Manicol, an Aromatic Sesquiterpene from *Dulacia guianensis* (*Liriosma* cf. *acuta*)

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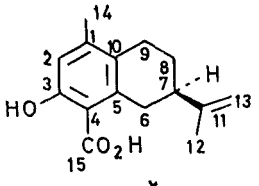
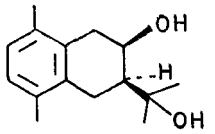
A eudesmane-type sesquiterpene acid with an aromatic A-ring isolated from a Guyanan tree *Dulacia guianensis* (Olacacea) was assigned a structure and an absolute stereochemistry (1) on the basis of spectroscopic evidence and partial synthesis. The isolate had moderate antileukaemic activity in P-388 lymphocytic leukaemia.

A EUDESMANE-TYPE sesquiterpene acid with an aromatic A-ring (1) for which the name manicol is suggested was isolated from the root bark of a Guyanan tree *Dulacia guianensis* (Engl.) O. Ktze (Olacaceae) (known locally as 'Balata kamwi' and 'switi udu'). The tree is uncommon, and the sample obtained was from a tree sited



(1)*



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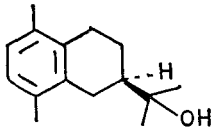


(3)

* Numbering throughout the Discussion section is that associated with eudesmane-type sesquiterpenes.

in the forest at Gallion at a location 20 km from the sea, south of Cayenne.†

Among the eudesmane sesquiterpenes which have been isolated containing an aromatic A-ring are rishitinol (2), a stress metabolite from the potato [1] and occidol (3) from *Thuja occidentalis*.[2]

The new sesquiterpene (1), which crystallised as needles, was optically active, $[\alpha]_D$ +90.6° (*c*, 0.94, $CHCl_3$). A high-resolution mass spectrum and elemental analysis of the compound gave the molecular formula as $C_{15}H_{18}O_3$. Bands in the i.r. spectrum of the sesquiterpene (1) were present in the hydroxy (3 300 cm^{-1}) (in KBr) and carbonyl (1 646 cm^{-1}) (in $CHCl_3$) stretching regions. The ^1H n.m.r. spectrum had signals due to a single aromatic proton (δ 7.38), two vinyl protons (δ 4.75), an aromatic methyl group (δ 2.38), one vinyl methyl group (δ 1.78), and a resonance at δ 8.2 which was assigned to a hydroxy-group. This last signal exchanged on deuteriation and was not present in the ^1H n.m.r. spectrum of the methylated product. Also present in the ^1H n.m.r. spectrum of (1) was a resonance δ 1.6—3.4 due to seven aliphatic protons.

The product from the methylation (MeI–K_2CO_3) of (1) had a ^1H n.m.r. spectrum which showed signals in the region of an aromatic methyl ether (δ 3.95) and an aromatic methyl ester (δ 3.88). The assignment of the latter signal was supported by the i.r. spectrum which contained an absorption band at 1 700 cm^{-1}. The mass spectrum of the methylated product confirmed that two additional methyl groups were present.

The carboxylic acid group and phenolic group are *ortho* to each other as seen from the chelating effect in the i.r. spectrum and the green colouration with ethanolic ferric chloride.

Inspection of the ^{13}C n.m.r. spectrum of manicol revealed a substantial amount of structural information from which it was ascertained that the new compound has a sesquiterpene structure containing an aromatic A-ring with the isopropylene group located at position 7.

The off-resonance decoupled ^{13}C n.m.r. spectrum showed the presence of the following: 2 CH_3, 3 CH_2, 1 CH, 1 CH_2=, 1 CH=, 6 sp^2 fully substituted carbons, and 1 CO group; it also accounted for 16 protons. The two remaining protons were observed as D_2O-exchangeable protons in the ^1H n.m.r. spectrum. The carbon resonances were assigned (see Table) by comparison with the resonance positions of a variety of known compounds of similar structure.

^{13}C N.m.r. spectrum of compound (1)

Carbon *	(p.p.m.)	Carbon	(p.p.m.)	Carbon	(p.p.m.)
1	141.4 [a]	6	37.5	11	148.5
2	123.7	7	40.7	12	20.9
3	157.7	8	26.1	13	109.8
4	134.2	9	28.5	14	26.9
5	156.0	10	138.4 [a]	15	163.7

* See formula (1) for numbering of eudesmane-type sesquiterpenes. [a] Signals may be reversed.

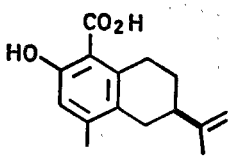
Aromatic sesquiterpenes of this nature and also aromatic steroids, triterpenes, and sapogenins arise biosynthetically by a dienone–phenol type rearrangement,[3] consequently structures (1) or (4) would be acceptable for the compound.

The ^1H n.m.r. spectrum of compound (1) was not useful in differentiating between the two proposed structures (1) and (4), since the signals for the aromatic protons at position 3 in structure (4) and position 2 in structure (1), when calculated, occur at the same position

† The material studied was collected in February 1976 by one of us (H. J.) and a sample (No. HJ 2165) deposited in the Herbier du Museum d'Histoire Naturelle, Paris.

as the observed signal in the natural product (δ 7.38). The breakdown pattern in the mass spectrum supports either structure for the sesquiterpene.

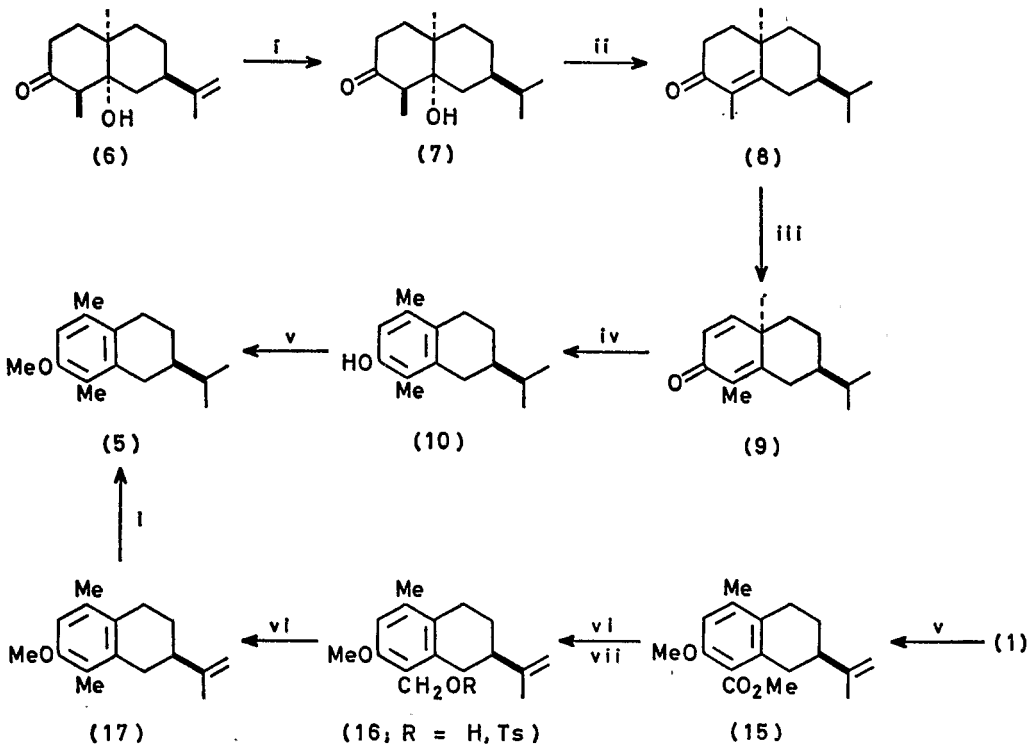
To determine unambiguously the structure for manicol



(4)

and to establish the absolute stereochemistry, an authentic synthesis was undertaken. The methyl ether (5) was synthesised from the ketol (6), $[\alpha]_D$ +51° (*c* 0.95, $CHCl_3$). The reagent phenylseleninic anhydride was more favoured, since the reaction time was much shorter (20 min) and the yield better (89%). Treatment of the dienone (9) with HCl yielded the phenol (10) in a typical dienone–phenol rearrangement. The ketone stretch of the dienone was absent in the i.r. spectrum of the product whereas a phenol OH stretch was present at 3 450 cm^{-1}. The ^1H n.m.r. spectrum of the product showed a signal for a single aromatic proton at δ 6.55 corresponding to the proton at position 2. Also, signals for two aromatic methyl groups were present at δ 2.18 and 2.15.

The phenolic acetate was also prepared by treatment of the dienone (9) with toluene-*p*-sulphonic acid [7] and acetic anhydride. This acetate was found to be identical with the acetate prepared from the phenol (10). Methylation of the phenol (10) with methyl iodide yielded the required methyl ether (5). It is of interest that hydrogenation of the isopropylene double bond is necessary at an early stage in the reaction scheme, because if the dienone–phenol rearrangement is carried out on the dienone (11), addition of HCl occurs to yield the phenol (12).



SCHEME

Reagents: i, H_2–Pd/C; ii, NaOMe–MeOH;[5] iii, DDQ–dioxan; $Ph_2Se_2O_3$–C_6H_5Cl;[6] iv, HCl; v, MeI–Me_2CO; vi, $LiAlH_4$; vii, TsCl–C_6H_6 [7]

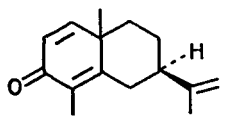
The latter compound was originally obtained from (+)-dihydrocarvone, the absolute stereochemistry of which is known.[4] The synthetic methyl ether (5) was compared with that obtained from methylation and reduction of the natural compound (1). Also, by comparison of the specific rotation of both samples, the absolute stereochemistry should be established for the new sesquiterpene. The synthetic scheme followed is outlined (see Scheme).

Dehydrogenation of the enone (8) with DDQ in dioxan or with phenylseleninic anhydride in chlorobenzene [6] yielded the dienone (9), which was easily identified from its ^1H n.m.r. spectrum showing doublets at δ 6.33 and δ 6.87 for the protons at positions 1 and 2.

The natural product (1) when treated with hydrogen and Pd–C yielded not the expected acid (13) but the reduced product (14). This probably arises from the existence of an equilibrium between the phenol (1) and a dienone which is stabilized by hydrogen bonding.

The natural product (1) was methylated and afforded the methyl ester (15). Reduction of this ester with

lithium aluminium hydride resulted in formation of the alcohol (16; R = H). The i.r. spectrum showed a hydroxy-band and in the ^{1}H n.m.r. spectrum the methyl ester signal was absent while the hydroxymethylene signal occurred at δ 4.80 as a doublet (*J* 4 Hz). The tosyl compound (16; R = Ts) was formed from the alcohol and



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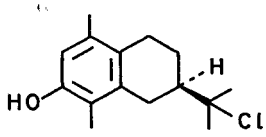

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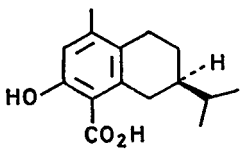

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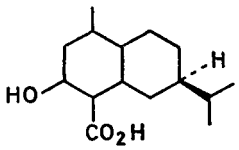

(14)

subsequently reduced with lithium aluminium hydride to yield the methyl compound (17). In the ^{1}H n.m.r. spectrum of the product, two aromatic methyl signals were distinguishable at δ 2.18 and 2.15. Finally, hydrogenation of the side-chain double bond yielded the required methyl ether (5) which was identical in every respect with the methyl ether synthesised from (+)-dihydrocarvone. The specific rotation of the methyl ether (5) synthesised from the ketol (6) was +48.2° and the specific rotation of the same methyl ether synthesised from the natural product was +48.0°. Therefore the natural product has the structure (1) and a stereochemistry at carbon 7 similar to (+)-dihydrocarvone.

The biological activity of manicol showed moderate antileukaemic activity in P-388 leukemia (T/C = 127%) at a non-toxic dose (14 mg kg^{-1} day^{-1}).* Further evaluation of manicol's antineoplastic properties is in progress.

EXPERIMENTAL

M.p.s were determined using a Kofler hot-stage microscope and are uncorrected. Optical rotations were determined at room temperature on a Roussel-Jouan Quick polarimeter. I.r. spectra were recorded with a Perkin-Elmer model 257 spectrometer for chloroform solutions. The u.v. spectra were measured with a Spectronic model 505 spectrometer (Bausch and Lomb). Electron-impact mass spectra were taken on an MS 50-AEI spectrometer. The ^{1}H n.m.r. spectra were recorded with a Varian T60 in deuteriochloroform; absorptions are given in δ units (p.p.m.) and coupling constants in Hz. Tetramethylsilane was used as internal standard. The ^{13}C n.m.r. spectrum was measured with a Bruker HXE 90 (22.63 MHz) spectrometer in deuteriochloroform.

Extraction of Root Bark of Dulacia guianensis.—The root bark (1 kg) of *Dulacia guianensis* was exhaustively extracted with n-hexane. Concentration of the extract gave red crystals (1.4 g) which were recrystallised from ethyl acetate, benzene, or methanol to yield manicol (1) as pale yellow prisms, m.p. 139—140 °C, sublimation from 134 °C; $\lambda_{max.}$ (EtOH) (log ε) 260 (4.61), 332 (3.81), and 380 nm (3.97); $[\alpha]_D^{21}$ +90.6° (*c* 0.94, $CHCl_3$) (Found: C, 73.3; H, 7.5. $C_{15}H_{18}O_3$ requires C, 73.1; H, 7.4%), M^+ 246.1248.

3-*Isopropenyl*-6-*methoxy*-5-*methoxycarbonyl*-8-*methyl*-1,2,3,4-*tetrahydronaphthalene* (15).*—The acid (1) (300 mg) was refluxed in acetone (50 ml) with methyl iodide (100 mg) and potassium carbonate (300 mg) for 6 h. The solids were filtered off and the solvent evaporated to yield on oil. Purification by p.l.c. afforded the methylated product (15) as an oil (124 mg); δ ($CDCl_3$) 6.95 (1 H, s, Ar-H), 4.90br (2 H, s, $=CH_2$), 3.95 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 2.38 (3 H, s, CH_3), 1.88 (3 H, s, CH_3), and 3.2—1.2 (7 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 610 cm^{-1}; $[\alpha]_D$ +34.6° (*c* 0.91, $CHCl_3$) (Found: C, 74.3; H, 8.2. $C_{17}H_{22}O_3$ requires C, 74.4; H, 8.1%); M^+ 274.

5-*Hydroxymethyl*-3-*isopropenyl*-6-*methoxy*-8-*methyl*-1,2,3,4-*tetrahydronapthalene* (16; R = H).—To the methyl ester (15) (200 mg) in ether (50 ml) was added lithium aluminium hydride (200 mg) and the mixture was stirred at 20 °C for 3 h. The excess of hydride was destroyed by the addition of ethyl acetate to the cooled solution. Brine was then added, and the organic phase was separated and dried (Na_2SO_4). The solvent was evaporated, and the resulting oil was purified by p.l.c. (chloroform) to afford the required alcohol (16; R = H) (134 mg) as an oil; δ ($CDCl_3$) 6.75 (1 H, s, aromatic), 4.85br (2 H, s, $=CH_2$), 4.80 (2 H, d, *J* 4 Hz, $-CH_2OH$), 3.91 (3 H, s, OCH_3), 2.30 (3 H, s, CH_3), 1.86 (3 H, s, CH_3), and 3.4—1.4 (7 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 3 500, 1 610, and 1 600 cm^{-1}; $[\alpha]_D$ ($CHCl_3$) +24.6° (*c* 0.74) (Found: C, 78.2; H, 9.1. $C_{16}H_{22}O_2$ requires C, 78.0; H, 9.0%).

3-*Isopropenyl*-6-*methoxy*-8-*methyl*-5-*tosyloxymethyl*-1,2,3,4-*tetrahydronaphthalene* (16; R = Ts).—The alcohol (16; R = H) (60 mg) was treated with toluene-*p*-sulphonyl chloride (50 mg) in refluxing benzene (50 ml) for 4 h. The reaction mixture was cooled, washed with water, and the solvent was evaporated. The resulting oil was purified by p.l.c. (chloroform) to afford the tosylate (16; R = Ts) (35 mg) as an oil; δ ($CDCl_3$) 6.73 (1 H, s, aromatic), 4.9 br (2 H, s, $=CH_2$), 4.81 (2 H, d, *J* 4Hz, CH_2OTs), 3.94 (3 H, s, OCH_3), 2.30 (3 H, s, CH_3), 1.86 (3 H, s, CH_3), and 3.4—1.4 (7 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 1 610 and 1 600 cm^{-1}; $[\alpha]_D$ +34.2° (*c* 0.64 $CHCl_3$) (Found: C, 69.2; H, 7.1. $C_{23}H_{28}O_4S$ requires C, 69.0; H, 7.0%).

3-*Isopropenyl*-6-*methoxy*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (17).—The tosylate (16; R = Ts) (34 mg) was dissolved in diethyl ether (20 ml) and treated with lithium aluminium hydride (100 mg) for 4 h at 25 °C. Work-up afforded an oil which was purified by p.l.c. (chloroform) to yield 3-isopropenyl-6-methoxy-5,8-dimethyl-1,2,3,4-tetrahydronaphthalene (17) (20 mg) as an oil; δ ($CDCl_3$) 6.54 (1 H, s, H-7), 4.75br (2 H, s, $=CH_2$), 3.95 (3 H, s, OCH_3), 2.18 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 1.86 (3 H, s, CH_3), and 2.80—0.70 (7 H, m, aliphatic); $\nu_{max.}$ ($CHCl_3$) 1 610 and 1 600 cm^{-1}; $[\alpha]_D$ +42.3° (*c* 0.78, $CHCl_3$) (Found: C, 83.1; H, 9.3. $C_{16}H_{22}O$ requires C, 83.5; H, 9.5%).

3-*Isopropyl*-6-*methoxy*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (5).—3-Isopropenyl-6-methoxy-5,8-dimethyl-1,2,3,4-tetrahydronaphthalene (17) (31 mg) was dissolved in

* The *in vivo* activity tests were carried out under the auspices of the National Cancer Institute, Bethesda, U.S.A., by the courtesy of Dr. M. Suffness.

* Throughout the Experimental section the numbering of compounds is that associated with naphthalene derivatives rather than eudesmone-type sesquiterpenes.

ethanol (30 ml) and hydrogenated over Pd–C (10%, 100 mg) until uptake of hydrogen had ceased. The catalyst was filtered off and the solvent evaporated to yield an oil. Purification by p.l.c. (chloroform) gave the required product (24.8 mg) as an oil; δ ($CHCl_3$) 6.56 (1 H, s, H-7), 4.00 (3 H, s, OCH_3), 2.18 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 0.97 (6 H, d, *J* 6 Hz, 2 × CH_3), and 2.80—0.70 (8 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 2 950 and 1 610 cm^{-1} (Found: C, 82.5; H, 10.3. $C_{16}H_{24}O$ requires C, 82.7; H, 10.4%); M^+ 232; $[\alpha]_D$ +48.0° (*c* 0.95, $CHCl_3$).

The Ketol (7).— The ketol (6) (1.0 g) in absolute ethanol (20 ml) was hydrogenated over palladium–charcoal (10% 400 mg) until uptake of hydrogen had ceased. The catalyst was filtered off, and the solvent was evaporated to afford the ketol (7) as an oil (0.94 g); δ ($CDCl_3$) 3.20—0.60 (16 H, m, aliphatic H), 1.28 (3 H, s, CH_3), 0.98 (6 H, d, *J* 6 Hz, 2 × CH_3); $\nu_{max.}$ ($CHCl_3$) 3 450, 3 950, and 1 640 cm^{-1} (Found: C, 75.8; H, 11.1. $C_{15}H_{26}O_2$ requires C, 75.6; H, 11.0%); $[\alpha]_D$ + 84.1° (*c* 0.84, $CHCl_3$).

(–)-*Dihydro*-epi-α-*cyperone* (8).—The alcohol (7) (850 mg) was heated under reflux in methanol (60 ml) with sodium methoxide (1 g) for 14 h. The reaction mixture was cooled, diluted with water, and extracted into chloroform. The solvent was dried (Na_2SO_4) and evaporated to yield the enone dihydro-*epi*-α-cyperone (8) (813 mg) as an oil; δ ($CDCl_3$) 1.82 (3 H, s, CH_3), 1.25 (3 H, s, CH_3), and 3.0—0.7 (m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 1 645 cm^{-1} (Found: C, 81.6; H, 10.8. $C_{15}H_{24}O$ requires C, 81.8; H, 11.0%); $[\alpha]_D$ −106.5° (*c* 0.92, $CHCl_3$).

The Dienone (9).—*Method A*. The enone (8) (330 mg) was refluxed with DDQ (233 mg) in dioxan (20 ml) for 14 h. The reaction mixture was cooled, diluted with water, extracted with chloroform, and dried (Na_2SO_4). The solvent was evaporated to yield an oil. Purification by p.l.c. (1 : 1, ether–hexane) yielded the required dienone (9) (111 mg) as an oil; δ ($CHCl_3$) 6.87 (1 H, d, *J* 10 Hz), 6.33 (1 H, d, *J* 10 Hz, H-1), 3.20—0.50 (8 H, m, aliphatic H), 1.97 (3 H, s, CH_3), 1.30 (3 H, s, CH_3), and 0.95 (6 H, d, *J* 8 Hz, 2 × CH_3); $\nu_{max.}$ ($CHCl_3$) 1 650 and, 1 610 cm^{-1} (Found: C, 82.4; H, 10.1. $C_{15}H_{22}O$ requires C, 82.5; H, 10.2%); $[\alpha]_D$ −97.8° (*c* 0.65, $CHCl_3$); M^+ 218.

Method B. The enone (8) (31 mg, 0.14 mmol), in chlorobenzene (20 ml) was refluxed under nitrogen with phenylselininic anhydride (250 mg, 0.56 mmol) for 20 min. The reaction mixture was cooled, and the solids filtered off. The filtrate mixture was evaporated and the residue chromatographed (p.l.c., 1 : 1 ether–hexane) to afford the dienone (9) (25 mg) as an oil.

6-*Hydroxy*-3-*isopropyl*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (10).—The dienone (9) (100 mg) was refluxed in HCl (36%, 3 ml) for 3 h. The reaction mixture was cooled, diluted with ice–water, and extracted into chloroform. The solvent was evaporated and the residual oil purified by p.l.c. (1 : 1 ether–hexane) to give the required phenol (10) (79 mg) as an oil; δ ($CDCl_3$) 6.55 (1 H, s, H-7), 4.68br(1 H, s, OH), 2.18 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 0.98 (6 H, d, *J* 6 Hz), 2 × CH_3), and 2.80—0.70 (8 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 3 600, 3 450, 2 950, and 1 610 cm^{-1} (Found: C, 82.3; H, 10.1. $C_{15}H_{22}O$ requires C, 82; H, 10.2%); $[\alpha]_D$ +50.1° (*c* 0.73, $CHCl_3$); M^+ 218.

3-*Isopropyl*-6-*methoxy*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (5).—The phenol (10) (71 mg) was refluxed in acetone (20 ml) with methyl iodide (20 mg) and potassium carbonate (100 mg) for 6 h. The solids were filtered off, and the solvent evaporated to yield an oil. Purification by p.l.c. (2 : 1 hexane–ether) gave the methyl ether (5) as an oil (51 mg); δ ($CDCl_3$) 6.56 (1 H, s, H-7), 4.00 (3 H, s, OCH_3), 2.18 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), 0.97 (6 H, d, *J* 6 Hz, 2 × CH_3), 2.80—0.70 (8 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 2 950, and 1 610 cm^{-1} (Found: C, 82.5; H, 10.3. $C_{16}H_{24}O$ requires C, 82.7; H, 10.4%); $[\alpha]_D$ +48.2° (*c* 0.81, $CHCl_3$).

6-*Acetoxy*-3-*isopropyl*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene*.—*Method A*. The phenol (10) (79 mg) was treated with acetic anhydride (2 ml) and pyridine (2 ml) and retained at 20 °C for 18 h. The reaction mixture was poured onto ice–HCl, extracted with chloroform, dried (Na_2SO_4), and the solvent evaporated to yield the crude acetate. Purification by p.l.c. (1 : 1 ether–hexane) afforded the acetate of (10) (75 mg) as an oil; δ ($CDCl_3$) 6.20 (1 H, s, H-7), 2.35 (3 H, s, $COCH_3$), 2.23 (3 H, s, CH_3), 2.05 (3 H, s, CH_3), 1.00 (6 H, d, *J* 6 Hz, 2 × CH_3), and 2.90—0.95 (8 H, m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 1 740 and 1 610 cm^{-1} (Found: C, 78.7; H, 9.03. $C_{17}H_{24}O_2$ requires C, 78.5; H, 9.23%); $[\alpha]_D$ +52.4° (*c*, 0.85, $CHCl_3$); M^+ 260.

Method B. The dienone (9) (269 mg) was heated on a steam-bath with toluene-*p*-sulphonic acid (44 mg) and acetic anhydride (5 ml) for 4 h. The mixture was cooled, diluted with water, and extracted with chloroform. The solvent was evaporated, and the resulting oil purified by p.l.c. (1 : 1 ether–hexane) to yield the acetate (90 mg) as an oil.

The Trienone (11).—*epi*-α-Cyperone (120 mg) was heated under reflux with DDQ (125 mg) in dioxan (20 ml) for 17 h and then cooled. Water (100 ml) was added to the mixture which was then extracted with chloroform, dried ($MgSO_4$), and the solvent evaporated to yield an oil. The oil was chromatographed (p.l.c. 1 : 1 ether–hexane) to yield *epi*-α-cyperone (43 mg) and the product (11) (17 mg); $[\alpha]_D^{21}$ −99.5° ($CHCl_3$); M^+ 216; δ ($CDCl_3$) 6.81 (d, *J* 10 Hz, 1 H), 6.28 (d, *J* 10 Hz, 1 H), 4.75 (d, *J* 9 Hz, 2 H), 3.2—1.0 (m, 7 H), 2.00 (s, 3 H), 1.75 (s, 3 H), and 1.30 (s, 3 H); $\nu_{max.}$ ($CHCl_3$) 1665 and 1615 cm^{-1}; $\lambda_{max.}$ (MeOH) 240 and 270sh nm.

3-(1-*Chloro*-1-*methylethyl*)-6-*hydroxy*-5,8-*dimethyl*-1,2,3,4-*tetrahydronaphthalene* (12).—The trienone (11) (110 mg) and concentrated hydrochloric acid (3 ml) were heated at reflux for 3 h; the mixture was then cooled, diluted with water, and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated to yield an oil which was purified by p.l.c. (ether–hexane 1 : 1) to yield the phenolic product (77 mg, 70%); δ ($CDCl_3$) 6.50 (s, 1 H), 2.90—0.60 (m, 7 H), 2.22 (s, 3 H), 1.20 (s, 3 H), and 1.09 (s, 3 H); $\nu_{max.}$ ($CHCl_3$) 3 600, 3 450br, 2 950, 1 610, and 1 605 cm^{-1}; $[\alpha]_D$ −80° (*c* 0.95, $CHCl_3$) (Found: C, 71.0; H, 8.3; Cl, 13.7. $C_{15}H_{21}ClO$ requires C, 71.2; H, 8.3; Cl, 14.0%).

6-*Hydroxy*-8-*methyl*-3-*isopropyl*-1,2,3,4,4a,5,6,7,8,8a-*decahydronaphthalene*-5-*carboxylic Acid* (14).—The acid (1) (300 mg) was dissolved in ethyl acetate (40 ml) and hydrogenated over palladium (10% on C, 100 mg) until uptake of hydrogen had ceased. The catalyst was filtered off and the solvent evaporated to yield a colourless oil. Chromatography (p.l.c., chloroform) yielded the reduced sesquiterpene (14) (260 mg) as an oil; δ ($CDCl_3$) 0.5—3.5 (m, aliphatic H); $\nu_{max.}$ ($CHCl_3$) 3 050 and 1 640 cm^{-1}; $[\alpha]_D$ +46° (*c* 0.95, $CHCl_3$) (Found: C, 70.5; H, 9.9. $C_{15}H_{26}O_3$ requires C, 70.9; H, 10.2%); M^+ 254.

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