Isopimarane Diterpenoids from *Lycopus europaeus*†

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A reinvestigation of the diterpene metabolites of *Lycopus europaeus* allowed the isolation of five new compounds, namely, four isopimarane derivatives (**1**−**4**) and 5,9-dihydroxygeranyllinalool (**5**). The structures of these substances were established by chemical and spectroscopic means.

Some years ago, Milosavljevic and co-workers[1,2] isolated two diterpenoids from the aerial parts of *Lycopus europaeus* L. (Labiatae) assigning a pimarane-type structure for these compounds. Recently,[3] we isolated several diterpenes from the same plant, with one of these being identical to one of the two substances reported by the Yugoslav authors.[1] From exhaustive spectroscopic studies and chemical transformations, we concluded[3] that all the diterpenes isolated by our group, including that described by Milosavljevic and co-workers,[1] belonged to the isopimarane- rather than the pimarane-type hydrocarbon skeleton.

With the aim of reexamining the structure of the second pimarane described previously as a constituent of *L. europaeus*,[2] we have undertaken a careful reinvestigation of the extract of the plant. Unfortunately, our attempts were unsuccessful, although five minor diterpene constituents (**1**−**5**) were isolated. We report herein the structure elucidation of these new compounds. Repeated rechromatography of the more polar chromatographic fractions of an Me_2CO extract of the aerial parts of *L. europaeus* (see Experimental Section) led to the isolation of four new isopimaranes (**1**−**4**), along with a dihydroxy derivative of geranyllinalool (**5**).

Compound **1** had the molecular formula $C_{25}H_{34}O_7$, and its ^1H and ^{13}C NMR spectra (Tables 1 and 2, respectively) were very similar to those of **6** ($C_{25}H_{36}O_7$), another constituent of *L. europaeus*,[3] showing almost identical signals for an 8,15-isopimaradiene with acetoxyl groups at the C-1α and C-7α positions and a carbomethoxyl group at C-18. The observed differences between the ^1H and ^{13}C NMR spectra of these diterpenoids were consistent with the presence in **1** of a ketone at C-14 [δ_C 129.6 s (C-8), 164.9 s (C-9), 47.5 s (C-13), and 199.7 s (C-14)] instead of the 14α-hydroxyl group of **6** [$\delta_{H-14\beta}$ 3.58 br s; δ_C 127.5 s (C-8), 146.3 s (C-9), 39.4 s (C-13), and 76.5 d (C-14)].[3] This was also in agreement with typical absorptions for an α,*β*-unsaturated ketone in the IR and UV spectra of **1** [ν_{max} 1680 and 1630 cm^{-1}; λ_{max} 237 nm (log ϵ 4.01)]. Oxidation of **6** with Jones's reagent[4] yielded a substance identical in all respects (mp, mixed mp, $[\alpha]_D$, ^1H NMR, MS, and TLC) with **1**, thus confirming its structure and establishing[3] a *normal* isopimarane absolute configuration for this diterpenoid.

Another of the new diterpenoids, **2** ($C_{23}H_{34}O_6$), was a regioisomer of 7α-acetoxy-11α,14α-dihydroxy-8,15-isopimaradien-18-oic acid methyl ester (**7**, $C_{23}H_{34}O_6$) previously found in the same plant.[3] Acetic anhydride−pyridine treatment of **2** yielded a peracetyl derivative (**8**) identical with that obtained by acetylation of **7**.[3] This correlation established for **2** a *normal* methyl 8,15-isopimaradien-18-oate structure with two secondary alcohols at the C-7α and C-11α positions and an acetoxyl group at the C-14α position. The attachment of the acetoxyl group at C-14 was deduced from the HMBC spectrum of **2**, because connectivity between the carboxyl carbon of the acetate (δ 171.1 s) and the H-14*β* proton (δ 5.14 s) was observed.

Compound **3** ($C_{23}H_{32}O_6$) possessed an α,*β*-unsaturated ketone [UV λ_{max} 232 nm (log ϵ 4.00); δ_C 128.6 s (C-8), 165.4 s (C-9), 47.2 s (C-13), and 199.6 s (C-14)] as in **1**, and an 8,15-isopimaradien-18-oic acid methyl ester structure with a secondary alcohol and an acetoxyl group at the C-11 and C-7 positions (see Tables 1 and 2). Oxidation of **3** gave the enedione derivative **9** ($C_{23}H_{30}O_6$), previously obtained[3] from **7**, thus supporting the location of the acetoxyl and hydroxyl groups of **3** at the C-7α and C-11 positions, respectively. This conclusion was also in agreement with the HMBC spectrum of **3**, which displayed connectivities between the carbonyl carbon at C-14 and the H-7*β*, H-15, and Me-17 protons (δ 5.84, 6.10, and 1.17, respectively). The 11α-configuration of the hydroxyl group of **3** was established from the NOESY spectrum, because the H-11*β* proton showed NOEs with the Me-17 and Me-20 protons. As **3** was chemically correlated with the *normal* isopimarane **7**[3] (see above), the former must have a *normal* isopimarane absolute stereochemistry.

Methyl 7α-acetoxy-1α,11α,14α-trihydroxy-8,15-isopimaradien-18-oate (**4**, $C_{23}H_{34}O_7$) was also found in the extract of *L. europaeus*. Comparison of the ^1H and ^{13}C NMR spectra of **4** (Tables 1 and 2) with those of other isopimarane derivatives isolated from the same plant (**2**, **6**, **7**, and others[3]) strongly supported structure **4** for this new diterpenoid. In particular, the location of the acetoxyl group at C-7 was established from the HMBC spectrum [connectivities between the carboxyl carbon of the acetate (δ 170.9 s) and the H-7*β* proton (δ 5.12 dd) and between the C-7 carbon (δ 71.3 d) and the H-5α, H-6α, and H-6*β* protons (δ 2.90 dd, 1.50 ddd, and 1.84 ddd, respectively)]. The relative stereochemistry of **4** was in agreement with its NOESY spectrum, which showed NOEs between the Me-20 and H-1*β*, H-7*β*, H-11*β*, and Me-17 protons, as well as between the Me-17 and H-11*β*, H-14*β*, and Me-20 protons, thus defining a *cis* spatial relationship for all these hydrogens.

The absolute configuration of **4** was not ascertained. However, we suppose that it belongs to the *normal* isopimarane series, like the other diterpenoids isolated from the same plant (**1**−**3**, **6**, **7**, and others[3]).

The last of the new diterpenoids found in this study was 3,7,11,15-tetramethyl-1,6,10,14-hexadecatetraene-3,5,9-

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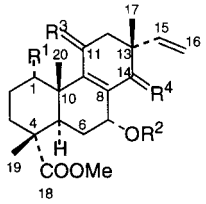
Table 1. ^{1}H NMR Spectral Data for Compounds **1**−**4**

proton(s)	**1**	**2**	**3**	**4**	$J_{H,H}$ (Hz)	**1**	**2**	**3**	**4**
H-1α		∼1.88[a]	1.87 (ddd)		1α,1β		*a*	12.5	
H-1β	4.97 (t)	∼1.63[a]	1.78 (ddd)	4.09 (t)	1α,2α		*a*	4.2	
H-2α	∼1.88[a]	∼1.63[a]	∼1.65[a]	1.79 (dddd)	1α,2β		*a*	12.5	
H-2β	∼1.88[a]	∼1.63[a]	∼1.65[a]	1.92 (dddd)	1β,2α	2.8	*a*	3.7	2.3
H-3α	∼1.98[a]	∼1.63[a]	∼1.60[a]	2.28 (ddd)	1β,2β	2.8	*a*	2.5	2.3
H-3β	1.44 (ddd)	∼1.86[a]	∼1.72[a]	1.39 (ddd)	2α,2β	*a*	*a*	*a*	13.6
H-5α	2.78 (dd)	2.41 (dd)	2.43 (dd)	2.90 (dd)	2α,3α	*a*	*a*	*a*	4.5
H-6α	1.62 (ddd)	1.40 (ddd)	1.56 (ddd)	1.50 (ddd)	2α,3β	3.3	*a*	*a*	2.6
H-6β	1.71 (ddd)	1.77 (ddd)	1.72 (ddd)	1.84 (ddd)	2β,3α	*a*	*a*	*a*	13.6
H-7β	5.75 (ddd)	3.95 (br d)	5.84 (ddd)	5.12 (dd)	2β,3β	3.3	*a*	*a*	4.1
H-11α	2.27 (ddd)				3α,3β	13.0	*a*	*a*	13.6
H-11β	2.08 (dddd)	4.28 (dd)	4.35 (dddd)	4.45 (ddd)	5α,6α	2.3	1.9	2.0	2.0
H-12α	1.74 (ddd)	2.18 (dd)	2.38 (dd)	2.30 (dd)	5α,6β	12.7	13.2	13.0	13.3
H-12β	∼1.88[a]	∼1.74[a]	2.00 (dd)	1.58 (dd)	6α,6β	14.8	14.2	14.9	14.8
H-14β		5.14 (s)		3.62 (d)	6α,7β	1.7	1.7	1.8	2.0
H-15	5.69 (dd)	5.98 (dd)	6.10 (dd)	6.10 (dd)	6β,7β	4.0	3.7	4.2	4.7
H_A-16	4.92 (dd)[b]	5.10 (dd)[c]	4.93 (dd)[b]	5.14 (dd)[c]	7β,11β	1.3	0	1.0	0
H_B-16	5.02 (dd)[c]	5.13 (dd)[b]	5.11 (dd)[c]	5.15 (dd)[b]	11α,11β	18.3			
Me-17	1.12 (3H, s)	0.93 (3H, s)	1.17 (3H, s)	0.87 (3H, s)	11α,12α	4.5			
Me-19	1.21 (3H, s)	1.20 (3H, s)	1.19 (3H, s)	1.18 (3H, s)	11α,12β	3.5			
Me-20	1.10 (3H, s)	0.94 (3H, s)	1.03 (3H, s)	0.92 (3H, s)	11β,12α	11.4	2.2	2.6	1.2
OAc	2.04 (3H, s)	2.07 (3H, s)	2.00 (3H, s)	2.09 (3H, s)	11β,12β	2.8	5.6	3.9	6.4
	1.99 (3H, s)				12α,12β	13.5	14.9	14.4	15.5
COO*Me*	3.63 (3H, s)	3.68 (3H, s)	3.62 (3H, s)	3.63 (3H, s)	15,16A	17.6	11.0	17.9	10.6
1α-OH				4.61 (br s)	15,16B	10.8	17.6	10.7	17.8
11α-OH		*d*	2.46 (d)	4.93 (d)	16A,16B	0.6	1.0	0.4	1.0
14α-OH				3.18 (d)	11β−11OH			11.1	8.5
					14β,14OH				4.5

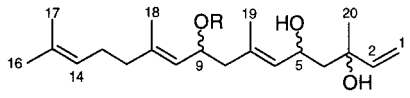
[a] This is an overlapped signal; approximate δ value was measured from the HSQC spectrum. [b] This is the *trans*-hydrogen with respect to H-15. [c] This is the *cis*-hydrogen with respect to H-15. [d] This signal was not observed.

Table 2. ^{13}C NMR Spectral Data for Compounds **1**−**4**

carbon	**1**	**2**	**3**	**4**
C-1	72.4 (d)	34.8 (t)	34.2 (t)	69.9 (d)
C-2	21.7 (t)	18.1 (t)	17.9 (t)	24.1 (t)
C-3	29.9 (t)	36.3 (t)	36.3 (t)	29.6 (t)
C-4	46.4 (s)	47.2 (s)	46.5 (s)	46.8 (s)
C-5	34.8 (d)	40.2 (d)	40.0 (d)	34.2 (d)
C-6	26.6 (t)	29.7 (t)	27.3 (t)	27.3 (t)
C-7	64.3 (d)	67.6 (d)	64.3 (d)	71.3 (d)
C-8	129.6 (s)	131.1 (s)	128.6 (s)	135.5 (s)
C-9	164.9 (s)	149.5 (s)	165.4 (s)	148.8 (s)
C-10	42.8 (s)	38.5 (s)	39.2 (s)	43.4 (s)
C-11	21.7 (t)	63.0 (d)	63.3 (d)	62.6 (d)
C-12	35.2 (t)	41.6 (t)	44.4 (t)	39.9 (t)
C-13	47.5 (s)	40.8 (s)	47.2 (s)	42.1 (s)
C-14	199.7 (s)	79.0 (d)	199.6 (s)	76.5 (d)
C-15	140.5 (d)	143.6 (d)	145.6 (d)	145.0 (d)
C-16	114.6 (t)	114.1 (t)	115.1 (t)	113.4 (t)
C-17	23.6 (q)	26.1 (q)	25.0 (q)	26.6 (q)
C-18	177.5 (s)	178.5 (s)	178.0 (s)	178.0 (s)
C-19	16.4 (q)	16.5 (q)	16.6 (q)	16.1 (q)
C-20	18.5 (q)	18.6 (q)	19.2 (q)	18.4 (q)
OAc	170.4 (s)	171.1 (s)	169.8 (s)	170.9 (s)
	170.1 (s)	21.5 (q)	21.0 (q)	21.4 (q)
	21.3 (q)			
	21.0 (q)			
COOCH_3	52.0 (q)	52.0 (q)	51.9 (q)	51.9 (q)



	R^1	R^2	R^3	R^4
1	OAc	Ac	H,H	O
2	H	H	α-OH,β-H	α-OAc,β-H
3	H	Ac	α-OH,β-H	O
4	OH	Ac	α-OH,β-H	α-OH,β-H
6	OAc	Ac	H,H	α-OH,β-H
7	H	Ac	α-OH,β-H	α-OH,β-H
8	H	Ac	α-OAc,β-H	α-OAc,β-H
9	H	Ac	O	O



5 R=H
10 R=Ac

triol (**5**, 5,9-dihydroxygeranyllinalool). The ^{1}H NMR spectrum of **5** was almost identical to that of 9-acetoxy-5-hydroxygeranyllinalool (**10**), a compound previously isolated[5] from a *Geigeria* species (Compositae). In fact, the observed differences between the ^{1}H NMR spectra of **5** and **10** were in agreement with the presence in **5** of a hydroxyl group at C-9 (δ_{H-9} 4.61, 1H, ddd; absence of OAc signals, see Experimental Section, spectrum recorded in C_6D_6 solution) instead of the C-9 acetoxyl group of **10** [δ_H 1.82, 3H, s (OAc), 5.94, 1H, ddd (H-9)].[5] The unambiguous assignment of the ^{1}H and ^{13}C NMR spectra of **5**, supported by HSQC and HMBC experiments, are reported in the Experimental Section.

Experimental Section

General Experimental Procedures. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. IR spectra were obtained on a Perkin-Elmer 681 spectrophotometer. UV spectra were recorded on a Perkin-Elmer Lambda 2 UV/vis spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian INOVA 400 apparatus at 400 and 100 MHz, respectively, and chemical shifts are reported with respect to residual $CHCl_3$ (δ 7.25) for protons and to solvent signals (δ_{CDCl_3} 77.00) for carbons. ^{13}C NMR assignments were determined by HSQC and HMBC spectra. MS were recorded in the positive EI mode on a Hewlett-Packard HP 5989A instrument (70 eV), and no fragments below *m*/*z* 50 were registered, except for **2**. Elemen-

tal analyses were made with a Carlo Erba EA 1108 apparatus. Merck Si gel no. 7734 (70−230 mesh) deactivated with 10% H_2O (w/v) was used for column chromatography.

Isolation of Compounds 1−5. For details on the collection and extraction of the aerial parts of *L. europaeus* L. see Hussein et al.[3] The chromatographic fractions eluted with petroleum ether−EtOAc (2:1−1:1) in the initial chromatography of the acetone extract of the plant yielded a residue (4.8 g), which on TLC showed several spots more polar than the other diterpenoids isolated previously.[3] Repeated chromatography [Si gel columns, petroleum ether−EtOAc (3:1−1:1) and benzene−EtOAc (2:1) as eluents] of that residue yielded **1** (68 mg, 0.007% of dry plant material), **3** (160 mg, 0.016%), **2** (76 mg, 0.008%), **4** (48 mg, 0.005%), and **5** (30 mg, 0.003%) in order of increasing chromatographic polarity.

Methyl 1α,7α-diacetoxy-14-oxo-8,15-isopimaradien-18-oate (1): colorless needles (EtOAc−petroleum ether); mp 184−186 °C; $[\alpha]^{20}_D$ +102.1° (*c* 0.533, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 237 (4.01); IR (KBr) ν_{max} 3080, 1670 (vinyl), 1730 br (OAc and COOMe), 1680, 1630 (α,β-unsaturated ketone), 1240 (OAc), 2940, 1460, 1445, 1330, 1110, 1055, 1030, 1015, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; EIMS *m/z* $[M]^+$ absent, 403 $[M - Ac]^+$ (11), 386 $[M - AcOH]^+$ (5), 326 $[M - 2AcOH]^+$ (13), 311 (19), 283 (12), 267 (26), 238 (27), 216 (100), 199 (18), 176 (37), 171 (36), 157 (22), 155 (21), 143 (24), 129 (22), 105 (29), 91 (23), 55 (18); *anal.* C 67.16%, H 7.41%, calcd for $C_{25}H_{34}O_7$ C 67.24%, H 7.68%.

Methyl 14α-acetoxy-7α,11α-dihydroxy-8,15-isopimaradien-18-oate (2): colorless thick oil; $[\alpha]^{20}_D$ −9.9° (*c* 0.242, $CHCl_3$); IR (NaCl) ν_{max} 3470 br (OH), 3080, 1670, 930 (vinyl), 1730 br (OAc and COOMe), 1245 (OAc), 2960, 2940, 1435, 1375, 1110, 1020, 975, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; EIMS *m/z* $[M]^+$ absent, 346 $[M - AcOH]^+$ (4), 328 $[M - AcOH - H_2O]^+$ (10), 285 (5), 283 (7), 278 (57), 225 (14), 216 (14), 203 (19), 201 (23), 185 (30), 159 (25), 145 (27), 131 (22), 121 (23), 119 (23), 105 (32), 91 (34), 79 (21), 55 (30), 43 (100), 41 (28); *anal.* C 68.09%, H 8.51%, calcd for $C_{23}H_{34}O_6$ C 67.95%, H 8.43%.

Methyl 7α-acetoxy-11α-hydroxy-14-oxo-8,15-isopimaradien-18-oate (3): colorless needles (EtOAc−petroleum ether); mp 192−195 °C; $[\alpha]^{20}_D$ +138.0° (*c* 0.321, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 232 (4.00); IR (KBr) ν_{max} 3500 (OH), 3080, 1655, 920 (vinyl), 1745, 1245 (OAc), 1705 (COOMe), 1675, 1630 (α,β-unsaturated ketone), 2960, 1450, 1375, 1370 1320, 1180, 1120, 1020, 950, 815 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; EIMS *m/z* $[M]^+$ absent, 344 $[M - AcOH]^+$ (2), 293 (3), 285 (5), 276 (66), 216 (100), 201 (39), 188 (51), 187 (29), 173 (22), 159 (30), 105 (20), 91 (24), 79 (13), 55 (16); *anal.* C 68.36%, H 7.84%, calcd for $C_{23}H_{32}O_6$ C 68.29%, H 7.97%.

Methyl 7α-acetoxy-1α,11α,14α-trihydroxy-8,15-isopimaradien-18-oate (4): colorless prisms (EtOAc−petroleum ether); mp 171−173 °C; $[\alpha]^{20}_D$ +89.1° (*c* 0.514, $CHCl_3$); IR (KBr) 3400, 3250 (OH), 3080, 1650, 915 (vinyl), 1727, 1240 (OAc), 1700 (COOMe), 2930, 1440, 1370, 1285, 1210, 1110, 1090, 1060, 1050, 1025, 945, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; EIMS *m/z* $[M]^+$ absent, 344 $[M - AcOH - H_2O]^+$ (1), 326 $[M - AcOH - 2H_2O]^+$ (7), 294 (18), 276 (7), 201 (21), 199 (17), 187 (12), 183 (100), 157 (57), 145 (23), 144 (28), 143 (22), 131 (22), 105 (26), 101 (22), 91 (23), 51 (21); *anal.* C 65.12%, H 8.19%, calcd for $C_{23}H_{34}O_7$ C 65.38%, H 8.11%.

3,7,11,15-Tetramethyl-1,6,10,14-hexadecatetraene-3,5,9-triol (5): colorless oil; $[\alpha]^{20}_D$ +8.8° (*c* 0.466, $CHCl_3$); IR (NaCl) 3320 br (OH), 3090, 1640, 920 (vinyl), 1670 (olefins), 2970, 2920, 1445, 1385, 1265, 1175, 1050, 1025, 995, 845, 825, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.89 (1H, dd, *J* = 17.1, 10.7 Hz, H-2), 5.34 (1H, dd, *J* = 17.1, 1.5 Hz, H_B-1), 5.25 (1H, br d, *J* = 8.3 Hz, H-6), 5.13 (1H, dd, *J* = 10.7, 1.5 Hz, H_A-1), 5.13 (1H, dd, *J* = 8.5, 0.9 Hz, H-10), 5.06 (1H, br t, *J* = 7.0 Hz, H-14), 4.58 (1H, ddd, *J* = 10.7, 8.3, 1.8 Hz, H-5), 4.44 (1H, ddd, *J* = 9.1, 8.5, 4.5 Hz, H-9), 4.10 (1H, br, OH), 3.63 (1H, br, OH), 2.41 (1H, br, OH), 2.12 (1H, dd, *J* = 13.3, 9.1 Hz, H_B-8), 2.06 (3H, m, H_A-8 and 2H-13), 1.97 (2H, t, *J* = 7.4 Hz, 2H-12), 1.80 (1H, dd, *J* = 14.5, 10.7 Hz, H_B-4), 1.66 (6H, br s, Me-16 and Me-19), 1.65 (3H, d, *J* = 0.9 Hz, Me-18), 1.58 (3H, br s, Me-17), 1.49 (1H, dd, *J* = 14.5, 1.8 Hz, H_A-4), 1.24 (3H, s, Me-20); ^1H NMR (C_6D_6, 400 MHz) δ 5.92 (1H, dd, *J* = 17.1, 10.5 Hz, H-2), 5.64 (1H, dd, *J* = 17.1, 1.9 Hz, H_B-1), 5.50 (1H, br d, *J* = 8.2 Hz, H-6), 5.44 (1H, dd *J* = 8.2, 1.2 Hz, H-10), 5.30 (1H, br t, *J* = 6.9 Hz, H-14), 5.23 (1H, dd, *J* = 10.5, 1.9 Hz, H_A-1), 4.79 (1H, ddd, *J* = 10.7, 8.2, 2.2 Hz, H-5), 4.61 (1H, ddd, *J* = 9.2, 8.2, 3.8 Hz, H-9), 4.13 (1H, br, OH), 3.68 (1H, br, OH), 2.77 (1H, br, OH), 2.33 (1H, dd, *J* = 13.5, 9.2 Hz, H_B-8), 2.26 (2H, dd, *J* = 7.6, 6.9 Hz, 2H-13), 2.19 (1H, dd, *J* = 13.5, 3.8 Hz, H_A-8), 2.13 (2H, t, *J* = 7.6 Hz, 2H-12). 1.98 (1H, dd, *J* = 14.4, 10.7 Hz, H_B-4), 1.78 (3H, br s, Me-16), 1.73 (3H, d, *J* = 1.0 Hz, Me-19), 1.70 (3H, d, *J* = 1.2 Hz, Me-18), 1.67 (3H, br s, Me-17), 1.51 (1H, dd, *J* = 14.4, 2.2 Hz, H_A-4), 1.34 (3H, s, Me-20); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.0 (d, C-2), 138.1 (s, C-11), 134.1 (s, C-7), 131.6 (s, C-15), 130.9 (d, C-6), 127.3 (d, C-10), 123.9 (d, C-14), 112.6 (t, C-1), 73.9 (s, C-3), 66.7 (d, C-5), 66.0 (d, C-9), 47.8 (t, C-8), 46.8 (t, C-4), 39.5 (t, C-12), 29.9 (q, C-20), 26.4 (t, C-13), 25.6 (q, C-16), 17.7 (q, C-17), 16.6 and 16.5 (both q, C-18 and C-19); EIMS *m/z* $[M]^+$ absent, 286 $[M - 2H_2O]^+$ (1), 223 (1), 153 (49), 95 (30), 82 (39), 71 (55), 69 (100), 59 (17), 55 (18); *anal.* C 74.29%, H 10.39%, calcd for $C_{20}H_{34}O_3$ C 74.49%, H 10.63%.

Preparation of Compound 1 from Methyl 1α,7α-Diacetoxy-14α-hydroxy-8,15-isopimaradien-18-oate (6). To a solution of **6**[3] (50 mg, 0.11 mmol) in Me_2CO (10 mL) was added an excess of Jones's reagent[4] (0.4 mL) at 18 °C with stirring. After 10 min, the excess of Jones's reagent was destroyed by addition of EtOH, and then the reaction mixture was diluted with H_2O (30 mL). Extraction with CH_2Cl_2 (4 × 10 mL), drying (Na_2SO_4), filtration, and evaporation of the solvents gave a residue (44 mg) that was crystallized from EtOAc−petroleun ether, yielding a compound (36 mg, 0.08 mmol, 72%) identical in all respects (mp, mixed mp, $[\alpha]_D$, ^1H NMR, MS, and TLC) with the natural diterpenoid **1**.

Reaction of Compound 2 with Acetic Anhydride−Pyridine To Give Methyl 7α,11α,14α-Triacetoxy-8,15-isopimaradien-18-oate (8). Treatment of **2** (17 mg, 0.04 mmol) with Ac_2O−pyridine (1:1, 3 mL) at room temperature for 48 h yielded **8** (19 mg, 0.038 mmol, 93%, after crystallization of the crude of the reaction from petroleum ether): colorless needles; mp 132−133 °C; $[\alpha]^{20}_D$ −8.1° (*c* 0.212, $CHCl_3$). This derivative was identical in all respects (mp, mixed mp, $[\alpha]_D$, ^1H NMR, MS, and TLC) to the compound described previously [mp 132−134 °C (*n*-hexane); $[\alpha]^{18}_D$ −7.9° (*c* 0.253, $CHCl_3$)].[3]

Oxidation of Compound 3 To Give Methyl 7α-Acetoxy-11,14-dioxo-8,15-isopimaradien-18-oate (9). Treatment of **3** (25 mg, 0.06 mmol) with Jones's reagent[4] at room temperature for 20 min and workup as described above gave **9** (21 mg, 0.052 mmol, 84%, after crystallization from EtOAc−petroleum ether) as yellowish prisms: mp 153−155 °C; $[\alpha]^{20}_D$ +79.9° (*c* 0.221, $CHCl_3$); IR, UV, ^1H NMR, and MS identical with those of the isopimarane derivative described previously [mp 156−158 °C (EtOAc−*n*-hexane); $[\alpha]^{18}_D$ +81.8° (*c* 0.582, $CHCl_3$)][3]. Comparison (mixed mp, TLC) with an authentic sample confirmed the identity.

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