Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis and Mass Spectral Data of four Potential Biomarkers Related to the C_{19}Tricyclanes Found in Australian Oils and Puget Sound Sediments

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Published online: 23 Sep 2006.

To cite this article: Teodoro S. Kaufman (1995) Synthesis and Mass Spectral Data of four Potential Biomarkers Related to the C_{19}Tricyclanes Found in Australian Oils and Puget Sound Sediments, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:8, 1205-1221

To link to this article: http://dx.doi.org/10.1080/00397919508012684

SYNTHETIC COMMUNICATIONS, 25(8), 1205-1221 (1995)

SYNTHESIS AND MASS SPECTRAL DATA OF FOUR POTENTIAL BIOMARKERS RELATED TO THE C_{19} TRICYCLANES FOUND IN AUSTRALIAN OILS AND PUGET SOUND SEDIMENTS

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Abstract: The synthesis of four potential biomarkers, 13α-, 13β-, 14α- and 14β-ethyl-8β(H)-podocarpane is reported. GC-MS comparison with an Australian oil C_{19} tricyclane and the mass spectra of two Puget Sound C_{19}-terpanes evidenced non-identity of the synthetic compounds with the natural products; thus, proposed structures should be revised.

Petroleum diagenesis is a complex process of conversion of the lipid fraction of biological systems mostly to hydrocarbons, during sedimentation and maturation. These transformations are increasingly being used to provide information about the factors affecting organic matter in geological environments and, furthermore, studies of the carbon structures of chemically stable terpenoid and steroid hydrocarbons have been successful in providing useful

information for petroleum exploration. Because biomarkers have survived unchanged or little altered from their original structures, they also provide details about the molecular systems that synthesized them or their close relatives as well as give clues regarding the source, maturation degree, migration and age of an oil, and the degree to which it has been affected by heat, burial, rock catalysis and biodegradation.[1]

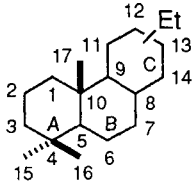
The complexity of the geological samples containing low concentration of these biomarkers often precludes their isolation, being GC-MS comparison with an authentic synthetic sample the usual method for their precise and definitive structural characterization.

Recently, Philp and coworkers[2] have detected a new C_{19} tricyclic terpenoid in Australian crude oils from the Gippsland Basin, to which they tentatively attributed structure **1**, based on a careful analysis of its mass spectrum. Simultaneously, Barrick and Hedges[3] published the mass spectra of two previously unknown C_{19} tricyclic nor-diterpanes found among the sedimentary hydrocarbons of the Puget Sound region of western Washington State.

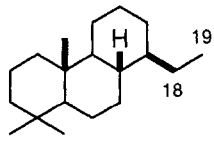
Since the involvement of our laboratory in the preparation of authentic standards of potential molecular fossils for GC-MS comparison and structural elucidation, we have elaborated many different bi-,[4] tri-[5] and tetracyclic[6] terpenoid derivatives, contributing to the discovery of an entirely new family of biomarkers in Chinese bituminous sandstones[7] and confirming the proposed structure for an

unusual C_{20} carboxylic acid found in the Canadian degraded oil sands of Athabasca.[8]

The present paper describes the synthesis of compounds **2 - 5** and their GC-MS comparison with the unknown Australian C_{19} tricyclane as well as their mass spectral confrontation with data of the Puget Sound C_{19} terpanes.



1



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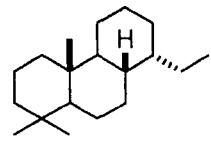

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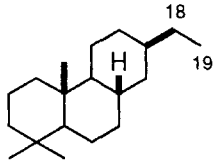

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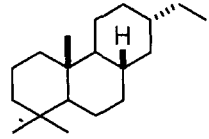


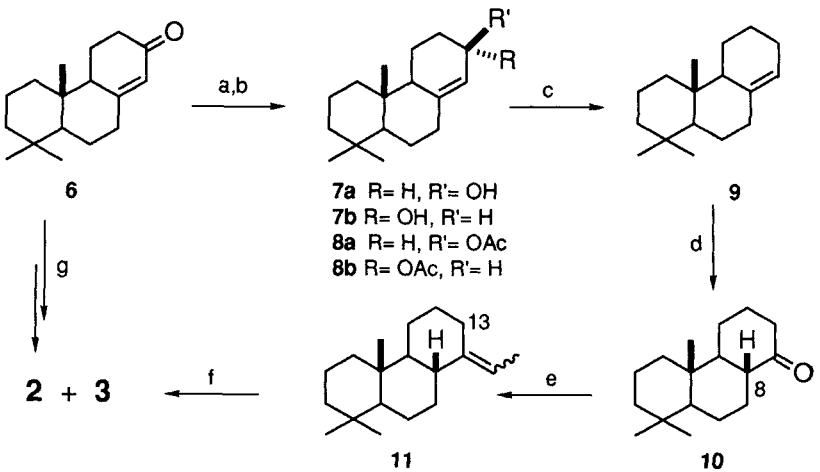
5

Those are the most likely structures corresponding to the new biomarkers since, to the best of our knowledge, neither C-11 nor C-12 substituted tricyclic podocarpane-type hydrocarbons have been reported to date in oil extracts and, moreover, the source of these terpenoids seems to be related to reduction, rearrangement and demethylation processes[2, 9] in the resinite maceral of the coal, being originated in resin acids from higher vascular plants.[2]

For the syntheses, it was decided to use the same starting material, the readily available enone **6**,[10] and to apply the widely used strategy of carrying out the elaboration of one

representative of each epimeric pair in its pure form, while the other targets could be part of a mixture to be simultaneously separated and analyzed during the GC-MS comparison step.[11] This decision simplified matters, since we have previously described an efficient synthesis of **2**.[9]

SCHEME 1



Reagents and Conditions: a. $NaBH_4$, $CeCl_3$, MeOH, 100%; b. Ac_2O, pyridine, CH_2Cl_2, 85%; c. 1. Li/NH_{3liq}, -33°C, 90 min, 2. NH_4Cl, RT, 54% + 46% of **7**; d. 1. BH_3SMe_2, THF, NaOH, 30% H_2O_2, 2. Jones' reagent, acetone, 0°C, 3. NaEtO, EtOH, RT, overnight, 81%; e. $Ph_3P^+EtBr^-$, MeLi, Et_2O, 88%; f. H_2, Rh/Al_2O_3, 1 atm., RT, MeOH-THF, 96%; g. See ref. 9.

As shown in Scheme 1, for the preparation of the C-14 susbtituted compounds, enone **6** was submitted to a reduction with sodium borohydride and cerium (III) chloride in methanol, to quantitatively furnish the known epimeric alcohols **7a** and **7b**,[12] which were transformed into an unseparable mixture of their related allylic acetates **8a** and **8b**.

Then, reduction of **8** with lithium in liquid ammonia, as reported by Ando and coworkers,[13] afforded the key intermediate **9**.

Olefin **9** was next submitted to a hydroboration-oxidation protocol with borane-dimethyl sulfide followed by alkaline hydrogen peroxide, and the resulting mixture of alcohols was oxidized with Jones' reagent to give a pair of ketones, epimeric on carbon 8; these were readily equilibrated to the thermodynamically more stable ketone **10**, an intermediate in the synthesis of phyllocladene,[14] in 81% overall yield from **9**, employing sodium methoxide in anhydrous methanol.

Then, the C-14 side chain was introduced by alkenylation of **10** by the Wittig method with ethylidenetriphenyl phposphorane, affording an 88% yield of a 10:1 mixture of E-**11** and Z-**11**, crystallization of which allowed to obtain pure E-**11**. The configuration of this solid was confirmed by analysis of its ^{13}C NMR spectrum and comparison of the estimated ^{13}C resonances[15] for E-**11** and Z-**11** at C-13 (δ 30.6 and 35.1, respectively) with the observed C-13 chemical shift (30.5 ppm). When olefin **11** was hydrogenated at atmospheric pressure and room temperature with 5% rhodium on alumina[16] as catalyst, a 1.6:1 mixture of the C_{19} tricyclanes **2** and **3** was obtained, as deduced from exhaustive analysis and comparison of ^{13}C NMR and GC data of the mixture and authentic **2**. Selection of a rhodium-based catalyst stemmed from the fact that these compounds promote hydrogenation to predominantly give axially-oriented products.

For elaboration of the remaining pair of epimers enone **6** was subjected to a Birch reduction, affording the known ketone **12**,[10a] to which the C-13 two-carbon side chain was appended by means of a Wittig reaction, furnishing an unseparable mixture of the olefinic key intermediates E-**13** and Z-**13**.

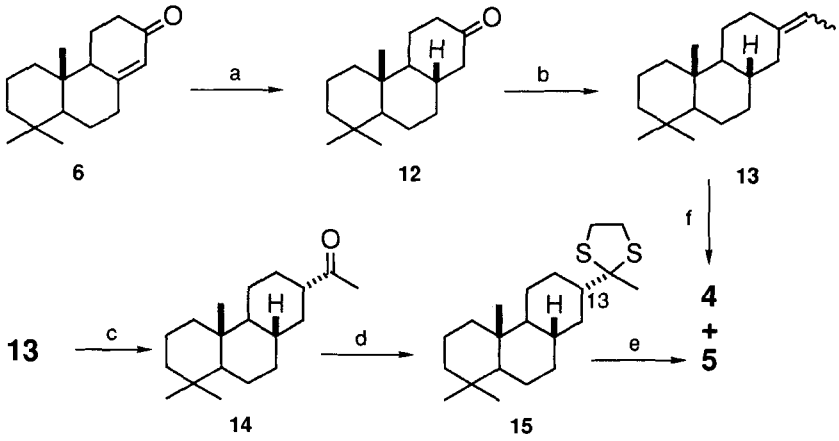
As shown in Scheme 2, by analogy with the synthesis of **10** and following a strategy which resembles that previously employed by Bauer,[17] and Corbett,[18] hydroboration-oxidation of **13**, followed by reaction with Jones' reagent and base-mediated equilibration, furnished methyl ketone **14** in 83% overall yield from **13**.

That the two-carbon side chain of **14** assumed the proposed equatorial configuration was assessed by comparison of calculated ^{13}C chemical shifts of C-13 of both possible epimers[15] with the observed resonance of C-13 in the synthetic compound. In fact, predicted signals at δ 38.9 and 52.5 were obtained for the axial and the equatorial methyl ketone respectively, being the observed chemical shift value of 51.2 ppm.

Ketone **14**, in turn, was smoothly and quantitatively converted into the related ethylene dithioketal **15** by boron trifluoride etherate-catalyzed reaction with 1,2-ethanedithiol and, finally, Raney nickel desulfurization of **15** in boiling ethanol furnished the desired target **5** in pure form.

Again, comparison of calculated[15] and observed ^{13}C resonances of C-13 of **4** and **5** confirmed that no epimerization occurred during the thioketalization-desulfurization process

SCHEME 2



Reagents and Conditions: a. 1. Li/NH_{3liq}, -33°C, 35 min, 2. NH_4Cl, 96%; b. $Ph_3P^+EtBr^-$, MeLi, Et_2O, 90%; c. 1. BH_3SMe_2, THF, NaOH, 30% H_2O_2, 2. Jones' reagent, acetone, 0°C, 3. NaMeO, MeOH, RT, overnight, 83%; d. $HSCH_2CH_2SH$, $BF_3.Et_2O$, CH_2Cl_2, RT, overnight, 100%; e. Raney Nickel, EtOH, reflux, overnight, 86%; f. H_2, Rh/Al_2O_3, 1 atm., RT, MeOH-THF, 93%.

and, therefore, the C-13 side chain was equatorial; values of δ 39.0 and 30.6 were calculated for **5** and **4**, respectively, whereas the observed chemical shift was 39.1 ppm.

To complete the synthesis of the required targets, an epimeric mixture containing **4** was obtained by rhodium on alumina-mediated catalytic hydrogenation of **13**, which gave **5** and **4** in a 3.2:1 ratio, as demonstrated by extensive analysis of their gas chromatogram and ^{13}C NMR spectrum, compared with retention time and chemical shift information of authentic diterpane **5**.

However, gas chromatographic and mass spectral comparison of the synthetic tricyclanes **2** - **5** with data of

Australian oil extracts revealed that the m/e 233 signal (M^+ - Et), while being the base-peak of the natural terpane, is entirely missing from the mass spectra of the synthetic hydrocarbons.

This indicates that the natural product must have a carbon skeleton different from that of **2** - **5**, on account that the trans-anti-trans ABC-ring configuration of the tricyclic system, being the thermodynamically more stable one, is that found in known tricyclic biomarkers.

In addition, the mass spectral data of the synthetic compounds did not match with any of both C_{19} hydrocarbons reported by Barrick and Hedges, also displaying prominent M^+ - Et peaks.[3]

These results, although not solving the identity problem of the C_{19} tricyclanes, constitute the basis for further reasearch into new possible candidates for GC-MS comparison.

EXPERIMENTAL SECTION

Melting points were measured on an Ernst Leitz hot-stage microscope apparatus and are uncorrected. IR spectra were taken on a Perkin Elmer Acculab-8 spectrometer with solid samples as KBr pellets and liquid samples as films. ^1H and ^{13}C NMR spectra were recorded in deuteriochloroform, on a Bruker WP 80 SY instrument at 80.13 and 20.15 MHz respectively, with tetramethylsilane as the internal standard. High and low resolution mass spectral data were obtained from Drs. O. S. Giordano (University of San Luis, Argentina) and R. P. Philp, (University of Oklahoma). Microanalyses were performed by Atlantic Microlab, Norcross, GA. The silica gel used for column chromatography was Merck Kieselgel 60 (0.04-0.063 mm). All reactions were carried out in a dry nitrogen atmosphere.

13α- and 13β-Hydroxy-podocarp-8(14)-ene (**7a** and **7b**): A solution of enone **6** (100 mg, 0.4 mmol) in absolute methanol (9.1 mL), was treated with sodium borohydride (6.8 mg, 0.18 mmol) and cerium III chloride heptahydrate (17.2 mg). Stirring was effected for 1 h in an ice-water bath, acetone (2.5 mL) was added and after 30 min at room temperature most of the solvent was evaporated under reduced pressure, brine (5 mL) was added and the organic products were extracted with ethyl acetate (4 x 40 mL). The combined extracts were washed with brine (5 mL), dried over sodium sulfate and concentrated under reduced pressure to give a 5:1 mixture of alcohols **7a** and **7b** (100 mg, 0.4 mmol, 100%); **7a**: mp: 126-127.5°C (recryst. from hexane; lit.[12] 127.5-128°C); IR ν 3400, 2940, 2880, 1660, 1450, 1390, 1370, 1050 and 870 cm^{-1}; ^1H NMR δ 0.79 (3 H, s), 0.80-2.29 (17 H, m), 0.85 (3 H, s), 0.88 (3 H, s), 4.09 (1 H, br s, $w_{1/2}$= 10.1 Hz) and 5.63 (1 H, d, J= 5.6 Hz); ^{13}C NMR δ 14.8 (C-17), 16.4 (C-11), 18.9 (C-2), 22.0 (C-16), 22.2 (C-6), 30.4 (C-12), 33.2 (C-4), 33.5 (C-15), 35.5 (C-7), 38.2 (C-10), 39.3 (C-1), 42.0 (C-3), 51.1 (C-9), 54.5 (C-5), 64.2 (C-13), 122.9 (C-14) and 143.9 (C-8); **7b**: mp: 109-111°C (recryst. from hexane; lit.[12] 109-111°C); IR ν 3400, 2940, 2880, 1660, 1450, 1390, 1370, 1050 and 870 cm^{-1}; ^1H NMR δ 0.74 (3 H, s), 0.79-2.29 (17 H, m), 0.84 (3 H, s), 0.88 (3 H, s), 4.14 (1 H, br s, w1/2= 16 Hz) and 5.47 (1 H, d, J= 1.8 Hz); ^{13}C NMR δ 14.2 (C-17), 18.7 (C-2), 19.7 (C-11), 21.9 (C-16), 22.3 (C-6), 33.1 (C-4 and C-12), 33.5 (C-15), 35.2 (C-7), 38.2 (C-10), 38.8 (C-1), 41.9 (C-3), 50.8 (C-9), 54.6 (C-5), 67.1 (C-13), 126.1 (C-14) and 140.3 (C-8).

Podocarp-8(14)-ene (**9**): A mixture of acetic anhydride (0.125 mL) and pyridine (0.5 mL) was added to alcohols **7** (98 mg, 0.4 mmol), dissolved in methylene chloride (7 mL). After stirring the reaction for 15 h at room temperature, it was acidified with cold 4% HCl (7 mL) and the products were extracted with ether (4 x 25 mL). The organic extracts were washed with saturated sodium bicarbonate (5 mL), dried over sodium sulfate and concentrated, giving acetates **8a** and **8b** (110 mg, 0.38 mmol, 95%); IR ν 3030, 2950 and 1740 cm^{-1}.
The foregoing acetates (102 mg, 0.35 mmol) in THF (1 mL) were introduced via syringe into refluxing dry liquid ammonia (5 mL), lithium wire (20 mg) was added portionwise and the reaction was kept at -33°C for 90 min. Ammonium chloride

(100 mg) quench was followed by solvent removal at room temperature, then the residue was dissolved in water (15 mL) and extracted with ether (3 x 15 mL). The extracts were concentrated under reduced pressure and chromatographed to furnish **9** (43 mg, 0.189 mmol, 54%) and a mixture of alcohols **7a** and **7b** (40 mg, 0.16 mmol, 46%), which was recycled; **9**: IR ν 2920, 2860, 1450, 1370, 880 and 810 cm^{-1}; ^1H NMR δ 0.76 (3 H, s), 0.84 (3 H, s), 0.87 (3 H, s), 0.90-2.00 (17 H, m), 2.02-2.30 (1 H, m) and 5.45 (1 H, m, $w_{1/2}$= 10 Hz); ^{13}C NMR δ 14.6 (C-17), 19.0 (C-2), 22.0 (C-16), 22.7 (C-6 and C-11), 22.9 (C-12), 25.2 (C-13), 33.2 (C-4), 33.6 (C-15), 36.0 (C-7), 38.3 (C-10), 39.2 (C-1), 42.2 (C-3), 51.3 (C-9), 54.9 (C-5), 121.4 (C-14) and 138.5 (C-8); mass spectrum, m/e (relative intensity) 232 (M^+, 27), 231 (30), 217 (16), 205 (5), 189 (10), 175 (13), 161 (36), 147 (40), 137 (100), 123 (72), 120 (82), 107 (74) and 91 (80); Anal. Calcd. for $C_{17}H_{28}$: C, 87.85; H, 12.15. Found C, 87.89; H, 12.10.

8β(H)-Podocarpan-14-one (**10**): A solution of olefin **9** (65 mg, 0.28 mmol) in anhydrous THF (5 mL) was dropwise treated with a 1.4 M solution of borane-dimethyl sulfide (0.24 mL, 0.33 mmol). The reaction was stirred overnight at room temperature, then 3N NaOH (2 mL) and 30% hydrogen peroxide (1 mL) were alternatively added dropwise. After 1 h, the reaction was diluted with brine (15 mL) and the organic products were extracted with ether (4 x 30 mL). The combined extracts were washed, dried over sodium sulfate and concentrated to give a crude oil, which was dissolved in acetone (10 mL) and cooled to 0°C. Jones reagent was slowly added and left to react for 30 min, the slight excess of reagent was destroyed with isopropyl alcohol (0.3 mL) and 30 min later the reaction products were partitioned between distilled water (10 mL) and ether (3 x 25 mL). The combined organic extracts were washed with brine (1 x 10 mL), dried, concentrated and dissolved in ethanol (5 mL) containing 0.25 M of sodium ethoxide. After equilibrating the ketone overnight at room temperature, the reaction was diluted with water (10 mL) and the product was extracted with ether (4 x 30 mL). The combined organic extracts were dried (Na_2SO_4), concentrated under reduced pressure and chromatographed to furnish ketone **10** (56 mg, 0.23 mmol, 81%) as a solid, mp: 67.5-68°C (recryst. from hexane; lit.[14] 67-68°C); IR ν 2940, 2870, 1715

and 1450 cm^{-1}; ^1H NMR δ 0.80-2.35 (19 H, m), 0.83 (3 H, s), 0.85 (3 H, s) and 0.93 (3 H, s); ^{13}C NMR δ 13.7 (C-17), 18.8 (C-2), 20.4 (C-6), 21.7 (C-16), 24.2 (C-11), 26.1 (C-7), 26.2 (C-12), 33.0 (C-4), 33.3 (C-15), 37.4 (C-10), 39.2 (C-1), 41.6 (C-13), 41.8 (C-3), 49.4 (C-8), 54.3 (C-9), 57.0 (C-5) and 213.4 (C-14); mass spectrum, m/e (relative intensity) 248 (M^+, 12), 233 (6), 215 (6), 163 (5), 150 (18), 138 (24), 123 (55), 109 (24) 97 (52) and 41 (100).

Wittig olefination of **10**: A 1.52 M solution of methyl lithium in hexane (0.36 mL, 0.548 mmol) was added to a suspension of ethyl triphenyl phosphonium bromide (212 mg, 0.575 mmol) in anhydrous ether (5 mL). After 2 h at room temperature, it was reacted with ketone **10** (34 mg, 0.137 mmol), dissolved in the same solvent (7 mL) and the reaction was stirred for 24 h. Then, distilled water (10 mL) was added and the reaction products were extracted with ether (4 x 30 mL). Drying, concentration and chromatography of the ethereal extract furnished a 10:1 mixture of E-**11** and Z-**11** (31 mg, 0.121 mmol, 88%). Crystallization from ether provided pure E-**11** as a solid, mp: 88-89.5°C; IR ν 2940, 2860, 1460, 1380, 915 and 830 cm^{-1}; ^1H NMR δ 0.80-2.03 (19 H, m), 0.85 (3 H, s), 0.89 (6 H, s), 1.58 (3 H, d, J= 6.4 Hz) and 5.10 (1 H, q, J= 6.4 Hz); ^{13}C NMR δ 12.8 (C-19), 14.2 (C-17), 18.9 (C-2), 21.5 (C-6), 21.9 (C-16), 25.4 (C-11), 27.5 (C-12), 29.0 (C-7), 30.5 (C-13), 33.1 (C-4), 33.6 (C-15), 37.4 (C-10), 39.4 (C-1), 41.3 (C-8), 42.0 (C-3), 55.2 (C-9), 57.2 (C-5), 111.9 (C-18) and 144.1 (C-14); mass spectrum, m/e (relative intensity) 260 (M^+, 50), 245 (11), 190 (11), 177 (6), 163 (7), 149 (13), 136 (37), 122 (100), 107 (74) and 95 (49); found for M^+ m/e 260.2508 ($C_{19}H_{32}$ requires m/e 260.2504).

14β- and 14α-Ethyl-8β(H)-podocarpanes (**2** and **3**): A solution of **11** (28 mg, 0.11 mmol) in a 1:1 THF-methanol mixture (8 mL) was hydrogenated for 24 hs at room temperature and atmospheric pressure employing 5% rhodium on alumina as catalyst (3 mg). Then, the catalyst was filtered off and washed with THF (2 x 2 mL), the solvent was evaporated and the resulting oil was distilled under reduced pressure to give a 1.6:1 mixture (GC) of **2** and **3** (27 mg, 0.106 mmol, 96%); **2**:[9] IR ν 2940, 2860, 1460 and 1380 cm^{-1}; ^1H NMR

δ 0.79-2.03 (25 H, m) and 0.81 (9 H, s); ^{13}C NMR δ 10.4 (C-19), 14.4 (C-17), 19.1 (C-2), 21.8 (C-6), 22.0 (C-16), 25.3 (C-11), 25.5 (C-12), 26.7 (C-18), 31.7 (C-13), 32.1 (C-7), 33.3 (C-4), 33.6 (C-15), 37.0 (C-10), 39.4 (C-1), 40.1 (C-8), 42.3 (C-3), 45.1 (C-14), 55.2 (C-5) and 56.0 (C-9); mass spectrum m/e (relative intensity) 262 (M^+, 45), 247 (6), 177 (96), 149 (100), 136 (26), 123 (72), 109 (49) and 95 (56); found for M^+ m/e 262.2661 ($C_{19}H_{34}$ requires m/e 262.2657); **3**: ^1H NMR δ 0.78-2.06 (25 H, m), 0.81 (3 H, s) and 0.83 (6 H, s); ^{13}C NMR δ 13.0 (C-19), 14.4 (C-17), 18.5 (C-18), 19.1 (C-2), 20.4 (C-12), 21.8 (C-6), 21.9 (C-16), 25.5 (C-11), 29.3 (C-13), 31.3 (C-7), 33.3 (C-4), 33.6 (C-15), 37.0 (C-10), 39.4 (C-1), 40.1 (C-8), 40.5 (C-14), 42.3 (C-3), 49.1 (C-9) and 55.5 (C-5); mass spectrum m/e (relative intensity) 262 (M^+, 34), 247 (6), 177 (70), 149 (100), 136 (22), 123 (86), 109 (61) and 95 (74); Anal. Calcd. for the mixture of $C_{19}H_{34}$: C, 86.94; H, 13.06. Found C, 87.17; H, 12.91.

8β(H)-Podocarpan-13-one (**12**): A solution of enone **6** (492 mg, 2 mmol) in dry THF (5 mL) was added dropwise to refluxing dry liquid ammonia (15 mL) containing lithium wire (34 mg). The blue solution was stirred for 15 min, ammonium chloride (100 mg) was added and the solvent was removed at room temperature under a nitrogen stream. The residue was taken with distilled water (10 mL) and partitioned with ether (3 x 50 mL). The organic extracts were washed with brine (10 mL), dried over sodium sulfate, concentrated under reduced pressure and chromatographed to afford ketone **12** (471 mg, 1.91 mmol, 96%) as a solid, mp: 92-94°C (recryst. from hexane; lit.[10a] 96-97°C); IR ν 2920, 2860, 1715, 1450 and 1370 cm^{-1}; ^1H NMR δ 0.70-2.38 (19 H, m), 0.85 (6 H, s) and 0.88 (3 H, s); ^{13}C NMR δ 14.0 (C-17), 18.6 (C-2), 21.4 (C-6), 21.8 (C-16), 25.4 (C-11), 33.1 (C-4), 33.5 (C-15), 35.7 (C-7), 36.9 (C-10), 37.9 (C-8), 39.3 (C-1), 41.1 (C-12), 42.07 (C-3), 49.0 (C-14), 54.3 (C-5), 55.1 (C-9) and 211.6 (C-13); mass spectrum m/e (relative intensity) 248 (M^+, 93), 233 (100), 215 (37), 192 (74), 177 (5), 163 (27), 147 (7), 135 (30), 123 (99), 110 (86) and 95 (42).

Wittig olefination of **12**: A solution of ketone **12** (450 mg, 1.81 mmol) in anhydrous ether (3 mL) was dropwise reacted with a red solution formed by reaction of 1.52 M methyl lithium (4.5 mL, 6.8 mmol) and ethyltriphenyl

phosphonium bromide (7 mmol) in ether (6 mL) at room temperature. After stirring for 24 h, saturated ammonium chloride (10 mL) was added and the reaction products were extracted with ether (3 x 30 mL). Drying, concentration and chromatography of the combined extracts afforded a 1:1 unseparable mixture of olefins Z-**13** and E-**13** (423 mg, 1.63 mmol, 90%) as an oil; IR ν 2920, 2840, 1450, 1390 and 830 cm^{-1}; ^1H NMR δ 0.76-2.00 (15 H, m), 0.79 (3 H, s), 0.82 (3 H, s), 0.85 (3 H, s), 1.53 + 1.59 (3 H, d, J= 5Hz), 2.07 (2 H, m, 12-H), 2.63 (2 H, m, H-14) and 5.09 (1 H, q, J 5 Hz); irradiation at δ 5.09 collapsed the 1.53 and 1.59 doublets to singlets, while irradiation at δ 2.07 transformed the δ 1.53 doublet into a singlet; ^{13}C NMR δ Z-**13**: 12.5 (C-19), 14.2 (C-17), 18.8 (C-2), 21.6 (C-16), 21.9 (C-6), 26.7 (C-11), 33.2 (C-4), 33.5 (C-15), 35.5 (C-12), 36.2 (C-7), 36.7 (C-14), 36.8 (C-10), 38.5 (C-8), 39.2 (C-1), 42.3 (C-3), 55.4 (C-5), 56.3 (C-9), 114.3 (C-18) and 139.5 (C-13); E-**13**: 12.5 (C-19), 14.2 (C-17), 18.8 (C-2), 21.6 (C-16), 21.9 (C-6), 25.8 (C-11), 27.8 (C-12), 33.2 (C-4), 33.5 (C-15), 35.8 (C-7), 36.8 (C-10), 37.5 (C-8), 39.2 (C-1), 42.3 (C-3), 45.1 (C-14), 55.4 (C-5), 56.3 (C-9), 114.3 (C-18) and 139.5 (C-13); mass spectrum m/e (relative intensity) 260 (M^+, 100), 177 (18) and 121 (49).

13β- and 13α-Ethyl-8β(H)-podocarpanes (**4** and **5**): A solution of **13** (100 mg, 0.36 mmol) in a 4:1 mixture of methanol-THF (8 mL) was hydrogenated for 48 h at room temperature and atmospheric pressure in the presence of 5% rhodium supported on alumina (8 mg). The catalyst was filtered off and washed with THF (2 x 2 mL). The organic solvents were removed and the residue was distilled at room temperature under reduced pressure (8 mm Hg) to furnish a 3.2:1 mixture of **5** and **4** (93 mg, 0.34 mmol, 93%); IR ν 2940, 2860, 1460, 1390 and 980 cm^{-1}; **4**: ^1H NMR δ 0.80-1.90 (25 H, m), 0.82 (6 H, s) and 0.83 (3 H, s); ^{13}C NMR δ 12.4 (C-19), 14.2 (C-17), 18.9 (C-2), 21.7 (C-6 and C-11), 21.9 (C-16), 24.9 (C-8), 29.7 (C-18), 30.6 (C-13), 33.2 (C-4 and C-12), 33.6 (C-15), 36.0 (C-7), 36.8 (C-10), 38.9 (C-1), 41.8 (C-14), 42.3 (C-3), 55.5 (C-5) and 56.7 (C-9); mass spectrum m/e (relative intensity) 262 (M^+, 21), 247 (4), 191 (2), 177 (34), 149 (69), 136 (7), 123 (68), 110 (54), 95 (70) and 81 (100); Anal. Calcd. for the mixture of $C_{19}H_{34}$: C, 86.94; H, 13.06. Found C, 86.88; H, 12.99.

13α-Acetyl-8β(H)-podocarpane (**14**): To an ice-cooled solution of olefin **13** (73 mg, 0.28 mmol) in anhydrous THF (4 mL), was added dropwise an excess of 1.4 M borane-dimethyl sulfide. After 2.5 h at room temperature, the solution was cooled to 0°C, 3 N NaOH (2 mL) and 30% hydrogen peroxide solution (1 mL) were alternatively added, and 1 h later, the organic products were extracted with ether (3 x 40 mL). The combined extracts were washed with distilled water (10 mL), 1M sodium bisulfite (20 mL) and brine (2 x 20 mL), then dried, dissolved in ice-cooled acetone (5 mL) and reacted with a slight excess of Jones reagent. After 15 min the excess of oxidant was destroyed with isopropanol (0.2 mL), the reaction was diluted with brine (5 mL) and extracted with ether (3 x 20 mL). The combined organic extracts were dried and concentrated to give a crude which was dissolved in 0.05 M sodium methoxide in methanol (5 mL) and equilibrated overnight with stirring. 10% citric acid (5 mL) was added, most of the methanol was evaporated under reduced pressure and the residue was extracted with ether (4 x 20 mL). The ethereal extracts were dried over sodium sulfate, concentrated under reduced pressure and chromatographed to give ketone **14** (65 mg, 0.23 mmol, 83%) as a solid, mp: 97.5-98°C (recryst. from hexane); IR ν 2930, 2860, 1715, 1455 and 1360 cm^{-1}; ^1H NMR δ 0.80-2.08 (20 H, m), 0.82 (6 H, s), 0.84 (3 H, s), and 2.11 (3 H, s); ^{13}C NMR δ 14.0 (C-17), 18.7 (C-2), 21.5 (C-6), 21.7 (C-16), 24.0 (C-11), 27.6 (C-19), 28.5 (C-12), 33.0 (C-4), 33.6 (C-15), 35.2 (C-7 and C10), 35.8 (C-8), 36.5 (C-14), 38.8 (C-1), 42.0 (C-3), 51.2 (C-13), 55.2 (C-5 and C-9) and 211.7 (C-18); mass spectrum m/e (relative intensity) 276 (M^+, 100), 261 (64), 258 (20), 243 (37), 233 (32), 205 (7),191 (26), 177 (12), 163 (34), 149 (21), 137 (20), 123 (55), 109 (41) and 95 (67); found for M^+ m/e 276.2452 ($C_{19}H_{32}O$ requires m/e 276.2457).

13α-Acetyl-8β(H)-podocarpane ethylenedithioketal (**15**): A solution of ketone **14** (60 mg, 0.22 mmol) in methylene chloride (5 mL) was treated with ethanodithiol (0.15 mL) and boron trifluoride etherate (0.05 mL). After stirring overnight at room temperature, 1.5 N NaOH (5 mL) was added, the biphasic system was stirred for another 30 min and then extracted with ether (4 x 25 mL). Drying, concentration and chromatography of the combined extracts furnished 1,3-dithiolane **15** (77 mg,

0.22 mmol, 100%) as a solid, mp: 94-96°C (recryst. from ether); IR ν 2920, 2840, 1450 and 1370 cm^{-1}; ^1H NMR δ 0.80-2.20 (20 H, m), 0.81 (6 H, s), 0.84 (3 H, s), 1.69 (3 H, s) and 3.27 (4 H, s, ethylenedithioketal); ^{13}C NMR δ 14.1 (C-17), 18.8 (C-2), 21.8 (C-6 and C-16), 24.8 (C-11), 29.5 (C-19), 30.5 (C-12), 33.1 (C-4), 33.5 (C-15), 35.4 (C-7), 36.4 (C-8), 36.6 (C-10), 38.8 (C-14), 39.1 (C-1), 39.4 (2 x C, ethylenedithioketal), 42.2 (C-3), 50.5 (C-13), 55.4 (C-5), 55.6 (C-9) and 71.8 (C-18); mass spectrum m/e (relative intensity) 352 (M^+, 3), 337 (0.5), 243 (0.5), 174 (0.4), 149 (0.7), 133 (0.9) and 119 (100).

13α-Ethyl-8β(H)-podocarpane (**5**): A solution of 1,3-dithiolane **15** (70 mg, 0.2 mmol) in ethanol (1 mL) was refluxed overnight with Raney nickel. Then, the catalyst was separated by filtration and washed with hot ethanol (3 x 2 mL). The solvent was evaporated and the resulting oil was submitted to a distillation under reduced pressure, affording compound **5** (44 mg, 0.17 mmol, 86%); IR ν 2940, 2860, 1460, 1390 and 980 cm^{-1}; ^1H NMR δ 0.70-1.90 (25 H, m), 0.81 (6 H, s) and 0.83 (3 H, s); ^{13}C NMR δ 11.4 (C-19), 14.2 (C-17), 18.9 (C-2), 21.7 (C-6), 21.9 (C-16), 24.8 (C-11), 29.9 (C-18), 33.2 (C-4 and C-12), 33.5 (C-15), 35.7 (C-7), 36.4 (C-8), 36.8 (C-10), 39.1 (C-1 and C-13), 41.8 (C-14), 42.2 (C-3), 55.5 (C-5) and 56.2 (C-9); mass spectrum m/e (relative intensity) 262 (M^+, 32), 247 (6), 191 (2), 177 (57), 163 (3), 149 (100), 136 (17), 123 (71), 109 (49) and 95 (76); Anal. Calcd. for $C_{19}H_{34}$: C, 86.94; H, 13.06. Found C, 87.02; H, 12.94.

ACKNOWLEDGEMENTS

The author is grateful to Dr. R. P. Philp, University of Oklahoma, U.S.A. for GC-MS data. Helpful discussions with Drs. E. A. Rúveda and M. Gonzalez Sierra are gratefully acknowledged. Thanks are due to CONICET for financial support.

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(Received in the USA 11 October 1994)