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A MYRTENYLFUROHELIANGOLIDE FROM *CALEA RUPICOLA*

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Key Word Index—*Calea rupicola*; Compositae; sesquiterpene lactones; furoheliangolides; myrtenylfuroheliangolide.

Abstract—The aerial parts of *Calea rupicola* afforded in addition to known furoheliangolides two new ones, 9α-hydroxyatripliciolide-8-*O*-isobutyrate and a myrtenyl substituted sesquiterpene lactone 5β-myrtenyl-4α,5-dihydroatripliciolide-8-*O*-isovalerate.

Many species of the large genus *Calea* (Compositae, tribe Heliantheae, subtribe Neurolaeninae) have been studied chemically. Furoheliangolides and other highly oxygenated germacranolides are widespread [1]. However, from a few species other constituents were reported [2, 3]. This is in agreement with the placement of some of these species in other genera like *Alloisospermum* [4] and *Tetrachyron* [5]. We have studied a further species from Paraguay and the results are discussed in this paper.

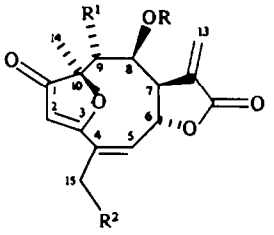
The aerial parts of *Calea rupicola* Chod. gave thymohydroquinone dimethyl ether and its 8,9-dehydro derivative as well as the known atripliciolide derivatives **1** [6], **2** [7], **3** [6] and **5** [8]. Furthermore, two new ones were obtained, 9α-hydroxyatripliciolide-8-*O*-isobutyrate (**4**) and a further myrtenyl substituted lactone (**6**). The structure of **4** followed from the ^{1}H NMR spectrum which was close to that of **3** [6]. However, the presence of a hydroxyl group at C-9 caused the replacement of a pair of double doublets (H-9) by a doublet at much lower field (δ4.03). The stereochemistry followed from the value of $J_{8,9}$ and the downfield shift of H-7. Furthermore, the spectrum was close to that of the corresponding methacrylate [9].

The structure of **6** could be deduced from the ^{1}H NMR spectrum in combination with spin decoupling and NOE difference spectroscopy. The presence of a myrtenyl residue followed from the typical ^{1}H NMR signals which were close to those of similar atripliciolide derivatives with a myrtenyl residue at C-5 [10, 11]. Though the configurations at C-4 and C-5 were deduced from the couplings it was desirable to verify these proposals. NOE difference spectroscopy clearly established the stereochemistry at all chiral centres. Thus, clear effects were observed between H-15, H-6 (5%) and H-2 (10%), between H-14 and H-9α (3%), between H-7, H-8 (4%) and H-5 (7%), between H-5, H-7 (6%) and H-4 (6%) as well as between H-10′, H-9′ (6%) and H-7′ (10%). Also the ^{13}C NMR data agreed with the structure (see Experimental).

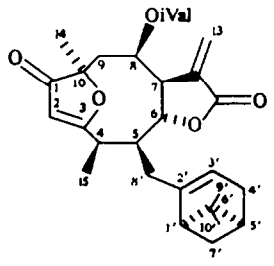
Furoheliangolides with a myrtenyl residue at C-5 so far have been isolated only from *Calea* species [10, 11]. The isolation of several furoheliangolides from *C. rupicola* again showed that these lactones are characteristic for the genus. However, such compounds are also present in related genera.

EXPERIMENTAL

The aerial parts of *Calea rupicola* Chod. 1.68 kg voucher Schmeda 680) were extracted with EtOH–Et_2O (1:1) and the extract obtained was separated first by CC (silica gel) affording two fractions (Fr. 1: Et_2O–petrol, 1:10; Fr. 2: Et_2O and



	1	2	3	4	5
R	iVal	MeBu	iBu	iBu	MeBu
R^1	H	H	H	OH	H
R^2	H	H	H	H	OH



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Et_2O–MeOH, 9:1). TLC (silica gel, PF 254, Et_2O–petrol, 1:20) of fraction 1 gave 40 mg thymohydroquinonedimethyl ether and 20 mg of the 9,10-dehydro derivative. Fraction 2 was separated again by flash chromatography (silica gel, ϕ 30–60 μ, Et_2O–petrol, 1:1, Et_2O and Et_2O–MeOH, 9:1) affording 15 mg **1**, 10 mg **2**, 20 mg **3**, 12 mg **4**, 24 mg **5** and 12 mg **6** which was purified by HPLC (RP 8, MeOH–H_2O, 7:3, R_t 7.5 min).

9α-Hydroxyatripliciolide-8-O-isobutyrate (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1740 (CO_2R), 1705 (C=CC=O); MS *m/z* (rel. int.): 362.136 $[M]^+$ (23) (calc. for $C_{19}H_{22}O_7$: 362.136), 347 $[M-Me]^+$ (7), 275 $[M-OCOR]^+$ (10), 274 $[M-RCO_2H]^+$ (9), 232 $[275-C_3H_7]^+$ (45), 71 $[RCO]^+$ (62), 57 (100); ^1H NMR (400 MHz, $CDCl_3$): δ5.63 (*s*, H-2), 5.98 (*dq*, H-5), 5.30 (*dq*, H-6), 3.86 (*ddd*, H-7), 5.07 (*dd*, H-8), 4.03 (*d*, H-9), 6.36 (*d*, H-13), 5.75 (*d*, H-13'), 1.57 (*s*, H-14), 2.07 (*t*, H-15); 2.48 (*qq*), 1.09 and 1.12 (*d*, $COCHMe_2$); [*J* (Hz): 5,6 = 2.5; 5,15 = 6,15 = 7,8 = 2; 7,13 = 3; 7,13' = 2.5; 8,9 = 5; 2',3' = 2',4' = 7].

5β-Myrtenyl-4α,5-dihydroatripliciolide-8-O-isovalerate (**6**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1730 (CO_2R), 1710 (C=CC=O), 1595 (C=COR); MS *m/z* (rel. int.): 496.283 $[M]^+$ (2.6) (calc. for $C_{30}H_{40}O_6$: 496.283), 481 $[M-Me]^+$ (0.5), 412 $[M-O=C=CHC_3H_7]^+$ (2.5), 394 $[M-RCO_2H]^+$ (1), 268 (51), 232 (50), 135 (22), 125 (78), 85 $[RCO]^+$ (37), 57 $[85-CO]^+$ (100); ^1H NMR (C_6D_6): δ5.46 (*d*, H-2), 2.54 (*dq*, H-4), 2.81 (*ddt*, H-5), 4.64 (*dd*, H-6), 2.69 (*ddd*, H-7), 5.06 (*dd*, H-8), 2.66 (*dd*, H-9), 1.55 (*dd*, H-9'), 6.29 (*d*, H-13), 5.14 (*d*, H-13'), 1.17 (*s*, H-14), 0.86 (*d*, H-15), 2.03 (*m*, H-1'), 5.13 (*br s*, H-3'), 2.20 (*ddd*, H-4'), 2.03 (*m*, H-5'), 2.37 (*dt*, H-7_1·), 1.31 (*d*, H-7_2·), 2.28 (*dd*, H-8_1·), 2.00 (*dd*, H-8_2·); [*J* (Hz): 2,4 = 1; 4,5 = 5,6 = 6,7 = 8,9 = 5; 4,15 = 7; $5,8_1$· = $5,8_2$· = 7; 7,13 = 3; 7,13' = 2.5; 8,9 = 5; 8,9' = 2; 9,9' = 15; 1',7_1· = 5',7_1· = 5.5; 4_1·,4_2· = 8; 7_1·,7_2· = 8.5; 8_1·,8_2· = 15]; ^{13}C NMR ($CDCl_3$, C-1–C-15): δ205.6 *s*, 104.3 *d*, 193.3 *s*, 44.1 *d*, 36.9 *d*, 75.1 *d*, 45.5 *d*, 73.9 *d*, 42.6 *t*, 88.0 *s*, 168.9 *s*, 138.8 *s*, 123.8 *t*, 9.7 *q*, 20.9 *q*; C-1'–C-10': 52.9 *d*, 145.2 *s*, 118.4 *d*, 31.3 *t*, 40.8 *d*, 38.1 *s*, 31.6 *t*, 34.8 *t*, 26.2 *q*, 22.9 *q*; OCOR: 171.4 *s*, 43.2 *t*, 25.2 *d*, 22.3 *q*, 22.3 *q* (assignment based on comparison with the data of α-pinene, other isovalerates and related sesquiterpene lactones).

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