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EUDESMANOLIDES FROM *CALEA TRICHOMATA*

ALFONSO G. OBER, LEOVIGILDO QUIJANO*, LOWELL E. URBATSCH† and NIKOLAUS H. FISCHER‡

Department of Chemistry and †Department of Botany, Louisiana State University, Baton Rouge, LA 70803, U.S.A.

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Key Word Index—*Calea trichomata*; Asteraceae; Heliantheae; sesquiterpene lactones; eudesmanolides.

Abstract—Chemical analysis of *Calea trichomata* yielded, besides four known eudesmanolides, a new eudesmanolide, trichomatolide A. The structure of the new compound was established by chemical and spectral methods.

INTRODUCTION

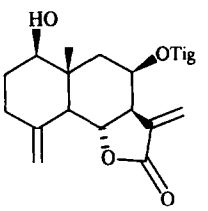
In continuation of our biochemical systematic study of members of the subtribe Galinsoginae, tribe Heliantheae [1] we have analysed *Calea trichomata* of section *Calea* from Chiapas, Mexico for their sesquiterpene lactone constituents. Besides the known 1β-hydroxy-8β-tigloxy-eudesman-6α,12-olide derivatives (**1**–**4**) which had previously been isolated from *Calea rotundifolia* [2] and *Liatris laevigata* [3], a new eudesmanolide was found. The identities of the known lactones (**1**–**4**) were established by ^{1}H NMR and mass spectral correlations [2, 3] and the new compound was characterized by chemical and spectral methods.

RESULTS AND DISCUSSION

Trichomatolide A (**5**), $C_{20}H_{26}O_6$, is a gum with an IR spectrum showing the presence of hydroxyl groups (absorption bands at 3415 and 3325 cm^{-1}), a γ-lactone moiety (1745 cm^{-1}) and an α,β-unsaturated ester(s) (1695 cm^{-1}). The ester function was assigned to a tiglate group on the basis of diagnostic ^{1}H NMR signals (a one-proton quartet of quartets at δ6.89, and two three-proton methyl singlets at 1.82 and 1.81, respectively), together

*On leave from Instituto de Quimica, UNAM, Mexico D.F., Mexico.

‡To whom correspondence should be addressed.



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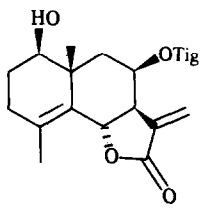

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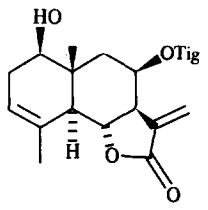

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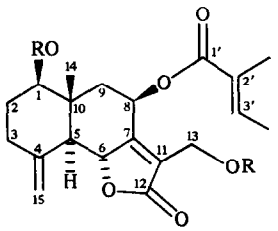
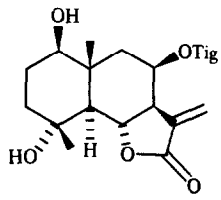


R

5 H

6 OAc



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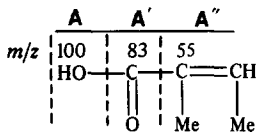

with the characteristic mass spectral peaks for tiglate side-chains at m/z 83 (A') and 55 (A''). On the basis of the chemical shift of H-8 (δ6.19) the tiglate ester must be attached at C-8. Further assignments of the proton signals were deduced from detailed double irradiation experiments (Table 1).

The ^{1}H NMR spectrum of compound **5** was very similar to the one of 8β-tigloxyreynosin (**1**) and in agreement with an eudesmanolide type skeleton, except for the following differences: (a) the typical signals for the exocyclic methylene lactone protons near δ6 were missing, and instead, a two-proton doublet at 4.57 (J = 1.5 Hz) was found; (b) the H-6 signal did not appear as a triplet as in compounds **1**–**4**, but as a broad doublet at 5.13 (J = 11.0 Hz); (c) there was no H-7 signal in the spectrum of **5**.

These differences between the ^{1}H NMR spectrum of compound **5** and the spectra of the other four eudesmanolides (**1**–**4**) suggested an arbusculin D type lactone ring [4] with an endocyclic 7(11)-double bond and a saturated C-13. Moreover, the chemical shift of the two-proton signal H-13 (δ4.57) suggested the presence of a hydroxyl group at C-13. Acetylation of compound **5** provided the diacetate **6**, $C_{24}H_{32}O_8$, which lacked hydroxyl absorptions in the IR spectrum, but instead showed an additional carbonyl band at 1735 cm^{-1} which was assigned to the acetate groups. The ^{1}H NMR spectrum of the diacetate **6** (Table 1) showed a paramagnetic shift of H-1 from δ3.44 to 4.65, and a shift of the two-proton H-13 doublet which now appeared as two doublets centered at 5.19 (J = 14.0 Hz) and 4.74 (J = 14.0; 1.8 Hz) in a typical AB pattern. These paramagnetic shifts in the diacetate **6** confirmed the presence of hydroxyl groups on C-1 and C-13 in compound **5**.

The proposed structure for lactone **5** was in agreement with the obtained ^{13}C NMR data given in the Experimental. Comparison of these data with the ones reported for 8β-tigloxyreynosin (**1**) [3] showed two major differences: (a) the C-7 signal, which was a doublet at δ53.39 in **1** [3] appeared as a singlet at 157.1 in **5** confirming the quarternary and olefinic character of C-7 in **5**. (b) C-13 which was a triplet at δ119.49 in **1** underwent a diamagnetic shift to 56.9 in compound **5** indicating that C-13 represents a saturated carbon atom bearing an hydroxyl group.

The stereochemistry at C-1 and C-8 was assigned by correlation of the dihedral angles of the protons with the experimentally measured coupling constants. The large coupling ($J_{1,2\beta}$ = 11.2 Hz) suggested an equatorial, β-oriented hydroxyl group at C-1; similarly, the small coupling constants $J_{8,9a}$ = 2.0 Hz and $J_{8,9b}$ = 4.6 Hz indicated that the tiglate ester substituent at C-8 be in a β position. The large splitting ($J_{5,6}$ = 11 Hz) was in accord with an antiperiplanar arrangement of the protons at C-5 and C-6.

EXPERIMENTAL

Calea trichomata D. Smith was collected on July 29, 1978 in Chiapas, Mexico, 2.8 miles south of La Trinataria along Highway 190 (L. Urbatsch, No. 3335, voucher deposited at LSU, U.S.A.). The air-dried plant material (652 g) was extracted and worked up as previously described [5], providing 9.1 g of crude syrup which was chromatographed on a silica gel column with petrol–Me_2CO mixtures of increasing polarity; 38 fractions of 200 ml each were taken.

Fractions 16–18 (1.4 g) were re-chromatographed on a silica gel column with petrol–EtOAc mixtures of increasing polarity; 25 fractions of 100 ml each were taken. Fractions 11–14 afforded 230 mg of **1**, 20 mg of **2**, and 7 mg of **3**. Fractions 15–16 provided 65 mg **5**, and fraction 17–18 gave 78 mg **4**. The ^{1}H NMR parameters of the known lactones **1**–**4** were identical with the ones of the compounds described in the literature [2, 3].

Trichomatolide A (**5**). $C_{20}H_{26}O_6$, gum; UV λ_{max}^{MeOH} nm: 220 (ε 1.14 × 10^4); CD (MeOH; c 4.56 × 10^{-3}): $[\theta]_{280}$ +2.9 × 10^2, $[\theta]_{243}$ −8.02 × 10^4; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3415 (OH), 3325 (OH),

Table 1. ^{1}H NMR spectral data of compounds **4** and **6** (200 MHz, $CDCl_3$, TMS as int. standard)

	5	**6**
H-1	3.44 *dd* (J = 11.2; 5.0 Hz)	4.65 *dd* (J = 12.0; 5.0 Hz)
H-2a H-2b	1.66 *m*	1.55–1.95*
H-3a	2.38 *ddd* (J = 14.0; 5.0; 2.0 Hz)	2.40 *ddd* (J = 15.0; 5.6; 2.2 Hz)
H-3b	2.0–2.1*	—
H-5	1.81 *d* (J = 11.0 Hz)	1.91 *d* (J = 11.0 Hz)
H-6	5.13 *ddd* (J = 11.0; 1.0; 1.0 Hz)	5.17 *d* (J = 11.0 Hz)
H-8	6.19 *dd* (J = 4.6; 2.0 Hz)	6.17 *dd* (J = 4.8; 2.0 Hz)
H-9a	2.58 *dd* (J = 15.5; 2.0 Hz)	2.27 *dd* (J = 16.0; 2.0 Hz)
H-9b	1.66 *dd* (J = 15.5; 4.6 Hz)	1.64 *dd* (J = 16.0; 4.8 Hz)
H-13a	4.57 *d* (J = 1.5 Hz)	5.19 *d* (J = 14.0 Hz)
H-13b		4.74 *dd* (J = 14.0; 1.8 Hz)
C-10-Me	1.13 *s*	1.19 *s*
H-15a	5.06 *br s*	5.09 *br s*
H-15b	5.00 *br s*	5.04 *br s*
H-3'	6.89 *qq* (J = 7.2; 1.8 Hz)	6.84 *qq* (J = 7.8; 2.0 Hz)
C-3'-Me	1.82 *br*	1.83 *br*
C-2'-Me	1.81 *s*	1.80 *s*

*Obscured by other signals.

1745 (γ-lactone), 1695 (conj. ester), 1650 (double bond); EIMS (probe) *m/z* (rel. int.): 362 $[M]^+$ (2.6), 262 $[M-A]^+$ (41.1), 244 $[M-A-H_2O]^+$ (12.5), 200 $[M-A-CO_2]^+$ (10.6), 83 $[A']^+$ (100), 55 $[A'']^+$ (39.8); ^{13}C NMR (50.32 MHz, $CDCl_3$, TMS as internal standard): 76.8 *d* (C-1), 31.2 *t* (C-2), 33.7 *t* (C-3), 142.3 (C-4), 55.3 *d* (C-5), 78.6 *d* (C-6), 157.1 *s* (C-7), 65.5 *d* (C-8), 41.4 *t* (C-9), 41.1 *s* (C-10), 128.1 *s* (C-11), 172.4 *s* (C-12), 56.9 *t* (C-13), 12.2 *q* (C-14), 110.8 *t* (C-15), 168.2 *s* (C-1'), 128.2 *s* (C-2'), 140.0 *d* (C-3'), 14.8 *q* (C-2'-Me), 13.0 *q* (C-3'-Me). (Calc. for $C_{20}H_{26}O_6$: 362.1693. Found: MS 362.1675.)

Trichomatolide A diacetate (**6**). Acetylation of 10 mg **5** in pyridine–Ac_2O for 20 hr, followed by usual work-up, gave the diacetate (**6**), $C_{24}H_{32}O_8$, gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1735 (acetate, ester), 1720 (conj. ester), 1655 (double bond); EIMS (probe) *m/z* (rel. int.): 446 $[M]^+$ (4), 386 $[M-HOAc]^+$ (4), 304 $[M-A-C_2H_2O]^+$ (4.0), 286 $[M-A-HOAc]^+$ (4.3), 244 $[M-HOAc-A-C_2H_2O]^+$ (21.5), 226 $[M-2HOAc-A]^+$ (35.3), 211 $[M-HOAc-A-Me]^+$ (17.1), 83 $[A']^+$ (100), 55 $[A'']^+$ (28.4), 43 $[Ac]^+$ (43.4).

Acknowledgement—We thank Helga D. Fischer for technical assistance.

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INTEGRIFOLIN, A GUAIANOLIDE FROM *ANDRYALA INTEGRIFOLIA**

G. M. MASSANET, I. GONZÁLEZ COLLADO, F. A. MACÍAS, F. RODRÍGUEZ LUIS and C. VERGARA

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, Apdo. 40 Puerto Real, Cádiz, Spain

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Key Word Index—*Andryala integrifolia*; Compositae; Lactuceae; sesquiterpene lactones; guaianolide; integrifolin.

Abstract—Integrifolin, the major constituent of *Andryala integrifolia*, has been isolated and characterized as 3β,8β-dihydroxy-4(15),10(14),11(13)-trien-(1αH), (5αH) guaian-6,12-olide (8-epi-desacylcynaropicrin).

INTRODUCTION

Only one species of the genus Andryala (tribe Lactuceae) has been investigated chemically [1, 2]. We have now initiated the study of the constituents of *A. integrifolia* L., a species found in mediterranean Europe [3]. The main constituent in this plant is a sesquiterpene lactone of the guaiane series, which has been named integrifolin (**1a**). In addition, the flavonoids luteolin [4] and apigenin [5] were isolated.

RESULTS AND DISCUSSION

Integrifolin, mp 206–208°, $[\alpha]_D$ −17.5°, IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1750 (α,β-unsaturated-γ-lactone ring), 1655, 1630 (double bonds); MS *m/z*: 262.120 $[M]^+$, was obtained from the medium polar fractions. Its ^1H NMR data (Table 1) showed it was 3β,8β-dihydroxy-4(15), 10(14),11(13)-trien-(1α-H,5α-H)-guaian-6,12-olide (**1a**). The most characteristic features of this spectrum are signals of the α-methylene-γ-lactone grouping, two exocyclic methylenes (C-14 and C-15), and the C-6 lactonic

Table 1. ^1H NMR spectral data for integrifolin **1a** (ppm from TMS)

H-1	2.66	*ddd*	H-9	2.38	*dd*
H-2	1.52	*ddd*	H-9'	2.11	*dd*
H-2'	1.98	*ddd*	H-13	5.42	*d*
H-3	4.28	*dddd*	H-13'	6.14	*d*
H-5	2.53	*dd*	H-14	4.71	*br s*
H-6	4.32	*dd*	H-14'	4.83	*br s*
H-7	2.78	*dddd*	H-15	5.09	*br s*
H-8	4.08	*ddd*	H-15'	5.20	*br s*

J (Hz): 1,2 = 7.5; 1,2' = 9.5; 1,5 = 9.5; 2,2' = 13; 2,3 = 9; 2',3 = 7.5; 3,15 = 1.5; 5,6 = 10; 6,7 = 9; 7,8 = 3; 7,13' = 3.5; 7,13 = 3; 8,9 = 8, 9' = 6 and 9,9' = 13.5.

*Part 1 in the series "Structure and Chemistry of Secondary Metabolites from Compositae".