Lichens and Fungi. Part IX.[1] 17α*H*-Hopane and 17α*H*-Moretane and their Derivatives

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17α*H*-Hopane and the C-21 epimer 17α*H*-moretane have been synthesized. The methyl resonances in the ^{1}H n.m.r. spectra of these compounds and some of their derivatives have been assigned.

THE triterpene 17α*H*-hopane † (12) has been synthesized by Tsuda and his co-workers,[3] but the C-21 epimer 17α*H*-moretane (8) has not been reported. Recently it became necessary to prepare both of these compounds in order to compare their physical and spectral characteristics with those of hydrocarbons obtained as degradation products from certain lichen triterpenes. The route developed permitted the concurrent synthesis of both hydrocarbons (Scheme).

The starting substance was 22,29,30-trisnor-21-oxo-17α*H*-hopane (1), which was readily obtained from the lichen triterpenoid 7β-acetoxy-22-hydroxyhopane by a series of standard degradative steps.[4] The transformations leading to both 17α*H*-moretane and 17α*H*-hopane are outlined in the Scheme. Alkenylation of compound (1) by the Wittig method gave two isomeric alkenes (2a and b), which have been named 29-nor-17α*H*-hop-21-ene-(A) and 29-nor-17α*H*-hop-21-ene-(B). These isomers were readily separated by preparative layer chromatography (p.l.c.) on silver bitrate-impregnated silica gel, but it has not proved possible to distinguish their structures on the basis of ^{1}H n.m.r. data. The Grignard method was used to convert compound (4) into the olefin (7) rather than the Wittig method, because the basic conditions of the Wittig reaction could cause isomerization of the ketone (4) to the more stable epimer (10). The Grignard method was also used for the conversion (10) ⟶ (11) *via* the intermediate 17α*H*-hopan-22-ol.

17α*H*-Hopane was also synthesized by the method of Tsuda and his co-workers.[3] A key step in their synthesis was the separation of the epimeric 17α*H*-hopan-20-ols from the epimeric 17α*H*-moretan-20-ols, which can be readily achieved by p.l.c. In addition, we found it possible to separate 17α*H*-hopan-20β-ol from the 20α-epimer. Steric control of the metal hydride reduction

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† Pending clarification of the structure of hopane by *X*-ray crystallography,[2] it is assumed that the isopropyl side-chain at C-21 has the α-orientation.

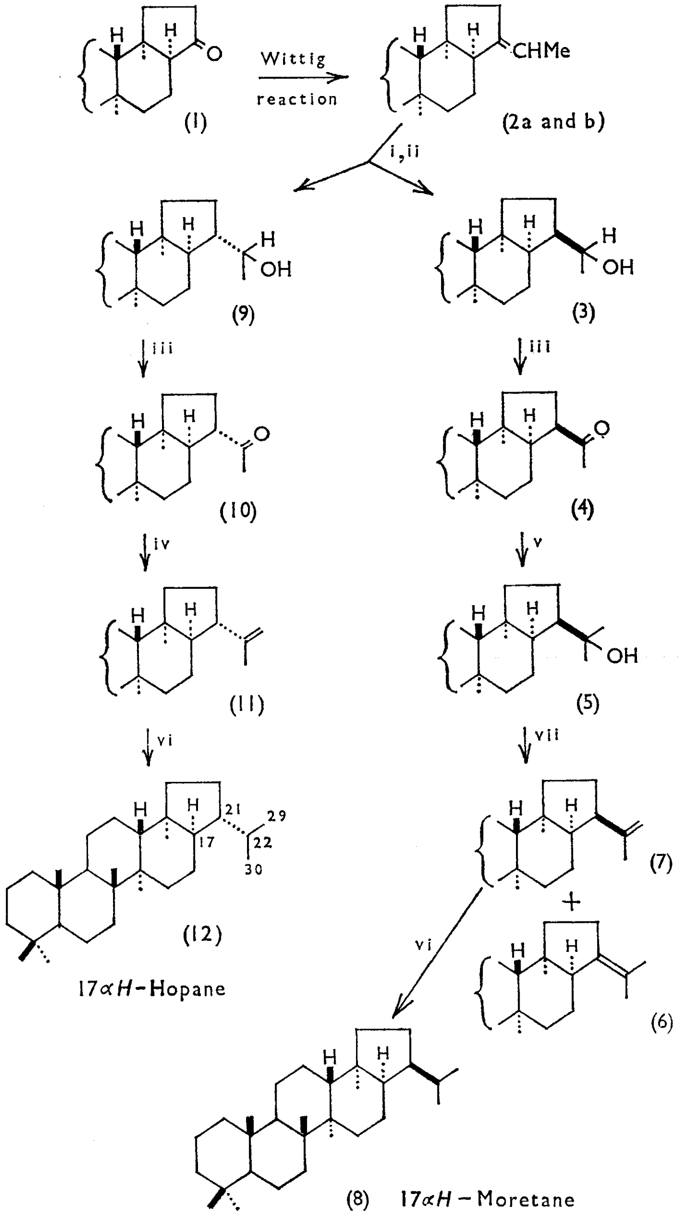
[1] Part VIII, R. E. Corbett and Miss H. L. Ding, preceding paper.

[2] I. Yosioka, T. Nakanishi, and I. Kitagawa, *Tetrahedron Letters*, 1968, 1485.

[3] Y. Tsuda, K. Isote, S. Fukushima, H. Ageta, and K. Iwata, *Tetrahedron Letters*, 1967, 23.

[4] R. E. Corbett and H. Young, *J. Chem. Soc.* (*C*), 1966, 1556.

of 17α*H*-hopan-20-one would be expected to favour the formation of the β-epimer, and because a β-hydroxy-group at C-20 is more sterically hindered than the α-epimer, the β-alcohol would be expected to move more rapidly on t.l.c. The major product was the faster moving of the two epimers, and it was assigned the 17α*H*-hopan-20β-ol structure. The ^{1}H n.m.r. spectrum was consistent with this formulation. Models show that the dihedral angle between the carbinol proton of the β-epimer and the C-19β proton is approximately 90° and so the C-19β proton will not contribute appreciably to the coupling. As a result the half-band width of the n.m.r. signal from the carbinol proton of the 20β-ol is less than that in the case of the 20α-ol.



SCHEME

Reagents: i, BF_3–Et_2O/$LiAlH_4$; ii, H_2O_2–NaOH; iii, RuO_4–CCl_4; iv, Wittig reaction; v, MeMgI; vi, H_2–PtO_2; vii, $POCl_3$–C_5H_5N.

The methyl signals in the n.m.r. spectra of 17α*H*-hopane and 17α*H*-moretane and their derivatives have been assigned by similar methods to those used for other hopane derivatives. In Part IV[5] methyl assignments were made for hopane and for 21α*H*-hopane (moretane) but the ring A methyl signals for positions 4β, 4α, and 10β were not distinguished. It is now clear[6] that the chemical shifts of the ring A methyl groups are at progressively lower field in the order 4β > 4α > 10β, so that the complete assignment of all the methyl signals from hopane and moretane is possible.

There was the expected close similarity between the 4β, 4α, 10β, and 8β methyl signals of hopane and moretane and their 17α*H*-epimers (Table); it remained to distinguish the 14α-methyl and 18α-methyl signals. The 14α-methyl signal is unlikely to be affected by modifications in the structure of 17α*H*-hopane at C-22 whereas the 18α-methyl signal could be affected. On this basis the signal at 1·00 p.p.m. is assigned to the 14α-methyl group and that at 0·91 p.p.m. to the 18α-methyl group in 17α*H*-hopane. The corresponding signals in 17α*H*-moretane are at 1·02 and 0·92 p.p.m. and neither of these will be effected by structural modifications at C-22. On the other hand the 8β-methyl signal, not unexpectedly, does reflect structural changes at this centre. Assignments are listed in the Table.

Chemical shifts of methyl groups expressed as p.p.m. (δ) from tetramethylsilane

	Position					
	4β	4α	10β	8β	14α	18α
Hopane	0·78	0·81	0·84	0·94	0·94	0·69
17α-*H*Hopane	0·80	0·83	0·85	0·96	1·00	0·91
17α*H*-Hop-22(29)-ene	0·80	0·84	0·84	0·97	0·99	0·99
17α*H*-Hopan-22-ol	0·79	0·83	0·85	0·97	1·02	0·95
29-Nor-17α*H*-hopan-22-one	0·79	0·84	0·84	0·97	1·00	0·99
29-Nor-17α*H*-hopan-22-ol	0·80	0·83	0·84	0·97	1·02	0·95
Moretane	0·78	0·81	0·84	0·95	0·92	0·64
17α*H*-Moretane	0·81	0·81	0·85	0·94	1·02	0·92
17α*H*-Moret-22(29)-ene	0·81	0·81	0·85	1·01	1·03	0·90
17α*H*-Moretan-22-ol	0·81	0·83	0·86	0·93	1·00	0·89
29-Nor-17α*H*-moretan-22-one	0·80	0·80	0·84	1·00	1·04	0·90
29-Nor-17α*H*-moretan-22-ol	0·79	0·79	0·85	0·95	1·03	0·91

EXPERIMENTAL

Experimental procedures were as described in Part VI.[7] Unless stated otherwise optical rotation measurements were made for solutions in chloroform. N.m.r. data were obtained with a Varian 100A instrument.

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[5] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (*C*), 1967, 1622.

[6] R. E. Corbett and Susan D. Cumming, *J. Chem. Soc.* (*C*), 1971, 955.

[7] R. E. Corbett and R. A. J. Smith, *J. Chem. Soc.* (*C*), 1969, 44.

29-*Nor*-17αH-*hop*-21-*ene*-(A) (2a) *and* 29-*Nor*-17αH-*hop*-21-*ene*-(B) (2b).—Sodium hydride (720 mg as 50% dispersion in mineral oil) in a three-necked flask was washed with dry n-pentane (×4) to remove the mineral oil. The flask was then fitted with a magnetic stirrer, a nitrogen inlet tube, a self-sealing Teflon stopper, and a reflux condenser. The system was flushed with nitrogen for 15 min and dimethyl sulphoxide (refluxed over calcium hydride for 4 h, distilled under reduced pressure, and collected over calcium hydride; 30 ml) was introduced with a syringe. The mixture was heated at 75—80° until evolution of hydrogen had ceased. The resulting greenish-grey solution of methylsulphinylmethylide was cooled in an ice–water bath, and ethyltriphenylphosphonium bromide (11·1 g) in dimethyl sulphoxide (60 ml) was added. The resultant dark orange-red solution of the ethylidenephosphorane was stirred at room temperature for 20 min.

A solution of 22,29,30-trisnor-17α*H*-hopan-20-one[4] (1) (1·8 g) in dry tetrahydrofuran (100 ml) was then added to the solution and the mixture was kept at 55° for 36 h. Dilution with water (2 l) and extraction with ether gave a product (1·2 g) which was shown [t.l.c. on silver nitrate-impregnated silica gel (type H)] to be a mixture of two compounds of similar R_F values. The mixture was separated by multiple p.l.c. on silver nitrate-impregnated silica gel (four plates; 20 cm × 100 cm × 1·25 mm; hexane × 3).

Crystallization of the compound of higher R_F value from ethanol–hexane gave 29-*nor*-17αH-*hop*-21-*ene*-(A) (2a) (590 mg); m.p. 159—161°; $[\alpha]_D^{20}$ +83·2° (*c* 0·50); $\nu_{max.}$ 825 (trisubstituted double bond) cm^{-1}; δ 0·70(3H), 0·81(3H), 0·84(6H), 0·98(3H), 1·00(3H), 1·59 and 1·68(3H), and 5·17 (1H, m, $W_{\frac{1}{2}}$ 12 Hz) p.p.m. (Found: C, 87·5; H, 12·5. $C_{29}H_{48}$ requires C, 87·8; H, 12·2%).

Crystallization of the other compound from ethanol–hexane gave 29-*nor*-17αH-*hop*-21-*ene*-(B) (2b) (450 mg); m.p. 170—172°; $[\alpha]_D^{20}$ +17·6° (*c* 0·17), $\nu_{max.}$ 819 (trisubstituted double bond) cm^{-1}; δ 0·80(3H), 0·81(3H), 0·84(3H), 0·89(3H), 0·91(3H), 1·05(3H), 1·57 and 1·64(3H), and 5·30 (1H, m, $W_{\frac{1}{2}}$ 15 Hz) p.p.m. (Found: C, 87·7; H, 12·3%).

29-*Nor*-17αH-*hopan*-22-*ol* (9) *and* 29-*Nor*-17αH-*moretan*-22-*ol* (3).—(*a*) 29-Nor-17α*H*-hop-21-ene-(B) (2a) (330 mg) in anhydrous ether (50 ml) was added to a solution of lithium aluminium hydride (250 mg) in ether (15 ml). Boron trifluoride–ether complex [1·7 g in ether (17 ml)] was then added dropwise during 30 min under nitrogen with stirring and continuous cooling in ice–water. The mixture was stirred for 1 h at room temperature and water was carefully added. The organic layer was washed with saturated sodium hydrogen carbonate solution and water. Evaporation left the organoborane; this was dissolved in tetrahydrofuran (20 ml) and aqueous sodium hydroxide (10%; 8 ml) was added. The solution was cooled in ice–water and hydrogen peroxide (30%; 6 ml) was added dropwise with stirring and cooling. The mixture was stirred for another 1 h, and water and ether were added. The organic layer was washed with sodium hydrogen sulphite solution and water and evaporated to leave a product (300 mg) which was separated by p.l.c. on silica gel [three plates; 20 cm × 20 cm × 1·25 mm; E–H (1 : 3)].

The compound of higher R_F value, 29-*nor*-17αH-*hopan*-22-*ol* (9) (105 mg), had m.p. 187—189° (from methanol–acetone); $[\alpha]_D^{20}$ +35·5° (*c* 0·48); δ 0·80(3H), 0·83(3H), 0·84(3H), 0·95(3H), 0·97(3H), 1·02(3H), 1·15 and 1·21 (3H, d), and 3·72 (1H, m, $W_{\frac{1}{2}}$ 16 Hz) p.p.m. (Found: C, 84·1; H, 12·3. $C_{29}H_{50}O$ requires C, 83·9; H, 12·1%).

The other compound, 29-*nor*-17αH-*moretan*-22-*ol* (3) (135 mg), had m.p. 204—205° (from acetone); $[\alpha]_D^{20}$ −0·9° (*c* 0·44); δ 0·79(6H), 0·85(3H), 0·91(3H), 0·95(3H), 1·03(3H), 1·17 and 1·24 (3H, d), and 3·67 (1H, m, $W_{\frac{1}{2}}$ 16 Hz) p.p.m. (Found: C, 84·2; H, 12·4. $C_{29}H_{50}O$ requires C, 83·9; H, 12·1%).

(*b*) Hydroboration of a mixture of 29-nor-17α*H*-hop-21-ene-(A) and 29-nor-17α*H*-hop-21-ene-(B) (400 mg) and oxidation of the resultant organoborane were carried out as in (*a*). The product (380 mg) was shown (t.l.c.) to be a mixture of two compounds and was separated by p.l.c. on silica gel [four plates; 20 cm × 20 cm × 1·25 mm, E–H (1 : 3)].

After crystallization from methanol–acetone, the compound of higher R_F value, 29-nor-17α*H*-hopan-22-ol (9) (90 mg), had m.p. 188—189°, and was identical (t.l.c. and mixed m.p.) with an authentic specimen.

After crystallization from acetone the other compound, 29-nor-17α*H*-moretan-22-ol (3) (220 mg), had m.p. 204—205° and was identical (t.l.c. and mixed m.p.) with an authentic specimen.

29-*Nor*-17αH-*Hopan*-22-*one* (10).—A solution of ruthenium tetroxide (Hopkin and Williams Ltd.) in carbon tetrachloride was added dropwise to a stirred solution of 29-nor-17α*H*-hopan-22-ol (90 mg) in carbon tetrachloride (20 ml) and water (5 ml) until a yellow colour persisted in the carbon tetrachloride phase. The excess of ruthenium tetroxide was destroyed with propan-2-ol (3 ml) and the mixture was filtered. The carbon tetrachloride layer was washed with water, dried (Na_2SO_4), and evaporated to leave 29-*nor*-17αH-*hopan*-22-*one* (10) (65 mg), m.p. 177—179° (from acetone); $[\alpha]_D^{20}$ +24·5° (*c* 0·48); δ 0·79(3H), 0·84(6H), 0·97(3H), 0·99(3H), 1·00(3H), and 2·12(3H), p.p.m. (Found: C, 84·3; H, 11·6. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%).

29-*Nor*-17αH-*moretan*-22-*one* (4).—Treatment of 29-nor-17α*H*-moretan-22-ol (100 mg) in carbon tetrachloride (25 ml) and water (5 ml) with ruthenium tetroxide as just described gave 29-*nor*-17αH-*moretan*-22-*one* (4) (80 mg), m.p. 201—203° (from acetone); $[\alpha]_D^{20}$ −24·1° (*c* 0·44); δ 0·80(6H), 0·84(3H), 0·90(3H), 1·00(3H), 1·04(3H), and 2·10(3H) p.p.m. (Found: C, 84·1; H, 11·4%).

17α*H*-*Hop*-22(29)-*ene* (11).—A solution of methylsulphinylmethylide was prepared as before from sodium hydride (25 mg as a 50% dispersion in mineral oil) and dimethyl sulphoxide (5 ml). A solution of methyltriphenylphosphonium bromide (350 mg) in dimethyl sulphoxide (10 ml) was added to give an orange solution of the alkylidenephosphorane.

29-Nor-17α*H*-hopan-22-one (60 mg) dissolved in dry tetrahydrofuran (10 ml) was added to the ylide solution and kept at 60° for 24 h. The mixture was worked up in the usual way; p.l.c. of the product on silver nitrate-impregnated silica gel [E–H (1 : 9)] gave 17αH-*hop*-22(29)-*ene* (11) (40 mg), m.p. 135—136°; $[\alpha]_D^{20}$ +48·4° (*c* 0·25); δ 0·80(3H), 0·84(6H), 0·97(3H), 0·99(6H), 1·64(3H), and 4·68 (2H, s) p.p.m. (Found: C, 88·0; H, 12·4. $C_{30}H_{50}$ requires C, 87·7; H, 12·2%).

17αH-*Hopane* (12).—17α*H*-Hop-22(29)-ene (40 mg) in AnalaR ethyl acetate (10 ml) was hydrogenated over Adams catalyst for 1 h (uptake 1·1 mol. equiv.) to give 17α*H*-hopane (40 mg), m.p. 154—156° (from hexane–ethanol) identical (i.r. and n.m.r. spectra, mixed m.p.) with an authentic specimen;[3] δ 0·76(1·5H), 0·80(3H), 0·83(4·5H), 0·85(4·5H), 0·91(4·5H), 0·96(3H), and 1·00(3H) p.p.m.

17αH-*Moretan*-22-*ol* (5).—29-Nor-17α*H*-moretane-22-one

(50 mg) in dry benzene (4 ml) and anhydrous ether (4 ml) was added to the Grignard reagent obtained by treating magnesium (250 mg) with methyl iodide (1 ml) in anhydrous ether (5 ml). The mixture was heated under reflux for 3 h and excess of Grignard reagent was destroyed with methanol. The mixture was acidified (2N-HCl) and extracted with ether. Evaporation of the extract, and p.l.c· of the product on silica gel [E–H (3 : 7)] gave 17αH-*moretan*-22-*ol* (5) (60 mg), m.p. 190—191° (from hexane); δ 0·81(3H), 0·83(3H), 0·86(3H), 0·89(3H), 0·93(3H), 1·00(3H), 1·20(3H), and 1·25(3H), p.p.m. (Found: C, 84·3; H, 12·0. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

17αH-*Moret*-22(29)-*ene* (7).—Phosphoryl chloride (0·5 ml) was added to 17α*H*-moretan-22-ol (60 mg) dissolved in anhydrous pyridine (8 ml), and the mixture was kept at room temperature for 30 h. It was then worked up in the usual way; the product (50 mg) was separated by p.l.c. on silver nitrate-impregnated silica gel (two plates, 20 cm × 20 cm × 1·25 mm, H).

Crystallization of the isomer of higher R_F value from ethyl acetate gave 17αH-*hop*-21-*ene* (6) (30 mg), m.p. 163—164° (from ethyl acetate); δ 0·80(3H), 0·81(3H), 0·84(3H), 0·85(3H), 0·90(3H), 1·05(3H), 1·59(3H), and 1·63(3H) p.p.m. (Found: C, 87·5; H, 12·1. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

Crystallization of the other isomer from hexane–ethanol gave 17αH-*moret*-22(29)-*ene* (7) (25 mg), m.p. 210°, $[\alpha]_D^{20}$ +4·5° (*c* 0·134); δ 0·81(6H), 0·85(3H), 0·90(3H), 1·01(3H), 1·03(3H), 1·69(3H), and 4·62 and 4·74 (2H, d) p.p.m. (Found: C, 88·0; H, 12·1. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

17αH-*Moretane* (8).—17α*H*-Moret-22(29)-ene (25 mg) in AnalaR ethyl acetate (10 ml) was hydrogenated over Adams catalyst to give 17αH-*moretane* (25 mg), m.p. 201—202° (from hexane–ethanol); $[\alpha]_D^{20}$ +12·2° (*c* 0·164); δ 0·81(7·5H), 0·85(4·5H), 0·89(1·5H), 0·92(4·5H), 0·94(3H), and 1·02(3H) p.p.m. (Found: C, 87·4; H, 12·9. $C_{30}H_{52}$ requires C, 87·3; H, 12·7%).

17αH-*Hopan*-22-*ol*.—29-Nor-17α*H*-hopan-22-one (50 mg) in dry benzene (4 ml) and dry ether (4 ml) was added to the Grignard reagent obtained from magnesium (250 mg) and methyl iodide (1 ml) in anhydrous ether (5 ml). The mixture was heated under reflux for 3 h, and excess of Grignard reagent was destroyed with methanol. The mixture, worked up in the usual way, gave 17αH-*hopan*-22-*ol* (50 mg), m.p. 169—171° (from hexane) (Found: C, 84·3; H, 12·0. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

17αH-*Hop*-21-*ene* (6) *and* 17αH-*Hop*-22(29)-*ene* (11).—Phosphoryl chloride (0·5 ml) was added to a solution of 22-hydroxy-17α*H*-hopane (50 mg) in anhydrous pyridine (7 ml) and the mixture was kept at room temperature for 30 h. Work-up in the usual way gave a mixture of two alkenes (t.l.c. on silver nitrate-impregnated silica gel). P.l.c. on silver nitrate-impregnated silica gel (one plate, 20 cm × 20 cm × 1·25 mm, H) gave 17α*H*-hop-21-ene (20 mg) (higher R_F value), m.p. 163—165° (from ethyl acetate), identical (i.r. and n.m.r. spectra, mixed m.p.) with an authentic sample; and 17α*H*-hop-22(29)-ene (25 mg.), m.p. 135—137° (from ethanol–hexane), identical (mixed m.p.) with an authentic specimen.

17αH-*Hopan*-20β-*ol and* 17αH-*Hopan*-20α-*ol*.—Hop-17(21)-en-20-one [3] (240 mg) in dry ether (10 ml) was added to a stirred solution of lithium (200 mg) in liquid ammonia (150 ml). The solution was vigorously stirred for 10 min and solid ammonium chloride (2 g) was added. The ammonia was allowed to evaporate off at room temperature; work-up then gave a mixture. P.l.c. on silica gel [two plates, 20 cm × 20 cm × 1·25 mm, E–H (1 : 4)] gave a mixture of saturated ketones (180 mg) which we could not separate by multiple p.l.c. The mixture (180 mg) was treated with a slight excess of lithium aluminium hydride in anhydrous ether (30 ml) and heated under reflux for 2 h. The usual work-up gave a product (170 mg) which showed three spots on t.l.c. P.l.c. [two plates, 20 cm × 20 cm × 1·25 mm, E–H (1 : 9)] then gave three fractions (10 mg, 140 mg, and 20 mg in order of decreasing R_F value).

The fraction of intermediate R_F value was shown (t.l.c. in benzene × 5) to be a mixture of two compounds. Multiple p.l.c. on silica gel (benzene × 5) gave 17αH-*hopan*-20α-*ol* (50 mg), a mixture of the 20α- and 20β-ols (45 mg), and 17αH-*hopan*-20α-*ol* (25 mg).

17α*H*-Hopan-20β-ol, the component of higher R_F value, had m.p. 181—182° (from methanol); δ 0·80(3H), 0·82(3H), 0·85(4·5H), 0·89(4·5H), 1·02(9H), and 4·0 (1H, m, *W* 12 Hz) p.p.m. (Found: C, 83·9; H, 12·2. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

17α*H*-Hopan-20α-ol, the third component, had m.p. 176° (from methanol); δ 0·80(3H), 0·82(3H), 0·84(6H), 0·95(3H), 1·00(3H), 1·07(6H), and 4·28 (1H, m, $W_{\frac{1}{2}}$ 15 Hz) p.p.m. (Found: C, 84·4; H, 12·5. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

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