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ISOCEDRENE DERIVATIVES AND OTHER COMPOUNDS FROM CHILEAN *PEREZIA* SPECIES

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Key Word Index—*Perezia* spp.; Compositae; sesquiterpenes; isocedrene derivatives; guaiane derivative.

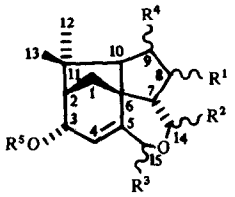
Abstract—The aerial parts of nine *Perezia* species from Chile afforded, in addition to various other compounds, isocedrene derivatives, eight being new. The structure of two compounds has been revised. Furthermore, a guaiane derivative was isolated. Four species gave only triterpenes.

INTRODUCTION

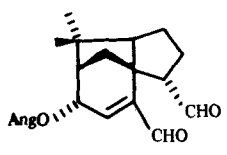
The genus *Perezia* with about 30 species is mainly distributed over South America in the Anden region. The chemistry differs remarkably from that of *Acourtia* which was previously a section of *Perezia* [1, 2]. We have studied eight further species and *P. carthamoides* (D. Don) H. et A. from Chile. The latter species afforded the isocedrene derivatives **3** [2] and **4–6** while the 5-methylcoumarin isolated from an Argentinian source [3], could not be detected.

RESULTS AND DISCUSSION

Four species, *P. lactucoides*, *P. linearis*, *P. lyrata* and *P. nutans* gave only triterpenes. *Perezia nutans* also contains isocedrenes but the amounts were insufficient for identification. From *P. magalantha* the isocedrenes **7**, **8/9** [4], **11/12** and **13/14** as well as the coumarins **17** [5] and scopoletin were isolated. In all cases the isovalerates could not be separated from the corresponding 2-methylbutyrates *P. pedicularifolia* gave the angelate **3** [2, 4] and the methoxy derivative **10**, *P. pilifera* the isocedrenes



	1	2	3	4	5	6	7	8	9	10	11	12	13	14
R^1	H	H	αOAng	αOAng	αOSen	αOSen	βOH	βOH	βOH	αOAng	βOH	βOH	βOH	βOH
R^2	βOAc	αOAc	αOAc	αOAc	αOAc	αOAc	αOAc	αOAc	αOAc	αOAc	βOAc	βOAc	αOAc	αOAc
R^3	αOMe	βOMe	βOAc	βOAc	βOAc	βOAc	βOMe	βOMe	βOMe	βOMe	αOMe	αOMe	βOAc	βOAc
R^4	H	H	H	H	H	H	αO*i*Bu	αOMeBu	αO*i*Val	H	αMeBu	αO*i*Val	βOMeBu	β*i*Val
R^5	Ang	Ang	Ang	Sen	Ang	Sen	Ang	Ang	Ang	Ang	Ang	Ang	Ang	Ang



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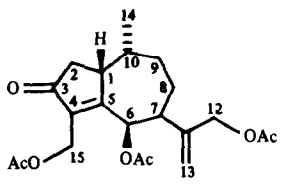

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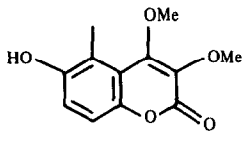

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Table 1. ^{1}H NMR spectral data of compounds **5**–**7** and **11**–**15** (400 MHz, $CDCl_3$)

H	5	6	7	11/12*	13/14*	15
1	2.20 *m*	2.20 *m*	2.19 *d*	2.25 *dd*	2.19 *d*	2.29 *dd*
				2.04 *br d*		
2	2.30 *br t*	2.25 *br t*	2.35 *br t*	2.28 *br t*	2.33 *br t*	2.37 *m*
3	5.87 *dd*	5.82 *dd*	5.87 *dd*	5.80 *dd*	5.87 *dd*	6.40 *dd*
4	5.33 *q*	5.33 *q*	5.37 *q*	5.48 *br t*	5.38 *q*	6.03 *dd*
7	2.05 *m*	2.05 *m*	2.01 *m*	2.10 *br dd*	2.01 *d*	2.37 *m*
8	5.03 *dt*	5.03 *dt*	4.07 *dd*	4.02 *br t*	4.09 *dd*	1.45 *m*
9	2.10 *m*	2.10 *m*	4.91 *dd*	4.88 *dd*	4.92 *dd*	1.73 *m*
10	2.25 *m*	2.25 *m*	2.33 *m*	2.62 *dd*	2.33 *br d*	2.37 *m*
12	1.27 *s*	1.26 *s*	1.30 *s*	1.31 *s*	1.30 *s*	1.18 *s*
13	1.02 *s*	1.02 *s*	1.09 *s*	1.10 *s*	1.10 *s*	1.02 *s*
14	6.04 *br s*	6.04 *br s*	6.12 *br s*	6.13 *d*	6.12 *d*	9.23 *s*
15	6.71 *t*	6.71 *t*	6.76 *t*	5.01 *br s*	6.76 *t*	9.59 *s*
3OCOR	6.09 *qq*	5.65 *br s*	6.11 *qq*	6.09 *qq*	6.11 *qq*	—
	2.00 *dq*	2.18 *d*	2.01 *dq*	2.02 *dq*	2.01 *dq*	—
	1.88 *dq*	1.90 *d*	1.88 *dq*	1.89 *dq*	1.88 *dq*	—
	5.61 *br s*	5.62 *br s*	2.60 *qq*	2.44 *q*	2.43 *tq*	—
	2.14 *br s*	2.15 *br s*	1.19 *d*	1.68 *q*	1.69 *q*	—
OCOR	1.88 *br s*	1.88 *br*	1.18 *d*	1.51 *q*	1.51 *q*	—
				0.92 *t*	0.93 *t*	—
				1.16 *d*	1.17 *d*	—
OAc	2.07 *s*	2.07 *s*	2.08 *s*	2.11 *s*	2.07 *s*	—
	2.05 *s*	2.05 *s*	2.07 *s*		2.06 *s*	—
OMe	—	—	—	3.48 *s*	—	—

*iVal 2.24 *d*, 2.08 *m*, 0.98 *d*.

J[Hz]: 2,3 = 4,5; 3,4 = 3,15 = 4,15 = 7,14,1.5; compounds **5** and **6**: 1,2 = 4.5; 7,8 = 8,9 = 9; 8,9′ = 5; compounds **7**, **13** and **14**: 1,2 = 2; 7,8 = 8,9 = 9; 9,10 = 11; compounds **11/12**: 1,1′ = 11; 1,2 = 4.5; 1′,10 = 1.5; 7,8 = 8,9 = 5.5; 7,14 = 6.5; 9,10 = 10; OAng: 3,4 = 7; 3,5 = 4,5 = 1.5; OMeBu: 2,3 = 3,4 = 2,5 = 7; 3,3′ = 14; OiVal: 2,3 = 3,4 = 3,5 = 7.

1 [2] and **2** [2] and *P. recurvata*, in addition to **1** [2], two new compounds, the guaiane derivative **16** and the dialdehyde **15**.

The structure of the latter followed from its ^{1}H NMR spectrum (Table 1) which was in part very similar to that of the corresponding 3-desacyloxy derivative [2, 5], its structure being established by synthesis [6]. The presence of a 3α-angeloyloxy derivative was deduced by comparing the new downfield signals with those of related compounds. The structure of **16** was also deduced from the ^{1}H NMR data (see Experimental) which were similar to those of the 12,15-bis-desacetoxy derivative [7, 8]. The olefinic methyl signals were replaced by a doublet at δ 4.76 and double doublet at δ4.86 as well as by a pair of doublets at δ 4.65 and 4.58. Furthermore, three acetate methyl singlets were visible. All the other signals were nearly identical with those of the desacetoxy derivative [7, 8]. Accordingly, also the stereochemistry was the same.

The ^{1}H NMR spectra of **5** and **6** (Table 1) indicated that these compounds differed from **3** [2] by the nature of the ester groups at C-3 and/or C-8. As the shift of H-8 was identical in **5** and **6** but differed slightly from that of **3** the senecioyl group was at C-8. Consequently the chemical shift of H-3 differed in the spectra of **3** and **6**, the senecioate **4** could not be obtained free from **5**.

The spectral data of **7** (Table 1) indicated that this isocedrene differed from **8** [4] only by the ester group at C-8. The presence of an isobutyrate was easily deduced from the typical ^{1}H NMR signals and the relative position of the ester groups again followed from the chemical shifts. As that of H-3 was unchanged in the spectra of **7** and **8** both were 3α-angeloyloxy derivatives. The configuration at C-8 and C-9 is discussed below.

The ^{1}H NMR spectral data of **11** and **12** (Table 1) differed from that of **8** and **9** [4] by the signals of H-14 and H-15. As pointed out previously [5], the stereochemistry at these centres follows from the coupling $J_{7,14}$. The observed ones indicated a 14α-H-orientation and the upfield shift of H-15 required a 15α-methoxy group. Accordingly, the acetoxy group was at C-14. The broadened triplet at δ 4.01 was due to H-8 as followed from spin decoupling. Therefore a hydroxy group was at C-8 and an ester group at C-9. The stereochemistry was deduced from the observed NOE's (Table 2). Especially the effects between H-10, H-8, H-14 and H-13 as well as between H-9, H-13 and H-1 indicated the configurations at the chiral carbons.

As the stereochemistry of the esters **8**/**9** was not established by NOE difference spectroscopy and as at that time no complete assignment of all signals was possible [4], we have returned to this problem. It turns out that these compounds were only isomeric with **11**/**12** at C-14 and C-15 (Table 2). Due to the 15α-methoxy group in the isomers **11**/**12** the H-10 signals were shifted downfield. Furthermore, small differences in the couplings in the spectra of the two pairs of isomers were visible probably due to different hydrogen bridge bonds. The structure of

Table 2. Observed NOE's of compounds **8/9** and **11/12**

Irradiated	**8/9**	**11**/12
H-1/1′	H-3 (10%), H-9 (7%)	
H-2	H-3 (8%)	
H-3	H-2 (6%), H-4 (6%)	H-2 (5%), H-4 (6%), H-1′ (6%)
H-4	H-3 (5%), H-15 (4%)	H-3 (5%), H-15 (15%)
H-8	H-10 (4%), H-14 (7%)	H-10 (4%), H-14 (8%)
H-9	H-13 (5%)	H-1 (3%), H-13 (5%)
H-10		H-8 (5%), H-13 (3%), H-14 (4%)
H-12	H-10 (12%), AngMe (7%)	H-10 (15%), AngMe (6%)
H-13	H-2 (10%), H-9 (12%)	H-9 (12%)
H-14	H-7 (5%), H-8 (5%)	H-8 (6%), H-14 (2%), OMe (3%)
H-15	H-4 (4%), H-10 (3%), OMe (8%)	H-4 (12%), OMe (8%)

12a/b in the literature [4] therefore has to be revised to **8/9**.

The ^{1}H NMR spectra of the diacetates **13/14** (Table 1) were similar to those of **8/9**. However, the signal of the 15-methoxy group was replaced by that of an acetate methyl and the H-15 signal was shifted downfield as in the spectra of **4–6**. The coupling of H-14 indicated identical stereochemistry at this centre.

The chemistry of the Chilean *Perezia* species shows that for this genus isocedrenes are characteristic as for most of the other genera of the subtribe Nassauviinae [5]. The North and Central American genus *Acourtia* (previously a section of *Perezia*) has yielded no isocedrenes but instead has given perezone derivatives. The absence of characteristic compounds in some species again shows that chemical results have to be interpreted with care.

EXPERIMENTAL

The air-dried plant was collected in Chile and the vouchers are deposited in the Herbarium of the University of Concepción, Chile.

Table 3. Compounds isolated from *Perezia* species

Species voucher No. and location	Quantity (g)	Isolated compounds
P. carthamoides (D. Don) H. et A. (1957), Termas del Flaco, Jan. 1988	52	4 mg α and 4 mg β-selinene, 4 mg elemene, 13 mg **3**, 2 mg impure **4**, 10 mg **5**, 6 mg **6**, 10 mg lupeol, 5 mg taraxasterol
P. lactucoides (Vahl) Less Ssp. palustris (Phil) Vuill. (1860, Parque Nacional, IX. Region Jan. 1986)	47	8 mg β-elemene, 26 mg mixture of lupeol, taraxasterol and β-amyrin
P. linearis Less (2170, VIII.-Region, Pico de Pilque, April 1987)	33	10 mg lupeol, 10 mg taraxasterol, 5 mg β-amyrin
P. lyrata (Remy) Wedd. (1114, Forestal alto Bio, VIII. Region, Jan. 1986)	86	20 mg lupeol, 10 mg taraxasterol
P. megalantha Spey (726, Provincia Ultima Esperanza, XII. Region, Jan. 87)	578	15 mg **7**, 15 mg **8/9**, 10 mg **11/12**, 8 mg **13/14**, 6 mg **17**, 50 mg mixture of lupeol and taraxasterol, 8 mg scopoletin
P. nutans Less (1882, Laguna verde IX. Region, Jan. 88)	30	7 mg lupeol
P. pedicularifolia Less (1880, Laguna verde, IX. Region, Jan. 1988)	14	7 mg **3**, 4 mg **10**, 5 mg lupeol
P. pilifera (D. Don) H. et A. (750, Provincia Ultima Esperanza, XII. Region, Jan. 1988)	356	4 mg β-selinene, 4 mg β-elemene, 4 mg **1**, 16 mg **2**, 10 mg lupenon
P. recurvata (Vahl) Less (744, Provincia Ultima Esperanza, Jan. 1987)	423	10 mg α-selinene, 10 mg β-selinene, 10 mg β-elemene, 10 mg lupeol, 10 mg β-amyrin acetate, 17 mg **16**, 22 mg **1**, 25 mg **15**

Extraction was performed with MeOH–Et_2O–petrol (1:1:1) and the extracts were sepd first by CC and by TLC or medium pressure chromatography (silica gel ϕ 30–60 μ, using mixtures of Et_2O–petrol as eluants) as reported previously [9]. Complex mixtures were sepd by HPLC (RP8, MeOH–H_2O–mixtures, 100 bar, flow rate 3 ml/min). The final sepn conditions for new compounds are given with the description of them. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material. The results are summarized in Table 3.

14α,15β-*Diacetoxy*-3α-*angeloyloxy*-8α-*senecioyloxy*-14β,15α-*epoxy*-α-*isocedrene* (**5**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750(OAc), 1715, 1655 (C=CO_2R); MS: *m/z* (rel. int.) 470.230 [M – HOAc]$^+$ (1.5) (calc. for $C_{27}H_{34}O_7$ 470.230), 430 [M – RCO_2H]$^+$ (0.4), 388 [430 – ketene]$^+$ (9), 83 [RCO]$^+$ (100), 55 [83 – CO]$^+$ (65) (HPLC: MeOH – H_2O, 7:3, R_t 14.5 min).

14α,15β-*Diacetoxy*-3α,8α-*disenecioyloxy*-14β,15α-*epoxy*-α-*isocedrene* (**6**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (OAc), 1715, 1650 (C=CCO_2R); MS: *m/z* (rel. int.) 470.230 [M – HOAc]$^+$ (1) (calc. for $C_{27}H_{34}O_7$ 470.230), 430 [M – RCO_2H]$^+$ (2.5), 388 [430 – ketene]$^+$ (12), 83 [RCO]$^+$ (100) (HPLC: MeOH – H_2O, 7:3, R_t 16.4 min).

14α-*Acetoxy*-15β-*methoxy*-3α-*angeloyloxy*-9α-*isobutyryloxy*-14β,15α-*epoxy*-α-*isocedren*-8β-*ol* (**7**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (CO_2R), 1715 (C=CCO_2R); MS: *m/z* (rel. int.) 474.225 [M – MeOH]$^+$ (1) (calc. for $C_{26}H_{34}O_8$ 474.225), 446 [M – HOAc]$^+$ (1.2), 406 [M – RCO_2H)$^+$ (0.5), 392 [474 – O=C=C(Me)CH=CH_2]$^+$ (1.8), 364 [406 – ketene]$^+$ (1.7), 83 [C_4H_7CO]$^+$ (100), 71 [C_3H_7CO]$^+$ (44) (HPLC: MeOH – H_2O, 4:1, R_t 11.5 min).

14β-*Acetoxy*-15α-*methoxy*-3α-*angeloyloxy*-9α-[*2-methylbutyryloxy*] *and isovaleryloxy*-14α,15β-*epoxy*-α-*isocedrene* 8β-*ol* (**11** and **12**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH), 1760 (CO_2R), 1720, 1650 (C=CCO_2R); MS: *m/z* (rel. int.) 460.246 [M – HOAc]$^+$ (8) (calc. for $C_{26}H_{36}O_7$ 460.246), 378 [460 – O=C=C(Me)CH=CH_2]$^+$ (12), 85 [C_4H_9CO]$^+$ (25), 83 [C_4H_7CO]$^+$ (100), 57 [85 – CO]$^+$ (68), 55 [83 – CO]$^+$ (63) (HPLC: MeOH – H_2O, 4:1, R_t 11.9).

14α,15β-*Diacetoxy*-3α-*angeloyloxy*-9α-[*2-methylbutyryloxy*] *and isovaleryloxy*-14β,15α-*epoxy*-α-*isocedren*-8β-*ol* (**13** and **14**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH), 1760 (CO_2R), 1715, 1650 (C=CO_2R); MS: *m/z* (rel. int.) 488.241 [M – HOAc]$^+$ (2) (calc. for $C_{27}H_{36}O_8$ 488.241), 448 [M – RCO_2H]$^+$ (0.5), 446 [M – RCO_2H]$^+$ (0.4), 428 [488 – HOAc]$^+$ (0.5), 328 [428 – RCO_2H]$^+$ (3), 85 [C_4H_9CO]$^+$ (9), 83 [C_4H_7CO]$^+$ (100) (HPLC: MeOH – H_2O, 4:1, R_t 13.1).

3α-*Angeloyloxy*-α-*isocedren*-14,15-*dial* (**15**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715 (*br*, C=CCO_2R, CHO); MS: *m/z* (rel. int.) 330.183 [M]$^+$ (0.7) (calc. for $C_{20}H_{26}O_4$ 330.183), 248 [M – O=C=C(Me)CH=CH_2]$^+$ (12), 83 [RCO]$^+$ (100), 55 [83 – CO]$^+$ (22), $[\alpha]_D^{24}$ – 35 ($CHCl_3$; *c* 2.32) (TLC Et_2O–petrol, 1:2, 2 ×, R_f 0.25).

6β,12,15-*Triacetoxy*-1β,7α,10βH-*guaia*-4,11(13)-*dien*-3-*one* (**16**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 (OAc), 1700, 1640 (C=CC=O); MS: *m/z* (rel. int.) 392.183 [M]$^+$ (2) (calc. for $C_{21}H_{28}O_7$ 392.183), 332 [M – HOAc]$^+$ (3), 290 [332 – ketene]$^+$ (34), 272 [332 – HOAc]$^+$ (21), 230 [290 – HOAc]$^+$ (100), 212 [272 – HOAc] (52); ^{1}H NMR ($CDCl_3$): δ 3.02 (*br* 9, H-1), 245 and 2.15 (*dd*, H-2), 6.07 (*br s*, H-6), 2.29 (*br dd*, H-7), 2.35 (*m*, H-10), 4.65 and 4.58 (*d*, H-12), 5.21 and 5.14 (*br s*, H-13), 1.00 (*d*, H-14), 4.86 (*dd*, H-15), 4.76 (*d*, H-15'), 2.12, 2.09, 2.07 (*s*, OAc); *J*[Hz]: 1,2 = 6.5; 1,2' = 4; 2,2' = 18; 6,15 = 1; 7,8 = 12; 7,8' = 4; 13,13' = 15,15' = 13; $[\alpha]_D^{24}$ – 22 ($CHCl_3$; *c* 1.43), (TLC Et_2O–petrol, 3:1, R_f 0.25).

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