



Minor eudesmanolides from *Artemisia canariensis*

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Abstract

Two new eudesmanolides and 12 known ones, two of which have not previously been obtained from natural sources, were isolated from the aerial parts of *A. canariensis*. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *Artemisia canariensis*; Asteraceae; Anthemidae; Sesquiterpene lactones; Eudesmanolides

1. Introduction

Eudesmanolides are the group of sesquiterpene lactones which exhibit the highest antibacterial activity (Picman, 1986) and they are widely present in plants of the genus *Artemisia*. *A. canariensis* Lee (Anthemidae, Asteraceae) is a plant endemic of the Canary Islands from which six eudesmanolides have previously been isolated (González, Bermejo, Bretón, & Fajardo, 1973; González, Bermejo, & Zaragoza, 1983) as well as a germacranolide of the heliangolide type (Bretón et al., 1985). During the process to obtain vulgarin **1**, a lactone abundant in *A. canariensis*, for use as a synthetic precursor, we obtained in addition to acetyltabarin **2**, 4-epivulgarin **3**, 11 β ,13-dihydrosantamarin **4**, 11 β ,13-dihydroreynosin **5** and tabarin **6**, previously isolated from the plant (González et al., 1973; González et al., 1983), 1-oxo-eudesm-4(15)-en-5 α ,6 β ,7 α ,11 β H-12,6-olide **7** (Ando & Takase, 1977), 1-oxo-eudesm-2,4(15)-dien-5 α ,6 β ,7 α ,11 β H-12,6-olide **8** (Ando & Takase, 1977), 1 α ,4 α -dihydroxyeudesm-2-en-5 α ,6 β ,7 α ,11 β H-12,6-olide **9** (Marco, Sanz, Sancenon, Rustaiyan, & Saberi, 1993), artapshin **10** (Fernández, García, & Pedro, 1987), 8 α -hydroxy-11 β ,13-dihydrobalchanin **11** (Fernández et al., 1987), 1 β -hydroxycolartin **12** (Ando & Takase, 1977; Sanz,

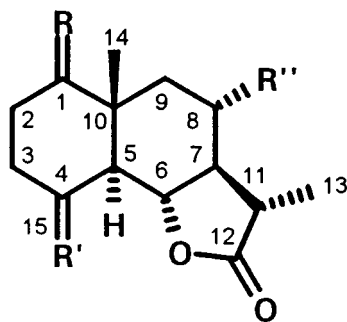
Falcó, & Marco, 1990) and the new eudesmanolides **13** and **14**. Although lactones **7** and **8** have been described as synthetic intermediates (Ando & Takase, 1977), to the best of our knowledge this is the first time that they have been obtained as natural products.

2. Results and discussion

Compound **13** showed IR bands of hydroxyl, γ -lactone and ester groups and a molecular peak in the mass spectrum at m/z 308, which agreed with the formula $C_{17}H_{24}O_5$. A fragment at m/z 248 ($M^+ - 60$) indicates the presence of an acetate group. The 1H NMR spectrum (Table 1) of **13** was very similar to that exhibited by 8 α -hydroxy-11 β ,13-dihydrobalchanin **11** (Fernández et al., 1987). The only significant differences are the presence of a methyl of the acetate group as a singlet at δ 2.04 and the downfield shift of the proton at C_8 (δ 5.18) which in **11** resonates at δ 4.03 ppm. The ^{13}C NMR spectrum of **13** (Table 2) shows the presence of 17 carbon atoms of which two correspond to an acetate group. Hydrolysis of **13** with aq. NaOH in EtOH gave **11** and confirmed that the former compound is the acetyl derivative of **11** at C_8 the 8 α -acetoxy-1 β -hydroxyeudesm-3-en-5 α ,6 β ,7 α ,11 β H-12,6-olide.

Compound **14** showed IR bands of hydroxyl and γ -lactone groups and a molecular ion at m/z 268 (M^+) with a composition $C_{15}H_{24}O_4$. Its 1H NMR spectrum

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- 1 R = O; R' = α -OH, β -Me; R'' = H; $\Delta^{2,3}$
 2 R = O; R' = α -OH, β -Me; R'' = OAc; $\Delta^{2,3}$
 3 R = O; R' = β -OH, α -Me; R'' = H; $\Delta^{2,3}$
 4 R = α -H, β -OH; R' = Me; R'' = H; $\Delta^{3,4}$
 5 R = α -H, β -OH; R' = CH₂; R'' = H
 6 R = O; R' = α -OH, β -Me; R'' = OH; $\Delta^{2,3}$
 7 R = O; R' = CH₂; R'' = H
 8 R = O; R' = CH₂; R'' = H; $\Delta^{2,3}$
 9 R = β -H, α -OH; R' = α -OH, β -Me; R'' = H; $\Delta^{2,3}$
 10 R = α -H, β -OH; R' = CH₂; R'' = OH
 11 R = α -H, β -OH; R' = Me; R'' = OH; $\Delta^{3,4}$
 12 R = α -H, β -OH; R' = α -OH, β -Me; R'' = H
 13 R = α -H, β -OH; R' = Me; R'' = OAc; $\Delta^{3,4}$
 14 R = β -H, α -OH; R' = α -OH, β -Me; R'' = H
 15 R = H₂; R' = α -OH, β -Me; R'' = H
 16 R = O; R' = α -OH, β -Me; R'' = H

Table 1 is very similar to that observed for compound **12** (Sanz et al., 1990). The most significant differences between both compounds are observed in the signal corresponding to the proton H₅ which in **14** is a doublet further downfield (δ 2.18 ppm) than in **12**, in which the said doublet appears at δ 1.73 ppm, as well as in the shape of the signal corresponding to H₁, which in **14** appears as a broad singlet indicating the absence of a trans-diaxial disposition between the said hydrogen and one of the hydrogens at C₂, while for compound **12** H₁ appears as a broad doublet indicating the existence of the said disposition. The most noteworthy

Table 1

¹H NMR data of lactones **13** and **14** (400 MHz, CDCl₃)^a

	13	14
H-1	3.67 dd (6.8; 9.8)	3.39 br s
H-3	5.35 br s	
H-5	2.26 br d (12.3)	2.18 d (11.6)
H-6	4.04 dd (11.0; 11.0)	4.09 dd (10.7; 11.2)
H-8	5.18 ddd (11.0; 11.0; 4.5)	
H-11	2.52 dq (12.4; 6.8)	2.28 dq (12.7; 6.7)
H-13	1.24 d (6.9)	1.22 d (6.9)
H-14	0.94 s	0.98 s
H-15	1.82 br s	1.35 s
OAc	2.07 s	
others		3.10 s (OH)

^a Coupling constant values are in parentheses.

Table 2

¹³C NMR data of lactones **13** and **14** (100 MHz, CDCl₃)

C	13	14
1	75.1	73.1
2	32.7	26.5
3	121.6	36.3
4	132.8	71.5
5	49.9	50.4
6	78.5	81.3
7	57.1	52.9
8	70.2	23.1
9	41.1	32.9
10	40.0	41.5
11	40.1	40.6
12	178.4	178.6
13	12.1	12.4
14	13.9	19.8
15	23.1	24.2
-COCH ₃	170.3	—
-COCH ₃	21.0	—

feature of the ¹³C NMR spectrum Table 2 is the upfield shift of the C₅ signal in relation to the same signal in compound **12** (Sanz et al., 1990). Thus, on the basis of the ¹³C NMR spectrum of colartin **15** (Blay, Cardona, García, & Pedro, 1993), in which there is no hydroxyl at C₁, compound **12** displays a difference of a 1.3 ppm upfield shift in the C₅ signal. The said difference increases to 6.8 ppm for **14**, clearly indicating the existence of a γ effect (El-Ferally & Benigni, 1983) and therefore an α -axial disposition of H₅ and of the hydroxyl group at C₁. The lactone **14** is thus the epimer of **12** at C₁. Indeed, oxidation of both compounds with PDC in CH₂Cl₂ afforded dihydrovulgarin **16**, confirming the structure of **14** as 1 α -hydroxycolartin or 1 α ,4 α -dihydroxyeudesman-5 α ,6 β ,7 α ,11 β H-12,6-olide.

3. Experimental

3.1. General

CC: silica gel (Merck, particle size 40–63 μ m).

3.2. Plant material

Aerial parts of *A. canariensis* were collected in January 1997 at Mesa Mota (Tenerife, Spain). A voucher specimen is deposited in the herbarium of the Department of Botany, Universidad de La Laguna, Tenerife, Spain.

3.3. Extraction and isolation

Dried and powdered aerial parts (10 kg) were extracted as described in Bretón et al. (1985). The

resulting extract (67.4 g) was prefractionated by cc using successively hexane and hexane–EtOAc mixtures (4:1, 4:3, 1:1, 3:4 and 1:4). Similar frs were grouped together and rechromatographed with hexane–EtOAc mixts as eluents to obtain the following products in order of increasing polarity: **8** (28 mg), **7** (41 mg), **2** (409 mg), **1** (7.1 g), **3** (1.2 g), **4** (2.6 g), **5** (3.4 g), **13** (145 mg), **6** (328 mg), **9** (226 mg), **10** (523 mg), **11** (380 mg), **14** (84 mg) and **12** (45 mg).

3.4. *8 α -Acetoxy-1 β -hydroxyeudesm-3-en-5 α ,6 β ,7 α ,11 β H-12,6-olide (13)*

White needles (from hexane–CH₂Cl₂): mp 137–139°C; $[\alpha]_D^{25} + 61^\circ$ (CHCl₃; *c* 0.5); IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1770 (γ -lactone), 1735 (-OAc). EIMS (probe) *m/z* (rel. int.): 308 [M⁺] (4), 290 [M⁺-H₂O] (36), 248 [M⁺-HOAc] (37), 230 (95), 175 (78), 124 (100). HRMS *m/z*: found: 308.1644 [M⁺], C₁₇H₂₄O₅ requires: 308.1624. NMR, Tables 1 and 2.

3.5. *1 α ,4 α -Dihydroxyeudesman-5 α ,6 β ,7 α ,11 β H-12,6-olide (14)*

Colorless oil; $[\alpha]_D^{25} + 31^\circ$ (CHCl₃; *c* 0.5); IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3550 (OH), 1770 (γ -lactone). EIMS (probe) *m/z*

(rel. int.): 268 [M⁺] (2), 253 [M⁺-CH₃] (22), 250 [M⁺-H₂O] (16), 232 (100), 217 (29), 189 (14). HRMS *m/z*: found: 268.1670 [M⁺], C₁₅H₂₄O₄ requires: 268.1675. NMR, Tables 1 and 2.

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