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SESQUITERPENE LACTONES FROM *CHROMOLAENA OPADOCLINIA*

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Key Word Index—*Chromolaena opadoclinia*; Compositae; Eupatorieae; new sesquiterpene lactones; structural determination; NMR; 2D-COSY; germacranolides.

Abstract—One known and four new germacranolide-type sesquiterpene lactones were obtained from the dichloromethane extract of *Chromolaena opadoclinia*.

INTRODUCTION

Chromolaena (tribe Eupatorieae, Compositae) comprises 130 species found mostly in tropical America [1]. In continuation of our chemosystematic investigations of this genus, we report here the isolation and structure elucidation of one known and four new sesquiterpene lactones from the dichloromethane extract of the aerial parts of *Chromolaena opadoclinia* (Blake) King and H. Rob.

Most species of *Chromolaena* examined to date produce cadinanes or prostaglandin-like fatty acid derivatives [2–5]. However, germacrane-derived sesquiterpene lactones have previously been reported from *C. glaberrima* [6–7], which is considered on morphological grounds to be closely related to *C. opadoclinia* [8]. Although sesquiterpene lactones with double side chains have been reported from several unrelated genera of Eupatorieae [9–22] double side chains with terminal angelate derivatives are otherwise known only from *Eupatoriastrum* [9], a genus in which *C. opadoclinia* was once placed [23]. However, the morphological grounds for separating these two groups are very strong [24], and the chemical similarity is of doubtful taxonomic significance.

DISCUSSION

The structure of the known compound deltoidin A (**1**) was easily deduced from comparison of the spectral data for the compound isolated here with those previously reported (25). The same skeletal structure [i.e. 8-β-acyloxylated parthenolide] with different side chains was assigned for compounds **2**–**6** based on spectral data (see Table 1 and Experimental).

The ^{1}H NMR of the new compound **2**, $C_{25}H_{32}O_7$ (CIMS), displayed signals for a 5′-acyloxylated tiglate moiety (δ 7.11 *q*, 4.87 *s*, 1.97 *d*). The 5′-acyl group was identified as angelic acid from its characteristic signal pattern (δ 6.07 *qq*, 1.92 *dq*, 1.78 *q*). The mass spectral peaks observed at *m/z* 445 $[M+H]^+$, 345 $[M+H-$angelic acid$]^+$, 247 $[M+H-$side chain$]^+$, 199 [side chain + H]$^+$ and 101 [angelic acid + H]$^+$ were in accord with this conclusion. Thus, **2** is 8-β-[5′-angeloyloxy]-tigloyloxyparthenolide.

The second new compound **3**, $C_{25}H_{32}O_8$ (CIMS), showed a similar ^{1}H NMR to that of **2** with only few differences. The ^{1}H NMR spectrum of **3** displayed signals for a 4′-esterified dihydroxytiglate moiety (δ 6.74 *t*, 4.98 *dd*, 4.88 *dd*, 4.39 *bd*), and 2D NMR homonuclear COSY spectrum of **3** clearly confirmed the attachment of the terminal ester group to the C-4′ hydroxyl group of the dihydroxytiglate moiety. The second side chain was also easily identified as angelate on the basis of characteristic ^{1}H NMR signals (δ 6.16 *qq*, 1.98 *dq*, 1.88 *q*). Furthermore, the peaks observed at *m/z* 361 $[M+H-$angelic acid$]^+$, 247 $[M+H-$side chain$]^+$ and 101 [angelic acid + H]$^+$ in the CIMS of **3** were in agreement with the proposed structure. Thus, **3** is 8-β-[4′-angeloyloxy]-5′-hydroxytigloyloxyparthenolide.

The new compounds **4** and **5**, both $C_{25}H_{32}O_8$ (CIMS), could not be separated by conventional chromato-graphic procedures of HPLC. However, the ^{1}H, 2D-COSY and ^{13}C NMR for the mixture of **4** and **5** revealed the presence of epimeric side chains in **4** and **5**. Signals at δ 4.33 and 4.30 (H-4′a and H-4′b, the centres of the AB part of ABX systems), as well as two sets of signals at δ 6.22 and 6.19 (H-5′a, both *s*), and signals at δ 6.06 and

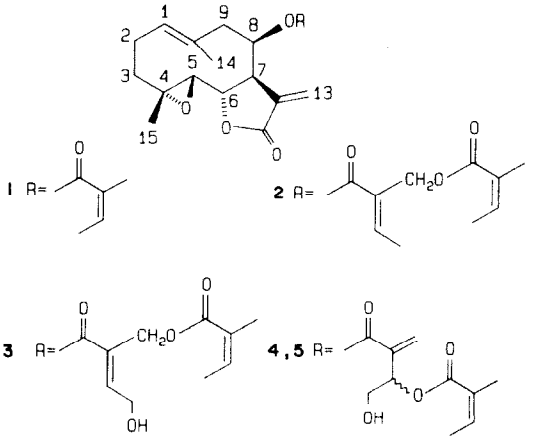

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Table 1. ^{1}H NMR data of compounds **2**–**5** [200 MHz, $CDCl_3$, TMS (coupling constants in Hz in parentheses)]

H	2	3	4	5
1	5.31 *br d* (10.5)	5.32 *br d* (10.7)	5.32 *br d* (10.6)	
5	2.83 *d* (8.5)	2.84 *d* (8.6)	2.83 *d* (8.4)	
6	4.42 *t* (8.5)	4.45 *t* (8.6)	4.42 *t* (8.4)	
7	3.18 *m*	3.19 *m*	3.18 *m*	
8	5.82 *br d* (3.9)	5.82 *br d* (3.8)	5.79 *br d* (3.9)	
9a	2.82 *dd* (5.8; 14.8)	2.81 *dd* (5.6; 14.8)	2.84 *dd* 4.9; 13.1)	
9b	2.40 *dd* (2.8; 14.8)	2.41 *dd* 2.8; 14.8	2.41 *br d* (13.1)	
13*a*	6.34 *d* (3.5)	6.39 *d* (3.5)	6.48 *d* (3.6)	
13*b*	5.70 *d* (2.9)	5.73 *d* (2.9)	5.70 *d* (2.9)	
14	1.71 *br s*	1.74 *br s*	1.73 *br s*	
15	1.37*s*	1.37 *s*	1.37 *s*	
3′	7.11 *q* (6.9)	6.73 *t* (6.3)	4.73 *br t* (5.1)	4.73 *br t* (5.1)
4′*a*	1.97 *d* (6.9)	4.98 *dd* (6.3; 14.5)	4.33†	4.30†
4′*b*		(4.88 *dd*) (6.3; 14.5)		
5′*a*	4.87 *s*	4.39 *br d* (5.5)	6.22 *s*	6.19 *s*
5′*b*			6.06 *s*	6.04 *s*
3″	6.07 *qq* (7.2; 1.4)	6.16 *qq* (7.2; 1.4)	6.09 *br q* (6.8)	6.09 *br q* (6.8)
4″	1.92 *dq* (7.2; 1.4)	1.98 *dq* (7.2; 1.4)	1.96 *dq* (6.8; 1.5)	1.96 *dq* (6.8; 1.5)
5″	1.78 *q* (1.4)	1.88 *q* (1.4)	1.86 *q* (1.5)	1.86 *q* (1.5)

*At 55°

†Centre of the AB art of an ABX signal.

6.04 (H-5′b, both *s*) in addition to a broad triplet at δ4.73 (H-3′) and characteristic angelic acid signals (δ6.09 *br q*, 1.98 *dq*, 1.86 *dq*) in the ^{1}H NMR of **4** and **5** confirmed the presence of epimeric 3′-angeloyloxylated 4′-hydroxyethacrylate side chains in these compounds. Furthermore, the relevant side chain carbon signals in the ^{13}C NMR spectrum of **4** and **5** (see Experimental) also supported these assignments.

The mass spectral peaks observed at *m/z* 361 $[M+H-$angelic acid$]^+$ 215 [side shain + H]$^+$ and 101 [angelic acid + H]$^+$ were also in accord with postulated structures.

EXPERIMENTAL

The aerial parts of *Chromolaena opadoclinia* (Blake) King and H. Rob were collected from Mexico: 4.7 miles east of Ejido Tziscao, Chiapas, 7, January 1984. The voucher specimen (S. Sundberg 2428) is deposited in the Plant Resources Center at the University of Texas at Austin (TEX).

Air-dried plant material (1100 g) was extracted twice with CH_2Cl_2 and the extract was concd and dissolved in 85% MeOH (500 ml) then left overnight at 4°. The concentrate was filtered and extracted with hexane (3 × 250 ml). The alcohol fraction was then concd and extracted with CH_2Cl_2 (3 × 300 ml), dried over dry $MgSO_4$, to yield, finally, 950 mg of gummy material. This gummy residue was chromatographed on a silica gel column (3 × 90 cm) using a hexane–EtOAc gradient. Fractions which were similar on TLC were combined and the resulting fractions chromatographed on a Sephadex LH-20 column using cyclohexane–CH_2Cl–MeOH (7:4:1) mixture. Final purification of the compounds was made by prep. TLC (silica gel) plates, 1.5 mm thickness, which were eluted with hexane–EtOAc (1:1) or C_6H_6–CH_2Cl_2–EtOAc–MeCN (4:4:2:1).

^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR at 125.8 MHz in $CDCl_3$, with TMS as int. standard.

8-*β*-[5′-*Angeloyloxy*]-*tigloyloxyparthenolide* (**2**). Oil (9 mg). IR ν_{max}^{NaCl} cm^{-1}: 2970, 2940, 2860, 1775, 1720, 1655 and 1270. CIMS (CH_4, 0.5 torr, direct probe) *m/z* (rel. int.): 445 $[M+H]^+$ (2.7); 345 $[M+H-$angelic acid$]^+$ (2.3), 247 $[M+H-$side chain$]^+$ (12.6); 229 $[M+H-$side chain $-H_2O]^+$ (14.6); 199 [side chain + H]$^+$ (16); 181 [side chain acylium]$^+$ (12.1), 101 [angelic acid + H]$^+$ (100); 83 [angelate]$^+$ (25.6).

8-β-[4′-*Angeloyloxy*]-5′-*hydroxytigloxyloxyparthenolide* (**3**). Oil (7 mg). IR ν_{max}^{NaCl} cm^{-1}: 3440 (OH), 2970, 2920, 2860 (CH_2), 1768, 1718, 1660, 1630, 1380. CIMS (CH_4, 0.5 torr, direct probe) *m/z* (rel. int.): 461 $[M+H]^+$ (4.5); 448 $[M+H-H_2O]^+$ (2.1), 247 $[M+H-$side chain$]^+$ (24.8), 229 $[M+H-$side chain $-H_2O]^+$ (64.3); 215 [side chain $+H]^+$ (7.7), 197 [side chain $+H-H_2O]^+$ (16.9), 101 [angelic acid $+H]^+$ (83), 83 [angelate]$^+$ (100).

8-β-[3′-*Angeloyloxy*]-4′-*hydroxyethacryloyloxyparthenolide* (**4**) *and* (**5**). Oil (6 mg). IR ν_{max}^{NaCl} cm^{-1}: 3450 (OH), 2970, 2940, 2860 (CH_2), 1772, 1720 *br*, 1655, 1265, 1240. CIMS (CH_4, 0.5 torr, direct probe) *m/z* (rel. int.) 461 $[M+H]^+$ (26.1); 443 $[M+H-H_2O]^+$ (17.8); 425 $[M+H-2H_2O]^+$ (9.3), 361 $[M+H-$angelic acid$]^+$ (9.2); 247 $[M+H-$side chain] (68.9), 229 $[M+H-$side chain$]^+$ (100); 215 [side chain $+H]^+$ (9.1); 197 [side chain $+H-H_2O]^+$ (22.2); 101 [angelic acid $+H]^+$ (22.1); 83 [angelate]$^+$ (37.2). ^{13}C data for **4** and **5**: ^{13}C NMR ($CDCl_3$, TMS) ppm δ129.30 *d* (C-1), 24.28 *t* (C-2), 35.85 *t* (C-3), 61.78 *s* (C-4), 66.63 *d* (C-5), 75.33 *d* (C-6), 49.63 *d* (C-7), 74.41–74.35 *d* (C-8), 43.95 *t* (C-9), 131.24 *s* (C-10), 135.95 *s* (C-11), 168.41 *s* (C-12), 122.73 *t* (C-13), 20.49 *q* (C-14) 17.22 *q* (C-15), 164.37–164.1 *s* (C-1′), 138.57 *s* (C-2′), 69.84–69.81 *d* (C-3′), 67.0 *t* (C-4′), 127.46 *t* (C-5′), 168.23 *s* (C-1″), 127.09–127.04 *s* (C-2″), 139.58–139.52 *d* (C-3″), 15.89 *q* (C-4″) and 19.68–19.61 *q* (C-5″).

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