

ISOCEDRENE AND GUAIANE DERIVATIVES FROM PLEOCARPUS REVOLUTUS

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ABSTRACT.—A reinvestigation of the aerial parts of *Pleocarpus revolutus* afforded, in addition to sesquiterpenes isolated previously, four new guaiane derivatives and four isocedrene derivatives, one of which is new. Furthermore, the configuration of the guaiane **5** has been revised. The structures were established by high field nmr spectroscopy.

The monotypic genus *Pleocarpus* (Compositae, tribe Mutisieae, subtribe Nassauviinae, endemic in northern Chile) previously was a section of *Jungia*. So far the chemistry of *Pleocarpus revolutus* D. Don. (1) has given no clear relationships to that of *Jungia*, where characteristic isocedrene derivatives have been isolated (1). We, therefore, have reinvestigated this *Pleocarpus* species. The extract of the aerial parts afforded large amounts of taraxasteryl acetate, 9-acetoxynerylidol (3), the acetate **8** (1), and the diol **5** (1), which was by far the main product. Furthermore, the guaiane derivatives **1**, **2** (1), **3** (1), **4**, **7** (1), and **9**, as well as the isocedrene derivatives **10** (4), **11** (2), **12** and **13** (2), were present.

The structure of **1** followed from its ¹H-nmr spectrum (Table 1) which was similar

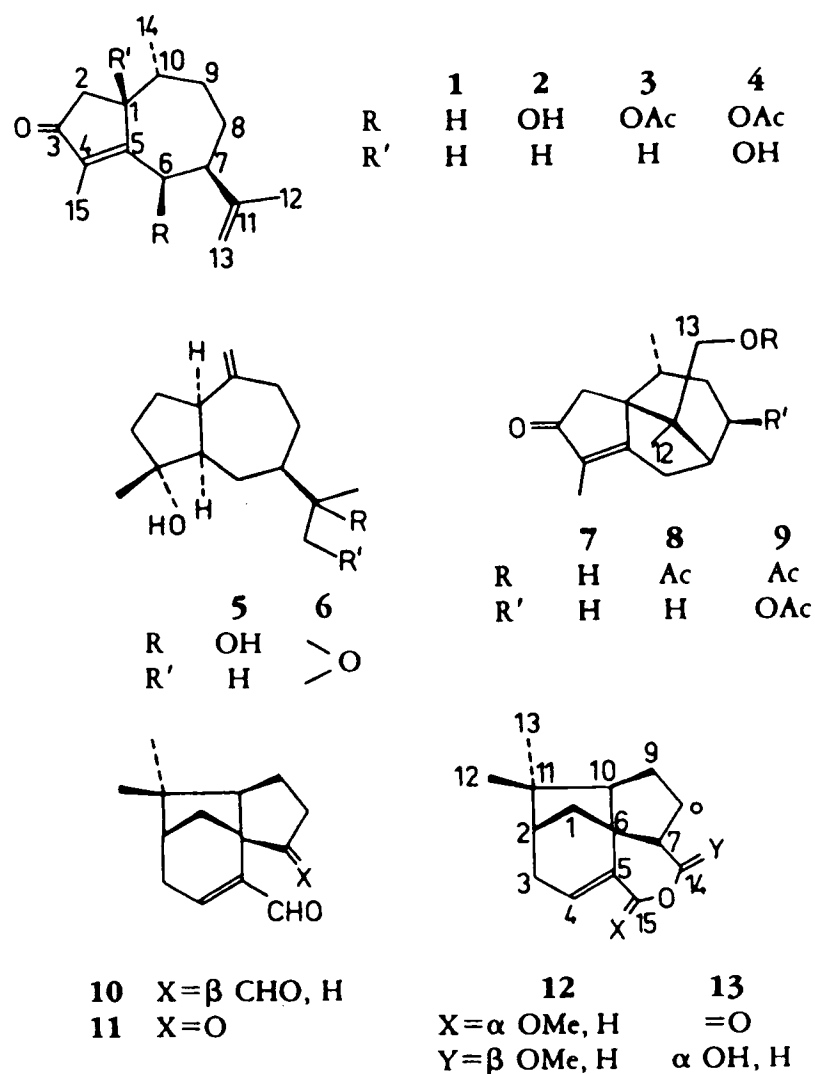


TABLE 1. ¹H nmr Spectral Data of Compounds **1**, **4**, **6**, **8**, and **9** (400 MHz, CDCl₃, δ values).

Proton	Compound				
	1	4	6 ^a (C ₆ D ₆)	8 ^b	9 ^c
1	2.99 m	—	2.98 br q	—	—
2	2.38 dd	2.46 d	1.80 m	2.21 d	2.28 d
2'	2.03 dd	2.27 d	1.60 m	2.15 d	2.20 d
5	—	—	1.73 m	—	—
6	2.73 br d	—	1.57 m	2.34 br d	2.27 br d
6'	2.37 dd	5.90 br s	0.90 ddd	2.64 br dd	2.69 br dd
7	1.96 m	1.97 m	1.11 dddd	2.15 m	2.46 br dd
10	2.13 br tq	2.24 m	—	2.15 tq	2.36 tq
12	1.76 br s	1.80 br s	1.04 s	0.84 s	0.85 s
13	4.75 dq	4.87 dq	2.35 dd	4.48 d	4.69 d
13'	4.72 br s	4.83 br s	2.26 d	4.21 d	4.32 d
14	0.98 d	1.07 d	4.91 br s 4.83 br s	0.63 d	0.67 d
15	1.70 d	1.83 br s	1.10 s	1.74 br s	1.75 br s
OAc	—	2.10 s	—	—	2.06 s (6H)

^aH-9 2.44 ddd, 1.80 m; H-8 2.07 dddd, 1.27 ddd; H-3 1.80 m, 1.57 m.

^bH-8 1.90 m, 1.47 m; H-9 1.67 m, 1.10 m.

^cH-8 4.12 br dd; H-9 1.40 m, 1.77 m.

J [Hz]: Compound **1** $J_{1,2} = 4$, $J_{2,2'} = 19$, $J_{6,6'} = 14$, $J_{6',7} = 5$, $J_{9,10} = J_{10,14} \sim 7$, $J_{12,13} = J_{13,13'} \sim 1$; compound **4** $J_{2,2'} = 18$, $J_{10,14} = 7$, $J_{12,13} = J_{13,13'} \sim 1$, compound **6** $J_{1,2} = J_{1,2'} = J_{1,5} \sim 9$, $J_{5,6\beta} = J_{6\alpha,6\beta} = J_{6\beta,7} = 12$, $J_{7,13} = 0.5$, $J_{8,9} = 3.5$, $J_{8',9} = 5.5$, $J_{9,9'} = 13$, $J_{13,13'} = 5$; compounds **8** and **9** $J_{2,2'} = 17$, $J_{6,6'} = 19$, $J_{9,10} = J_{10,14} \sim 7$, $J_{13,13'} = 12$; compound **8** $J_{6,7} = 7$; compound **9** $J_{6,7} = 7$, $J_{7,8} = 3.5$.

to that of the corresponding acetoxy derivative **3** (1), except that the low field H-6 signal was replaced by a broadened doublet at δ 2.73 and a double doublet at δ 2.37. An isomeric ketone has previously been prepared by Zn dust reduction of **2** (1), which differed in rotation from that of a synthetic sample (5). Most likely the configuration of **2** had been affected during the reduction. The stereochemistry of **1** was, therefore, studied again by nOe experiments.

Irradiation of H-10 gave effects with H-1 (8%), H-6 β (6%), and H-2 β (6%), while irradiation of H-1 gave nOe's with H-2 (9%) and H-10 (10%). Because all sesquiterpenes from Compositae with known stereochemistry have the 7 α -H configuration, the proposed stereochemistry most likely also represents the absolute configuration. Most likely ketone **1** is identical with that prepared by synthesis (5), although no direct comparison is possible and nmr data are not available; the optical rotations are negative for both ketones. The isomeric ketone prepared by Zn dust reduction of **2** (1) presumably is epimeric with **1** at C-1.

The ¹H-nmr spectrum of **4** (Table 1) was also similar to that of **3**. However, the presence of a 1-hydroxy group collapsed the H-2 signals to simple doublets. As the couplings of the remaining protons were identical with those of **3**, a 1 β -hydroxy group was very likely as a 1 α -hydroxy group would have changed the conformation. Accordingly, the data were close to those of the known desacetoxy derivative **2** from a *Jungia* species (2). Additional compounds with identical configuration at C-1, C-7, and C-10 have been reported from a *Moscharia* species (6), also placed in the Nassauviinae.

The ¹H- and ¹³C-nmr data of **5** were identical with those reported previously for a compound with the *epi* configuration at C-1 (1). The ¹H-nmr spectrum of **6** (Table 1) was similar to that of **5**. However, the changes in the signals corresponding to the side chain indicated the presence of an 11,13-epoxide. All couplings were the same as those

of diol **5**. NOe's between H-1 and H-5 (6%), H-5 and H-7 (10%), and H-15 and H-6 α (8%) unambiguously defined the complete stereochemistry except that at C-11; in particular, the stereochemistry at the ring junction must be *cis*. Most likely, therefore, the stereochemistry of **5** at C-1 must also be revised to that shown. Perhaps the degradation of **5** at C-10 to the corresponding ketone (**1**) was also accompanied by an epimerization at C-1.

The ^1H -nmr spectral data of **8** (Table 1) showed it to be the acetate of hydroxy-isopatchoulene-3-one [**7**], which had already been prepared by acetylation of the latter (**1**). Similarly, the data of **9** (Table 1) showed that an 8-acetoxy derivative of **8** was very likely. Spin decoupling established this assumption. Inspection of models showed that only an 8 β -acetoxy group agreed with the observed couplings of H-8 since an α -acetoxy derivative should show a large vicinal coupling.

The ^1H -nmr spectrum of **12** indicated the presence of an isocedrene derivative. The couplings of H-14 and H-15 were identical with those of the corresponding acetoxy derivative (**3**, **5**) where the configuration was established. Therefore, the stereochemistry of **12** was also clear. Perhaps **12** is an artifact formed from the corresponding 5,7-dialdehyde by reaction with MeOH.

The isolation of isocedrene derivatives from this species supports its placement in the subtribe Nassauviinae where these rare compounds are widespread. Isocedrene derivatives have been isolated from the genera *Jungia* (**2**), *Moscharia* (**6**), *Perezia* (**7**), *Proustia* (**2**, **3**), and *Trixis* (**8**–**10**). However, they have not so far been reported for a few other genera in this subtribe. Further taxonomic and chemical studies may show whether this subdivision of the tribe *Mutisieae* is valid for all genera proposed.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The air-dried plant material (402 g, voucher Conc 72991, deposited in the Herbarium of the University of Concepcion, collected near Vicuna, Cuarta Region, Chile) was extracted at room temperature with a mixture of Et₂O-MeOH-petroleum ether 1:1:1. The extract obtained was defatted with MeOH, and the soluble part was first separated by cc (Si gel) into three crude fractions [1, Et₂O-petroleum ether (E-PE), 1:9; 2, E-PE, 1:1 and Et₂O; and 3, Et₂O-MeOH, 9:1]. Tlc (Si gel, PF 254) of fraction 1 gave 600 mg taraxasteryl acetate. Fraction 2 was separated by flash chromatography (Si gel ϕ 30–60 μ , E-PE mixtures). After monitoring by tlc, the fractions were combined into four (2/1–2/4). Hplc of 2/1 (MeOH-H₂O, 19:1, RP-8, flow rate 3 ml/min in all separations) afforded 6 mg of compound **12** (Rt 3.6 min). Hplc of 2/2 (MeOH-H₂O, 17:3) gave 0.9 g of compound **3** (Rt 2.2 min), 350 mg of 9-acetoxynerylidol (Rt 2.7 min), 10 mg of compound **1** (Rt 3.7 min), and 5 mg of compound **10** (Rt 4.8 min). Further flash chromatography of 2/3 gave 600 mg of compound **3**, 400 mg of compound **8**, and a mixture which gave by hplc (MeOH-H₂O, 3:1) two mixtures (2/3/1 and 2/3/2). Fraction 2/3/1 afforded by tlc (E-PE, 3:1) 70 mg of compound **11** (*R_f* 0.50) and crude **9**. Tlc of this crude material (CHCl₃-C₆H₆-Et₂O, 1:1:1) gave 40 mg of compound **9** (*R_f* 0.4). Tlc of 2/3/2 (E-PE, 3:1) gave 800 mg of compound **2**, 150 mg of compound **7** and a mixture which by tlc (CHCl₃-C₆H₆-Et₂O, 1:1:1) afforded 150 mg of compound **13** and 60 mg of compound **4** (*R_f* 0.4). Tlc of fraction 2/4 (Et₂O) gave 10 mg of compound **9**, 10 mg of compound **11**, 5 mg of compound **13**, and 80 mg of crude **6** (*R_f* 0.5) which was purified by hplc (MeOH-H₂O, 3:1, Rt 7.2 min). Fraction 3 contained 10 g of compound **5**. Known compounds were identified by comparing their 400 MHz ^1H -nmr spectra with those of authentic material or by rigorous ^1H -nmr studies and comparing data with those in the literature.

1 β ,7 α ,10 β H-Guaia-4,11(13)-dien-3-one [**1**].—Colorless oil; ir ν (CCl₄) cm⁻¹ 1705, 1640, (C=C–C=O); ms *m/z* [M]⁺ 218.167 (calcd for C₁₅H₂₂O, 218.167) (100), [M–Me]⁺ 203 (20), 175 (46), 162 (32), 161 (40), 147 (42); [α]²⁴⁰_D –63° (CHCl₃, *c* = 0.75).

1 β -Hydroxy-6 β -acetoxy-7 α -10 β H-guaia-4,11(13)-dien-3-one [**4**].—Colorless oil; ir ν (CCl₄) cm⁻¹ 3550 (OH), 1745, 1240 (OAc), 1720, 1640 (C=C–C=O); ms *m/z* [M]⁺ 292.167, (calcd for C₁₇H₂₄O₄, 292.167) (4.5), [M–HOAc]⁺ 232 (42), 190 (50), 55 (100); [α]²⁴⁰_D –57° (CHCl₃, *c* = 0.6).

4 α -Hydroxy-11,13-epoxy-1 α ,5 α ,7 α H-guai-10(14)-ene [**6**].—Colorless oil; ir ν (CCl₄) cm⁻¹ 3600 (OH); ms *m/z* [M–H₂O]⁺ 218.167 (calcd for C₁₅H₂₂O, 218.167) (19), 203 (8), 187 (100), 160 (78), 145 (76), 119 (82), 105 (94), 93 (98), 91 (94); [α]²⁴⁰_D +5° (CHCl₃, *c* = 0.89).

8 β , 13-Diacetoxyisopatchoulen-3-one [9].—Colorless oil; ir ν (CCl₄) cm⁻¹ 1740, 1240 (OAc), 1705, 1630 (C=C—C=O); ms *m/z* [M]⁺ 334.178 (calcd for C₁₉H₂₆O₅, 334.178) (27), [M—HOAc]⁺ 274 (36), [274—ketene]⁺ 232 (48), [274—HOAc] 214 (100), [214—Me]⁺ 199 (38), 173 (71), 159 (50); [α]²⁴⁰_D -13 (CHCl₃, *c* = 0.42).

14 β , 15 α -Dimethoxy-14,15-epoxy- α -isocedrene [12].—Colorless oil; ir ν (CCl₄) cm⁻¹ 1470, 1450, 1405, 1390, 1370; ms *m/z* [M]⁺ 278.188 (calcd for C₁₇H₂₆O₃, 278.188) (28), [M—Me]⁺ 263 (8), [M—OMe]⁺ 247 (17), [M—MeOH]⁺ 246 (30), [246—Me]⁺ 231 (10), [247—CHO]⁺ 218 (26), [218—OMe] 187 (24), 149 (46), 117 (44), 91 (51), 73 (100); [α]²⁴⁰_D -35 (CHCl₃, *c* = 0.53); ¹H nmr (CDCl₃, 400 MHz) 1.50 (dd, H-1), 2.25 (m, H-2, H-3), 5.42 (t, H-4), 1.83 (m, H-7), 1.09 (s, H-12), 0.97 (s, H-13), 4.52 (d, H-14), 5.04 (br s, H-15), 3.50 and 3.42 (s, OMe); *J*_{1,1'} = 10, *J*_{1,3} = 1.5, *J*_{3,4} = 3, *J*_{7,14} = 7 Hz.

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