Functionalization of Methyl Groups in Isopimaran-8β-ol, Hopan-7α-ol, and Hopan-15β-ol and Derivatives

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Treatment of isopimaran-8β-ol and derivatives with 'long-range' oxidants has resulted in functionalization of the 10β- and 4β-methyl groups but not of the 13β-methyl group. Similar oxidation of hopan-7α-ol and hopan-15β-ol and their 21αH-epimers has led to functionalization of the 14α-, 18α-, and 8β-methyl groups.

THE diterpene alcohol isopimar-15-en-8β-ol from the leaf oil of *Dacrydium colensoi*[1] appeared to be a useful substrate for possible cyclization to tetracyclic diterpenoid structures *via* a C-8 carbocation and for studies of selective long-range functionalization of the 10β-, 13β-, and 4β-methyl groups. The results of the attempted cyclizations have been published;[2] the results of long-range functionalization studies are now reported.

The functionalization of angular methyl groups in di- and tri-terpenoid molecules by intramolecular free radical decomposition of certain alcohol derivatives has been the subject of a number of investigations.[3] Oxidation of alcohols by lead tetra-acetate, photolysis of nitrites, and thermolysis or photolysis of hypohalites have all been used for the functionalization of methyl groups in a 1,3-diaxial relation to the original hydroxy-function. Wenkert *et al.*[4] have reported the extension of the method to the functionalization of methyl groups at some distance from the hydroxy-group site. They consider that these long-range oxidations consist of two consecutive alkoxyl-radical-generated 1,5-hydrogen shifts and refer to this new synthetic method as a 'billiard reaction,' giving examples of both V-shaped and linear billiard shots.

Kitadani[5] has suggested structures (2) and (3), respectively, for an epoxide and an iodo-epoxide isolated from the oxidation of the alcohol (1) by lead tetra-acetate–iodine. The same epoxide has now been isolated from the oxidation of the alcohol (1) with silver acetate, mercury(II) acetate, potassium t-butoxide, and mercury(II) oxide under u.v. irradiation. The dominance of the fragments (a) and (b) in the mass spectra of (2) and (3) confirms the presence of an 8β,20-rather than an 8β,17-epoxide linkage in these compounds. Functionalization of the 13β-methyl group did not appear to occur in these reactions. Reduction of the iodo-epoxide (3) with lithium aluminium deuteride gave the deuterio-derivative (4), showing the expected lower intensity of the ^{1}H n.m.r. signal at δ 0·92 (Table 1). Photolysis of the nitrite ester (5) gave only the aldoxime (6). A vinylic group at C-13 did not effect the course of this reaction. Photolysis of the nitrite ester (8) gave the C-20 oxime (9). Both oximes (6) and (9) were converted into the hemiacetal (10).

The relationship of the 10β-methyl to the 8β-hydroxy-group is rigidly fixed by the carbon framework. The

[1] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (C), 1967, 300.

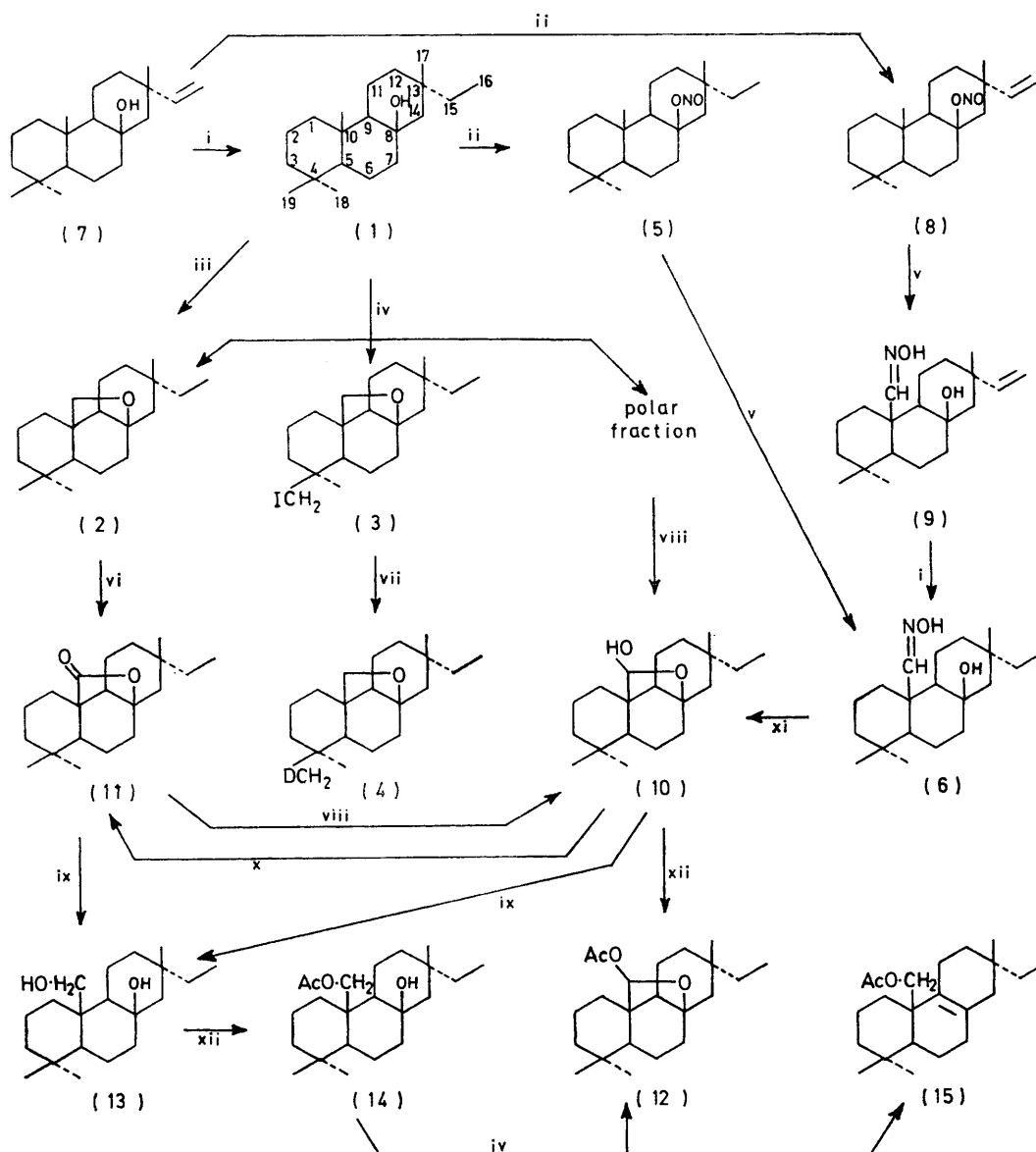[2] W. J. Chin, R. E. Corbett, D. R. Lauren, and R. A. J. Smith, *Austral. J. Chem.*, 1969, **22**, 2033.

[3] (a) M. Akhtar and D. H. R. Barton, *J. Amer. Chem. Soc.*, 1964, **86**, 1528; (b) C. Djerassi, 'Steroid Reactions,' Holden-Day San Francisco, 1963, p. 327 and references cited therein; (c) C. Meystre, K. Heusler, J. Kaluoda, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, 1962, **45**, 1317.

[4] E. Wenkert and B. L. Mylari, *J. Amer. Chem. Soc.*, 1967, **89**, 174.

[5] M. Kitadani, *Nippon Kagaku Zasshi*, 1970, **91**, 664.

apparent lack of reactivity of the 13β-methyl group suggests that it is not in a true 1,3-diaxial relation to the 8β-hydroxy-group. Rings A and C are more flexible

ization of the 4β-methyl group indicates that ring A does not deviate significantly from a chair conformation. Ring C, on the other hand, must be appreciably flattened,

SCHEME i, H_2–Pt; ii, NOCl–C_5H_5N; iii, HgO–I_2,hv, or KOBu^t–I_2,hv, or Hg(OAc)$_2$–I_2,hv, or AgOAc–I_2,hv; iv, Pb(OAc)$_4$–I_2; v, hv; vi, CrO$_3$–Ac$_2$O–HOAc–H_2O, 100 °C; vii, LiAlD$_4$; viii, LiAlH$_4$–Et$_2$O, 20 °C; ix, LiAlH$_4$–[CH$_2$]$_4$O, 64 °C; x, Jones reagent; xi, HCl–MeOH–H_2O; xii, Ac$_2$O–C_5H_5N

than ring B and any distortion or flattening of these rings would affect the 13β-methyl group, which is two carbon atoms removed from the ring junction, more

(a) m/e 191   (b) m/e 178
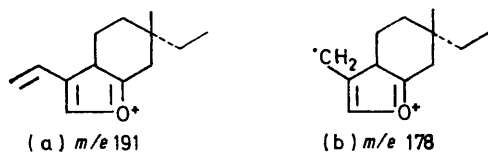
than the 4α- and 4β-methyl groups which are one carbon atom removed. The over-oxidative functional-

thus moving the 13β-methyl group away from its theoretical 1,3-diaxial relation to the 8β-hydroxy-group.

In our hands the oxidation of the alcohol (1) by lead tetra-acetate–iodine gave a polar fraction which on reduction with lithium aluminium hydride afforded the hemiacetal (10). The independent preparation of (10) by the sequence (2) ⟶ (11) ⟶ (10) (Scheme) established its structure and the elimination of formic acid in the mass spectral fragmentation of this compound is also consistent with its formulation as a hemiacetal. The most favourable configuration for (10) would be

that with the 20R-orientation. The hydroxy-group in the 20S-epimer would be subject to steric interaction from the 4β-methyl group. In any case reduction of the lactone (11) by metal hydride would be expected to give the less hindered 20R-epimer. The ease with which acetylation gives the hemiacetal acetate (12) supports the 20R assignment.

Reduction of (10) or (11) by lithium aluminium hydride in refluxing tetrahydrofuran gave the diol (13), which showed a mass spectrum consistent with its structure. Protective acetylation of the primary alcohol group of the diol followed by oxidation with lead tetra-acetate–iodine gave a hemiacetal acetate and the dehydration product (15). This method of preparation would be expected to give the hemiacetal isomer in which the most bulky group occupies the least hindered position, and the product was in fact identical with (12). This appears to be the first report of a long-range oxidation at an oxidized angular methyl group. It proceeds with retention of the original functionality.

The methyl assignments in the ^{1}H n.m.r. spectra of compounds (1)—(15) are listed in Table 1. 8β,20-

TABLE 1

	Methyl group resonances (δ values)			
Compound	4α-	4β-	10β-	13β-
Isopimar-15-en-8β-ol (7)	0·85	0·85	0·99	1·21
Isopimaran-8β-ol (1)	0·85	0·85	0·97	1·05
8β,20-Epoxyisopimarane (2)	0·88	0·91		0·95
8β,20-Epoxy-19-iodoisopimarane (3)	1·03			0·94
19-Deuterio-8β,20-epoxyisopimarane (4)	0·88	0·92*		0·95
8β,20-Epoxyisopimaran-19-ol	1·06			0·97
(20R)-8β,20-Epoxyisopimaran-20-ol (10)	0·88	0·89		1·04
(20R)-20-Acetoxy-8β,20-epoxyisopimarane (12)	0·95	1·00		1·03
Isopimaran-8β,20-olide (11)	0·89	0·89		0·93
Isopimarane-8β,20-diol (13)	0·90	1·02		1·09
20-Acetoxyisopimaran-8β-ol (14)	0·87	0·89		1·06
20-Acetoxyisopimar-8-ene (15)	0·88	0·88		0·96
Isopimaran-8β-yl nitrite (5)	0·86	0·86	0·99	1·06
Isopimar-15-en-8β-yl nitrite (8)	0·86	0·86	1·00	1·23
8β-Hydroxyisopimaran-20-al oxime (6)	0·88	0·72		1·06
8β-Hydroxyisopimar-15-en-20-al oxime (9)	0·88	0·75		1·23

* CH$_2$D.

Epoxyisopimaran-19-ol, which is included in the Table, was prepared from the iodo-derivative (3). The assignments follow from arguments already outlined here and from the recognition of usual substituent chemical shift effects, for example the downfield shift of ca. 0·17 p.p.m. of the 13β-methyl signal in the compounds with a 13α-vinyl group [(7)—(9)].

Extension of these long-range functionalization studies to hopan-7α-ol[6] (16) and hopan-15β-ol[7] (18) and their 21α-H-epimers (17)[6] and (19),[7] respectively, was expected to give useful information about the possibilities of methyl group functionalization in the hopane skeleton. As the 8β-, 10β-, and 4β-methyl groups are sited in consecutive 1,3-diaxial relations with the 15β-hydroxy-group there was the possibility

that products resulting from three consecutive 1,5-hydrogen shifts might be isolated.

(16) 21βH
(17) 21αH

(18) 21βH
(19) 21αH

(20) 21βH
(21) 21αH

(22) 21βH
(23) 21αH

(24) 21βH
(25) 21αH

(26) 21βH
(27) 21αH

(28)

(29)

Oxidation of the four alcohols with lead tetra-acetate–iodine gave mixtures of products which were separated by preparative t.l.c. on silica gel. In each case the major product, $C_{30}H_{50}O$, was an epoxide and showed only five of the six tertiary methyl group signals usually present in the ^{1}H n.m.r. spectra of hopane derivatives. Over-oxidation products were isolated from the oxidation of the 7α-ols (16) and (17) only. With the 15β-ols (18) and (19), a number of unidentified minor products were isolated, but surprisingly all gave negative results in tests for iodine and were not further investigated.

The structures (20)—(23) assigned to the oxidation products followed from a study of the methyl signals in the ^{1}H n.m.r. spectra of these compounds and were confirmed by an analysis of the low-field proton signals.

The five tertiary methyl group signals of the epoxides can be readily assigned (Table 2) by comparison with the

[6] R. E. Corbett, R. A. J. Smith, and H. Young, J. Chem. Soc. (C), 1968, 1823.
[7] R. E. Corbett and R. A. J. Smith, J. Chem. Soc. (C), 1969, 44.

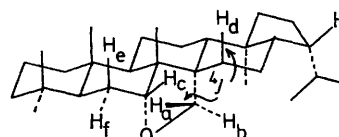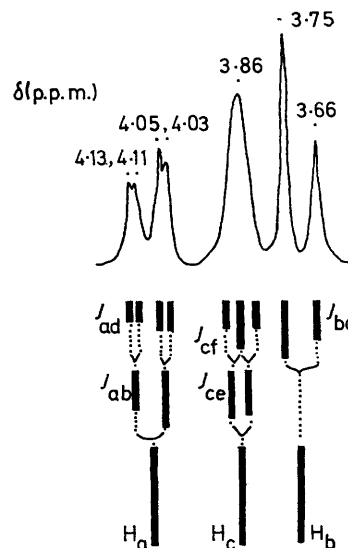methyl group resonances of hopane and 21α-*H*-hopane.[8] The formation of an epoxide linkage between an angular

long-range-coupled AB patterns, the coupling in epoxides (22) and (23) being between the 7β- and 26-*pro-S* protons. The assignments made for the low-field proton signals from the four epoxides are listed in Table 3.

TABLE 2
Methyl resonances (δ values)

Compound	4β-	4α-	10β-	8β-	14α-	18α-
Hopane	0·78	0·81	0·84	0·94	0·94	0·69
7α,27-Epoxyhopane (20)	0·80	0·84	0·84	0·94		0·65
7α,27-Epoxy-28-iodo-hopane (24)	0·80	0·85	0·85	0·95		
15β,26-Epoxyhopane (22)	0·80	0·85	0·85		0·92	0·73
21α*H*-Hopane	0·78	0·81	0·84	0·95	0·92	0·64
7α,27-Epoxy-21α*H*-hopane (21)	0·80	0·84	0·84	0·94		0·62
7α,27-Epoxy-28-iodo-21α*H*-hopane (25)	0·79	0·85	0·85	0·95		
15β,26-Epoxy-21α*H*-hopane (23)	0·80	0·85	0·85		0·91	0·68

methyl group and a 1,3-diaxial-related hydroxy group does not introduce significant additional strain or steric compression into the hopane framework and the close similarity between the methyl resonances of the epoxide and the parent hopane is not unexpected. The only significant variations from the methyl resonances of the parent structures are in the 18α-methyl resonances in the 15β,26-epoxides (22) and (23), where the anisotropic effects of the epoxide oxygen atoms deshield the 18α-methyl groups by about 0·04 p.p.m. The methyl resonances of the iodo-epoxides (24) and (25) were similar to those of the epoxides (20) and (21) (Table 2) except that the high field 18α-methyl signal had been replaced by a quartet [δ 2·87, 2·97, 3·09, and 3·21 (2H, CH_2I)] indicating that functionalization of this group had occurred.

The analysis of the signals in the region δ 3·60—4·20 in the [1]H n.m.r. spectrum of 7α,27-epoxyhopane (20) is illustrated in the Figure. Decoupling experiments

Partial [1]H n.m.r. spectrum of 7α,27-epoxyhopane (20)

The iodo-compounds (24) and (25) were unstable in air and decomposed to give brown products even when

TABLE 3
Low-field proton resonances (δ values)

Epoxide	Singlet		Doublet		Quartet	
(20)	7β-	3·86	27-*pro-S*-	3·65, 3·75	27-*pro-R*-	4·03, 4·05, 4·11, 4·13
(21)	7β-	3·85	27-*pro-S*-	3·63, 3·72	27-*pro-R*-	4·02, 4·04, 4·10, 4·12
(22)	15α-	3·86	26-*pro-R*-	3·68, 3·77	26-*pro-S*-	4·01, 4·03, 4·10, 4·12
(23)	15α-	3·82	26-*pro-R*-	3·68, 3·76	26-*pro-S*-	4·03, 4·05, 4·12, 4·14
Average coupling	$W_{\frac{1}{2}}$ 5 Hz		9 Hz (O·HCH)		9 Hz (O·HCH); 2 Hz ([4]J)	

established that the doublet at δ 3·66 and 3·75 (1H) was coupled to the quartet at δ 4·03, 4·05, 4·11, and 4·13 (1H). This permitted the assignment of the broadened singlet at δ 3·86 (1 H, $W_{\frac{1}{2}}$ 5 Hz) to the 7β-proton. Molecular models of (20) indicate that the 27-*pro-R* proton only is suitably oriented for highly stereospecific coplanar W-coupling[9] and this must be with the 15β-proton. The sharp doublet (δ 3·66, 3·75) is therefore produced by the 27-*pro-S* proton, while the more hindered long-range-coupled 27-*pro-R* proton resonates at lower field as a quartet. These assignments are consistent with the anisotropic effects of the adjacent oxygen.[10] All four epoxides gave similar

stored in a vacuum desiccator. Satisfactory analyses could not be obtained for these compounds but they could be hydrolysed to the stable alcohols (26) and (27).

Dehydration of the parent alcohol is usually observed to some extent in lead tetra-acetate–iodine oxidations. In the experiments with each of the four hopanols, hydrocarbon fractions (*ca.* 10%) were isolated, but not further investigated.

[8] R. E. Corbett and C. K. Heng, *J. Chem. Soc.* (C), 1971, 1885.
[9] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 115.
[10] Ref. 9, p. 187.

Hemiacetal and related lower R_F value products are invariably formed in up to 25% yield in lead tetra-acetate–iodine oxidations. Although polar products were isolated in the present investigation the complex mixtures could not be separated into identifiable products. Reduction of the polar fraction from the oxidation of (17) with lithium aluminium hydride under reflux in ether gave as the major product a diol assigned structure (28). When the reaction was carried out at room temperature the major product was the hemiacetal which is given the least hindered structure (29). When (29) was heated under reflux in ether with lithium aluminium hydride it gave the diol (28). Identifiable products could not be isolated from similar treatment of the polar fractions from the oxidations of the other three hopanols.

EXPERIMENTAL

Experimental procedures are as described in ref. 7.

Oxidation of Isopimaran-8β-ol (1) *with Lead Tetra-acetate–Iodine.*—A mixture of dry lead tetra-acetate (1·0 g), iodine (300 mg), and calcium carbonate (1·0 g) in benzene (20 ml) was heated under reflux with stirring in an atmosphere of nitrogen for 10 min. A solution of the alcohol (1) (250 mg) in benzene (5 ml) was added and refluxing was continued for a further 3 h. The mixture was filtered, washed with aqueous sodium thiosulphate solution, then with water, and evaporated under reduced pressure. Separation of the products by multiple preparative layer chromatography (p.l.c.) (×2) on silica gel with E–H (1 : 49) gave in order of decreasing R_F value, a hydrocarbon fraction (20 mg), compounds (2) (90 mg) and (3) (22 mg), and a polar fraction (80 mg). The hydrocarbon fraction was shown by t.l.c. on silver nitrate impregnated silica gel to consist of a major (highest R_F) and two minor components. From the work of Chin *et al.*[2] it is probable that these were isopimar-8-ene, isopimar-7-ene, and isopimar-8(14)-ene, in order of decreasing R_F value. 8β,20-Epoxyisopimarane (2) had m.p. 33—35° (lit.,[5] 33—35°); $\nu_{max.}$ 1011 (C–O–C) and 819 cm⁻¹; δ 3·85 (2H, q, O·CH₂); *m/e* 290 (*M*⁺, 100%), 191, and 178 (Found: C, 82·4; H, 11·7. Calc. for C₂₀H₃₄O: C, 82·7; H, 11·8%). 8β,20-Epoxy-19-iodoisopimarane (3) had m.p. 103—104° (from hexane–ethanol) (lit.,[5] 104·5—105·5°); $\nu_{max.}$ 1010 (C–O–C) and 821 cm⁻¹; δ 3·53 (2H, q, CH₂I) and 3·83 (2H, q, O·CH₂); *m/e* 416 (*M*⁺, 100%), 289, 191, and 178.

The polar fraction (80 mg) in ether (20 ml) was refluxed with an excess of lithium aluminium hydride (LAH) for 2 h. The excess of reagent was destroyed with wet ether and the mixture worked up in the usual way. P.l.c. on silica gel with E–H (1 : 3) gave (20R)-8β,20-*epoxyisopimaran-20-ol* (10) (25 mg), m.p. 86—88° (sublimed sample); $\gamma_{max.}$ 3300 (OH), 1015 (C–O–C), 952, and 820 cm⁻¹; δ 5·46 (1H, s, O·CH·OH); *m/e* 306·2560 (*M*⁺, 100%), 260·2504 (*M*⁺ − HCO₂H), and 245·2270 (Found: C, 78·2; H, 11·4. C₂₀H₃₄O₂ requires C, 78·4; H, 11·2%).

Repetition of the oxidation with cyclohexane as solvent and u.v. irradiation of the reaction mixture did not increase the yield of iodo-epoxide (14).

Oxidation of isopimaran-8β-ol (1) with mercury(II) oxide–iodine,[3a] potassium t-butoxide,[3a] mercury(II) acetate–calcium carbonate–iodine,[3b,c] and silver acetate–iodine[3b,c] by the usual methods, gave in each case 8β,20-epoxyisopimarane in good yield as the only identifiable product.

19-Deuterio-8β,20-epoxyisopimarane (4).—A solution of 8β,20-epoxy-19-iodoisopimarane (3) (20 mg) in ether (10 ml) was heated at reflux temperature with lithium aluminium deuteride (30 mg) for 10 h. The excess of reagent was destroyed with wet ether and after washing with water the solvent was removed under reduced pressure. Sublimation of the product gave 19-deuterio-8β,20-epoxy-isopimarane (4) (10 mg), δ 3·84 (2H, q, O·CH₂).

8β,20-Epoxyisopimaran-19-ol.—A solution of 8β,20-epoxy-19-iodoisopimarane (3) (20 mg) in ethanolic 20% potassium hydroxide (10 ml) was refluxed for 6 h, diluted with water (100 ml), and worked up in the usual way. P.l.c. on silica gel with E–H (1 : 3) gave 8β,20-*epoxyisopimaran-19-ol* (11 mg), m.p. 115—116° (sublimed sample); $\nu_{max.}$ 3320 (OH) and 1011 cm⁻¹ (C–O–C); δ 3·35—4·16 (4H, overlapping q, CH₂·OH and O·CH₂) (Found: C, 78·7; H, 11·0. C₂₀H₃₄O₂ requires C, 78·4; H, 11·2%).

(20R)-20-Acetoxy-8β,20-epoxyisopimarane (12).—A solution of (20R)-8β,20-epoxyisopimaran-20-ol (10) (30 mg) in pyridine (5 ml) was stirred with acetic anhydride (5 ml) for 24 h at room temperature. The mixture was worked up in the usual way and the product dissolved in benzene and filtered through alumina (2 g) to give as a wax, the *acetate* (12) (30 mg), $\nu_{max.}$ 1740, 1225 (OAc), 1020, 958, and 821 cm⁻¹; δ 2·10 (3H, s, OAc) and 6·12 (1H, s, O·CH·-OAc) (Found: C, 75·6; H, 10·4. C₂₂H₃₆O₃ requires C, 75·6; H, 10·4%).

Isopimaran-8β,20-olide (11).—(*a*) A solution of (20R)-8β,20-epoxyisopimaran-20-ol (10) (25 mg) in acetone (20 ml) was stirred with a slight excess of Jones reagent for 5 min at room temperature and worked up in the usual way. P.l.c. on silica gel with E–H (1 : 9) gave isopimaran-8β,20-olide (11) (20 mg), m.p. 124—126° (lit.,[5] 125·5—126·5°); $\nu_{max.}$ 1755 (C=O) and 1125 cm⁻¹ (CO–O–C) (Found: C, 78·7; H, 10·6. Calc. for C₂₀H₃₂O₂: C, 78·9; H, 10·6%).

(*b*) A solution of 8β,20-epoxyisopimarane (2) (200 mg) in acetic anhydride (10 ml) was heated to 100° and a solution of chromium trioxide (250 mg) in glacial acetic acid (9 ml) and water (1 ml) was added dropwise over 30 min. After heating for a further 1 h at 100° the mixture was cooled and the excess of oxidant destroyed with ethanol (1 ml). The usual work-up and purification by p.l.c. on silica gel with E–H (1 : 9) gave isopimaran-8β,20-olide (11) (130 mg), identical (t.l.c., i.r. spectrum, m.p., and mixed m.p.) with the sample from (*a*).

Isopimarane-8β,20-diol (13).—A solution of (20R)-8β,20-epoxyisopimaran-20-ol (10) (100 mg) in redistilled tetrahydrofuran (25 ml) was refluxed with an excess of LAH for 6 h and worked up in the usual way. P.l.c. on silica gel with E–H (3 : 2) gave *isopimarane-8β,20-diol* (13) (75 mg), m.p. 154—155° (sublimed sample); $\nu_{max.}$ 3540 and 3240 cm⁻¹ (OH); δ 3·78 (2H, q, CH₂·OH); *m/e* 308 (*M*⁺), 290, 277, 260 (100%), and 245 (Found: C, 78·0; H, 11·9. C₂₀H₃₆O requires C, 77·9; H, 11·8%).

Reduction of isopimaran-8β,20-olide (11) and (20R)-20-acetoxy-8β,20-epoxyisopimarane (12) with LAH in tetrahydrofuran in the manner described above gave in each case isopimarane-8β,20-diol (13).

20-Acetoxyisopimaran-8β-ol (14).—A solution of isopimarane-8β,20-diol (13) (90 mg) in pyridine (5 ml) was stirred with acetic anhydride (5 ml) for 6 h at room temperature and worked up in the usual way. The product in ether was filtered through alumina (3 g) to give 20-*acetoxyisopimaran-8β-ol* (14) (88 mg), m.p. 94—96° (sublimed sample); $\nu_{max.}$ 3520 (OH), 1730, and 1235 cm⁻¹ (OAc);

δ 2·05 (3H, s, OAc) and 4·57 (2H, q, CH_2·OAc) (Found: C, 75·2; H, 10·8. $C_{22}H_{38}O_3$ requires C, 75·4; H, 10·9%).

Isopimaran-8β-yl Nitrite (5).—Nitrosyl chloride was passed into a solution of isopimaran-8β-ol (2) (300 mg) in pyridine (30 ml) until a brown colour persisted. Nitrogen was passed into the mixture for 10 min to remove the excess of nitrosyl chloride and the solution was diluted with hexane (40 ml). After washing (2N-HCl and water) the product in hexane was filtered through Florisil (10 g) and the solvent removed under reduced pressure at 30° to give an unstable oil (300 mg). Isopimaran-8β-yl nitrite (5) had $v_{max.}$ 1620 (N–O), 785, 753, and 728 cm^{-1} (ONO).

Photolysis of Isopimaran-8β-yl Nitrite (5).—A solution of isopimaran-8β-yl nitrite (5) (250 mg) in redistilled benzene (20 ml) was irradiated under nitrogen at 20°. After 2 h the solvent was removed under reduced pressure and the products separated by p.l.c. on silica gel with E–H (2 : 3) to give, in order of decreasing R_F value, isopimaran-8β-ol (2) (25 mg), 8β-*hydroxyisopimaran-20-al oxime* (6) (173 mg), and a minor product (5 mg). The oxime (6) had m.p. 119—121° (from hexane–acetone); $v_{max.}$ 3470, 3210 (OH), and 1695 cm^{-1} (C=N); δ 7·55 (1H, s, CH=N·OH); m/e 321 (M^+), 303, 286 (100%), 260, 256, 244, and 154 (Found: M^+, 321·2658. $C_{20}H_{35}NO_2$ requires M, 321·2657). The minor product, an isomeric oxime, had m.p. 115—117° (from acetone–hexane); $v_{max.}$ 3520, 3250 (OH), 1695 cm^{-1} (C=N) (Found: M^+, 321·2656).

Isopimar-15-en-8β-yl Nitrite (8).—Nitrosyl chloride was passed into a solution of isopimar-15-en-8β-ol (7) (300 mg) in pyridine (30 ml) until a brown colour persisted. Nitrogen was passed into the mixture for 10 min to remove the excess of nitrosyl chloride and the solution was diluted with hexane (40 ml). After washing (2N-HCl and water) the product, in hexane, was filtered through Florisil (10 g) and the solvent removed under reduced pressure (at 30°) to give an unstable oil (295 mg). Isopimar-15-en-8β-yl nitrite (8) had $v_{max.}$ 3080, 990, 910 (–CH=CH$_2$), 1640 (C=C), 1620 (N–O), 785, 753, and 738 cm^{-1} (ONO); δ 4·79 (1H, q, CH=HCH), 4·94 (1H, q, CH=HCH), and 5·72 (1H, q, CH=CH$_2$).

Photolysis of Isopimar-15-en-8β-yl Nitrite (8).—A solution of isopimar-15-en-8β-yl nitrite (8) (250 mg) in redistilled benzene (20 ml) was irradiated under nitrogen at 20°. After 2 h the solvent was removed under reduced pressure and the products separated by p.l.c. on silica gel with E–H (2 : 3) to give, in order of decreasing R_F value, isopimar-15-en-8β-ol (7) (23 mg), 8β-*hydroxyisopimar-15-en-20-al oxime* (9) (180 mg), and a minor product (4 mg). The oxime (9) had m.p. 95—97° (from hexane–acetone); $v_{max.}$ 3470, 3240 (OH), 3080, 980, 905 (CH=CH$_2$), and 1690 cm^{-1} (C=N); δ 4·78 (1H, q, CH=HCH), 4·84 (1H, q, CH=HCH), 5·72 (1H, q, CH=CH$_2$), and 7·58 (1H, s, CH=N·-OH); m/e 319 (M^+), 302, 301, 283 (100%), and 154 (Found: M^+, 319·2512. $C_{20}H_{33}NO_2$ requires M, 319·2511). The minor product, an isomeric oxime, had m.p. 93—94° (from hexane–acetone); $v_{max.}$ 3570, 3250 (OH), 3080, 975, 905 (CH=CH$_2$), 1695 (C=N), and 1635 cm^{-1} (C=C).

Hydrogenation of 8β-Hydroxyisopimaran-15-en-20-al Oxime (9).—A solution of the oxime (9) (150 mg) in ethyl acetate (25 ml) was hydrogenated over Adams catalyst for 15 min (1·0 mol. equiv. uptake). Filtration and removal of the solvent gave 8β-hydroxyisopimaran-20-al oxime (6) (150 mg), identical (t.l.c., i.r., and n.m.r. spectra) with the sample isolated from the photolysis of (5).

Acidic Rearrangement of 8β-Hydroxyisopimaran-20-al

Oxime (6).—A solution of the oxime (6) (200 mg) in water–acetone (1 : 5) (30 ml) was stirred with concentrated hydrochloric acid (0·4 ml) at room temperature. After 2 h, crystallization of the product commenced. Stirring was continued for a further 8 h and after the addition of water (20 ml) the mixture was filtered and the product (155 mg) recrystallized from acetone–hexane to give (20R)-8β,20-epoxyisopimaran-20-ol (10) (140 mg), identical (t.l.c., i.r. spectrum, m.p., and mixed m.p.) with an authentic sample.

Oxidation of 20-Acetoxyisopimaran-8β-ol (14) *with Lead Tetra-acetate–Iodine.*—Oxidation of the alcohol (14) (60 mg) in the usual way and separation of the products by p.l.c. on silica gel with E–H (1 : 19) gave 20-*acetoxyisopimar-8-ene* (15) (18 mg), (20R)-20-acetoxy-8β,20-epoxyisopimarane (12) (34 mg), and a minor product (3 mg) of low R_F value. Compound (15) (of highest R_F value) was a waxy substance, $v_{max.}$ 1735, 1230 (OAc), 965, 908, and 824 cm^{-1}; δ 2·04 (3H, s, OAc) and 4·64 (2H, q, CH_2·OAc) (Found: C, 79·3; H, 10·6. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9%). (20R)-20-Acetoxy-8β,20-epoxyisopimarane (12), (medium R_F value) was identical (t.l.c., i.r., and n.m.r. spectra) with the sample prepared by acetylation of (20R)-8β,20-epoxyisopimaran-20-ol (10).

Oxidation of Hopan-7α-ol (16) *with Lead Tetra-acetate–Iodine.*—Oxidation of the alcohol (16)[6] (300 mg) in the usual way and separation of the products by p.l.c. on silica gel with E–H (1 : 49) gave, in order of decreasing R_F value, a mixture of hydrocarbons (30 mg), compounds (20) (105 mg) and (24) (32 mg), and a polar fraction (60 mg). 7α,27-*Epoxyhopane* (20) had m.p. 201—203° (sublimed sample); $v_{max.}$ 1036 cm^{-1} (C–O–C); m/e 426 (M^+), 395, (100%), 257, 204, 202, 191, 189, and 187 (Found: C, 84·6; H, 11·8. $C_{30}H_{50}O$ requires C, 84·4; H, 11·9%). 7α,27-Epoxy-28-iodohopane (24) gave a positive result in a test for iodine and had $v_{max.}$ 1038 and 1020 cm^{-1} (C–O–C). This compound could not be crystallized or analysed and on storage gave a brown wax. The polar fraction had $v_{max.}$ 3340 (OH), 1740, 1240 (OAc), and 1040 cm^{-1} (C–O–C). Jones oxidation of the mixture gave a complex mixture of products with overlapping R_F values, which was not further investigated.

7α,27-*Epoxyhopan-28-ol* (26).—A solution of 7α,27-epoxy-28-iodohopane (24) (15 mg) in ethanolic 15% potassium hydroxide (15 ml) was refluxed for 6 h, diluted with water (100 ml), and worked up in the usual way. P.l.c. on silica gel with E–H (1 : 3) gave 7α,27-*epoxyhopan-28-ol* (26) (8 mg), m.p. 234—235° (sublimed sample); $v_{max.}$ 3450 (OH) and 1040 cm^{-1} (C–O–C) (Found: C, 81·3; H, 11·2. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

Oxidation of 21αH-Hopan-7α-ol (17) *with Lead Tetra-acetate–Iodine.*—Oxidation of the alcohol (17)[6] (450 mg) in the usual way and separation of the products by p.l.c. on silica gel with E–H (1 : 49) gave, in order of decreasing R_F value, a mixture of hydrocarbons (48 mg), compounds (21) (220 mg) and (25) (65 mg), and a polar fraction (130 mg). 7α,27-*Epoxy-21αH-hopane* (21) had m.p. 179—180° (sublimed sample); $v_{max.}$ 1042 cm^{-1} (C–O–C); m/e 426 (M^+), 395 (100%), 257, 204, 202, 191, 189, and 187 (Found: C, 84·2; H, 11·5. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). 7α,27-Epoxy-28-iodo-21αH-hopane (25) gave a positive result in a test for iodine and had $v_{max.}$ 1040 and 1018 cm^{-1} (C–O–C). This compound could not be crystallized or analysed and on storage gave a brown wax.

The polar fraction had $v_{max.}$ 3360 (OH), 1740, 1230 (OAc),

and 1045 cm^{-1} (C–O–C). Reduction of a portion of the polar fraction (60 mg) with an excess of LAH in refluxing tetrahydrofuran for 3 h gave a complex mixture. Separation by multiple (×3) p.l.c. on silica gel with E–H (2 : 3) gave as the major component 21αH-*hopane*-7α,28-*diol* (28) (15 mg), m.p. 247° (sublimed sample); $v_{max.}$ 3490 cm^{-1} (OH) (Found: C, 81·8; H, 10·8. $C_{30}H_{52}O_2$ requires C, 81·8; H, 11·0%).

Reduction of a portion of the polar fraction (60 mg) with an excess of LAH in ether at room temperature for 3 h gave a mixture separated by multiple (×3) p.l.c. on silica gel with E–H (1 : 9). The major product, 7α,27-*epoxy*-21αH-*hopan*-27-*ol* (29) (12 mg) had m.p. 220—222° (from acetone); $v_{max.}$ 3480 cm^{-1} (OH) (Found: C, 81·2; H, 11·2. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

Reduction of (29) with an excess of LAH in refluxing tetrahydrofuran gave (28).

7α,27-*Epoxy*-21αH-*hopan*-28-*ol* (27).—A solution of 7α,27-epoxy-28-iodo-21αH-hopane (25) (15 mg) in ethanolic 15% potassium hydroxide (15 ml) was refluxed for 6 h, diluted with water (100 ml), and worked up in the usual way. P.l.c. on silica gel with E–H (1 : 3) gave 7α,27-*epoxy*-21αH-*hopan*-28-*ol* (27) (9 mg), m.p. 252—254° (sublimed sample); $v_{max.}$ 3440 (OH) and 1040 cm^{-1} (C–O–C) (Found: C, 81·2; H, 11·6. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

Oxidation of Hopan-15β-*ol* (18) *with Lead Tetra-acetate–Iodine.*—Oxidation of the alcohol (18) [7] (250 mg) in the usual way and separation of the products by multiple (×3) p.l.c. on silica gel with E–H (1 : 49) gave a mixture of hydrocarbons (45 mg), compound (22) (30 mg), and a polar fraction (55 mg). 15β,26-*Epoxyhopane* (22) had m.p. 203—204° (sublimed sample); $v_{max.}$ 1045 cm^{-1} (C–O–C) (Found: C, 84·5; H, 11·7. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). T.l.c. indicated the presence of at least five minor products with R_F values slightly less than that of the epoxide (22). Less than 5 mg of each of these products was estimated to be present, and they could not be isolated in sufficient quantities for characterization.

Oxidation of 21αH-*Hopan*-15β-*ol* (19) *with Lead Tetra-acetate–Iodine.*—Oxidation of the alcohol (19) [7] (250 mg) in the usual way and separation of the complex mixture by multiple (×3) p.l.c. on silica gel with E–H (1 : 49) gave a mixture of hydrocarbons (40 mg), compound (23) (88 mg) and a polar fraction. 15β,26-*Epoxy*-21αH-*hopane* (23) had m.p. 210—211° (sublimed sample); $v_{max.}$ 1045 cm^{-1} (C–O–C) (Found: C, 84·3; H, 11·6. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).