; 21·1, t, C 11; 25·2, t, C 12; 29·4, t, C 13; 70·0, t, C 14; 33·4, q, C 18; 21·7, q, C 19; 14·6, q, C 20; 37·3, q, Ms. *m*/*z* 344 (M).

(v) (13*RS*)-15-Norlabd-8(17)-en-14-ol (24) (0·51 g) gave, after p.l.c. (20% ether/hexane):

(A) At higher R_F: (E)(*13*RS)-*15,17-dinor-8,9-secolabd-9(11)-en-8,14-olide* (26) (80 mg), m.p. 75–76°, sublimed 60°/0·04 mm (Found: C, 77·5; H, 11·0. $C_{18}H_{30}O_2$ requires C, 77·6; H, 10·9%). ν_{max} 1730 (C=O); 1250, 1160, 1150, 1040 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·90, 0·90, 0·91 (d, *J* 6 Hz), 0·93; 3·56, bm, 14-H; 4·75, bm, 14-H; 5·15, m, $W_{h/2}$ 18 Hz, CH=CH. ^{13}C n.m.r.: 38·3, t, C 1; 18·5, t, C 2; 41·9, t, C 3; 34·8, s, C 4; 52·1, 51·7, d, C 5; 22·2, 21·9, t, C 6; 38·0, t, C 7; 173·3, 172·9, s, C 8; 143·3, 142·6, d, C 9; 39·8, s, C 10; 126·7, 124·3, d, C 11; 40·4, 40·1, t, C 12; 32·8, 31·8, d, C 13; 69·8, 69·6, t, C 14; 18·3, 18·0, q, C 16; 33·2, q, C 18; 21·6, q, C 19; 16·2, q, C 20. *m*/*z* 278 (M).

(B) At lower R_F: (*13*RS)-*14-mesyloxy-15,17-dinorlabdan-8-one* (25) (0·25 g), b.p. 75°/0·01 mm (Found: C, 63·9; H, 9·9; S, 8·6. $C_{19}H_{34}O_4S$ requires C, 63·7; H, 9·6; S, 8·9%). ν_{max} 1700 (C=O) 1172, 1060 cm^{-1} (SO_2O). ^{1}H n.m.r.: methyls at δ 0·70, 0·83, 0·95, 0·98 (d, *J* 6 Hz), 3·0 (OMs); 4·05, d, *J* 6 Hz, CH_2OMs. ^{13}C n.m.r.: 39·1, t, C 1; 18·8, t, C 2; 41·8, t, C 3; 33·3, s, C 4; 54·1, d, C 5; 23·9, t, C 6; 42·5, t, C 7; 211·5, s, C 8; 64·3, d, C 9; 42·5, s, C 10; 18·8, t, C 11; 32·7, 32·2, t, C 12; 33·3, s, C 13; 74·4, t, C 14; 16·5, 16·2, q, C 16; 21·5, q, C 19; 14·5, q, C 20; 37·0, q, Ms. *m*/*z* 358 (M).

(vi) (13*RS*)-13-Fluoro-15-norlabd-8(17)-en-14-ol (27) (1·12 g) gave, after p.l.c. (20% ether/hexane):

(A) At highest R_F: (E)-*13ξ-fluoro-15,17-dinor-8,9-secolabd-9(11)-en-8,14-olide* (29a) (60 mg), m.p. 95–96°, sublimed 80°/0·04 mm (Found: C, 72·8; H, 10·2. $C_{18}H_{29}FO_2$ requires C, 72·9; H, 9·9%). ν_{max} 1735 (C=O); 1220, 1150, 1060, 1000 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·90, 0·90, 0·93, 1·45, d, $J_{H,F}$ 22 Hz; 3·52, q, ^2J 11 Hz, $J_{H,F}$ 7·5 Hz, 14-H; 4·90, bd, ^2J 11 Hz, $J_{H,F}$ 2 Hz, 14-H; 5·12, m, $W_{h/2}$ 9 Hz, CH=CH. ^{13}C n.m.r.: 39·9, t, C 1; 18·4, t, C 2; 41·8, t, C 3; 34·8, s, C 4; 51·3, d, C 5; 22·1, t, C 6; 37·7, t, C 7; 172·5, s, C 8; 146·4, d, C 9; 40·2, s, C 10; 120·4, t, C 11 ($^3J_{C,F}$ 14 Hz); 44·2, t, C 12 ($^2J_{C,F}$ 23 Hz); 93·8, s, C 13 ($^1J_{C,F}$ 166 Hz); 67·7, t, C 14 ($^2J_{C,F}$ 44 Hz); 22·5, q, C 16 ($^2J_{C,F}$ 22 Hz); 33·2, q, C 18; 21·5, q, C 19; 17·9, q, C 20. *m*/*z* 296 (M).

(B) (E)-*13ξ-Fluoro-15,17-dinor-8,9-secolabd-9(11)-en-8,14-olide* (29b) (120 mg), m.p. 85–86°, sublimed 75°/0·04 mm (Found: C, 72·6; H, 10·2. $C_{18}H_{29}FO_2$ requires C, 72·9; H, 9·9%). ν_{max} 1740 (C=O); 1250, 1170, 1060, 990 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·91, 0·91, 0·97, 1·30, d, $J_{H,F}$ 21 Hz; 3·63, q, ^2J 13 Hz, $J_{H,F}$ 9 Hz, 14-H; 4·77, d, ^2J 13 Hz, $J_{H,F}$ 0 Hz, 14-H; 5·13, m, $W_{h/2}$ 9 Hz, CH=CH. ^{13}C n.m.r.: 40·3, t, C 1; 18·4, t, C 2; 41·8, t, C 3; 34·8, s, C 4; 52·1, d, C 5; 21·9, t, C 6; 38·0, t, C 7; 172·9, s, C 8; 144·7, d, C 9; 39·8, s, C 10; 121·7, d, C 11 ($^3J_{C,F}$ 5 Hz); 43·0, t, C 12 ($^2J_{C,F}$ 23 Hz); 94·6, s, C 13 ($^1J_{C,F}$ 177 Hz); 68·0, t, C 14 ($^2J_{C,F}$ 20 Hz); 25·0, q, C 16 ($^2J_{C,F}$ 23 Hz); 33·0, q, C 18; 21·4, q, C 19; 18·0, q, C 20. *m*/*z* 296 (M).

(C) At lowest R_F: (*13*RS)-*13-fluoro-14-mesyloxy-15,17-dinorlabdan-8-one* (28) (300 mg) as an oil, b.p. 85°/0·04 mm (Found: C, 60·9; H, 9·0; S, 8·2. $C_{19}H_{33}O_4SF$ requires C, 60·6; H, 8·8; S, 8·5%). ν_{max} 1700 cm^{-1} (C=O). ^{1}H n.m.r.: methyls at δ 0·70, 0·81, 0·95, 1·38 (d, $J_{H,F}$

22 Hz), 3·30 (Ms); 4·20, d, $J_{H,F}$ 22 Hz and 4·25, d, $J_{H,F}$ 22 Hz, CH_2OMs. ^{13}C n.m.r.: 38·9, t, C1; 18·7, t, C2; 41·7, t, C3; 33·4, s, C4; 53·9, d, C5; 23·7, t, C6; 42·4, t, C7; 211·2, s, C8; 63·8, d, C9; 42·2, s, C10; 15·2, t, C11 ($^3J_{C,F}$ 4 Hz); 34·8, 36·3, t, C12 ($^2J_{C,F}$ 11 Hz, 11 Hz); 94·6, s, C13 ($^1J_{C,F}$ 173 Hz); 71·9, 73·6, t, C14 ($^2J_{C,F}$ 12 Hz, 11 Hz); 19·9, 21·5, q, C16 ($^2J_{C,F}$ 17 Hz, 18 Hz); 33·2, q, C18; 21·4, q, C19; 14·4, q, C20; 37·3, q, Ms. *m*/*z* 296 (M).

(vii) (13*RS*)-Labd-8(17)-en-15-ol (30) (0·3 g) gave, after p.l.c. (60% ether/hexane), (*13*RS)-*15-mesyloxy-17-norlabdan-8-one* (31) (0·18 g) as an oil, b.p. 75°/0·01 mm (Found: C, 64·7; H, 9·5; S, 8·5. $C_{20}H_{36}O_4S$ requires C, 64·5; H, 9·7; S, 8·6%). ν_{max} 1700 cm^{-1} (C=O). ^1H n.m.r.: methyls at δ 0·70, 0·83, 0·93, 0·95 (d, *J* 6 Hz), 3·00 (Ms); 4·23, t, *J* 6 Hz, CH_2OMs. *m*/*z* 372 (M).

(viii) 14-Hydroxymethyl-16-norlabd-8(17)-en-15-ol (32) (0·4 g) gave, after p.l.c. (ether), *14-mesyloxymethyl-15-mesyloxy-17-norlabdan-8-one* (33) (0·25 g) as an oil, b.p. 95°/0·01 mm (Found: C, 54·0; H, 8·0; S, 13·4. $C_{21}H_{38}O_7S_2$ requires C, 54·1; H, 8·2; S, 13·7%). ν_{max} 1700 (C=O), 1170, 1070 cm^{-1} (OSO_2). ^1H n.m.r.: methyls at δ 0·70, 0·86, 0·96, 3·00 (Ms), 3·00 (Ms); 4·20, t, *J* 6 Hz, CH_2OMs. *m*/*z* 466 (M).

(ix) 14,15,16-Trinorlabd-8(17)-en-13-oic acid (34) (1 g) gave, after p.l.c. (ether), *8-oxo-14,15,16,17-tetranorlabdan-13-oic acid* (35) (0·74 g), m.p. 91–92°, b.p. 110°/0·02 mm (Found: C, 72·3; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·1; H, 9·8%). ν_{max} 3300–2800 (OH); 1700 cm^{-1} (C=O). ^1H n.m.r.: methyls at δ 0·70, 0·83, 0·95. ^{13}C n.m.r.: 39·2, t, C1; 19·0, t, C2; 41·9, t, C3; 33·7, s, C4; 54·2, d, C5; 24·0, t, C6; 42·5, t, C7; 212·1, s, C8; 63·1, d, C9; 42·7, s, C10; 17·2, t, C11; 33·1, t, C12; 179·5, s, C13; 33·5, q, C18; 21·7, q, C19; 14·6, q, C20. *m*/*z* 266 (M).

(x) (14*RS*)-Labd-8(17)-ene-13,14-diol (36) (0·5 g) gave, after p.l.c. (60% ether/hexane):

(A) At higher R_F: (*14*RS)-*8,13:8,14-diepoxy-17-norlabdane* (39) (0·16 g, 13%) as an oil, b.p. 95°/0·02 mm (Found: C, 78·0; H, 11·0. $C_{19}H_{32}O_2$ requires C, 78·0; H, 11·0%). ν_{max} 1188, 1100, 1080, 1046, 1013 cm^{-1} (C–O). ^1H n.m.r.: methyls at δ 0·80, 0·84, 0·99, 1·14, 1·20 (d, *J* 6 Hz); 3·60, q, *J* 6 Hz, CHOC; 3·93, q, *J* 6 Hz, CHOC. ^{13}C n.m.r.: 40·2, t, C1; 18·7, t, C2; 42·1, t, C3; 33·2, s, C4; 51·0, d, C5; 19·7, t, C6; 37·7, t, C7; 107·7, s, C8; 54·5, d, C9; 38·6, s, C10; 17·0, t, C11; 28·7, t, C12; 81·3, s, C13; 78·2, 75·8, d, C14; 16·6, 16·2, q, C15; 23·0, q, C16; 33·9, q, C18; 21·8, q, C19; 13·9, q, C20. *m*/*z* 292 (M).

(B) (E)(*14*RS)-*14-hydroxy-17-nor-8,9-secolabd-9(11)-en-8,13-olide* (37) (0·17 g, 35%), m.p. 125–126°, sublimed 92°/0·01 mm (Found: C, 74·0; H, 10·6. $C_{19}H_{32}O_3$ requires C, 74·0; H, 10·5%). ν_{max} 3340 (OH); 1720 (C=O); 1270, 1220, 1165, 1090, 1020 cm^{-1} (C–O). ^1H n.m.r.: methyls at δ 0·87, 0·87, 1·00, 1·14, (d, *J* 6 Hz), 1·30; 4·17, q, *J* 6 Hz, CHO; 5·29, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 39·5, t, C1; 18·4, t, C2; 41·8, t, C3; 34·8, s, C4; 53·0, d, C5; 23·5, t, C6; 39·3, t, C7; 175·7, s, C8; 148·9, d, C9; 40·5, s, C10; 120·3, d, C11; 35·0, 37·2, t, C12; 89·7, 90·5, s, C13; 71·3, 72·1, d, C14; 17·1, q, C15; 22·7, 23·2, q, C16; 32·7, q, C18; 21·0, q, C19; 18·3, q, C20. *m*/*z* 308 (M).

(C) At lowest R_F: (E)(*14*RS)-*13-hydroxy-17-nor-8,9-secolabd-9(11)-en-8,14-olide* (38) (0·13 g, 26%), m.p. 110–111°, sublimed 93°/0·02 mm (Found: C, 73·9; H, 10·5. $C_{19}H_{32}O_3$ requires C, 74·0; H, 10·5%). ν_{max} 3400 (OH); 1710 (C=O); 1265, 1220, 1170, 1100, 1060 cm^{-1} (C–O). ^1H n.m.r.: methyls at δ 0·89, 0·89, 1·01, 1·21, 1·23 (d, *J* 6 Hz); 4·91, q, *J* 6 Hz, CH–OCO; 5·36, m, $W_{h/2}$ 12 Hz, CH=CH. ^{13}C n.m.r.: 40·4, t, C1; 18·7, t, C2; 42·0, t, C3; 35·0, s, C4; 58·5, d, C5; 21·9, t, C6; 37·8, t, C7; 178·0, s, C8; 145·2, d, C9; 39·2, s, C10; 123·0, s, C11; 44·4, t, C12; 73·3, s, C13; 77·8, d, C14; 15·9, q, C15; 23·7, q, C16; 33·2, q, C18; 21·6, q, C19; 19·6, q, C20. *m*/*z* 308 (M).

(xi) (12*RS*)-14,15,16-Trinorlabd-8(17)-ene-12,13-diol (40) (0·5 g) gave, after p.l.c. (50% ether/hexane), (E)(*12*RS)-*12-hydroxy-14,15,16,17-tetranor-8,9-secolabd-9(11)-en-8,13-olide* (41) (0·2 g) as an oil, b.p. 75°/0·02 mm (Found: C, 72·2; H, 9·6. $C_{16}H_{26}O_3$ requires C, 72·1; H, 9·8%). ν_{max} 3420 (OH); 1720 (C=O); 1250, 1225, 1130, 1045 cm^{-1} (C–O). ^1H n.m.r.: methyls at δ 0·84, 0·84, 0·99; 4·48, m, $W_{h/2}$ 16 Hz, CH_2–O, CH–OH; 5·18, m, $W_{h/2}$ 11 Hz, CH=CH. ^{13}C n.m.r.: 39·9, t, C1; 18·3, t, C2; 41·9, t, C3; 34·8, s, C4; 53·8, d, C5; 23·2, t, C6; 38·4, t, C7; 174·7, s, C8; 146·5, d, C9; 40·8, s, C10; 125·9, d, C11; 72·3, d, C12; 67·0, t, C13; 33·1, q, C18; 21·4, q, C19; 16·9, q, C20. *m*/*z* 266 (M).

(xii) 13,14,15,16-Tetranorlabd-8(17)-en-12-ol (42) (0·3 g) gave, after p.l.c. (15% ether/hexane), many unidentified products. Ozone was bubbled through a solution of alcohol (42) (0·26 g) in dry methanol (10 ml) at −78° until the blue colour persisted. Removal of the solvent under vacuum at room temperature and p.l.c. (50% ether/hexane) gave the 'ozonolysis product' (43) and (44) (0·2 g). $\nu_{\max}$: 3310 (OH); 1155, 1120, 1105, 1052, 1047, 1020 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·83, 0·88; 3·90, br m, CH_2O. *m/z* 254, 238.

Lithium Aluminium Hydride Reduction of 'Ozonolysis Product'

Ozonolysis product (45) and (46) (0·23 g) in dry ether (50 ml) was refluxed with excess lithium aluminium hydride for $\frac{1}{2}$ h. Usual workup and p.l.c. (80% ether/hexane) gave (*8*RS)-*13,14,15,16,17-pentanorlabdane-8,12-diol* (45) (0·19 g) (Found: C, 74·7; H, 11·8. $C_{15}H_{28}O_2$ requires C, 74·9; H, 11·7%). $\nu_{\max}$ 3300 (OH); 1050, 1020 cm^{-1} (C–O).

Acetylation of Diol (45)

Diol (45) (0·18 g) in acetic anhydride (5 ml) and pyridine (5 ml) was stirred overnight at room temperature. Usual workup and p.l.c. (30% ether/hexane) gave:

(A) At higher R_F: *13,14,15,16,17-pentanorlabdan-8α,12-yl diacetate* (46) (0·06 g) as an oil, b.p. 65°/0·04 mm (Found: C, 70·2; H, 9·9; $C_{19}H_{32}O_4$ requires C, 70·3; H, 9·9%). $\nu_{\max}$ 1725 (C=O); 1250, 1045 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·83, 0·83, 0·93, 1·97 (OAc), 2·00 (OAc); 4·05, m, $W_{h/2}$ 14 Hz, CH_2OAc; 5·07, m, $W_{h/2}$ 10 Hz, CHOAc. *m/z* 324 (M).

(B) At lower R_F: *12-acetoxy-13,14,15,16,17-pentanorlabdan-8β-ol* (47) (0·1 g) as an oil, b.p. 78°/0·04 mm (Found: C, 72·1; H, 10·7. $C_{17}H_{30}O_3$ requires C, 72·3; H, 10·7%). $\nu_{\max}$ 3490 (OH), 1710 (C=O); 1240, 1030, 1000 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·85, 0·85, 1·00, 2·02 (OAc); 3·97, m, $W_{h/2}$ 6 Hz, CHOH; 4·13, t, *J* 6 Hz, CH_2OAc. *m/z* 282 (M).

Synthesis of Substrates

8(17)-En-13-ol Systems

t-Butyl hydroperoxide (4·5 g) was added dropwise to a refluxing solution of manool (3) (5 g) and vanadyl acetylacetonate (0·25 g) in benzene (50 ml). When the reaction was complete, partial evaporation of the solvent, filtration through alumina and elution with ether gave (14*RS*)-14,15-epoxylabd-8(17)-en-13-ol (19) (5 g) as an oil. ^{1}H n.m.r. and i.r. identical with reported data.[8] ^{13}C n.m.r.: 39·2, t, C 1; 19·4, t, C 2; 42·3, t, C 3; 33·6, s, C 4; 55·7, d, C 5; 24·5, t, C 6; 38·4, t, C 7; 148·6, s, C 8; 57·5, d, C 9; 39·9, s, C 10; 17·0, t, C 11; 38·0, t, C 12; 69·6, s, C 13; 57·9, d, C 14; 44·2, 40·6, t, C 15; 26·1, 22·9, q, C 16; 106·4, t, C 17; 33·6, q, C 18; 21·7, q, C 19; 14·4, q, C 20. The epoxide (19) (5 g) in dry ether (120 ml) was refluxed with excess lithium aluminium hydride for 1 h. Appropriate workup gave (14*RS*)-labd-8(17)-ene-13,14-diol (36) (4·7 g) as an oil, ^{1}H n.m.r. and i.r. identical with reported data.[8] ^{13}C n.m.r.: 39·3, t, C 1; 19·5, t, C 2; 42·3, t, C 3; 33·6, s, C 4; 55·8, d, C 5; 24·6, t, C 6; 38·5, t, C 7; 148·6, s, C 8; 57·9, d, C 9; 40·0, s, C 10; 17·5, t, C 11; 35·3, t, C 12; 75·0, s, C 13; 74·2, 72·8, d, C 14; 17·2, q, C 15; 23·4, 20·7, q, C 16; 106·7, t, C 17; 33·6, q, C 18; 21·8, q, C 19; 14·6, q, C 20. Sodium periodate (5 g) in water (100 ml) was added to the diol (36) (4·7 g) in methanol (100 ml) and the solution stirred overnight at room temperature. The usual workup gave methylene ketone (48) (3·5 g) which was dissolved in dioxan and oxidized with sodium hypobromite solution to give 14,15,16-trinorlabd-8(17)-en-13-oic acid (34) (3·2 g)[4] which was reduced with lithium aluminium hydride to 14,15,16-trinorlabd-8(17)-en-13-ol (15) (3 g).[4]

Sodium borohydride (250 mg) was added to the methylene ketone (48) (1·4 g) in methanol (80 ml) and water (4 ml) and the reaction mixture stirred for 40 min. Usual workup and p.l.c. (50% ether/hexane) gave (*13*RS)-*14,15-dinorlabd-8(17)-en-13-ol* (17) (1·4 g) as an oil, b.p. 90°/0·02 mm (Found: C, 81·6; H, 12·0. $C_{18}H_{32}O$ requires C, 81·8; H, 12·2%). $\nu_{\max}$ 3350 (OH); 3080, 1640, 888 cm^{-1} (C=CH_2). ^{1}H n.m.r.: methyls at δ 0·69, 0·81, 0·87, 1·17, d, *J* 6 Hz; 3·74, m, CHOH; 4·51, 4·81 (=CH_2). *m/z* 264 (M).

Methylmagnesium iodide was prepared by the dropwise addition of methyl iodide (2·3 ml) to magnesium turnings (2·3 g) in dry ether (40 ml). The reaction mixture was refluxed for 20 min to ensure complete reaction of the methyl iodide and the ethereal solution decanted from the unchanged magnesium. Excess methylmagnesium iodide solution was added dropwise to the methylene ketone (48) (1·3 g) in dry ether (25 ml) and the reaction mixture stirred at room

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[8] Sundararaman, P., and Herz, W., *J. Org. Chem.*, 1977, **42**, 806.

temperature for 20 min. Excess reagent was destroyed by the addition of saturated ammonium chloride. Usual workup and p.l.c. (30% ether/hexane) gave *15-norlabd-8(17)-en-13-ol* (2) (1·1 g), m.p. 91–92°, sublimed 80°/0·05 mm (Found: C, 81·9; H, 12·2. $C_{19}H_{34}O$ requires C, 82·0; H, 12·3%). ν_{max} 3300 (OH); 3080, 1640, 883 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·69, 0·80, 0·87, 1·20, 1·20; 4·52, 4·81 ($=CH_2$). ^{13}C n.m.r.: 39·2, t, C 1; 19·4, t, C 2; 42·3, t, C 3; 33·6, s, C 4; 55·6, d, C 5; 24·5, t, C 6; 38·4, t, C 7; 148·7, s, C 8; 57·4, d, C 9; 39·9, s, C 10; 18·1, t, C 11; 43·1, t, C 12; 71·2, s, C 13; 29·1, q, C 14; 29·3, q, C 16; 106·4, t, C 17; 33·6, q, C 18; 21·7, q, C 19; 14·5, q, C 20. *m/z* 278 (M).

8(17)-En-14-ol Systems

The alcohol (15) (0·5 g) was treated with methanesulfonyl chloride (0·2 ml) in pyridine (10 ml) in an ice/salt bath and after usual workup gave 14,15,16-trinorlabd-8(17)-en-13-yl methanesulfonate (49) (0·49 g), identical by i.r. and ^1H n.m.r. with an authentic sample.[4] Sodium cyanide (0·06 g) was added to the mesylate (49) (0·4 g) in dry hexamethylphosphoric triamide (20 ml) and the reaction mixture stirred overnight at room temperature.[9] Usual workup and p.l.c. (50% ether/hexane) gave *14,15,16-trinorlabd-8(17)-ene-13-carbonitrile* (50) (0·23 g) as an oil, b.p. 77°/0·04 mm (Found: C, 83·0; H, 11·3; N, 5·7. $C_{18}H_{29}N$ requires C, 83·3; H, 11·3; N, 5·4%). ν_{max} 2250 ($C{\equiv}N$); 3080, 1640, 890 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·67, 0·80, 0·87; 2·31, m, CH_2CN; 4·47, 4·83, ($=CH_2$). ^{13}C n.m.r.: 39·2, t, C 1; 19·4, t, C 2; 42·2, t, C 3; 33·6, s, C 4; 55·6, d, C 5; 24·6, t, C 6; 38·3, t, C 7; 148·1, s, C 8; 56·2, d, C 9; 39·8, s, C 10; 17·5, t, C 11; 23·0, t, C 12; 24·6, t, C 13; 119·7, s, C 14; 106·5, t, C 17; 33·6, q, C 18; 21·8, q, C 19; 14·5, q, C 20. *m/z* 259 (M). The nitrile (50) (0·54 g) in diethylene glycol (30 ml) and potassium hydroxide (40%, 40 ml) was refluxed for 4 h.[10] The reaction mixture was diluted with water (200 ml) and ether extracted to remove neutral material. The aqueous layer was acidified and gave, after p.l.c. (40% ether/hexane), *15,16-dinorlabd-8(17)-en-14-oic acid* (51) (0·3 g) as an oil, b.p. 90°/0·04 mm (Found: C, 77·6; H, 11·0. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·9%). ν_{max} 3400–2600, 1705 (COOH); 3080, 1640, 890 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·67, 0·78, 0·83; 2·35, t, *J* 6 Hz, CH_2COOH; 4·50, 4·80 ($=CH_2$). *m/z* 278 (M). The acid (51) (0·25 g) in dry ether (50 ml) was refluxed with excess lithium aluminium hydride for 1 h. Appropriate workup and p.l.c. (50% ether/hexane) gave *15,16-dinorlabd-8(17)-en-14-ol* (21) (0·21 g) as an oil, b.p. 80°/0·04 mm (Found: C, 81·6; H, 12·1. $C_{18}H_{32}O$ requires C, 81·8; H, 12·2%). ν_{max} 3340 (OH); 3080, 1640, 890 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·66, 0·78, 0·85; 3·57, m, $W_{h/2}$ 8 Hz, CH_2OH; 4·48, 4·78 ($=CH_2$). ^{13}C n.m.r.: 39·2, t, C 1; 19·5, t, C 2; 42·3, t, C 3; 33·6, s, C 4; 55·6, d, C 5; 24·6, t, C 6; 38·4, t, C 7; 148·7, s, C 8; 56·9, d, C 9; 39·7, s, C 10; 23·5, t, C 11; 25·0, t, C 12; 33·3, t, C 13; 62·9, t, C 14; 106·1, t, C 17; 33·6, q, C 18; 21·8, q, C 19; 14·5, q, C 20. *m/z* 264 (M).

Sodium hydride (50% dispersion, 1 g) was washed repeatedly with dry hexane and suspended in dry dimethyl sulfoxide (18 ml) in a nitrogen atmosphere. After stirring for 2 h at 45° the hydrogen evolution had ceased. The solution was cooled and sufficient dry tetrahydrofuran added to maintain solution when cooled in an ice/salt bath. Trimethylsulfonium iodide (3·8 g) in dry dimethyl sulfoxide (20 ml) was added over 5 min.[11] After stirring for a further 10 min methylene ketone (48) (4 g) in dry tetrahydrofuran (10 ml) was added and the reaction stirred at 0° for ½ h and then at room temperature, until the reaction was complete. Dilution with water and extraction of the product into ether gave, after p.l.c. (50% ether/hexane), (*13*RS)-*13,14-epoxy-15-norlabd-8(17)-ene* (52) (3·6 g) as an oil, b.p. 70°/0·02 mm (Found: C, 82·7; H, 11·7. $C_{19}H_{32}O$ requires C, 82·5; H, 11·7%). ν_{max} 3080, 1640, 885 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·67, 0·80, 0·86, 1·26; 2·50, s, CH_2–O; 4·48, 4·81 ($=CH_2$). *m/z* 276 (M). Freshly redistilled boron trifluoride etherate (0·4 ml) was added dropwise to the epoxide (52) (2 g) in dry ether (30 ml) cooled to 0° in an ice/salt bath. After 5 min the reaction was quenched by the addition of ice-cold water. Ether extraction with usual workup gave, after p.l.c. (50% ether/hexane):

(A) At higher R_F: *15-norlabd-8(17)-en-14-al* (53) (0·6 g) as an oil, b.p. 68°/0·02 mm. ν_{max} 2700, 1725 (CHO); 3080, 1640, 890 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·66, 0·80, 0·86, 1·00, d, *J* 6 Hz; 4·50, 4·80 ($=CH_2$); 9·40, d, *J* 2 Hz, CHO. *m/z* 276 (M).

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(B) At lower R_F: *13*(RS)-*13-fluoro-15-norlabd-8(17)-en-14-ol* (27) (0·9 g) as an oil, b.p. 70°/0·02 mm (Found: C, 77·3; H, 11·5. $C_{19}H_{33}FO$ requires C, 77·0; H, 11·2%). ν_{max} 3500 (OH); 1055 (C–O); 3080, 1640, 890 cm^{-1} (C=CH$_2$). ^{1}H n.m.r.: methyls at δ 0·70, 0·80, 0·86, 1·32, d, $J_{H,F}$ 20 Hz; 3·57, d, $J_{H,F}$ 20 Hz, CH$_2$OH; 4·46, 4·76 (=CH$_2$). ^{13}C n.m.r.: 39·0, t, C1; 19·3, t, C2; 42·1, t, C3; 33·5, s, C4; 55·5, d, C5; 24·4, t, C6; 38·3, t, C7; 148·2, s, C8; 57·1, d, C9; 39·7, s, C10; 17·0, t, C11 ($^3J_{C,F}$ 5 Hz); 35·2, t, C12 ($^2J_{C,F}$ 22 Hz); 97·8, s, C13 ($^1J_{C,F}$ 168 Hz); 67·8, t, C14 ($^2J_{C,F}$ 25 Hz); 20·7, q, C16 ($^2J_{C,F}$ 27 Hz); 106·6, t, C17; 33·5, q, C18; 21·6, q, C19; 14·4, q, C20. *m/z* 296 (M), 281 (M − CH$_3$), 276 (M − HF). The fluoro alcohol (27) (0·15 g) in pyridine (1 ml) and acetic anhydride (1 ml) was stirred at room temperature overnight. Usual workup and p.l.c. (40% ether/hexane) gave (*13*RS)-*13-fluoro-15-norlabd-8(17)-en-14-yl acetate* (54) (0·15 g) as an oil, b.p. 72°/0·02 mm (Found: C, 74·6; H, 10·6. $C_{21}H_{35}FO_2$ requires C, 74·5; H, 10·3%). ν_{max} 1735, 1230 (OAc); 1045 (C–O); 3080, 1640, 890 cm^{-1} (C=CH$_2$). ^{1}H n.m.r.: methyls at δ 0·66, 0·76, 0·86, 1·33, d, $J_{H,F}$ 20 Hz, 2·00; 4·07, d, $J_{H,F}$ 20 Hz, CH$_2$OAc; 4·46, 4·80 (=CH$_2$). *m/z* 338 (M), 323 (M − CH$_3$), 318 (M − HF). The aldehyde (53) (0·5 g) in dry ether (20 ml) was refluxed with excess lithium aluminium hydride for 1 h. Usual workup and p.l.c. (50% ether/hexane) gave (*13*RS)-*15-norlabd-8(17)-en-14-ol* (24) (0·5 g) as an oil, b.p. 66°/0·005 mm (Found: C, 81·6; H, 12·1. $C_{19}H_{34}O$ requires C, 81·9; H, 12·3%). ν_{max} 3300 (OH); 1040 (C–O); 3080, 1640, 890 cm^{-1} (C=CH$_2$). ^{1}H n.m.r.: methyls at δ 0·70, 0·83, 0·86, 1·00, d, *J* 6 Hz; 3·47, m, $W_{h/2}$ 8 Hz, CH$_2$OH; 4·46, 4·76, (=CH$_2$). *m/z* 278 (M), 263 (M − CH$_3$), 260 (M − H$_2$O).

8(17)-En-15-ol Systems

Dry sodium iodide (3 g) was added to the mesylate (49) (1·5 g) in dry acetone (60 ml) and the reaction mixture refluxed for 2 h.[12] Usual workup and p.l.c. (10% ether/hexane) gave *13-iodo-14,15,16-trinorlabd-8(17)-ene* (55) (1·2 g) as an oil, b.p. 85°/0·03 mm (Found: C, 56·4; H, 8·2. $C_{17}H_{29}I$ requires C, 56·7; H, 8·1%). ν_{max} 3080, 1640, 888 cm^{-1} (C=CH$_2$). ^{1}H n.m.r.: methyls at δ 0·67, 0·80, 0·83; 3·06, t, *J* 6 Hz, CH$_2$–I; 4·50, 4·83 (=CH$_2$). *m/z* 360 (M), 345 (M − CH$_3$). Freshly distilled diethyl malonate (1·27 g) in dry tetrahydrofuran (5 ml) was added to a suspension of sodium hydride (0·2 g, 100%) in dry tetrahydrofuran (10 ml) and the reaction mixture refluxed for ½ h by which time there was no unchanged hydride. To this solution the iodo compound (55) (1·3 g) in dry tetrahydrofuran (5 ml) was added dropwise and the reaction mixture refluxed for 2 h. The sodium iodide was filtered off and washed with ether and the combined solvent portions (ether and tetrahydrofuran) were worked up in the usual way to give after p.l.c. (benzene) the *diethyl ester* (56) (0·9 g) as an oil, b.p. 75°/0·01 mm (Found: C, 73·2; H, 10·4. $C_{24}H_{40}O_4$ requires C, 73·5; H, 10·2%). ν_{max} 1735, 1200 (COO); 3080, 1640, 890 cm^{-1} (C=CH$_2$). ^{1}H n.m.r.: methyls at δ 0·66, 0·80, 0·83, 1·23 (2), t, *J* 7 Hz; 4·18 (2), q, *J* 7 Hz, CH$_2$–O); 4·46, 4·80 (=CH$_2$). *m/z* 392 (M), 377 (M − CH$_3$). The diester (56) (0·8 g) in dry ether (35 ml) was refluxed with excess lithium aluminium hydride for 1 h. Usual workup and p.l.c. (ether) gave the *diol* (32) (0·5 g) as an oil, b.p. 80°/0·01 mm (Found: C, 77·7; H, 11·5. $C_{20}H_{36}O_2$ requires C, 77·9; H, 11·8%). ν_{max} 3330 (OH); 1040 cm^{-1} (C–O). ^{1}H n.m.r.: methyls at δ 0·66, 0·80, 0·86; 3·70, d, *J* 7 Hz, CH$_2$–OH; 4·46, 4·80 (=CH$_2$). *m/z* 308 (M), 293 (M − CH$_3$).

Manool (3) (5·8 g) in dichloromethane (20 ml) was added dropwise to a stirred suspension of pyridinium chlorochromate[13] (19·6 g) in dichloromethane (75 ml) and the reaction mixture stirred at room temperature for 18 h.[14] The precipitate was washed with ether and the combined solvents (dichloromethane and ether) worked up in the usual way to give, after p.l.c. (30% ether/hexane), (*13*EZ)-*labda-8(17),13-dien-15-al* (57) (5 g) as an oil, ^{1}H n.m.r. and i.r. identical with reported data.[15] A mixture of iron pentacarbonyl (3·1 g) and sodium hydroxide (0·32 g) in methanol/water (10 ml, 19 : 1) was stirred under a nitrogen atmosphere until the sodium hydroxide dissolved. The aldehyde (57) (1·1 g) in methanol/water (5·0 ml, 19 : 1) was added and the reaction mixture stirred at room temperature for 12 h and heated to 60° for 2 h.[16] Excess

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reducing agent was removed by the addition of an ethereal solution of iodine. Dilution, ether extraction and usual workup gave, after p.l.c. (30% ether/hexane), *(13RS)-labd-8(17)-en-15-al* (58) (0·3 g), as an oil, b.p. 80°/0·02 mm. ν_{max} 2700, 1720 (CHO); 3080, 1640, 890 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·66, 0·80, 0·86, 0·96, d, *J* 6 Hz; 4·43, 4·76 ($=CH_2$); 9·63, t, *J* 2 Hz, CHO. *m/z* 290 (M). The aldehyde (58) (0·9 g) in dry ether (45 ml) was refluxed with excess lithium aluminium hydride for 1 h. Usual workup and p.l.c. (50% ether/hexane) gave *(13RS)-labd-8(17)-en-15-ol* (30) (0·75 g) as an oil, b.p. 80°/0·03 mm (Found: C, 82·1; H, 12·2. $C_{20}H_{36}O$ requires C, 82·1; H, 12·4%). ν_{max} 3400 (OH); 1050 (C–O); 3080, 1635, 885 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·66, 0·80, 0·86, 1·10, d, *J* 6 Hz; 3·55, m, CH_2O; 4·46, 4·74 ($=CH_2$). ^{13}C n.m.r.: 39·7, t, C 1; 19·4, t, C 2; 42·2, t, C 3; 33·6, s, C 4; 55·6, d, C 5; 24·5, t, C 6; 38·4, t, C 7; 148·8, s, C 8; 57·4, 57·1, d, C 9; 39·6, s, C 10; 20·9, t, C 11; 36·3, t, C 12; 30·3, 30·1, d, C 13; 39·1, t, C 14; 60·9, t, C 15; 20·9, 19·8, q, C 16; 106·2, t, C 17; 33·6, q, C 18; 21·7, q, C 19; 14·5, q, C 20. *m/z* 292 (M).

8(17)-En-12-ol Systems

Dry tetrahydrofuran (10 ml) and diisopropylamine (1·33 ml) were added to a dry flask purged with nitrogen and maintained under a nitrogen atmosphere. The mixture was cooled to −20° and butyllithium (5 ml, 2 M) in hexane was added in a controlled manner to prevent the temperature exceeding 0°. The acid (34) (1·05 g) in dry tetrahydrofuran (15 ml) was added dropwise while maintaining the reaction temperature below 0° and the reaction mixture stirred at −5° for 2 h. The crystalline complex, diperoxo(oxohexamethylphosphoramido)molybdenum(VI), was prepared according to Vedejs.[17] The molybdenum complex (2·5 g), incorporated into the reaction vessel prior to the preparation of the dianion, was added in one addition. After the molybdenum complex had dissolved, the reaction mixture was quenched by the addition of saturated sodium sulfite (20 ml) and allowed to reach room temperature.

Dilution with water and appropriate workup gave, after p.l.c. (60% ether/hexane), unchanged acid (34) (0·34 g) and *(12RS)-12-hydroxy-14,15,16-trinorlabd-8(17)-en-13-oic acid* (59) (0·57 g) as an oil, b.p. 120°/0·02 mm (Found: C, 73·4; H, 9·4. $C_{17}H_{26}O_3$ requires C, 73·3; H, 9·4%). ν_{max} 3400 (OH), 3300–2600, 1700 (COOH); 3080, 1640, 890 ($C{=}CH_2$) cm^{-1}. ^1H n.m.r.: methyls at δ 0·69, 0·82, 0·88; 4·23, m, $W_{h/2}$ 18 Hz, CHOH; 4·47, 4·65, 4·87 (2:7:9) ($=CH_2$). *m/z* 278 (M).

The hydroxy acid (59) (0·71 g) in dry ether (50 ml) was refluxed with excess lithium aluminium hydride for 1 h. Usual workup and p.l.c. (80% ether/hexane) gave *(12RS)-14,15,16-trinorlabd-8(17)-ene-12,13-diol* (40) (0·6 g) as an oil, b.p. 105°/0·02 mm (Found: C, 76·3; H, 11·5. $C_{17}H_{30}O_2$ requires C, 76·6; H, 11·4%). ν_{max} 3390 (OH); 1080, 1045 (C–O); 3080, 1640, 888 cm^{-1} ($C{=}CH_2$). ^1H n.m.r.: methyls at δ 0·68, 0·81, 0·88; 3·48, m, $W_{h/2}$ 34 Hz, CHOH, CH_2OH; 4·38, 4·67, 4·83 (4:7:11) ($=CH_2$). ^{13}C n.m.r.: 39·0, t, C 1; 19·3, t, C 2; 42·1, t, C 3; 33·5, s, C 4; 55·4, d, C 5; 24·4, t, C 6; 38·4, t, C 7; 149·0, s, C 8; 53·5, 52·1, d, C 9; 39·2, s, C 10; 27·5, t, C 11; 71·9, 70·7, d, C 12; 67·4, 66·4, t, C 13; 107·0, 106·4, t, C 17; 33·5, q, C 18; 21·7, q, C 19; 14·5, q, C 20. *m/z* 266 (M).

Sodium periodate (0·4 g) in water (7 ml) was added to the diol (40) (0·14 g) in methanol (20 ml) and the reaction mixture stirred at room temperature overnight. Usual workup and p.l.c. (20% ether/hexane) gave 13,14,15,16-tetranorlabd-8(17)-en-12-al (60) (0·1 g) as an oil, ^1H n.m.r. and i.r. identical with reported data.[8]

The aldehyde (60) (0·12 g) in dry ether (30 ml) was refluxed with excess lithium aluminium hydride for ½ h. Usual workup and p.l.c. (40% ether/hexane) gave 13,14,15,16-tetranorlabd-8(17)-en-12-ol (42) (0·09 g) as an oil, ^1H n.m.r. and i.r. identical with reported data.[8] ^{13}C n.m.r.: 39·2, t, C 1; 18·4, t, C 2; 42·3, t, C 3; 33·7, s, C 4; 55·6, d, C 5; 24·5, t, C 6; 38·3, t, C 7; 148·9, s, C 8; 53·0, d, C 9; 39·5, s, C 10; 27·2, t, C 11; 62·6, t, C 12; 106·4, t, C 17; 33·7, q, C 18; 21·8, q, C 19; 14·6, q, C 20.

The dianion of the acid (34) (1·1 g) in dry tetrahydrofuran (25 ml), prepared as above, was cooled to −78° and dry oxygen[18] passed through the solution for ½ h. The reaction mixture was concentrated under partial vacuum to about 5 ml, diluted with ether (20 ml) and poured onto dilute hydrochloric acid (50 ml). Usual workup and p.l.c. (60% ether/hexane) gave the aldehyde

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(60) (0·05 g), unchanged acid (34) (0·31 g) and the (12*RS*)-hydroxy acid (59) (0·59 g). An ethereal solution of diazomethane (prepared from *N*-nitrosomethylurea) was added dropwise to the acid (34) (1 g) in ether (50 ml) at 0° until gas evolution ceased and the solution remained a yellow colour. Excess diazomethane was destroyed by the careful addition of acetic acid. Usual workup gave *methyl 14,15,16-trinorlabd-8(17)-en-13-oate* (61) (0·94 g) as an oil, b.p. 75°/0·02 mm (Found: C, 77·5; H, 10·7. $C_{18}H_{30}O_2$ requires C, 77·6; H, 10·9%). ν_{max} 1735, 1180 (COOMe); 3080, 1638, 885 cm^{-1} (C=CH_2). ^1H n.m.r.: methyls at δ 0·68, 0·79, 0·86, 3·64; 4·50, 4·83 (=CH_2). *m/z* 278 (M).

The monoanion of the ester (61) (1·0 g) in dry tetrahydrofuran (25 ml) was prepared as above and dry oxygen passed through the solution at −78° for ½ h. Workup as before gave unchanged ester (61) (0·18 g), the hydroxy acid (59) (0·25 g) and *methyl* (*12*RS)-*12-hydroxy-14,15,16-trinorlabd-8(17)-en-13-oate* (62) (0·36 g) as an oil, b.p. 80°/0·03 mm (Found: C, 73·5; H, 10·4. $C_{18}H_{30}O_3$ requires C, 73·4; H, 10·3%). ν_{max} 3330 (OH); 1725, 1200 (COOMe); 3080, 1640, 890 cm^{-1} (C=CH_2). ^1H n.m.r.: methyls at δ 0·67, 0·80, 0·87, 3·60; 4·23, m, $W_{h/2}$ 15 Hz, CHOH; 4·42, 4·50, 4·83 (4:6:11), (=CH_2).

To the dianion of the acid (34) (1·05 g) in dry tetrahydrofuran (25 ml), prepared as before, was added diphenyl disulfide (1·75 g) in dry tetrahydrofuran (10 ml) and the reaction mixture stirred for a further 1 h.[19] Usual workup and p.l.c. (30% ether/hexane) gave unchanged acid (34) (0·3 g) and (*12*RS)-*12-phenylthio-14,15,16-trinorlabd-8(17)-en-13-oic acid* (63) (0·68 g) as an oil, b.p. 105°/0·02 mm (Found: C, 74·2; H, 8·5; S, 8·8. $C_{23}H_{32}O_2S$ requires C, 74·2; H, 8·6; S, 8·6%). ν_{max} 3400–2500, 1700 (COOH); 3080, 1640, 890 (C=CH_2); 1580, 735, 688 cm^{-1} (aromatic). ^1H n.m.r.: methyls at δ 0·68, 0·79, 0·81; 3·73, m, $W_{h/2}$ 18 Hz, S–CH–COOH; 4·15, 4·35 (=CH_2); 7·23, m, (aromatic). *m/z* 372 (M).

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