

NEW HELIANGOLIDES FROM  
CONOCLINIOPSIS PRASIIFOLIA\*FERDINAND BOHLMANN,† CHRISTA ZDERO,† ROBERT M. KING‡  
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## INTRODUCTION

The new genus *Conocliniopsis* is based on a single species distributed widely in South America, *Eupatorium ballotaefolia* var. *caucense* B. L. Robinson (= *Conoclinium prasiifolium* DC), which now is named *C. prasiifolia* (DC) K. et R. [1]. We have investigated this species chemically; the roots afforded well known compounds and a new obliquine derivative, while the aerial parts contained two new heliangolides which may be of chemotaxonomical importance. One of these lactones is most probably identical to a compound from *Eupatorium ballotaefolium* H. B. K. (= *Lourteigia ballotaefolia* (H. B. K.) K. et R.) [1], for which the stereochemistry was not given [2].

## RESULTS AND DISCUSSION

The roots of *C. prasiifolia* afforded the pentayne 1 [14], germacrene D (2) [15], bicyclogermacrene (3) [16], caryophyllene (4) [17], alloaromadendrene (5) [18], 4 $\alpha$ -hydroxygermacrene (6) [19],  $\alpha$ -bisabolol (7) [20], the thymol derivatives 8 and 9, and a coumarin, dihydro-hydroxy-obliquine (10), already prepared from obliquine [3]. The data were in agreement with those reported for 10 [3]. The <sup>1</sup>H NMR spectrum was very similar to that of obliquine [3, 4], indicating the same relative position of the hydroxyisopropyl group as that of the isopropylidene group in obliquine. Also the optical rotation was nearly the same as that given for the synthetic sample [3].

The aerial parts also contained compounds 2-6 and an unidentified triterpene acetate (C<sub>32</sub>H<sub>52</sub>O<sub>2</sub>). The most polar fractions afforded two sesquiterpene lactones, which were heliangolides 11 and 12, as shown by <sup>1</sup>H NMR studies (Table 1). On acetylation both 11 and 12 led to the diacetate 13. Therefore the only difference between 11 and 12 was the free hydroxyl at C-5' in 12, which was acetylated in 11. The presence of an acetyl sarracinate group in 11 clearly followed from the <sup>1</sup>H NMR data ( $\tau$  7.10,  $\delta$  1.97,  $\delta$  4.86 and 4.71,  $s$  2.03), while the  $\beta$ -furanone part was indicated

by a typical singlet at 5.64 [5-11]. The <sup>1</sup>H NMR spectrum of 11 further displayed typical signals of a methylene lactone ( $\delta$  6.36,  $J$  = 2.8 and  $\delta$  5.73,  $J$  = 2.6); values less than 3 Hz are typical for heliangolides [12]. The presence of the hydroxyl group was seen after deuterium exchange. In the original <sup>1</sup>H NMR spectrum the signals of the hydroxyl and the C-9 proton were very broad multiplets. In the spectrum of 13, however, all signals were clearly separated. The stereochemistry therefore could be established by decoupling experiments and comparison of the chemical shifts and coupling constants with those of similar lactones [5-11]. Irradiation of the signal of the olefinic methyl ( $\delta$  2.08) in the spectrum of 13 collapsed the signals at 5.99 and 5.39 to a doublet and triplet, respectively. Irradiation at 5.99 collapsed the signal at 5.39 to a doublet of quartets, while irradiation at 3.63 collapsed the signals at 5.39, 5.51, 6.40 and 5.84 to a doublet of quartets and to doublets, respectively. These results clearly indicated that the signal at 3.69 must be assigned to 7-H and consequently 5.39 to 6-H and 5.51 to 8-H. Irradiation at 5.51 collapsed the doublet at 5.32 to a singlet and therefore the latter must be assigned to 9-H. Inspection of models showed that the 9-hydroxy group is most probably  $\beta$ -orientated as the 10-methyl group is deshielded ( $s$  1.68) in comparison with that in 14 [8], which otherwise seems to have a similar stereochemistry. Due to the flexibility of such systems, the stereochemistry at C-8 cannot be assigned with certainty [11]. However, comparison of the observed signals with those of similar compounds [5-11], especially the chemical shift of 8-H in 12 and 14, showed that, most probably, these lactones have the same C-8 stereochemistry. Therefore an 8 $\beta$ -acyloxy group in 11-13 is likely. The changed orientation of the 9-oxygen function also followed from the shift difference for 13'-H in the spectra of 11-13 relative to 14. Only in the latter case should this proton be deshielded by the hydroxyl group as seen by inspection of the models. Furthermore the  $J$  values for 8 and 9 are in good agreement with the stereochemistry given. We have named compound 12 conoprasiolide.

Most probably a lactone mentioned in a symposium report [2] isolated from *Eupatorium ballotaefolium* H. B. K. (= *Lourteigia ballotaefolia* (H. B. K.) K. and R. [1]), is identical to 11. However, only the gross structure without stereochemistry is given. As both genera

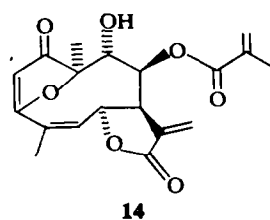
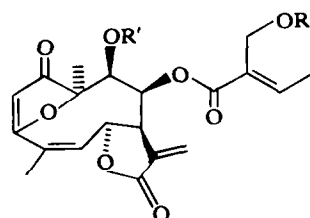
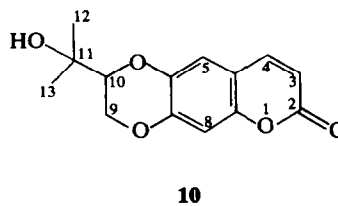
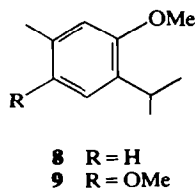
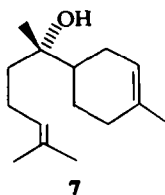
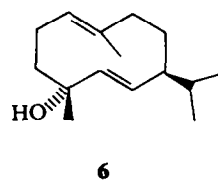
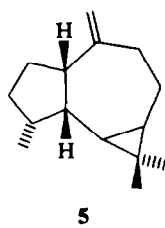
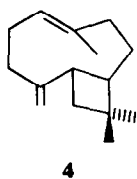
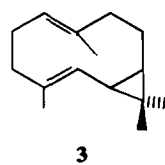
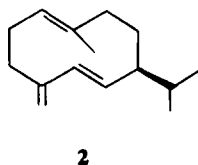
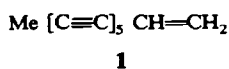
\* Part 275 in the series "Naturally Occurring Terpene Derivatives". For Part 274 see Bohlmann, F. and Zdero, C. (1980) *Phytochemistry* 19, 1550.

Table 1.  $^1\text{H}$  NMR spectral data of compounds data of **11**–**14** (270 MHz, TMS as internal standard)

	<b>11</b>		<b>12</b>		<b>13</b>	<b>14</b> [8]
	$\text{CDCl}_3$	$\text{C}_6\text{D}_6$ 77°	$\text{CDCl}_3$	$\text{C}_6\text{D}_6$	$\text{CDCl}_3$	$\text{CDCl}_3$
2-H	5.64 s	5.32 s	5.68 s	5.23 s	5.67 s	5.62 s
5-H	5.98 dq	5.56 dq	5.98 dq	5.48 dq	5.99 dq	5.99 dq
6-H	5.10 ddq	5.12 ddq	5.03 ddq	5.03 ddq	5.39 ddq	5.23 ddq
7-H	3.66 dddd	3.31 dddd	3.65 dddd	3.29 dddd	3.63 dddd	3.91 dddd
8-H	5.20 dd	5.29 dd	5.07 dd	5.14 dd	5.51 dd	5.07 dd
9-H	4.19 m	3.85 m*	4.19 m	3.85 m	5.32 d	4.10 dd
13-H	6.36 d	6.29 d	6.37 d	6.35 d	6.40 d	6.36 d
13'-H	5.73 d	5.18 d	5.70 d	5.20 d	5.84 d	6.05 d
14-H	1.68 s	1.52 s	1.67 s	1.53 s	1.52 s	1.58 s
15-H	2.07 dd	1.58 dd	2.06 dd	1.50 dd	2.08 dd	2.06 dd
3'-H	7.10 q	6.99 q	6.98 q	6.92 q	7.11 q	
4'-H	1.97 d	1.56 d	1.93 d	1.53 d	1.98 d	
5 <sub>1</sub> '-H	4.86 d	4.85 d	4.27 d	4.22 d	4.91 d	
5 <sub>2</sub> '-H	4.71 d	4.78 d			4.66 d	
OAc	2.03 s	1.80 s			2.04 s	
					2.12 s	
OH	4.19 m	3.75 m	4.08 d			2.74 d

\* After deuterium exchange  $d(J=3)$ .

$J(\text{Hz})$ : 5,6 = 4; 5,15 = 1.7; 6,7 = 4; 6,15 = 1.7; 7,8 ~ 1.5; 7,13 = 2.8, 7,13' = 2.6; 8,9 = 3; 3',4' = 7.5; 5<sub>1</sub>,5<sub>2</sub> = 12; **12**: 5, OH = 5.5; **14**: 5,6 = 3.5, 5,12 = 2.1; 6,7 = 4; 6,15 = 2; 7,8 = 1.5; 8,9 = 5; 7,13 = 3; 9,OH = 6.5.



are combined in the Gypitis group [13], lactones of this type may have chemotaxonomical importance. However, more representatives of this group have to be investigated chemically.

#### EXPERIMENTAL

IR:  $\text{CHCl}_3$ ;  $^1\text{H}$  NMR: 270 MHz, TMS as int. standard; MS: 70 eV; optical rotation:  $\text{CHCl}_3$ . The air-dried plant material (voucher No. RMK 7982, collected in North Brazil) was chopped and extracted with  $\text{Et}_2\text{O}$ -petrol (1:2) at room temp. The resulting extracts were separated first by CC (Si gel, act. grade II) and further by repeated TLC (Si gel, GF 254). The hydrocarbons were separated by  $\text{AgNO}_3$ -Si gel TLC ( $\text{Et}_2\text{O}$ -petrol, 1:20). Known compounds were identified by comparison of IR,  $^1\text{H}$  NMR and MS with authentic compounds. Roots (70 g) afforded 0.5 mg **1** [14], 2 mg **2** [15], 2 mg **3** [16], 30 mg **4** [17], 10 mg **5** [18], 8 mg **6** [19], 8 mg **7** [20], 5 mg **8**, 30 mg **9** and 2 mg **10** ( $\text{Et}_2\text{O}$ -petrol, 3:1), while aerial parts (345 g) afforded 10 mg **2**, 2 mg **3**, 20 mg **4**, 30 mg **5**, 40 mg **6**, 5 mg of a triterpene-acetate ( $\text{C}_{32}\text{H}_{52}\text{O}_2$ ), 40 mg **11** ( $\text{Et}_2\text{O}$ -MeOH, 50:1) and 75 mg **12** ( $\text{Et}_2\text{O}$ -MeOH, 50:1).

**11-Hydroxy-11,12-dihydroobliquine (10)**. Colourless crystals from  $\text{CHCl}_3$ -petrol, mp  $167^\circ$ . IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3600 (OH), 1735, 1640, 1570 (coumarin); UV  $\lambda_{\text{max}}^{\text{Et}_2\text{O}}$  nm: 339, 296, 286; MS  $m/e$  (rel. int.): 262.084 (100,  $\text{M}^+$ ) ( $\text{C}_{14}\text{H}_{14}\text{O}_5$ ); 204  $\text{M}^+$ - $\text{Me}_2\text{CO}$ , (51); 175 204- $\text{CHO}$ , (35);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.28 (d,  $J=9.5$ , 3-H), 7.57 (d,  $J=9.5$ , 4-H), 7.00 (s, 5-H), 6.87 (s, 8-H), 4.00 (dd,  $J=11$ , 9, 9-H), 3.93 (dd,  $J=9$ , 2, 9'-H), 4.52 (dd,  $J=11$ , 2, 10-H), 1.40 (s, 12-H), 1.34 (s, 13-H).  $[\alpha]_D^{25} + 171^\circ$  (C 0.2).

**Conoprasiolide-5'-O-acetate (11)**. Colourless gum: IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3620 (OH); 1772, 1735, 1705 (C=O), 1655, 1597 (C=C); MS  $m/e$  (rel. int.): 432.142 (20,  $\text{M}^+$ ) ( $\text{C}_{22}\text{H}_{24}\text{O}_9$ ); 390 ( $\text{M}^+-2$ ); 372 ( $\text{M}^+ - \text{HOAc}$ , 5); 274 ( $\text{M}^+ - \text{RCO}_2\text{H}$ , 11); 245 (274- $\text{CHO}$ , 14); 232 (274- $\text{C}_2\text{H}_2\text{O}$ , 55); 141 ( $\text{MeCH}=\text{C}(\text{CH}_2\text{OAc})\text{CO}^+$ , 49); 99 (141-ketene, 36); 81 (99- $\text{H}_2\text{O}$ , 63); 43 ( $\text{MeCO}^+$ , 100). 40 mg **11** in 1 ml  $\text{Ac}_2\text{O}$  was heated for 1 hr at  $70^\circ$ . After evapn and TLC ( $\text{Et}_2\text{O}$ -petrol, 2:1), 37 mg **13** were obtained, colourless gum; IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 1780, 1740, 1720 (C=O); 1660, 1610 (C=C); MS  $m/e$  (rel. int.): 474. 153 (23,  $\text{M}^+$ ) ( $\text{C}_{24}\text{H}_{26}\text{O}_{10}$ ); 432 ( $\text{M}^+ - \text{ketene}$ , 10); 414 ( $\text{M}^+ - \text{HOAc}$ , 17); 43 ( $\text{MeCO}^+$ , 100).

$$[\alpha]_{25}^{25} = \frac{589}{-29.6} \frac{578}{-30.1} \frac{546}{-35.4} \text{ nm} \quad (c = 3.7).$$

**Conoprasiolide (12)**. Colourless gum; IR  $\nu_{\text{max}}^{\text{CHCl}_3}$   $\text{cm}^{-1}$ : 3610 (OH), 1770, 1730, 1710 (C=O), 1655, 1600 (C=C); MS  $m/e$  (rel. int.): 390.132 (12,  $\text{M}^+$ ) ( $\text{C}_{20}\text{H}_{22}\text{O}_8$ ); 274 ( $\text{M}^+ - \text{RCO}_2\text{H}$ , 19); 99 ( $\text{MeCH}=\text{C}(\text{CH}_2\text{OH})\text{CO}^+$ , 100). 10 mg **12** were acetylated as above. TLC afforded 8 mg **13**,

identical with the diacetate obtained from **11**.

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