Synthesis of the Key Intermediate(±)-18,19-Dinor-14αH-cheilantha-12,15-dien-17-one and its Transformation into the Geochemical Marker 18,19-Dinor-13βH,14αH-cheilanthane and the Marine-type Sesterterpene Methyl Scalar-17-en-25-oate

Manuel González Sierra,* Raquel M. Cravero, María de los Angeles Laborde, and Edmundo A. Rúveda *
Instituto de Química Orgánica de Síntesis (CONICET-UNR), Facultad de Ciencias Bioquímicas y Farmacéuticas, Casilla de Correo 991, Suipacha 531, 2000 Rosario, Argentina

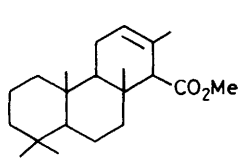
(±)-Methyl isocopalate (**1**) was converted into 18,19-dinor-14α*H*-cheilantha-12,15-dien-17-one (**5**). This key intermediate was then used as starting material for the synthesis of the tricyclane 18,19-dinor-13β*H*,14α*H*-cheilanthane (**6**) and its C-13 epimer (**19**). The hydrocarbon (**6**) is the most abundant member of a series of biological markers from petroleums and sediments. Starting from (**5**) the sesterterpene of marine-type scalar-17-en-25-oate (**8**) through the tricyclic esters (**21**) was also synthesized. The (*Z*) isomer of (**21**) possesses the carbon skeleton of the fern sesterterpene cheilanthatriol (**10**).

We have recently used methyl isocopalate (**1**) as starting material for the synthesis of various marine diterpenes, including isoagatholactone (**2**),[1,2] isocopal-12-ene-15,16-dial (**3a**), 14-*epi*-isocopal-12-ene-15,16-dial (**4**), and 15-acetoxy-isocopal-12-en-16-al (**3b**).[3] In this work we show how it can also be used as a precursor for the ketone (**5**), and through this key intermediate, for the synthesis of the tricyclane (**6**),† the cheilanthane derivative (**7**) and the tetracyclic sesterterpene of the scalarane group (**8**).‡

The C_{23} hydrocarbon (**6**) is the most abundant member of a new and widely occurring terpane series (C_{20}—C_{45}) that constitute an important class of biological markers used to provide information about the processes affecting organic matter in geological environments.[4–6] Compound (**6**) and the isomeric cyclane (**9**), were isolated from the Athabasca oil sand bitumen and their structures were suggested on the basis of the mass spectra and correlation of the ^{1}H n.m.r. methyl shifts of (**6**) with those of the sesterterpene cheilanthatriol (**10**).[7]§

Compound (**8**) is a tetracyclic intermediate possessing an arrangement of functional groups that make it attractive for the synthesis of a number of members of a growing group of sesterterpenes formally derived from the hypothetical hydrocarbon scalarane (**11**).[8] The scalaranes have recently been isolated from species of nudibranchs and sponges and some of them show interesting biological activities.[9–11]

In order to study the side-chain extension of (±)-methylisocopalate (**1**)¶ by Wittig olefination, we first attempted



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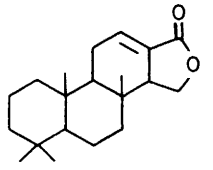

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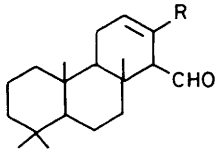
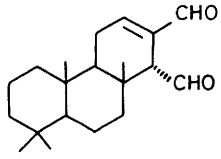


(3a) R = CHO
(3b) R = CH_2OAc



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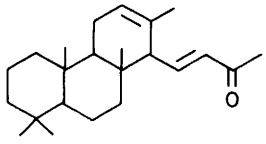

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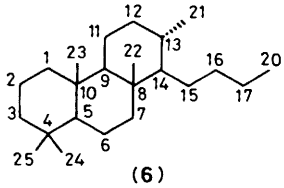
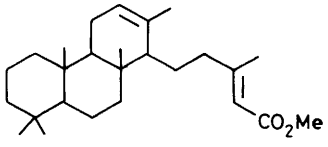


(6)



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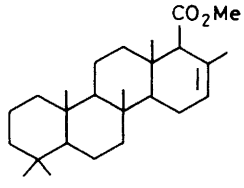

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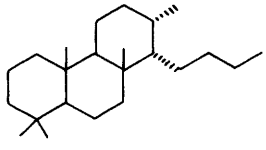
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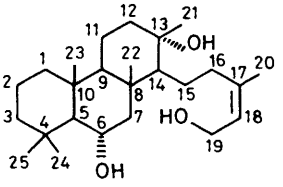


(10)

† Part of this work has been published in preliminary form: M. González Sierra, R. M. Cravero, M. A. Laborde, and E. A. Rúveda, *J. Chem. Soc., Chem. Commun.*, 1984, 417. Simultaneously, and following essentially the same sequence, the syntheses of (**6**) and some homologues have also been reported: D. Heissler, R. Ocampo, P. Albrecht, J. J. Riehl, and G. Ourisson, *J. Chem. Soc., Chem. Commun.*, 1984, 496. After acceptance of our preliminary communication, the syntheses of compounds (**6**) and (**18**) were reported, W. Herz and J. Siva Prassad, *J. Org. Chem.*, 1984, **49**, 326.

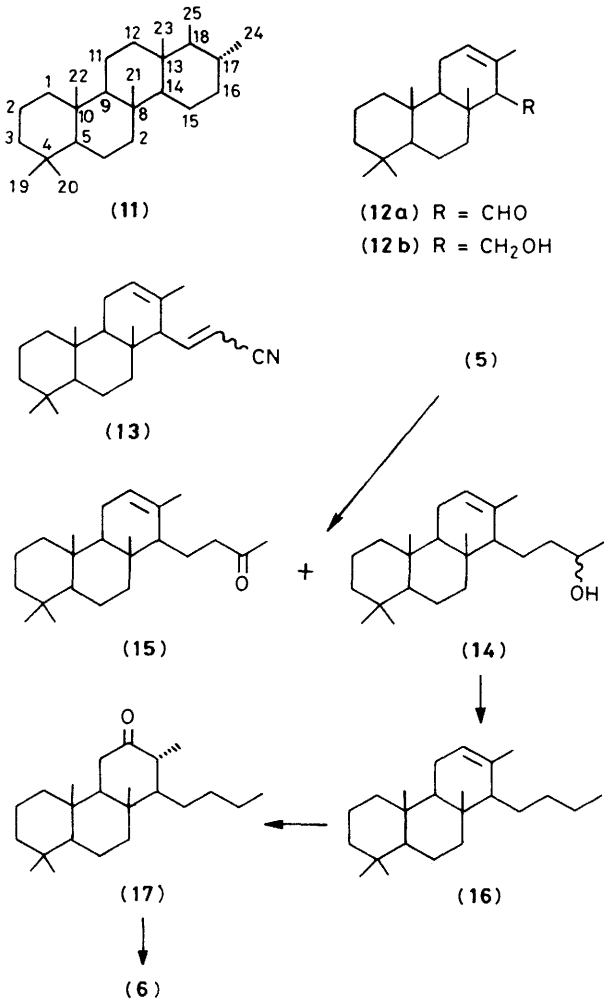
‡ The synthesis of (**8**) and (**22**) starting from manool has already been published by W. Herz, and J. Siva Prassad, *J. Org. Chem.*, 1982, **47**, 4171.

§ Attempts to the synthesis of precursors for cheilanthatriol (**10**), have been reported, R. V. Venkateswaran, D. Mukherjee, and P. C. Dutta, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1603.

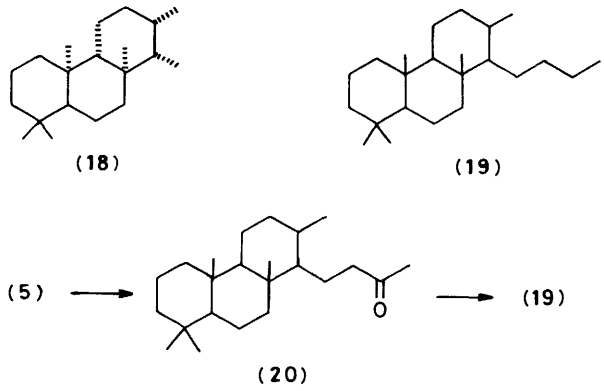
¶ Since the sample of copalic acid used for the preparation of methyl isocopalate was racemic, the structure of all intermediates and final products are written without considering their absolute configurations. The isolation of (±)-copalic acid form *Eperua purpurea* was recently reported, V. De Santis and J. D. Medina, *J. Nat. Products*, 1981, **14**, 370.

the preparation of (**12a**). We have found that the oxidation of the alcohol (**12b**)[2] with pyridinium chlorochromate adsorbed on neutral alumina[12] afforded an oily and fairly unstable product that shows carbonyl bands in its i.r. spectrum, suggesting that the aldehyde (**12a**) was contaminated with the conjugated isomer. This was confirmed by analysis of the ^{1}H n.m.r. spectrum which shows a doublet at δ 9.70 and a singlet at δ 10.26 in a 9:1 ratio. Treatment of (**12a**) with acetonylphosphorane led only to starting material, undoubtedly due to the severe steric hindrance at the carbonyl group. However, by reaction with the less bulky diethyl cyanomethylphosphonate, the conjugated nitrile (**13**) was obtained. Treatment of (**13**) with methyl-lithium followed by hydrolysis of the resulting imine afforded the desired αβ-unsaturated ketone (**5**) as a crystalline solid, showing the expected i.r. bands and ^{1}H n.m.r. signals. The analysis of the ^{13}C n.m.r. spectrum confirms the proposed structure and, further, on the basis of the signal at 54.4 p.p.m. assigned to C-9 by its multiplicity and comparison with related products previously studied,[2] shows that during the oxidation step and/or Wittig olefination no epimerization occurred at C-14, in spite of some isomerization to the conjugated aldehyde. This is a crucial point in our synthetic sequence since all the selected target molecules have an equatorial substituent at C-14.

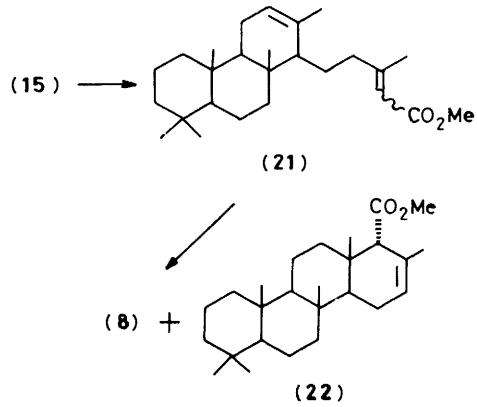
With access to the tricyclic ketone (**5**) secure, we focussed next on the synthesis of (**6**) (Scheme 1). Treatment of (**5**) with an excess of sodium in liquid ammonia afforded an epimeric mixture of the alcohols (**14**) together with a small amount of the ketone (**15**). The alcohols (**14**) were converted into the hydrocarbon (**16**) by tosylation and reduction with lithium aluminium hydride. Hydroboration of (**16**) followed by Jones oxidation and equilibration with sodium methoxide in methanol gave the saturated ketone (**17**). Finally, thioacetalization of (**17**) followed by treatment with Raney nickel afforded the low melting hydrocarbon (**6**). At this point, an exhaustive analysis of the ^{13}C n.m.r. spectrum of (**6**) was carried out. The shift data of isocopalane (**18**)[2] together with the information obtained from a APT spectrum[13] allowed the shift assignment of (**6**). It is worthwhile mentioning that the chemical shift of C-11 at 20.6 p.p.m. is a clear indicator that the methyl group at C-13 is equatorial. In order to obtain more rigorous evidence in favour of the foregoing stereochemical assignment at C-13, the synthesis of the epimeric hydrocarbon (**19**) was planned (Scheme 2). Catalytic hydrogenation of (**5**) from the less hindered α-face[2] gave the isomerically pure ketone (**20**) which, by thioacetalization and treatment with Raney nickel afforded (**19**). As expected, the signal of C-11 in the ^{13}C n.m.r. spectrum of (**19**) appears at a higher field than the corresponding one of (**6**), undoubtedly due to the γ effect imposed by the axial methyl group. The δ values calculated for hydrocarbons (**6**) and (**19**) by using the substituent parameters proposed by Bierbeck *et al.*[14] are in agreement with those observed. Finally, compound (**6**) was shown to be identical with the natural tricyclane, thus confirming the proposed structure and stereochemistry. It is worthwhile mentioning that the mass spectra of hydrocarbons (**6**) and (**19**), in spite of the different stereochemistry at C-13, are essentially identical.



Scheme 1.



Scheme 2.



Scheme 3.

Having established such a simple route, it was attractive to investigate further the chemistry of the ketone (**5**) in anticipation of being able to prepare the scalarane (**8**). As outlined in Scheme 3, treatment of (**15**) with trimethyl phosphonoacetate and sodium methoxide, produced the tricyclic esters (**21**), as a 2:1 mixture of *E*- and *Z*-isomers on the basis of the intensity of the 20-H ^{1}H n.m.r. signals. As expected, the signal corresponding to the *E*-isomer appears at δ 2.16 while that of the *Z*-isomer is at δ 1.89. By a careful column chromatography the pure isomer (**7**) was obtained and spectroscopically characterized.

Interestingly enough, the *Z*-isomer possesses the carbon skeleton of cheilanthatriol (**10**) and functional groups that could eventually allow the synthesis of the 6-deoxy derivative of the natural product. Cyclization of the mixture (**21**) with stannic chloride yielded again a 2:1 mixture of scalaranes (**8**) and (**22**) as shown by the relative intensity of the ^{1}H n.m.r signals of 18-H, at δ 2.89 ($W_{\frac{1}{2}}$ 8.6 Hz) and δ 2.47 ($W_{\frac{1}{2}}$ 4 Hz), respectively, in agreement with those reported for both compounds by Herz and Siva Prassad.* A careful recrystallization allowed the isolation, in pure form, of the major component of the mixture, showing m.p. and spectroscopic data identical with those previously reported for compound (**8**).

The synthesis described above is distinguished from those already reported by a higher overall yield of compounds (**6**) and (**8**) and by the fact that the entire sequence met with no separation problems.

Experimental

M.p.s were determined on an Ernst Leitz hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Beckman Acculab 8 spectrometer. ^{1}H and ^{13}C N.m.r. spectra were recorded at 80.13 and 20.15 MHz, unless otherwise stated, on a Bruker WP 80 SY spectrometer in deuteriochloroform with tetramethylsilane as internal standard. All solvents were purified and dried by standard techniques. All reactions were performed under a dry nitrogen atmosphere. Column chromatography was performed on silica gel 60 H, slurry packed, run under low pressure of nitrogen and employing increasing amounts of ethyl acetate in hexane as solvent. Ether refers to diethyl ether.

Isocopal-12-en-15-al (**12a**).—A stirred solution containing isocopal-12-en-15-ol (**12b**)[2] (605 mg, 2.08 mmol) in benzene (35 ml) was treated with pyridinium chlorochromate adsorbed on alumina (9.80 g, 8.03 mmol).[12] After the mixture had been stirred for 3 h at room temperature in the dark, the solid was filtered off through a silica gel 60 H and Celite pad and washed thoroughly with chloroform. The combined filtrates were evaporated to give crude aldehyde (**12a**) (390 mg) as an oil, $\nu_{max.}$ 1 730 (aldehyde), and 1 600 cm^{-1} (α,β-unsaturated aldehyde); δ_H 0.82 (3 H, s), 0.84 (3 H, s), 0.92 (3 H, s), 1.05 (3 H, s), 1.60 (3 H, s, 13-Me), 5.64 (1 H, br s, 12-H), 9.70 (d, *J* 4.8 Hz, aldehyde proton), and 10.26 (s, aldehyde proton of the α,β-unsaturated aldehyde). The crude material was used immediately for the next step.

18-19-*Dinor*-14αH-*cheilantha*-12,15-*dien*-17-*one* (**5**).—A suspension of 55—60% sodium hydride (157 mg, 3.6 mmol) in mineral oil was washed with hexane under an atmosphere of nitrogen, and then tetrahydrofuran (6 ml) was added. The mixture was cooled to 0 °C and a solution of diethyl cyanomethylphosphonate (761 mg, 4.3 mmol) in tetrahydrofuran (2 ml) was gradually added (15 min). After 1 h at room temperature, the mixture was again cooled to 0 °C and a solution of the aldehyde (**12a**) (390 mg, 1.35 mmol) in tetrahydrofuran (3.5 ml) was added dropwise. The mixture was stirred for an additional 2 h period at room temperature, diluted with water, and extracted with ether. The extract was washed with 10% aqueous sodium hydroxide, water, and brine, dried, and evaporated to give the conjugated nitrile (**13**) (490 mg) as an oil, $\nu_{max.}$ 2 200 (conjugated nitrile), and 1 660 cm^{-1} (C=C). To a cold (0 °C) and stirred solution of the crude nitrile (**13**) (490 mg, 1.58 mmol) in ether (15 ml) was added slowly a solution of methyl-lithium in ether (1.5M; 2.8 ml, 4.5 mmol). After the mixture had been stirred at 0 °C for 30 min, it was poured into water and extracted with ether. The ethereal extract was dried and evaporated. The residue was stirred at room temperature *in* a 9:1 mixture of acetone: aqueous N sulphuric acid for 1 h, poured into water, and extracted with ether. The organic extract was washed with 10% aqueous sodium hydrogen carbonate and water, dried, and evaporated to leave a residue which was chromatographed to give the conjugated ketone (**5**) [85 mg, 12% overall yield from (**12b**)], m.p. 105—106 °C (from MeOH); $\nu_{max.}$ 3 000—2 900, 1 680, and 1 390—1 370 cm^{-1}; δ_H 0.81 (3 H, s), 0.86 (3 H, s), 0.87 (3 H, s), 0.91 (3 H, s), 1.50 (3 H, s, 13-Me), 2.25 (3 H, s, CO-Me), 5.53 (1 H, br s, 12-H), 6.07 (1 H, d, *J* 16 Hz, =C*H*CO, and 6.67 (1 H, dd, *J* 16 and 11 Hz, C*H*=CHCO); δ_C 39.9 (t, C-1), 18.0 (t, C-2), 42.0 (t, C-3), 33.0 (s, C-4), 56.5 (d, C-5), 18.5 (t, C-6), 41.8 (t, C-7), 36.7 (s, C-8), 54.4 (d, C-9), 37.4 (s, C-10), 22.7 (t, C-11), 122.9 (d, C-12), 131.0 (s, C-13), 60.0 (d, C-14), 134.0 (d, C-15), 148.7 (d, C-16), 197.8 (s, C-17), 27.0 (q, C-20), 22.7 (q, C-21), 15.7 (q, C-22), 15.7 (q, C-23), 33.3 (q, C-24), and 21.6 (q, C-25) (Found: C, 84.1; H, 11.3. $C_{23}H_{36}C$ requires C, 84.09; H, 11.04%) (Found: M^+, 328.2743. Calc. for $C_{23}H_{36}O$: M^+, 328.2766).

18,19-*Dinor*-13βH,14αH-*cheilanthane* (**6**).—Small pieces of sodium metal (226 mg) were added to stirred, liquid ammonia (50 ml) at −69 °C. After the reaction mixture had been stirred for 30 min the temperature was raised to −33 °C and a solution of (**5**) (206 mg, 0.63 mmol) in ether was slowly added. The mixture was stirred for 1 h and then cooled again to −69 °C while solid ammonium chloride was carefully added until the blue colour faded away and ammonia evaporated. The residue was partitioned between water and ether and the aqueous layer was further extracted. The ether extract was dried and evaporated. The residue (200 mg) was chromatographed to yield (**14**) (136.5 mg, 65.3%) and (**15**) (47 mg, 22.6%). The epimeric mixture of (**14**) is a colourless oil; $\nu_{max.}$ 3 620, 2 940—2 860, 1 620, 1 470, and 1 380 cm^{-1}; δ_H 0.73 (3 H, s), 0.82 (3 H, s), 0.86 (3 H, s), 0.87 (3 H, s), 1.19 [3 H, d, *J* 6.4 Hz, CH(OH)Me], 1.66 (3 H, br s, 13-Me), 3.75 (1 H, br m, C*H*OH), and 5.35 (1 H, br s, 12-H); the ketone (**15**) was a colourless oil; $\nu_{max.}$ 2 940—2 860, 1 720, 1 680—1 640, 1 470, and 1 390—1 370 cm^{-1}; δ_H 0.73 (3 H, s), 0.82 (3 H, s), 0.86 (6 H, s), 1.67 (3 H, br s, 13-Me), 2.13 (3 H, s, COMe), and 5.36 (1 H, br s, 12-H). Jones oxidation of the alcohols (**14**) produced the ketone (**15**) quantitatively.

To a stirred solution of (**14**) (155 mg, 0.47 mmol) in dichloromethane (0.6 ml) and pyridine (1 ml) was gradually added a solution of toluene-*p*-sulphonyl chloride (500 mg, 2.6 mmol) in dichloromethane (2.7 ml) and pyridine (0.5 ml). After 15 h at room temperature, the mixture was poured into ice–water, stirred for an additional 3 h period at room temperature, and then extracted with ether. The ether extract was washed with 10% aqueous hydrochloric acid, 10% aqueous sodium hydrogen carbonate and brine, dried, and evaporated. Chromatographic purification of the crude product yielded an epimeric mixture of tosylates (207 mg, 91%); δ_H 0.60 (3 H, s), 0.82 (3 H, s), 0.85 (6 H, s), 1.26 [d, *J* 6.4 Hz, CH(OTs)Me], 1.30 [d, *J* 6.4 Hz, CH(OTs)Me], 2.43 (3 H, s, C_6H_4Me), 4.80 (1 H, m, C*H*OTs), 5.30 (1 H, br s, 12-H), 7.30 (2 H, d, *J* 9.6 Hz, ArH), and 7.85 (2 H, d, *J* 9.6 Hz, ArH).

To a stirred solution of lithium aluminium hydride (130 mg,

* [See footnote ‡ on p. 1227.]

3.4 mmol) in tetrahydrofuran was added a solution of the epimeric mixture of tosylates (207 mg, 0.42 mmol) in tetrahydrofuran. The mixture was heated for 2.5 h under reflux and then worked up, to give an oily residue. Chromatographic purification of the crude product yielded (**16**) (90.6 mg, 69%); δ_H 0.72 (3 H, s), 0.81 (3 H, s), 0.86 (6 H, s), 1.67 (3 H, br s, 13-Me), and 5.34 (1 H, br s, 12-H).

To a stirred solution of (**16**) (90 mg, 0.28 mmol) in tetrahydrofuran was added a solution of borane–methyl sulphide complex in tetrahydrofuran (2M; 2.4 ml). After the mixture had been stirred at room temperature for 20 h, 3M-sodium hydroxide (4 ml) and hydrogen peroxide (4 ml) were added and the whole stirred at 40 °C for 1.5 h; the mixture was then cooled and extracted with ether. The organic extract was dried and evaporated to yield an epimeric mixture of alcohols (95 mg); $\nu_{max.}$ 3 630 cm^{-1}; δ_H 3.57 (m, C*H*OH) and 3.89 (m, C*H*OH). To an ice-cold solution of this crude mixture in acetone was added dropwise a solution of Jones reagent until a slight excess was present. The mixture was stirred for 30 min and then worked up to give a product (93.2 mg) which was shown to be homogeneous by t.l.c. This was then equilibrated with sodium methoxide in methanol (prepared from 15 mg of sodium in 15 ml of methanol) at room temperature for 30 min. The residue obtained by removal of most of the solvent was diluted with water and the resulting mixture was extracted with ether. The organic extract was washed with brine, dried, and evaporated. Chromatographic purification of the crude product yielded (**17**) (35 mg); $\nu_{max.}$ 1 715 cm^{-1}; δ_H 0.83 (3 H, s), 0.86 (6 H, s), 0.90 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 1.04 (3 H, d, *J* 8 Hz, 13-Me), and 2.29 (2 H, m, CH_2CO); *m/z* 332 (M^+), and 191 (100%).

Boron trifluoride–ether (0.014 ml) was added to a stirred solution of (**17**) (35 mg) in dichloromethane (2 ml) and ethanedithiol (0.045 ml) and the whole stirred for 14 h at room temperature; the reaction was then complete (t.l.c.). Cooled 10% aqueous sodium hydroxide was then added and the mixture was extracted with dichloromethane. The organic extract was washed with brine, dried, and evaporated. A solution of the crude thioacetal (42.5 mg) in absolute ethanol (15 ml) was stirred under reflux 4 h in the presence of Raney nickel (*ca.* 500 mg). The mixture was filtered through Celite and the filtrate was evaporated to give a colourless low-melting solid [28.3 mg, 19% overall yield from (**14**)]. Sublimation of this product afforded crystalline (**6**) (24.4 mg), m.p. 39—41 °C; δ_H (400 MHz) 0.77 (3 H, s), 0.82 (6H, s), 0.86 (3 H, s), 0.85 (3 H, d, *J* 6.5 Hz, 13-Me), and 0.89 (3 H, t, *J* 7 Hz, 20-Me); δ_C 39.8 (t, C-1), 18.6 (t, C-2), 42.0 (t, C-3), 33.1 (t, C-4), 56.5 (s, C-5), 18.4 (t, C-6), 40.0 (t, C-7), 38.4 (s, C-8), 59.8 (d, C-9), 37.4 (s, C-10), 20.6 (t, C-11), 36.6 (t, C-12), 34.4 (d, C-13), 58.7 (d, C-14), 28.6 (t, C-15), 36.9 (t, C-16), 23.3 (t, C-17), 14.0 (q, C-20), 20.9 (q, C-21), 15.0 (q, C-22), 16.1 (q, C-23), 33.3 (q, C-24), and 21.4 (q, C-25); *m/z* 318 (M^+, 12%), 303 (12), 191 (100), 177 (5), 165 (5), 137 (25), 123 (31), 109 (31), 95 (47), 81 (42), 69 (52), and 55 (48) (Found: M^+, 318.3291. Calc. for $C_{23}H_{42}$: M^+, 318.3284).

18,19-*Dinor*-13α*H*,14α*H*-*cheilanthane* (**19**).—The ketone (**5**) (70 mg) in ethyl acetate (30 ml) was hydrogenated in the presence of platinum oxide (35 mg) for 4 h at room temperature and 4 atm. The catalyst was filtered off and the filtrate was concentrated to dryness. The residue (70 mg) afforded pure (**20**), m.p. 103—106 °C (from MeOH); $\nu_{max.}$ 1 720 cm^{-1}; δ_H 0.83 (12 H, br s), 0.90 (3 H, d, *J* 7 Hz, 13-Me), 2.13 (3 H, s, CO-Me); δ_C 39.9 (t, C-1), 18.6 (t, C-2), 42.1 (t, C-3), 33.2 (s, C-4), 56.5 (d, C-5), 18.1 (t, C-6), 41.5 (t, C-7), 38.5 (s, C-8), 61.4 (d, C-9), 37.5 (s, C-10), 16.1 (t, C-11), 34.7 (t, C-12), 29.1 (d, C-13), 53.2 (d, C-14), 19.9 (t, C-15), 42.4 (t, C-16), 209.5 (s, C-17), 29.7 (q, C-20), 15.1 (q, C-21), 16.2 (q, C-22), 17.4 (q, C-23), 33.3 (q, C-24), and 21.2 (q, C-25); *m/z* 332 (M^+, 10%), 317 (8), 259 (5), 191 (100), 177 (9), 163 (8), 150 (6), 137 (17), 123 (14), 109 (18), 95 (20), 81 (14), 69 (12), and 55 (10).

By following the same procedure described for the transformation of the ketone (**17**) into the hydrocarbon (**6**), the transformation of (**20**) (35 mg) into (**19**) [20 mg, 23% overall yield from (**5**)]. Sublimation of this product afforded crystalline (**19**) (15 mg), m.p. 73—74 °C; δ_H (400 MHz) 0.82 (3 H, s), 0.83 (3 H, s), 0.84 (3 H, s), 0.86 (3 H, s), 0.88 (3 H, d, *J* 8 Hz, 13-Me), and 0.90 (3 H, t, *J* 7.5 Hz, 20-Me); δ_C 39.9 (t, C-1), 18.6 (t, C-2), 42.1 (t, C-3), 33.2 (s, C-4), 56.5 (d, C-5), 18.1 (t, C-6), 41.5 (t, C-7), 38.5 (s, C-8), 61.4 (d, C-9), 37.5 (s, C-10), 16.2 (t, C-11), 34.9 (t, C-12), 29.2 (d, C-13), 53.7 (d, C-14), 25.0 (t, C-15), 30.2 (t, C-16), 23.0 (t, C-17), 14.0 (q, C-20), 15.4 (q, C-21), 17.5 (q, C-22), 16.2 (q, C-23), 33.2 (q, C-24), 21.3 (q, C-25); *m/z* 318 (M^+, 12%), 303 (12), 191 (100), 177 (5), 165 (5), 137 (25), 123 (28), 109 (28), 95 (42), 81 (41), 69 (61), and 55 (48) (Found: M^+, 318.3273. Calc. for $C_{23}H_{42}$: M^+, 318.3284).

Methyl Cheilantha-12,17-*dien*-19-*oate* (**21**).—To a stirred solution of the ketone (**15**) (100 mg, 0.3 mmol) and trimethylphosphonoacetate (405 mg, 2.24 mmol) in benzene (7 ml) was slowly added a solution of sodium methoxide in methanol (51.5 mg of sodium metal in 1.26 ml of methanol). After 1 h at 70 °C the mixture was cooled, treated with ice–water, and extracted with ethyl acetate. The organic extract was washed, dried, and evaporated. The residue was purified by chromatography yielding a 2:1 mixture of *E*- and *Z*-(**21**) (94 mg, 81%); δ_H 0.73 (3 H, s), 0.82 (3 H, s), 0.86 (6 H, s), 1.68 (3 H, s), 1.89 (d), 2.16 (d), 3.67 (OMe), 3.68 (OMe), 5.37 (1 H, br s), and 5.67 (1 H, m); *m/z* 386 (M^+, 4%), 371 (6), 272 (22), 177 (100), 192 (60), and 191 (51).

By very careful column chromatography the pure *E*-isomer (**7**) was obtained as an oil; $\nu_{max.}$ 2 920—2 840, 1 720, 1 650, 1 470—1 440, and 1 380 cm^{-1}; δ_H 0.73 (3 H, s), 0.82 (3 H, s), 0.86 (6 H, s), 1.68 (3 H, s), 2.17 (3 H, d), 3.68 (3 H, s), 5.37 (1 H, m), and 5.67 (1 H, m) (Found: M^+, 386.3144. Calc. for $C_{26}H_{42}O_2$: M^+, 386.3185).

Methyl Scalar-17-*en*-25-*oate* (**8**).—To a benzene solution of *E*- and *Z*-(**21**) (84 mg, 0.22 mmol) stannic chloride (0.12 ml, 1.08 mmol) was added. After being stirred for 4 h at room temperature, the mixture was treated with ice–water and extracted with ether. The organic extract was washed, dried, and evaporated. The residue was purified by chromatography to yield a mixture of ester (**8**) and (**22**) (65 mg, 78%); δ_H 2.47 [br s, $W_{\frac{1}{2}}$ 4 Hz, 18-H (**22**)], 2.89 (br s, $W_{\frac{1}{2}}$ 8.6 Hz (**8**)]. After crystallization pure (**8**) was obtained, m.p. 156—158 °C (from Et_2O) (lit.,* 165—169 °C); $\nu_{max.}$ 2 940—2 860, 1 740, 1 660—1 640, 1 470—1 450, and 1 390 cm^{-1}; δ_H 0.80—0.83 (6 H, br s), 0.92 (6 H, s), 1.56 (3 H, br s), 2.89 (1 H, br s, $W_{\frac{1}{2}}$ 8.6 Hz), 3.66 (3 H, s, OMe), 5.51 (1 H, br s, $W_{\frac{1}{2}}$ 9.8 Hz); *m/z* 386 (M^+, 20%), 260 (63), 205 (10), 191 (100), 137 (37), and 123 (40).

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* [See footnote ‡ on p. 1227.]

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