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EUPATOLIDE AND BORNEOL DERIVATIVES FROM *FLORESTINA TRIPTERIS*

X. A. DOMÍNGUEZ, H. SÁNCHEZ, J. SLIM, J. JAKUPOVIC,* T. V. CHAU-THI* and F. BOHLMANN*

Instituto Tecnológico y de Estudios Superiores de Monterrey, C.P. 64849, Monterrey, N.L., Mexico; *Institute of Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.

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Key Word Index—*Florestina tripteris*; Compositae; sesquiterpene lactones; eupatolide derivatives; borneol derivatives; diterpene manoyloxide derivative.

Abstract—The aerial parts of *Florestina tripteris* afforded in addition to eupatolide and eupatoriopicrin a new derivative and the corresponding 11,13-dihydro compound. Furthermore four substitution products of borneol and a trihydroxymanoyloxide were present. The structures were elucidated by high field NMR techniques. The chemotaxonomy is discussed briefly.

INTRODUCTION

The Central American genus *Florestina* is placed in the subtribe Chaenactidinae [1] and Bahiinae [2] respectively. So far nothing is known to the chemistry of this genus. We therefore have studied one species from Mexico, *F. tripteris* D.C.. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts afforded small amounts of eupatoriopicrin [3] and its 11β,13-dihydro derivative [4], eupatolide [3] as well as two new lactones, the β-hydroxyisovalerates **5** and **6**, four derivatives of borneol (**1–4**) and a trihydroxymanoyloxide (**7**). The structure of the latter followed from the ^{1}H NMR spectrum (see Experimental). In deuteriobenzene nearly all signals could be assigned by spin decoupling in combination with NOE difference spectroscopy. *W*-couplings of H-20 with H-1β, of H-18′ with H-3β and of H-17 with H-7β indicated the axial orientation of the corresponding methyl groups. H-20 showed NOE's with H-18 and H-17 and the latter with H-15. Thus the methyl signals could be assigned without doubt. H-16 only gave a NOE with H-15 and not with H-17. Accordingly, the methyl at C-13 was equatorial. The ^{13}C NMR data (see Experimental) also agreed with the proposed structure. The absolute configuration could not be established, but the negative optical rotation may support an *ent*-labdane as the corresponding manoyloxide showed positive optical rotation [5].

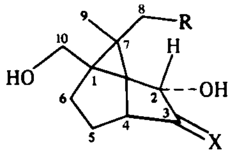
The structures of **5** and **6** could be easily deduced from their ^{1}H NMR spectra (Table 1) which were close to those of eupatoriopicrin and its dihydro derivative respectively. The nature of the ester group followed from the characteristic signals and from the molecular formulae. In the spectrum of **5** the ester group exhibited only two singlets [δ2.48 (2 H) and 1.28 (6 H)] while in the spectrum of **6** a pair of doublets (δ2.59 and 2.52) and two methyl singlets (δ1.33 and 1.32) were present.

The spectra of **1–4** (Table 2) indicated that we were probably dealing with derivatives of borneol, as several signals showed the typical splitting of these compounds. This was established by systematic spin decoupling and NOE difference spectroscopy. In the case of **1** a clear NOE was observed between H-2 and one methyl group. The latter gave a NOE with a hydroxymethyl proton. The coupling of H-2 further indicated the *cis*-relationship of H-2 and H-3. Thus **1** was 3α,10-dihydroxyborneol. The spectrum of the isomeric triol **2** was typically different from that of **1**. The missing coupling $J_{3,4}$ and the coupling of H-2 clearly showed that the 3β-epimer was present. This was supported by a NOE between H-8, H-9 and H-2. The ^{1}H NMR of the third triol **3** clearly showed that two primary hydroxyl groups were present. A *W*-coupling of H-9 with H-8 and a NOE between H-2 and H-8 established the relative position of the hydroxy groups, as the last one only could be placed at C-10. The configuration at C-2 followed from the observed couplings. The ^{1}H NMR signals of the ketone **4** could be assigned by spin decoupling and the relative position of the hydroxy group was deduced from the presence of *W*-couplings of H-2 with H-6β and H-4 as well as by the NOE between H-8 and H-2.

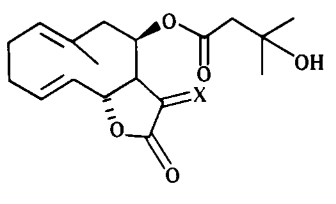
The overall picture of the chemistry of this *Florestina* species shows relationship to *Chaenactis* [6] and to *Schkuhria* [7] by the co-occurrence of eupatolide derivatives and to *Palafoxia* [8] and *Schkuhria* [9] by the presence of manoyloxide derivatives. Accordingly, the placement of these genera in one subtribe is supported by the chemistry.

EXPERIMENTAL

The air-dried plant material (300 g, voucher 8164, deposited in the Herbarium of ITESM, collected in El Cercado, N.L., 28 November 1986), was extracted (15 g) and worked-up as reported previously [10]. The CC fractions (silica gel) were combined to three which were further separated by TLC and HPLC (always RP 8, *ca* 100 bar). The first fraction gave *ca* 50 mg taraxasteryl and lupeyl acetate as well as *ca* 50 mg of the corresponding alcohols. The next one afforded after TLC (Et_2O–petrol, 3 : 2) by HPLC ($MeOH–H_2O$, 7 : 3) 1 mg **6** (R_t 8.3 min), 1 mg eupatolide



	R	X
1	H	αOH,H
2	H	βOH,H
3	OH	H_2
4	H	=O



5 X = CH_2

6 X = Me,H

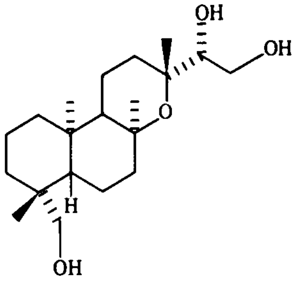


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Table 1. ^{1}H NMR spectral data of **5** and **6** (400 MHz, $CDCl_3$, δ-values)

H	**5**	**6**
1	4.88 *br dd*	4.87 *br dd*
5	4.76 *br d*	4.67 *br d*
6	5.09 *dd*	5.01 *dd*
7	2.92 *br ddd*	1.98 *ddd*
8	5.79 *br d*	5.44 *br d*
9	2.82 *br dd*	2.80 *br dd*
9′	2.35 *br d*	2.24 *dd*
11	—	2.35 *m*
13	6.32 *d*	1.28 *d*
13′	5.60 *d*	
14	1.48 *br s*	1.48 *br s*
15	1.75 *d*	1.72 *d*
OCOR	2.48 *s*	2.59 *d*
	1.28 *s* (6H)	2.52 *d*
		1.33 *s*
		1.32 *s*

J[Hz]: 1,2 = 12; 1,2′ = 4; 5,6 = 10; 5,15 = 1.5; 6,7 = 9; 7,8 = 1; 7,13 = 3.5; 7,13′ = 3; 8,9 = 5; 9,9′ = 15; (compound **6**: 7,11 = 12; 11,13 = 7).

Table 2. ^{1}H NMR spectral data of **1**–**4** (400 MHz, $CDCl_3$, δ-values)

H	**1**	**2**	**3**	**4**
2	4.19 *br d*	4.24 *br s*	3.99 *ddd*	4.32 *br s*
3	4.24 *br dd*	3.45 *br d*	0.98 *dd* 2.30 *dddd*	—
4	1.84 *dd*	1.62 *br d*	1.64 *dd*	2.27 *br d*
5α	1.74 *ddd*	1.18 *ddd*	1.33 *ddd*	1.49 *ddd*
5β	1.50 *dddd*	1.76 *dddd*	1.70 *dddd*	2.05 *dddd*
6α	1.95 *ddd*	1.97 *ddd*	1.89 *ddd*	2.15 *ddd*
6β	1.32 *ddd*	1.27 *dddd*	1.80 *dddd*	1.54 *dddd*
8	0.94 *s*	1.10 *s*	3.77 *d* 3.24 *d*	1.05 *s*
9	0.95 *s*	0.85 *s*	0.99 *s*	1.04 *s*
10	3.74 *d*	3.79 *d*	3.58 *br s*	3.77 *d*
10′	3.60 *br d*	3.58 *d*		3.92 *d*

J[Hz]: 4,5β = 5α,6β = 5β,6α ≈ 4; 5α,5β = 5β,6β = 12; 5α,6α = 9; compound **1**: 2,3 = 9; 3,4 = 4; 10.10′ = 11; compound **2**: 2,3 = 2,6β = 2.

and 1 mg **5** (R_t 12.3 min). Medium pressure chromatography of the third CC fraction gave three mixtures (3/1–3/3). HPLC of 3/1 (MeOH–H_2O, 1:1) gave 6 mg **4** (R_t 2.5 min) and 7 mg **1** (R_t 3.0 min) HPLC of 3/2 (MeOH–H_2O, 11:9) gave three mixtures (3/2/1–3/2/2). TLC of 3/2/1 ($CHCl_3$–MeOH, 19:1) gave 6 mg **3**. HPLC of 3/2/2 (MeOH–H_2O, 1:1) afforded 10 mg **2** (R_t 5.0 min) and HPLC of 3/2/3 (MeOH–H_2O, 11:9) gave 3 mg eupatoriopicrin, 3 mg 11,13-dihydroeupatoriopicrin and 8 mg **7** (R_t 9.5 min). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

3,10-*Dihydroxyborneol* (**1**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH); MS *m/z* (rel. int.): 168.115 $[M-H_2O]^+$ (13) (calc. for $C_{10}H_{16}O_2$: 168.115), 153 $[168-Me]^+$ (10), 137 $[168-CH_2OH]^+$ (48), 121 (36), 109 (81), 108 (100), 95 (98), 93 (58); $[\alpha]_{546}^{24°}$ −40 ($CHCl_3$; *c* 0.5).

3β,10-*Dihydroxyborneol* (**2**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH); MS *m/z* (rel. int.): 168.115 $[M-H_2O]^+$ (12) (calc. for $C_{10}H_{16}O_2$: 168.115), 153 (10), 137 (54), 121 (41), 109 (83), 108 (100), 95 (91); $[\alpha]_D^{24°}$ +21 ($CHCl_3$; *c* 0.1).

8,10-*Dihydroxyborneol* (**3**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH); CIMS *m/z* (rel. int.): 187 $[M+1]^+$ (3), 169 $[187-H_2O]^+$ (33), 151 $[169-H_2O]^+$ (108), 133 $[151-H_2O]^+$ (12); $[\alpha]_D^{24°}$ −10 ($CHCl_3$; *c* 0.36).

3-*Oxo*-10-*hydroxyborneol* (**4**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1740 (C=O); MS *m/z* (rel. int.): 184.110 $[M]^+$ (22) (calc. for $C_{10}H_{16}O_3$: 184.110), 156 $[M-CO]^+$ (5), 138 $[156-H_2O]^+$ (41), 123 $[138-Me]^+$ (20), 95 (28), 87 (100).

Eupatolide-[3-*hydroxyisovalerate*] (**5**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 230.131 $[M-RCO_2H]^+$ (25) (calc. for $C_{15}H_{18}O_2$: 230.131); CIMS *m/z* (rel. int.): 349 $[M+1]^+$ (46), 231 $[349-RCO_2H]^+$ (100); $[\alpha]_D^{24°}$ +40 ($CHCl_3$; *c* 0.1).

11β,13-*Dihydroeupatolide*-[3-*hydroxyisovalerate*] (**6**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (γ-lactone); MS *m/z* (rel. int.): 232.146 $[M-RCO_2H]^+$ (36) (calc. for $C_{15}H_{20}O_2$: 232.146); CIMS *m/z* (rel. int.): 351 $[M+1]^+$ (18), 233 $[351-RCO_2H]^+$ (100).

14,15,19-*Trihydroxy*-13-epi-ent-*manoyloxide* (**7**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 279.232 $[M-CH(OH)CH_2OH]^+$ (39) (calc. for $C_{18}H_{31}O_2$: 279.232), 261 $[279-H_2O]^+$ (100), 243 $[261-H_2O]^+$ (42), 231 $[261-CH_2O]^+$ (32), 123 (54), 95 (100); ^{1}H NMR (C_6D_6): 1.4–1.3 (*m*, H-1α, H-2β, H-7β, H-9, H-11β, H-12β), 0.70 (*br ddd*, H-1β), 1.46 (*ddddd*, H-2α), 1.82 (*dddd*, H-3α), 0.86 (*dddd*, H-3β), 0.91 (*dd*, H-5), 1.14 (*dddd*, H-6α), 1.58 (*dddd*, H-6β), 1.79 (*ddd*, H-7α), 1.22 (*m*, H-12α), 2.05 (*m*, H-12α), 3.62 (*dd*, H-14), 3.58 and 3.86 (*dd*, H-15), 1.24 (*s*, H-16), 1.11 (*d*, H-17), 3.45 (*d*, H-18), 3.22 (*dd*, H-18′), 0.93 (*s*, H-19), 0.63 (*s*, H-20); (*J*[Hz]: 1α,1β = 1β,2α = 2α,2β = 2α,3β = 3α,3β = 5,6α = 6α,6β = 6α,7β = 7α,7β = 13; 1β,2β = 1α,2α = 2α,3α = 2β,3β = 6α,7α = 6β,7β = 14,15 ~ 3; 1α,3α = 1.5; 3β,18 = 0.8; 15,6β = 2.5; 14,15′ = 7; 15,15′ = 11; 18,18′ = 10.5); ^{13}C NMR ($CDCl_3$; C-1–C-20): 27.0, 18.0, 39.0, 37.1, 57.2, 20.4, 35.7, 75.3, 52.6, 38.4, 14.1, 44.3, 77.0, 77.2, 65.4, 26.9, 25.9, 25.0, 63.1, 15.3 (a few signals may be interchangeable).

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