Synthesis of 11,14-Diacetoxy-13-(acetoxymethyl)podocarpa-8,11,13-triene. Correction of Proposed Structure for Premnolal

Takashi MATSUMOTO,* Sachihiko IMAI,* and Shuhei YUKI
Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Naka-ku, Hiroshima 730
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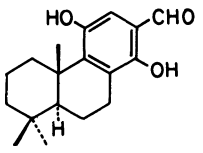
Oxidation of 11-acetoxyabieta-8,11,13-triene, derived from methyl 11-methoxyabieta-8,11,13-trien-18-oate, with chromium trioxide afforded 11,15-diacetoxyabieta-8,11,13-trien-7-one and 11-acetoxy-13-acetylpodocarpa-8,11,13-trien-7-one (**11**) in a ratio of *ca.* 2 : 1. The acetyl compound **11** was converted into a quinone, 13-(hydroxymethyl)podocarpa-8,12-diene-11,14-dione (**18**), by a series of reactions : iodoform reaction, esterification, acetylation, sodium borohydride reduction, dehydration, catalytic hydrogenation, lithium aluminium hydride reduction, and oxidation with Fremy's salt. Reductive acetylation of **18** produced 11,14-diacetoxy-13-(acetoxymethyl)-podocarpa-8,11,13-triene (**2**). The ^{1}H NMR spectrum of **2** was different from that of 15-acetoxypremnol diacetate which was prepared from natural premnolal. Based on this fact a corrected structure of premnolal is proposed.

Premnolal, a new aromatic bisnorditerpene, has recently been isolated from the root bark of *Premna latifolia* Roxb. (Verbenaceae) by Rao *et al.*[1] On the basis of chemical and spectroscopic studies, they deduced the structure of premnolal to be 11,14-dihydroxypodocarpa-8,11,13-triene-13-carbaldehyde (**1**). This structure is unique among the naturally-occurring tricyclic diterpenes, in that it contains a formyl group at C-13 and two hydroxyl goups at C-11 and C-14. To confirm the validity of their proposed structure, we now attempted the synthesis of **1** or its derivatives. This paper will describe the synthesis of the proposed 15-acetoxypremnol diacetate, 11,14-diacetoxy-13-(acetoxymethyl)-podocarpa-8,11,13-triene (**2**), and present a revised structure of natural premnolal.



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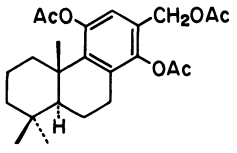

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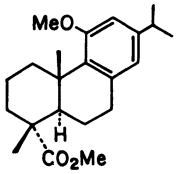

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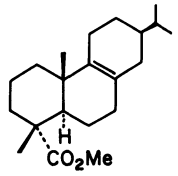

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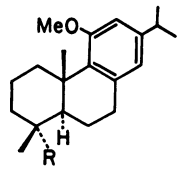
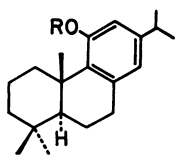
In the present study, methyl 11-methoxyabieta-8,11,13-trien-18-oate (**3**)[2] prepared from methyl (+)-13β-abiet-8-en-18-oate (**4**)[3] in our laboratory, was chosen as the starting material. Reduction of **3** with lithium aluminium hydride in refluxing ether afforded 11-methoxyabieta-8,11,13-trien-18-ol (**5**)[4,5] which, without purification, was oxidized at room temperature with pyridinium chlorochromate in dichloromethane to give 11-methoxyabieta-8,11,13-trien-18-al (**6**). The crude aldehyde **6** was immediately treated with 80% hydrazine hydrate in diethylene glycol at 125—140 °C and then with sodium hydroxide at 195—200 °C. Separation of the reaction mixture by column chromatography on silica gel yielded 11-methoxyabieta-8,11,13-triene (**7**)[4] and abieta-8,11,13-trien-11-ol (**8**) in a ratio of *ca.* 3 : 1. The methoxy compound **7** was easily demethylated at room temperature with boron tribromide in dichloromethane to give **8**, which was converted into the corresponding acetate (**9**) with acetic anhydride in pyridine. Oxidation of **9** with chromium trioxide in a mixture of acetic anhydride and acetic acid afforded two ketones, **10** and **11**, in yields of 48% and 23% respectively. The IR spectrum of **10** showed bands at 1768, 1735, and 1685 cm^{-1}, while that of **11** at 1768 and 1690 cm^{-1}. The ^{1}H NMR spectrum of **10** showed singlet signals at δ 1.74 (6H) due to two methyls, at δ 1.98 (3H) and 2.26 (3H) due to two acetoxyls, and two doublet signals at δ 6.98 (1H, J=2 Hz) and 7.84 (1H, J=2 Hz) assigned to two aromatic protons. On the other hand, the ^{1}H NMR spectrum of **11** showed an acetoxyl at δ 2.29 (3H, s), an acetyl at δ 2.57 (3H, s), and two aromatic protons at δ 7.57 (1H, d, J=2 Hz) and 8.35 (1H, d, J=2 Hz). From these spectral data, the structures of **10** and **11** were assigned respectively to be 11,15-diacetoxyabieta-8,11,13-trien-7-one and 11-acetoxy-13-acetylpodocarpa-8,11,13-trien-7-one.

Hydrolysis of **10** with sodium hydrogencarbonate in refluxing aqueous acetone afforded the known 11,15-dihydroxyabieta-8,11,13-trien-7-one (**12**) which was prepared by Kawazu *et al.*[6] from the natural fish-killing component, callicarpone (**13**).

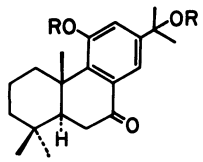
The ketone **11** was then converted into 11-acetoxy-13-(methoxycarbonyl)podocarpa-8,11,13-trien-7-one (**14**) by a series of reactions: iodoform reaction, esterification with diazomethane, and acetylation. The IR spectrum of **14** showed carbonyl absorptions at 1768, 1728, and 1690 cm^{-1}. Reduction of **14** with sodium borohydride in methanol, followed by dehydration with *p*-toluenesulfonic acid in refluxing benzene afforded 13-(methoxycarbonyl)podocarpa-6,8,11,13-tetraen-11-ol (**15**), whose ^{1}H NMR spectrum showed C-5, C-6, and C-7 protons at δ 2.20 (t, J=3 Hz), 6.03 (dd, J=10 and 3 Hz), and 6.48 (dd, J=10 and 3 Hz) respectively. The tetraene **15** was submitted to catalytic hydrogenation over Pd–C in ethanol and the resulting 13-(methoxycarbonyl)-podocarpa-8,11,13-trien-11-ol (**16**) was reduced with lithium aluminium hydride in refluxing ether to give



5 R=CH_2OH
6 R=CHO
7 R=Me



8 R=H
9 R=Ac



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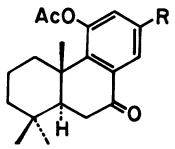
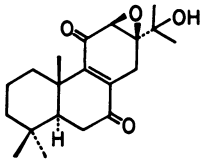
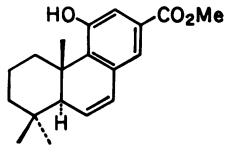
12 R=H



11 R=COMe
14 R=CO_2Me



13



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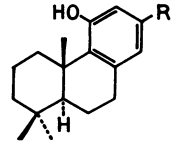
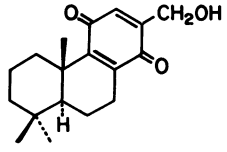
13-(hydroxymethyl)podocarpa-8,11,13-trien-11-ol (**17**). Introduction of oxygen function at C-14 was successfully achieved by oxidation of **17** in aqueous methanol with Fremy's salt in the presence of sodium dihydrogenphosphate and a *p*-quinone compound, 13-(hydroxymethyl)-podocarpa-8,12-diene-11,14-dione (**18**), was obtained. The ^1H NMR spectrum of **18** showed a broad singlet signal at δ 4.37 (2H) due to the hydroxymethyl group at C-13 and a triplet signal at δ 6.49 (1H, J=1.5 Hz) due to a vinylic proton at C-12. Reductive acetylation of **18** with zinc in acetic anhydride and pyridine afforded a triacetate **2**, whose ^1H NMR spectrum showed three acetoxyls at δ 1.98 (3H) and 2.24 (6H), a methylene of acetoxymethyl group at δ 4.87, and an aromatic proton at δ 6.78. Oxidation of **2** with chromium trioxide in acetic acid gave 11,14-diacetoxy-13-(acetoxymethyl)-podocarpa-8,11,13-trien-7-one (**19**), whose IR spectrum showed bands at 1763, 1745, and 1685 cm^{-1}. The presence of an aromatic proton at C-12 in **19** was supported by its chemical shift (δ 7.09) in the ^1H NMR spectrum; if the aromatic proton is located at C-14, the chemical shift might be expected to be δ *ca.* 8, like that (δ 7.94) of 12-acetoxyabieta-8,11,13-trien-7-one (**20**).[7]



16 R=CO_2Me
17 R=CH_2OH



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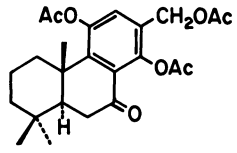

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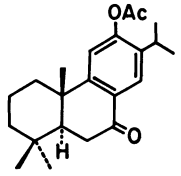

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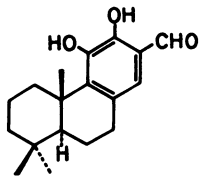

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Thus, the structure of **2** was conclusively assigned to be 11,14-diacetoxy-13-(acetoxymethyl)podocarpa-8,11,13-triene. Since the ^1H NMR spectrum of the synthetic **2** was different from that of 15-acetoxypremnol diacetate which was prepared from natural premnolal, all of the proposed structures[1] for premnolal and its derivatives should be revised. From the present study together with consideration of the published spectral data, we now propose the correct structure of premnolal to be 11,12-dihydroxypodocarpa-8,11,13-triene-13-carbaldehyde (**21**).

Experimental

All melting points are uncorrected. The IR and optical rotations were measured in chloroform, and the ^1H NMR spectra in carbon tetrachloride at 90 MHz, with tetramethylsilane as an internal standard, unless otherwise stated. The chemical shifts are presented in terms of δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, m: multiplet, dm: doublet of multiplet. The column chromatography was performed using Merck silica gel.

Abieta-8,11,13-trien-11-ol (8). *a)*: A solution of methyl 11-methoxyabieta-8,11,13-trien-18-oate (**3**)[2] (6.26 g) in dry ether (70 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (1.38 g) in dry ether (120 ml). The mixture was refluxed for 4 h, cooled, poured into ice–dilute hydrochloric acid, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo* to give 11-methoxyabieta-8,11,13-trien-18-ol (**5**)[4,5] (5.81 g) which, without purification, was used in the next reaction. IR: 3630, 3440 cm^{-1}; ^1H NMR (60 MHz): 0.81 (3H, s, C_4–CH_3), 1.21 (6H, d, J=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.27 (3H, s, C_{10}–CH_3), 2.16 (1H, s, –OH), 3.22 (2H, ABq, J_{AB}=11 Hz, δ_{AB}=20 Hz), 3.75 (3H, s, –OCH_3), 6.30 (2H, s, C_{12}–H and C_{14}–H).

A solution of the crude **5** (5.81 g) in dichloromethane (46 ml) was added to a stirred suspension of pyridinium chlorochromate (5.96 g) in dichloromethane (70 ml) at room temperature. The mixture was stirred for 105 min, diluted with ether, and then decanted from a tarry residue, which was washed with ether. The combined organic solution was washed with brine, passed through a short alumina column, and evaporated *in vacuo* to give the crude 11-methoxyabieta-8,11,13-trien-18-al (**6**) (5.20 g); IR: 2700, 1724 cm^{-1}; ^1H NMR (60 MHz): 1.12 (3H, s, C_4–CH_3), 1.19 (6H, d, J=7 Hz, –CH($C\underline{H}_3$)$_2$), 1.29 (3H, s, C_{10}–CH_3), 3.77 (3H, s, –OCH_3),

6.42 (2H, s, C_{12}–H and C_{14}–H), 9.18 (1H, s, –CHO).

A stirred mixture of the crude **6** (5.20 g) and 80% hydrazine hydrate (24.9 ml) in diethylene glycol (156 ml) was heated at 125—140 °C for 2 h, and then powdered sodium hydroxide (33.1 g) was added. The mixture was stirred at 195—200 °C for 3 h, cooled, diluted with water, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product (4.75 g) was chromatographed on silica gel (500 g), using hexane–benzene (99 : 1) as the eluent, to give 11-methoxyabieta-8,11,-13-triene (**7**)[4] (3.40 g: 62%) as an oil; $[\alpha]_D$ +125° (*c* 1.32); ^{1}H NMR: 0.92 and 0.94 (each 3H and s, –C(C$\underline{H}_3$)$_2$), 1.19 (6H, d, *J*=7 Hz, –CH(C$\underline{H}_3$)$_2$), 1.24 (3H, s, C_{10}–CH_3), 3.01 (1H, dm, *J*=13 Hz, $C_{1\beta}$–H), 3.74 (3H, s, –OCH_3), 6.36 (2H, s, C_{12}–H and C_{14}–H). Found: C, 84.19; H, 10.93%. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73%.

Further elution with hexane–benzene (2 : 3) gave abieta-8,11,13-trien-11-ol (**8**) (1.04 g: 20%) as a solid; $[\alpha]_D$ +94° (*c* 1.56); IR: 3595, 3340 cm^{-1}; ^{1}H NMR: 0.91 and 0.93 (each 3H and s, –C(C$\underline{H}_3$)$_2$), 1.14 (6H, d, *J*=7 Hz, –CH(C$\underline{H}_3$)$_2$), 1.27 (3H, s, C_{10}–CH_3), 3.04 (1H, dm, *J*=13 Hz, $C_{1\beta}$–H), 4.38 (1H, s, –OH), 6.05 (1H, bd, *J*=2 Hz, C_{12}–H), 6.35 (1H, bd, *J*=2 Hz, C_{14}–H). Found: C, 84.02; H, 10.69%. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56%.

b): A solution of boron tribromide (0.38 ml) in dichloromethane (1.5 ml) was added to a stirred solution of **7** (300 mg) in dichloromethane (3.0 ml) over a period of 5 min with cooling in an ice-bath. The mixture was stirred at the same temperature for 10 min and at room temperature for 2 h, poured into ice–water, and extracted with ether. The ether extract was washed successively with aqueous sodium thiosulfate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (30 g), using hexane–benzene (3 : 2) as the eluent, to give an oil (257 mg: 90%), whose IR and ^{1}H NMR spectra were identical with those of **8**.

11-Acetoxyabieta-8,11,13-triene (9). A solution of **8** (257 mg) and acetic anhydride (1.4 ml) in pyridine (1.4 ml) was allowed to stand overnight at room temperature. After the usual work-up, the crude product was recrystallized from methanol to give **9** (149 mg: 51%); mp 98.5—99.5 °C; $[\alpha]_D$ +94° (*c* 1.68); IR: 1748 cm^{-1}; ^{1}H NMR (60 MHz): 0.96 (6H, bs, –C(C$\underline{H}_3$)$_2$), 1.21 (6H, d, *J*=7 Hz, –CH(C$\underline{H}_3$)$_2$), 1.23 (3H, s, C_{10}–CH_3), 2.22 (3H, s, –$OCOCH_3$), 6.45 (1H, bs, C_{12}–H), 6.66 (1H, bs, C_{14}–H). Found: C, 80.64; H, 10.08%. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83%. The mother liquor of recrystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (15 g), using hexane–benzene (7 : 3) as the eluent, to give additional **9** (128 mg: 43%).

Oxidation of the Acetate 9 with Chromium Trioxide. Chromium trioxide (500 mg) was added portionwise at 0—5 °C to a stirred solution of **9** (328 mg) in acetic anhydride (2.3 ml) and acetic acid (3.3 ml). The mixture was further stirred at 0—5 °C for 1 h and at room temperature for 1 h. After the successive addition of aqueous sodium acetate (10%: 2.0 ml), methanol (1.5 ml), and brine (50 ml), the mixture was extracted with ether. The ether extract was washed with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel (40 g), using ether–benzene (1 : 99) as the eluent, to give 11,15-diacetoxyabieta-8,11,13-trien-7-one (**10**) (153 mg: 38%). This was recrystallized from methanol; mp 135—136 °C; $[\alpha]_D$ +45° (*c* 3.11); IR: 1768, 1735, 1685 cm^{-1}; ^{1}H NMR: 0.99 (6H, bs, –C(C$\underline{H}_3$)$_2$), 1.34 (3H, s, C_{10}–CH_3), 1.74 (6H, bs, –C(C$\underline{H}_3$)$_2$OCOCH_3), 1.98 (3H, s, C_{15}–$OCOCH_3$), 2.26 (3H, s, C_{11}–$OCOCH_3$), 6.98 (1H, d, *J*=2 Hz, C_{12}–H), 7.84 (1H, d, *J*=2 Hz, C_{14}–H). Found: C, 71.92; H, 8.15%. Calcd for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05%.

Further elution with the same solvent gave a mixture (148 mg) of **10** and 11-acetoxy-13-acetylopodocarpa-8,11,13-trien-7-one (**11**). This mixture was rechromatographed on silica gel (15 g), using ether–hexane (1 : 4) as the eluent, to give additional **10** (37 mg: 9%) and **11** (79 mg: 23%). The acetyl compound **11** was recrystallized from methanol; mp 111—112 °C; $[\alpha]_D$ +67° (*c* 0.925); IR: 1768, 1690, 1607 cm^{-1}; ^{1}H NMR: 1.01 (6H, s, –C(C$\underline{H}_3$)$_2$), 1.35 (3H, s, C_{10}–CH_3), 2.29 (3H, s, –$OCOCH_3$), 2.57 (3H, s, –$COCH_3$), 7.57 (1H, d, *J*=2 Hz, C_{12}–H), 8.35 (1H, d, *J*=2 Hz, C_{14}–H). Found: C, 73.95; H, 7.74%. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66%.

11,15-Dihydroxyabieta-8,11,13-trien-7-one (12). A mixture of **10** (220 mg) in hot aqueous acetone (50%: 44 ml) and sodium hydrogencarbonate (460 mg) was refluxed for 2 h. The mixture was diluted with brine and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The residue was recrystallized from chloroform to give **12** (74 mg: 43%); mp 220—222 °C; MS (*m/e*): 316 (M^+); $[\alpha]_D$ +45° (*c* 0.245, MeOH) (lit,[6] mp 220—222 °C, $[\alpha]_D^{25}$ +44° (MeOH)); ^{1}H NMR (acetone-d_6): 0.97 and 1.01 (each 3H and s, –C(C$\underline{H}_3$)$_2$), 1.43 (3H, s, C_{10}–CH_3), 1.48 (6H, s, –C(C$\underline{H}_3$)$_2$OH), 3.41 (1H, dm, *J*=13 Hz, $C_{1\beta}$–H), 3.91 (1H, s, C_{15}–OH), 7.28 (1H, d, *J*=2 Hz, C_{12}–H), 7.62 (1H, d, *J*=2 Hz, C_{14}–H), 8.40 (1H, s, C_{11}–OH). ^{1}H NMR (pyridine-d_5): 0.88 and 0.93 (each 3H and s, –C(C$\underline{H}_3$)$_2$), 1.58 (3H, s, C_{10}–CH_3), 1.71 (6H, s, –C(C$\underline{H}_3$)$_2$OH), 3.79 (1H, dm, *J*=12 Hz, $C_{1\beta}$–H), 7.90 (1H, d, *J*=2 Hz, C_{12}–H), 8.30 (1H, d, *J*=2 Hz, C_{14}–H). Found: C, 75.89; H, 8.91%. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92%. The mother liquor of recrystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (15 g), using ether–benzene (1 : 3) as the eluent, to give additional **12** (49 mg: 28%).

11-Acetoxy-13-(methoxycarbonyl)podocarpa-8,11,13-trien-7-one (14). A mixture of **11** (638 mg), iodine (710 mg), and pyridine (12 ml) was refluxed for 3 h. The mixture was allowed to stand overnight at room temperature, diluted with water, and extracted with chloroform. The chloroform extract was washed successively with dilute hydrochloric acid, aqueous sodium thiosulfate, and brine. After drying over sodium sulfate, the solution was evaporated *in vacuo*. The residual oil in ethanol (15 ml) was refluxed for 3 h with aqueous sodium hydroxide (10%: 8.2 ml), cooled, acidified with dilute hydrochloric acid, and extracted with chloroform. The chloroform extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo* to give a crude acid. This crude acid was immediately methylated with diazomethane in ether and the resulting methyl ester was acetylated with acetic anhydride (3.0 ml) in pyridine (3.0 ml) at room temperature overnight. After the usual work-up, the crude product was chromatographed on silica gel (70 g), using ether–benzene (2 : 98) as the eluent, to give **14** (299 mg: 45%); $[\alpha]_D$ +55° (*c* 0.725); IR: 1768, 1728, 1690 cm^{-1}; ^{1}H NMR: 1.01 (6H, s, –C(C$\underline{H}_3$)$_2$), 1.36 (3H, s, C_{10}–CH_3), 2.30 (3H, s, –$OCOCH_3$), 3.89 (3H, s, –CO_2CH_3), 7.62 (1H, d, *J*=2 Hz, C_{12}–H), 8.45 (1H, d, *J*=2 Hz, C_{14}–H). Found: C, 70.65; H, 7.40%. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31%.

13-(Methoxycarbonyl)podocarpa-6,8,11,13-tetraen-11-ol (15). A mixture of **14** (152 mg) and sodium borohydride (24 mg) in methanol (4.0 ml) was stirred at 0—5 °C for 1 h and at room temperature for 2 h. After the addition of acetone, the mixture was evaporated *in vacuo*. The residue was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried over sodium

sulfate, and evaporated *in vacuo* to give the corresponding alcohol.

A mixture of the above crude alcohol and *p*-toluenesulfonic acid (3.0 mg) in benzene (15 ml) was refluxed for 1 h, cooled, and then diluted with ether. The ether solution was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (15 g), using ether–benzene (1 : 99) as the eluent, to give **15** (116 mg: 90%). This was recrystallized from hexane; mp 147.5—149 °C; $[\alpha]_D$ −73° (*c* 1.11); IR: 3590, 3430, 1705 cm^{-1}; ^1H NMR ($CDCl_3$): 0.98 and 1.03 (each 3H and s, $-C(CH_3)_2$), 1.13 (3H, s, C_{10}–CH_3), 2.20 (1H, t, J=3 Hz, $C_{5\alpha}$–H), 3.00 (1H, m, $C_{1\beta}$–H), 3.89 (3H, s, $-CO_2CH_3$), 6.03 (1H, dd, J=10 and 3 Hz, C_6–H), 6.17 (1H, s, C_{11}–OH), 6.48 (1H, dd, J=10 and 3 Hz, C_7–H), 7.27 (1H, d, J=2 Hz, C_{12}–H), 7.43 (1H, d, J=2 Hz, C_{14}–H). Found: C, 75.98; H, 8.18%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%.

*13-(Methoxycarbonyl)podocarpa-8,11,13-trien-11-ol (**16**).* A mixture of **15** (169 mg) and 5% Pd–C (80 mg) in ethanol (5.0 ml) was submitted to catalytic hydrogenation with 1 atm hydrogen pressure at room temperature for *ca.* 2 h. After the usual work-up, the crude product was recrystallized from hexane to give **16** (118 mg: 69%); mp 180—181 °C; $[\alpha]_D$ +73° (*c* 1.56); IR: 3600, 3410, 1708 cm^{-1}; ^1H NMR ($CDCl_3$): 0.94 and 0.97 (each 3H and s, $-C(CH_3)_2$), 1.34 (3H, s, C_{10}–CH_3), 2.88 (2H, m, C_7–H_2), 3.18 (1H, dm, J=13 Hz, $C_{1\beta}$–H), 3.89 (3H, s, $-CO_2CH_3$), 5.97 (1H, bs, C_{11}–OH), 7.31 (2H, bs, C_{12}–H and C_{14}–H). Found: C, 75.54; H, 8.70%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%. The mother liquor of recrystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (5.0 g), using ether–benzene (2 : 98) as the eluent, to give additional **16** (33 mg: 19%).

*13-(Hydroxymethyl)podocarpa-8,11,13-trien-11-ol (**17**).* A mixture of **16** (149 mg) and lithium aluminium hydride (38 mg) in dry ether (10 ml) was refluxed for 2 h. The mixture was cooled, poured into a mixture of ice and dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was recrystallized from chloroform–hexane to give **17** (97 mg: 72%); mp 153—154 °C; $[\alpha]_D$ +77° (*c* 0.830); IR: 3600, 3330 cm^{-1}; ^1H NMR ($CDCl_3$): 0.94 and 0.96 (each 3H and s, $-C(CH_3)_3$), 1.32 (3H, s, C_{10}–CH_3), 2.18 (1H, bs, $-CH_2O\underline{H}$), 2.82 (2H, m, C_7–H_2), 3.13 (1H, dm, J=13 Hz, $C_{1\beta}$–H), 4.50 (2H, bs, $-C\underline{H}_2OH$), 5.73 (1H, bs, C_{11}–OH), 6.52 and 6.56 (each 1H and bs, C_{12}–H and C_{14}–H). Found: C, 79.00; H, 9.77%. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55%. The mother liquor of recrystallization was evaporated *in vacuo* and the residue was chromatographed on silica gel (5.0 g), using ether–benzene (1 : 1) as the eluent, to give additional **17** (33 mg: 24%).

*13-(Hydroxymethyl)podocarpa-8,12-diene-11,14-dione (**18**).* A solution of aqueous sodium dihydrogenphosphate [0.17 M (1 M=1 mol dm^{-3}): 4.0 ml] and Fremy's salt (150 mg) in water (8.0 ml) was added at 45 °C to a stirred solution of **17** (30 mg) in methanol (9.0 ml) over a period of 13 min. After being stirred at this temperature for 45 min, additional methanol (3.0 ml) and a solution of aqueous sodium dihydrogenphosphate (0.17 M: 4.0 ml) and Fremy's salt (150 mg) in water (8.0 ml) were added. The mixture was stirred at 45 °C for 45 more min, cooled, diluted with water, and extracted with chloroform. The chloroform extract was washed with brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (5.0 g), using ether–benzene (8 : 92) as the eluent, to give **18** (23 mg: 72%) as an oil; $[\alpha]_D$ −88° (*c* 1.01); IR: 3360, 1645 cm^{-1}; ^1H NMR: 0.92 and 0.94 (each 3H and s, $-C(CH_3)_2$), 1.26 (3H, s, C_{10}–CH_3), 4.37 (2H, bs, $-C\underline{H}_2OH$), 6.49 (1H, t, J=1.15 Hz, C_{12}–H). Found: C, 74.93; H, 8.39%. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39%.

*11,14-Diacetoxy-13-(acetoxymethyl)podocarpa-8,11,13-triene (**2**).* A mixture of **18** (47 mg), zinc (53 mg), acetic anhydride (0.5 ml), and pyridine (0.5 ml) was stirred at 0—5 °C for 10 min and then at room temperature for 1 h. The reaction mixture was filtered and the filtrate was diluted with ether. The ether solution was washed successively with aqueous sodium hydrogencarbonate, dilute hydrochloric acid, and brine. After drying over sodium sulfate, the ether solution was evaporated *in vacuo* to give an oil, whose IR spectrum showed a hydroxyl absorption band at 3330 cm^{-1}. The crude oil was immediately acetylated with acetic anhydride (0.5 ml) in pyridine (0.5 ml) at *ca.* 95 °C for 10 min. After the usual work-up, the crude product was chromatographed on silica gel (5.0 g), using ether–benzene (5 : 95) as the eluent, to give **2** (60 mg: 88%) as an oil; MS (*m/e*): 416 (M^+); $[\alpha]_D$ +61° (*c* 0.785); IR: 1765, 1745 cm^{-1}; ^1H NMR: 0.92 and 0.96 (each 3H and s, $-C(CH_3)_2$), 1.26 (3H, s, C_{10}–CH_3), 1.98 (3H, s, $-CH_2OCOC\underline{H}_3$), 2.24 (6H, s, C_{11}–$OCOCH_3$ and C_{14}–$OCOCH_3$), 2.60 (3H, m, $C_{1\beta}$–H and C_7–H_2), 4.87 (2H, bs, $-CH_2OAc$), 6.78 (1H, bs, C_{12}–H). ^1H NMR spectrum for natural 15-acetoxypremnol diacetate:[1] 0.90, 0.93, and 1.18 (each 3H and s, $3-CCH_3$), 1.92, 2.13, and 2.16 (each 3H and s, $3-OCOCH_3$), 2.45 (1H, dm, $C_{1\beta}$–H), 2.85 (2H, m, C_7–H_2), 4.86 (2H, s, $-C\underline{H}_2OAc$), 6.91 (1H, s, an aromatic proton). The ^1H NMR spectrum of **2** was not identical with that of natural 15-acetoxypremnol diacetate.

*11,14-Diacetoxy-13-(acetoxymethyl)podocarpa-8,11,13-trien-7-one (**19**).* A solution of chromium trioxide (35 mg) in acetic acid (0.16 ml) and water (0.04 ml) was added dropwise to a stirred solution of **2** (48 mg) in acetic acid (0.72 ml) at room temperature over a period of 3 min. The mixture was stirred at the same temperature for 15 h, poured into brine, and extracted with ether. The ether extract was washed successively with aqueous sodium hydrogencarbonate and brine, dried over sodium sulfate, and evaporated *in vacuo*. The crude product was chromatographed on silica gel (5.0 g), using ether–benzene (5 : 95) as the eluent, to give the starting **2** (23 mg: 47%). Further elution with the same solvent afforded **19** (17 mg: 34%) as an oil; $[\alpha]_D$ +72° (*c* 0.615); IR: 1763, 1745, 1685 cm^{-1}; ^1H NMR: 0.98 (6H, s, $-C(CH_3)_2$), 1.31 (3H, s, C_{10}–CH_3), 1.99 (3H, s, $-CH_2OCOC\underline{H}_3$), 2.26 (6H, s, C_{11}–$OCOCH_3$ and C_{14}–$OCOCH_3$), 4.95 (2H, bs, $-C\underline{H}_2$-OAc), 7.09 (1H, s, C_{12}–H). Found: C, 66.95; H, 7.20%. Calcd for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02%.

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