The Configuration at C-21 of Hydroxyhopanone

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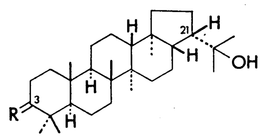
(Received March 29, 1974)

Hydroxyhopanone (**1**) was converted *via* two alternative routes (**1→9→11a→12→14→15→16** and **1→10→17→18→19→20**) to A-neohop-21-ene (**16**) and A-neohop-3-ene (**20**), respectively. These unsaturated hydrocarbons (**16** and **20**) were found to be identical; this provided evidence to confirm the 21β-H configuration for **1**.

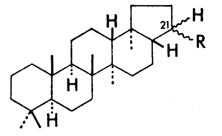
Hydroxyhopanone is a pentacyclic triterpene isolated from dammar resin.[1] The structure had been determined as **1**[2] with a 21β-H configuration based on an isomerization of the norketone (**2**) to its isomeric norketone (**3**).[2a]

Later, this configuration at C-21 of **1** was questioned in connection with studies which led to a revision of the 21β-H (**4a** and **5a**) to the 21α-H structures (**4b** and **5b**) for zeorin and hopane, respectively.[3] However, this revision has recently been withdrawn by the same authors[4] on re-investigation of some derivatives of leucotylin (**6**). The 21β-H configuration was thus confirmed for hopane (**5a**) in accordance with the earlier observation[2a] as well as with the results obtained for adipedatol (**7**)[5] and adiantol B bromoacetate (**8**).[6]



1 R=O

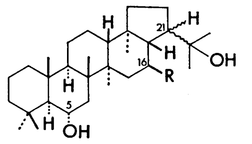
22 R=H_2



2 21β-H; R=$-COCH_3$(α)

3 21α-H; R=$-COCH_3$(β)

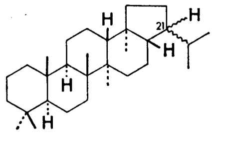
8 21β-H; R=$-\underset{CH_3}{CH}OCOCH_2Br$(α)



4a R=H; 21β-H

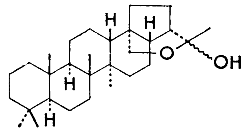
4b R=H; 21α-H

6 R=OH; 21β-H



5a 21β-H

5b 21α-H



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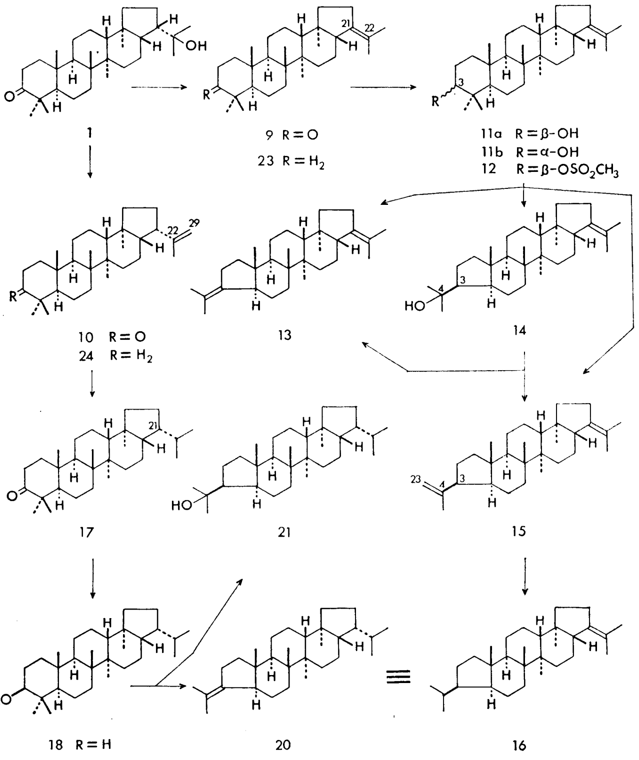
We wish to present another chemical evidence to confirm the 21β-H configuration for hydroxyhopanone (**1**).

Dehydration of **1** with phosphorus oxychloride in pyridine gave hop-21-en-3-one (hopenone-a) (**9**)[7] and hop-22(29)-en-3-one (hopenone-b) (**10**)[7] in a ratio of about 2: 1. The isopropylideneketone (**9**) was reduced with sodium borohydride to give hop-21-en-3β-ol (**11a**) and hop-21-en-3α-ol (**11b**) in a ratio of 4: 1. The former alcohol (**11a**) was converted to its mesylate (**12**). Solvolysis of **12** in a mixture of dioxane and water (1: 1) in the presence of calcium carbonate afforded A-neohopa-3,21-diene (**13**) (yield: 53%), A-neohop-21-en-4-ol (**14**) (y: 24%), and A-neohopa-4(23),21-diene (**15**) (y: 5%). Dehydration of **14** with phosphorus oxychloride in pyridine yielded **13** and **15** in a ratio of about 2: 1. The latter (**15**) in ethanol was hydrogenated over platinum catalyst to give A-neohop-21-ene (**16**).

On the other hand, hydrogenation of the isopropenylketone (**10**) in ethanol[4] over platinum catalyst yielded hopan-3-one (**17**) which was reduced with sodium borohydride to give hopan-3β-ol (**18**) as a main product. The alcohol (**18**) was converted to its mesylate (**19**) and then submitted to solvolysis to give A-neohop-3-ene (**20**) (y: 34%) and A-neohopan-4-ol (**21**) (y: 18%).

Two unsaturated hydrocarbons (**16** and **20**) thus obtained were found to be identical.



It has already been reported that dehydration of hydroxyhopane (**22**) with phosphorus oxychloride in pyridine gave hop-21-ene (hopene-a) (**23**) and hop-22(29)-ene (hopene-b) (**24**),[7] and that reaction of methylmagnesium iodide with the norketone (**2**), obtained by oxidation of **24**, reproduced **22**.[2a] This showed that the configurations of the side chain at C-21 of **24** and **22** are the same. A parallel argument could lead to the same configuration at C-21 for the isopropenylketone (**10**) and hydroxyhopanone (**1**).

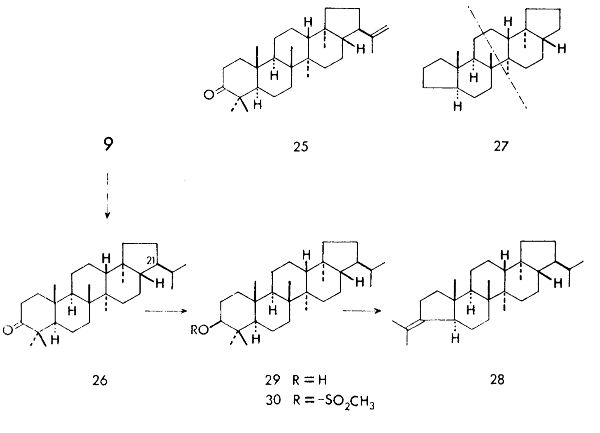
When treated with *p*-toluenesulfonic acid in chloroform, **10** isomerized completely to the isopropylideneketone (**9**). During hydrogenation of **10** in neutral conditions (ethanol, platinum catalyst) to give hopan-3-one (**17**), an isomerization of **10** *via* **9** to form an isomeric isopropenylketone (**25**) and successive hydrogenation leading to isohopan-3-one (**26**) are less probable. The isopropylideneketone (**9**) was found unchanged on hydrogenation in neutral conditions. The Wolff-Kishner reduction of **17** furnished hopane (**5a**)[8] whose configuration at C-21 has been shown to be the same as that of **1**.[8] Thus, no isomrization at C-21 has taken place during the hydrogenation of **10** to give **17**.

Based on a parallel argument, it could be concluded that the configurations at C-3 of **15** and **16** must be the same.

A β(equatorial) nature for the hydroxyl group at C-3 of **11a** and **18** was shown by the formation of A-neo derivatives from the tosylates (**13**, **14**, and **15** from **12**; **20** and **21** from **19**) in accordance with the stereochemistry required by the mechanism of ring contraction.[9] Thus, the side chains at C-3 of **14**, **15**, and **21** should be in a β-configuration.

These findings showed the structure with 3β-isopropyl side chain (**16**) for A-neohop-21-ene. The identity of **16** with **20** as shown above led to a 21α-configuration for the isopropyl group of A-neohop-3-ene (**20**) due to the C_2 symmetry of hexanor-A-neohopane (**27**). As stereochemistry at C-21 of **20** has been shown to be retained as that of **1**, the configuration at C-21 of hydroxyhopanone (**1**) should be 21β-H.

For a further confirmation of the result, A-neoisohop-3-ene (**28**) was prepared by the following transformation. Hydrogenation of **9** in acidic conditions (acetic acid, platinum catalyst)[4,10] gave isohopan-3-one (**26**) which was reduced with sodium borohydride to yield 3β-hydroxyisohopane (**29**) as a main product. The alcohol (**29**) was converted to the mesylate (**30**). Solvolysis of **30** gave **28** which was found to be not identical with **16** (=**20**).


9 25 27

26 29 R=H 30 R=$-SO_2CH_3$ 28

Thus, 21β-H configuration of hydroxyhopanone (**1**) was confirmed.

Experimental

IR spectra were measured using a Hitachi EPI-G2 spectrometer in Nujol mull, unless otherwise stated. NMR spectra were taken on a JEOL JNM-C-60 or a Hitachi R-24 spectrometer in deuteriochloroform solution containing tetramethylsilane as an internal standard. Mass spectra were measured using a Hitachi RMU-6-Tokugata mass spectrometer with a direct inlet system operating at 70 eV. Measurements of optical rotation were carried out using a JASCO polarimeter DIP-SL in chloroform solution. Gas chromatographic (glc) analyses were performed on a Shimadzu gas chromatograph model GC-4A. For column chromatography Wakogel C 200 (Wako Pure Chemical Industries) and Activated Alumina (Mesh 200—300, Showa Chemical Co.) were used. Thin layer chromatography (tlc) was carried out on Kieselgel PF_{254} (E. Merck, Darmstadt) in 0.25 mm thickness. All melting points were determined on a hot block and reported uncorrected.

Hydroxyhopanone (1): Hydroxyhopanone (**1**) was isolated from dammar resin by the procedure described by Dunstan *et al.*[7] Mp 249—250 °C; $[\alpha]_D^{19}$ +58° (*c* 0.76); IR 3450 (OH) and 1710 cm^{-1} (C=O); NMR δ 0.79, 0.95, 0.98, 1.09 (each 3H, s, *t*-CH_3), 1.03 (6H, s, 2×*t*-CH_3), and 1.23 (6H, s, $-C(OH)(C\underline{H}_3)_2$); mass *m/e* 442 ($M^+$), 424, 205, and 189 (base peak); Found: C, 81.51; H, 11.62%. Calcd for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38%; glc retention time 9.7 min (column: OV-1 (2%), 260 °C).

Dehydration of Hydroxyhopanone (1): To a solution of hydroxyhopanone (**1**; 0.6 g) in pyridine (55 ml), phosphorus oxychloride (6 ml) was added with stirring at 0 °C. The reaction mixture was allowed to stand overnight at room temperature, poured into ice-water, and extracted with ether. The ethereal extract was washed with diluted hydrochloric acid, sodium hydrogen carbonate solution and then water, and dried over sodium sulfate. After evaporation, the mixture was chromatographed on silica gel (50 g, impregnated with 25% silver nitrate; each fraction 200 ml). The fractions 34—41, eluted with petroleum ether–benzene (4: 1) were combined, and crystallized from acetone to afford hop-21-en-3-one (**9**; 0.35 g) as needles. Mp 209—210.5 °C; $[\alpha]_D^{14}$ +54° (*c* 1.10); IR 1700 cm^{-1} (C=O); NMR δ 0.61, 0.94, 0.98, 1.07 (each 3H, s, *t*-CH_3), 1.02 (6H, s, 2×*t*-CH_3), 1.58, and 1.73 (each 3H, s, $C=C(CH_3)_2$); mass *m/e* 424 (M^+), 205, and 189 (base peak); Found: C, 84.87; H, 11.34%. Calcd for $C_{30}H_{48}O$: C, 84.84; H, 11.39%; glc retention time 13.8 min (column: OV-1 (2%), 250 °C).

The fractions 43—51, eluted with petroleum ether–benzene (2: 1), gave 0.15 g of hop-22(29)-en-3-one (**10**) as needles after crystallization from acetone. Mp 219—220 °C; $[\alpha]_D^{19}$ +89° (*c* 0.57); IR 1700 (C=O), 1640, and 885 cm^{-1} ($C=CH_2$); NMR δ 0.75, 1.08 (each 3H, s, *t*-CH_3), 0.95, 1.03 (each 6H, s, 2×*t*-CH_3), 1.75 (3H, s, $C=C-CH_3$), and 4.78 (2H, br.s, $C=CH_2$); mass *m/e* 424 (M^+), 205, and 189; Found: C, 84.73; H, 11.58%. Calcd for $C_{30}H_{48}O$: C, 84.84; H, 11.39%; glc retention time 15.1 min (column: OV-1 (2%), 260 °C).

*Isomerization of Hop-22(29)-en-3-one (**10**) to Hop-21-en-3-one (**9**)*: Hop-22(29)-en-3-one (**10**; 27 mg) in chloroform was treated with *p*-toluenesulfonic acid overnight at room temperature. After usual work-up, the solvent was removed to afford crude crystals (one spot on tlc), which was recrystallized from acetone. The isomerized product (20 mg) was identical with hop-21-en-3-one (**9**) in respects of IR, NMR, mass spectra, and glc.

On the same treatment of hop-21-en-3-one (**9**; 22 mg), only the starting material (**9**; 19 mg) was recovered. No formation of the other product was observed.

*Reduction of Hop-21-en-3-one (**9**)*: To a solution of hop-21-en-3-one (**9**; 2.92 g) in ethanol (1.4 l), sodium borohydride (1.6 g) was added and allowed to stand overnight at room temperature. After the reaction mixture was concentrated, acetone was added and left overnight at room temperature to destroy the excess sodium borohydride. Evaporation of the solvents gave crude products (2.54 g), which were subjected to silica gel column chromatographic separation: fractions 1—12, benzene (each fraction 200 ml); and fractions 13—20, benzene-ether (5: 1, each fraction 100 ml).

Fractions 8—11, on evaporation of the solvent, gave crude crystals, which were recrystallized from ethanol to give hop-21-en-3α-ol (**11b**; 0.56 g). Mp 161—162.5 °C; $[\alpha]_D^{13}$ +3° (*c* 0.31); IR 3470 cm^{-1} (OH); NMR δ 0.60, 0.96 (each 3H, s, *t*-CH_3), 0.85, 1.00 (each 6H, s, 2×*t*-CH_3), 1.57, 1.73 (each 3H, br.s, $C{=}C(CH_3)_2$), and 3.39 (1H, t, *J*=3 Hz, $-CH_2-C\underline{H}-OH$).

Fractions 17 and 18 were combined, evaporated and crystallized from ethanol. Hop-21-en-3β-ol (**11a**; 1.91 g) was obtained. Mp 200—201.5 °C; $[\alpha]_D^{14}$ +40° (*c* 0.49); IR 3270 cm^{-1} (OH); NMR δ 0.60, 0.77, 0.83 (each 3H, s, *t*-CH_3), 0.97 (9H, s, 3×*t*-CH_3), 1.57, 1.72 (each 3H, br.s, $C{=}C(CH_3)_2$) and 3.20 (1H, dd, *J*=10 and 6 Hz, $-CH_2-C\underline{H}-OH$); mass *m/e* 426 (M^+), 207, and 189 (base peak); Found: C, 84.60; H, 11.51%. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81%.

*Mesylation of Hop-21-en-3β-ol (**11a**)*: Hop-21-en-3β-ol (**11a**; 1.32 g) was dissolved in dry pyridine (45 ml) and kept at 0 °C. To the solution, methanesulfonyl chloride (1 ml) in pyridine (5 ml) was added dropwise with agitation. The mixture was further stirred for 30 min and then left overnight at room temperature. The reaction mixture, after addition of ice-water in order to destroy the excess reagent, was extracted with ether and worked up as usual giving rise to 1.20 g of crude crystals. On recrystallization from acetone, hop-21-en-3β-yl mesylate (**12**; 0.70 g) was obtained as colorless needles. Mp 145—145.5 °C; $[\alpha]_D^{22}$ +26° (*c* 0.10); IR 1350 and 1180 cm^{-1}; NMR δ 0.59, 1.02 (each 3H, s, *t*-CH_3), 0.86, 0.97 (each 6H, s, 2×*t*-CH_3), 1.57, 1.73 (each 3H, s, $C{=}C(CH_3)_2$), and 2.97 (3H, s, CH_3-SO_2-).

*Solvolysis of Hop-21-en-3β-yl Mesylate (**12**)*: A mixture of hop-21-en-3β-yl mesylate (**12**; 0.44 g) and calcium carbonate (0.4 g) in dioxane-water (100 ml, 1: 1) was heated under reflux for several hours. Most of the solvents were removed under reduced pressure, acetic acid was added to dissolve calcium carbonate and the reaction product was extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution, water and then saturated sodium chloride solution, and the solvents were removed. The crude crystal in benzene was passed through a column of alumina (15 g) and eluted with the following solvents: fractions 1—3, benzene (each fraction 30 ml); fractions 4—6, benzene-ether (1: 1, each fraction 20 ml); and fractions 7 and 8, ether (each fraction 30 ml).

On evaporation of the solvent, fraction 1 gave white crystals (0.31 g, mp 168—188 °C; IR 892 cm^{-1}) which were shown to be a mixture of olefins by NMR measurement. Signals due to olefinic protons were observed at δ 4.78 and 5.74, and each was a broad singlet with intensity less than one proton. The mixture was further chromatographed on silica gel impregnated with 10% silver nitrate and eluted with petroleum ether-benzene (9: 1, each fraction 40 ml). Evaporation of fraction 3 followed by recrystallization from dichloromethane–methanol gave A-neohopa-3,21-diene (**13**; 190 mg) as colorless plates. Mp 190—191 °C; $[\alpha]_D^{14}$ +45° (*c* 0.77); NMR δ 0.60, 0.98 (each 6H, s, 2×*t*-CH_3), 1.59, and 1.73 (each 6H, s, $C{=}C(CH_3)_2$); mass *m/e* 408 (M^+) and 189 (base peak); Found: C, 87.98; H, 11.76%. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84%. Fractions 9—12 were combined and crystallized from chloroform–ethanol to afford A-neohopa-4(23),21-diene (**15**; 19 mg) as colorless needles. Mp 185—186 °C; IR 1640 and 894 cm^{-1} ($C{=}CH_2$); NMR δ 0.57, 0.72 (each 3H, s, *t*-CH_3), 0.95 (6H, s, 2×*t*-CH_3), 1.59 (3H, br.s, $C{=}C-CH_3$), 1.75 (6H, br.s, 2×$C{=}C-CH_3$), and 4.77 (2H, br.s, $C{=}CH_2$); mass *m/e* 408 (M^+) and 189 (base peak); Found: C, 88.04; H, 11.58%. Calcd for $C_{30}H_{48}$: C, 88.16; H, 11.84%.

Fraction 8 of the first chromatography afforded A-neohop-21-en-4-ol (**14**; 91 mg) as colorless needles by crystallization from chloroform–ethanol. Mp 193—194 °C; $[\alpha]_D^{20}$ +46° (*c* 0.17); IR 3400 cm^{-1} (OH); NMR δ 0.59, 0.78 (each 3H, s, *t*-CH_3), 0.98 (6H, s, 2×*t*-CH_3), 1.19, 1.22 (each 3H, s, $-C(OH)(C\underline{H}_3)_2$), 1.59, and 1.73 (each 3H, s, $C{=}C(CH_3)_2$); mass *m/e* 426 (M^+), 408, and 189 (base peak).

*Dehydration of A-Neohop-21-en-4-ol (**14**)*: To a solution of A-neohop-21-en-4-ol (**14**; 36 mg) in dry pyridine (10 ml), phosphorus oxychloride (1 ml) was added dropwise with stirring at 0 °C. The reaction mixture was allowed to stand overnight at room temperature, poured into ice-water and extracted with chloroform. The extract was washed with diluted hydrochloric acid, sodium hydrogen carbonate solution, water and then with saturated sodium chloride solution. After drying over sodium sulfate, evaporation of the solvent gave a residue (24 mg), which was chromatographed on silica gel impregnated with 10% silver nitrate and eluted with the following solvents (each fraction 20 ml): fractions 1—3, petroleum ether; fractions 4—7, petroleum ether-benzene (10: 1); fractions 8—10, petroleum ether-benzene (5: 1).

From fraction 4, on evaporation of the solvent, 15 mg of colorless crystal was obtained by crystallization from chloroform–ethanol. The mp and spectral data were identical with those of A-neohop-3,21-diene (**13**), obtained by solvolysis of hop-21-en-3β-yl mesylate (**12**).

Fractions 5—8, after crystallization from chloroform–ethanol, gave 7 mg of colorless needles, which was identical with A-neohopa-4(23),21-diene (**15**) in respects of IR, NMR, and tlc.

*Hydrogenation of A-Neohopa-4(23),21-diene (**15**)*: A-neohopa-4(23),21-diene (**15**; 17 mg) in ethanol (30 ml) was catalytically hydrogenated in the presence of platinum oxide (about 5 mg) with stirring at 40 °C overnight. The solvent was removed under reduced pressure to afford crude crystals, which were recrystallized from chloroform–ethanol. A-neohop-21-ene (**16**) was obtained and weighed 8 mg. Mp 191.5—192.5 °C; $[\alpha]_D^{16}$ +49° (*c* 0.30); IR (KBr disk) 1380, 1360, 1165, and 1145 cm^{-1}; NMR δ 0.59, 0.72 (each 3H, s, *t*-CH_3), 0.97 (6H, s, 2×*t*-CH_3), 1.57, and 1.73 (each 3H, s, $C{=}C(CH_3)_2$), (signals due to protons of two secondary methyls could not be assignable); tlc R_f 0.4 (10% $AgNO_3-SiO_2$, petroleum ether); mass *m/e* 410 (M^+), 191 (base peak), and 189; Found: C, 87.39; H, 12.54%. Calcd for $C_{30}H_{50}$: C, 87.73; H, 12.27%; glc retention time 19.1 min (column: SE-30 (0.7%), 220°) and 20.2 min (column: OV-17 (2%), 250 °C).

*Hydrogenation of Hop-22(29)-en-3-one (**10**)*: Hop-22(29)-en-3-one (**10**; 0.21 g) in ethanol (200 ml) was hydrogenated in the presence of platinum oxide (0.07 g) for 12 hr to the same procedure as above. Filtration of the catalyst followed by evaporation of the solvent gave a residue (0.21 g), which was recrystallized from acetone to afford hopan-3-one (**17**) as needles. Mp 230—232 °C; $[\alpha]_D^{19}$ +78° (*c* 0.75); IR 1700

0.97 (6H, s, 2×*t*-CH_3), 1.59, and 1.73 (each 3H, br.s, C=C-(each 3H, s, *t*-CH_3); mass *m/e* 426 (M^+), 205, and 191 (base peak); Found: C, 84.29; H, 11.91%. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81; glc retention time 14.6 min (column: OV-1 (2%), 260°) and 63.5 min (column: OV-17 (2%), 250 °C).

Hydrogenation of Hop-21-en-3-one (9): Hop-21-en-3-one (**9**; 62 mg) in ethanol (100 ml) was hydrogenated in the presence of platinum oxide (19 mg) overnight. Treatment as usual gave a substance (61 mg; one spot on tlc) which was found to be identical with the starting material (**9**). No formation of the other product was observed.

Reduction of Hopan-3-one (17): Hopan-3-one (**17**; 0.85 g) was dissolved in ethanol (650 ml), sodium borohydride (0.67 g) was added and left overnight at room temperature. After a small quantity of acetone was added, the solvents were removed. The residue, dissolved in chloroform, washed with water and evaporated, gave crude crystals (0.85 ; two spots on tlc), which were chromatographed on silica gel (100 g). The fractions 20—29 (one spot on tlc), eluted with benzene, were collected and recrystallized from ethanol to afford hopan-3β-ol (**18**; 0.46 g) as a main product. Mp 238—239 °C; IR 3300 cm^{-1} (OH); NMR δ 0.74, 0.78, 0.85, 0.99 (each 3H, s, *t*-CH_3), and 0.96 (6H, s, 2×*t*-CH_3); mass *m/e* 428 (M^+), 207, and 191 (base peak).

Mesylation of Hopan-3β-ol (18): To a solution of hopan-3β-ol (**18**; 0.4 g) in pyridine (20 ml), methanesulfonyl chloride (1 ml) in pyridine (9 ml) was added dropwise with agitation at 0 °C. The reaction mixture was allowed to stand overnight at room temperature and poured into ice-water. Extraction with ether and usual work-up gave a residue (0.39 g), which was recrystallized from ether to afford hopan-3β-yl mesylate (**19**; 0.12 g). Mp 119—120 °C; $[\alpha]^{21}_{D}$ +35° (*c* 0.49); IR 1170 cm^{-1} (SO_2); NMR δ 0.73, 1.02 (each 3H, s, *t*-CH_3), 0.87, 0.96 (each 6H, s, 2×*t*-CH_3), and 3.00 (3H, s, CH_3–SO_2–).

Solvolysis of Hopan-3β-yl Mesylate (19): A mixture of hopan-3β-yl mesylate (**19**; 0.32 g) and calcium carbonate (0.5 g) in dioxane (150 ml) and water (150 ml) was heated under reflux for 5 hr. The solvents were removed under reduced pressure and the residue was dissolved in ether. The ethereal solution was treated as usual manner and the residue was dissolved in petroleum ether–benzene, which was chromatographed on silica gel (10 g) and the following solvents (each fraction 40 ml) were eluted: fractions 1 and 2, petroleum ether–benzene (2: 1); fraction 3, petroleum ether–benzene (1: 1); and fraction 4, ether.

On evaporation of the solvents, fraction 1 gave a mixture (0.20 g) of olefins. IR 1640 and 894 cm^{-1}; NMR δ 1.58, 1.73 (each 3H, s, C=C(CH_3)$_2$), 4.8, and 5.4 (each less than 1H, olefinic proton); mass *m/e* 410 (M^+). The mixture gave four spots (R_f 0.9, 0.8, 0.5, and 0.2) on tlc (10% $AgNO_3$–SiO_2, petroleum ether). The olefin mixture was subjected to column chromatographic separation using silica gel impregnated with 10% silver nitrate, and eluted with petroleum ether (each fraction 30 ml). Fractions 8—15, after recrystallization from ethanol, gave A-neohop-3-ene (**20**; 88 mg) as colorless needles. Mp 193.5—193.7 °C; $[\alpha]^{16}_{D}$ +52° (*c* 0.28); IR (KBr disk) 1380, 1360, 1165, and 1145 cm^{-1}; NMR δ 0.60, 0.72 (each 3H, s, *t*-CH_3), 0.97 (6H, s, 2×*t*-CH_3), 1.58, and 1.73 (each 3H, s, C=C(CH_3)$_2$), (signals due to protons of two secondary methyls could not be assignable); tlc R_f 0.4 (10% $AgNO_3$–SiO_2, petroleum ether); mass *m/e* 410 (M^+), 191 (base peak), and 189; Found: C, 87.74; H, 12.42%. Calcd for $C_{30}H_{50}O$: C, 87.73; H, 12.27%; glc retention time 19.1 and 10.4 min (column: SE-30 (0.7%), 220 and 250 °C respectively) and 20.2 min (column: OV-17 (2%), 250 °C). This compound was shown to be identical (mp, mixed mp, IR, NMR, mass spectra, tlc, and glc) with **16**.

Fraction 4, eluted with ether, afforded A-neohopan-4-ol (**21**; 0.05 g). Mp 198.5—199 °C; $[\alpha]^{19}_{D}$ +64° (*c* 0.75); IR 3470 cm^{-1} (OH); NMR δ 0.70, 0.77 (each 3H, s, *t*-CH_3), 0.96 (6H, s, 2×*t*-CH_3), 1.18, and 1.21 (each 3H, s, –C(OH)-$(C\underline{H}_3)_2$); mass *m/e* 428 (M^+), 410, 191, and 189 (base peak); Found: C, 84.03; H, 12.42%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23%.

Reduction of Hopan-3-one (17): A mixture of hopan-3-one (**17**; 70 mg), potassium hydroxide (0.2 g), diethylene glycol (5 ml) and hydrazine hydrate (80%, 0.1 ml) was heated under reflux for 1 hr. After removal of water and hydrazine by distillation, the reaction mixture was further heated under reflux for 1 hr. Completion of the reaction was confirmed by tlc examination and then water was added to the reaction mixture. Extraction with ether, usual treatment and recrystallization from *n*-hexane–ethanol gave hopane (**5a**; 19 mg) as colorless needles. Mp 209.5—211 °C; $[\alpha]^{20}_{D}$ +50° (*c* 0.14); NMR δ 0.70, 0.79, 0.81, 0.84 (each 3H, s, *t*-CH_3) and 0.95 (6H, s, 2×*t*-CH_3), (signals due to protons of two secondary methyls could hardly be assignable); mass *m/e* 412 (M^+). These data coincide with those published for hopane (**5a**)[8] rather than for isohopane (**5b**) (moretane).[8]

Hydrogenation of Hop-21-en-3-one (9) in Acidic Condition: A solution of hop-21-en-3-one (**9**; 113 mg) in ethyl acetate (15 ml) and acetic acid (0.5 ml) was catalytically hydrogenated in the presence of platinum oxide at room temperature. After removal of the catalyst by filtration, evaporation under reduced pressure gave crude crystals, which were crystallized from chloroform–ethanol to give crude isohopan-3-one (**26**; 96 mg). IR 1700 cm^{-1} (C=O); NMR: signals due to vinyl methyls were not observed.

Reduction of Isohopan-3-one (26): Crude isohopan-3-one (**26**; 96 mg) without further purification, was dissolved in ethanol (50 ml) and treated with sodium borohydride and allowed to stand overnight. Addition of acetone followed by evaporation of the solvents under reduced pressure afforded a residue, which showed two spots on tlc. This was dissolved in benzene, passed through a column of silica gel (10 g) and eluted with the following solvents (each fraction 50 ml): fraction 1, benzene; fractions 2 and 3, benzene–ether (50: 1); and fractions 4—8, benzene–ether (10: 1).

A main component, isohopan-3β-ol (29), eluted in fractions 5 and 6, was obtained as crude crystals (78 mg), which gave one spot on tlc. IR 3350 cm^{-1} (OH).

Mesylation of Isohopan-3β-ol (29): Crude isohopan-3β-ol (**29**; 78 mg) obtained above, was dissolved in pyridine (6 ml) and kept at 0 °C. Methanesulfonyl chloride (about 0.5 ml) in pyridine was added and usual treatment gave crude isohopan-3β-yl mesylate (**30**; 90 mg) as pale yellow crystals, in which no starting material (**29**) was detected by tlc.

Solvolysis of Isohopan-3β-yl Mesylate (30): Calcium carbonate (0.1 g) and crude isohopan-3β-yl mesylate (**30**; 90 mg) without further purification, were suspended in dioxane (10 ml) and water (10 ml), and the mixture was heated under reflux for 13 hr. After the same treatment as in the case of solvolysis of hop-21-en-3β-yl mesylate (**12**), the residue was chromatographed on silica gel (5 g). Elution with benzene (30 ml) and evaporation of the solvent gave a mixture (52 mg) of olefins, which was subjected to column chromatographic separation on silica gel (3 g) impregnated with 10% silver nitrate using petroleum ether as eluent (each fraction 30 ml). Fractions 2—6, on crystallization from acetone, gave A-neoisohop-3-ene (**28**; 30 mg) as colorless needles. Mp 156—158 °C; IR (KBr disk) 1440, 1380, 1365, 1170, and 1140 cm^{-1}; NMR δ 0.62, 0.68 (each 3H, s, *t*-CH_3), cm^{-1} (C=O); NMR δ 0.73, 0.94, 0.96, 1.00, 1.03, and 1.10 ($(CH_3)_2$), (signals due to protons of two secondary methyls could not be assignable); mass *m/e* 410 (M^+); glc retention time 7.8 min (column: OV-1 (2%), 250 °C).

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