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SESQUITERPENE LACTONES FROM *HELOGYNE HUTCHISONII*

J. JAKUPOVIC, V. P. PATHAK, F. BOHLMANN, D. GAGE* and M. O. DILLON†

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany; *Department of Botany, University of Texas at Austin, U.S.A.; †Field Museum of Natural History, Chicago, IL 60605-2496, U.S.A.

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Key Word Index—*Helogyne hutchisonii*; Compositae; sesquiterpene lactones; heliangolides; germacranolides; guaianolides.

Abstract—The aerial parts of *Helogyne hutchisonii* afforded, in addition to known sesquiterpene lactones, two new heliangolides and two germacranolides. The structures were elucidated by high-field ^{1}H NMR spectroscopy.

INTRODUCTION

The South American genus *Helogyne* Nutt. [1], with about 12 species, is placed in the subtribe Alomiinae [2] although it is not very close to the principal genus in this group, *Brickellia* Ell. As nothing is known about the chemistry of this genus, we have studied a species from Peru, *H. hutchisonii* King et Robins. [3]. The results are discussed in this paper.

RESULTS AND DISCUSSION

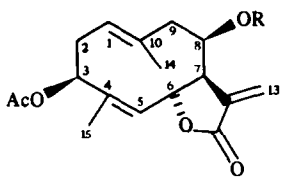
The aerial parts gave the heliangolides hiyodorilactone C [4], eucannabinolide (large amounts) [5], 5′-desoxy-eucannabinolide [6], the closely related lactones santhemoidins A and B [7] as well as the new compounds **1** and **2**. In addition, they gave the germacranolides **3** and **4**, the known guaianolides ligustrin [8] and the corresponding 4′-hydroxy- and 4′,5′-dihydroxytiglate [9, 10]. The structures of the known lactones were identified by direct comparison with authentic samples or, in the case of the santhemoidins, by ^{1}H NMR spectroscopy including spin decoupling. The data agreed with those in the literature. However, in the case of santhemoidin B, most likely an artefact formed by reaction of the corresponding semiacetal with methanol, the high-field ^{1}H NMR spectrum showed that 4′-epimeric methyl acetals were present (see Experimental). The corresponding epimeric semiacetals are also known [11].

The structure of **1** followed from the ^{1}H NMR spectrum (see Experimental). Most signals were nearly identical with those of eucannabinolide and similar lactones [6, 11]. The nature of the ester residue followed from the typical signals at δ 6.84 *q* (*br*) 1.80 *s* (*br*) and 1.74 *d* (*br*). The ^{1}H NMR spectrum of **2** (see Experimental) was also close to that of eucannabinolide. The presence of two additional acetate methyl singlets and the downfield shift of the H-4′ and H-5′ signals indicated that the diacetate of eucannabinolide was present. Accordingly, the spectral data agreed with those of the diacetate prepared by acetylation of eucannabinolide [6].

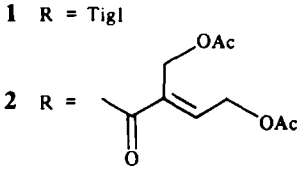
The molecular formula of **3** ($C_{19}H_{26}O_5$) indicated that it was most likely a sesquiterpene lactone with a hydroxyl group and a C-4 ester group. This was further supported by the fragmentation pattern. Elimination of $C_3H_7CO_2H$ and the base peak, *m/z* 71 (C_3H_7CO), agreed with the presence of a butyrate. The ^{1}H NMR spectrum (see Experimental) showed that it was an 8-isobutyryloxy-costunolide with a hydroxyl group at C-2, as followed from spin decoupling and the observed coupling.

The structure of **4** followed directly from the ^{1}H NMR data (see Experimental) which were close to those of similar germacranolides [11].

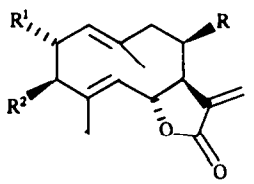
The relative position of the ester groups in **1**, **2**, and **4**



1 R = Tigl



2 R =

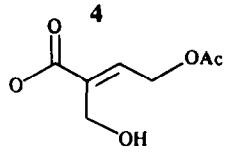


3

R OCOCHMe$_2$

R^1 OH

R^2 H



4

H

OAc

followed from the chemical shifts of H-3 and H-8, respectively.

The isolation of heliangolides like eucannabinolide and of guaianolides like ligustrin and its ester undoubtedly is of chemotaxonomic relevance. So far, from other genera which are placed in the subtribe Alomiinae mostly diterpenes [12–19] and in the case of an *Austrobrickellium* species traces of a guaianolide [20] have been isolated. However, similar lactones are reported from *Eupatorium* and *Liatris*, two genera which are not very closely related. Furthermore, heliangolides with 3β- and 8β-oxygen functions are reported from the tribe Heliantheae. Accordingly, the isolation of this type of sesquiterpene lactone may be an indication that *Helogyne* is a primitive element in this group and the production of diterpenes in the other genera of the Alomiinae could be an advanced character. Of course, further species of this subtribe should be examined chemically and morphologically to test this hypothesis.

EXPERIMENTAL

The air-dried plant material (270 g) was collected in the Depto. Arequipa, Prov. Caraveli, Peru, 15 km south of Atico on the Pan Americana Hwy, growing in sandy soil on loma formation, in November 1983. A voucher specimen (Dillon and Dillon 3847) has been deposited at the Herbarium of the University of Texas at Austin. After extraction with MeOH–Et_2O–petrol (1:1:1), the extract obtained was worked up as reported previously [21]. CC (silica gel) gave five crude fractions (Et_2O–petrol, 3:1; Et_2O; Et_2O–MeOH, 33:1, 9:1 and 17:3). Fraction 1 was separated by prep. TLC (silica gel PF 254; CH_2Cl_2–C_6H_6–Et_2O, 3:3:1; 2 developments) into four fractions (1/1–1/4). HPLC (MeOH–H_2O, 3:2; always RP 8; flow rate *ca* 3 ml/min; *ca* 100 bar) of one third of fraction 2/1 gave 8 mg epimeric santhemoidin B (R_t 7.7 min). HPLC of one third of fraction 2/2 (MeOH–H_2O, 3:2) gave 6 mg santhemoidin A (R_t 10.3 min) and 5 mg **1** (R_t 13.6 min). HPLC of fraction 2/3 (MeOH–H_2O, 13:7) gave 7 mg ligustrin (R_t 7.2 min) and 3 mg ligustrin-[4′-hydroxytiglate] (R_t 10.5 min). HPLC of fraction 2/4 (MeOH–H_2O, 7:3) gave 4 mg hiyodorilactone C (R_t 7.6 min). CC fraction 2 gave by prep. TLC ($CHCl_3$–MeOH, 33:1) 15 mg *p*-coumaric acid and prep. TLC of CC fraction 3 (same solvent, 3 developments) afforded 11 mg **4**, 5 mg 5′-desoxyeucannabinolide and 11 mg **2**. CC fraction 4 was separated again by CC ($CHCl_3$ with increasing amounts of MeOH) and by prep. TLC ($CHCl_3$–MeOH, 15:1) affording a mixture which gave by HPLC (MeOH–H_2O, 3:2) 3 mg **3** (R_t 8.7 min) and 5 mg ligustrin-[4′,5′-dihydroxytiglate] (R_t 9.8 min). Repeated CC ($CHCl_3$–MeOH, 33:1) of fraction 5 gave 1.8 g eucannabinolide.

3β-Acetoxy-8β-tigloyloxyheliangolide (**1**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (γ-lactone), 1740 (OAc), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 388.189 $[M]^+$ (3) (calc. for $C_{22}H_{28}O_6$: 388.189), 289 $[M-OCOR]^+$ (4.5), 288 $[M-RCO_2H]^+$ (1), 228 $[288-HOAc]^+$ (19), 83 $[C_4H_7CO]^+$ (100); ^1H NMR (400 MHz, $CDCl_3$): δ5.21 (*m*, H-1), 2.73 and 2.29 (*m*, H-2), 5.26 (*t*, H-3), 5.21 (*dq*, H-5), 5.92 [*d*(*br*), H-6], 2.96 [*s*(*br*), H-7], 5.20 (*m*, H-8), 2.75 and 2.41 [*d*(*br*), H-9], 6.35 and 5.75 (*d*, H-13), 1.75 [*s*(*br*), H-14], 1.78 [*s*(*br*), H-15]; OAc: 2.07 (*s*); OCOR: 6.84 [*q*(*br*)], 1.80 [*s*(*br*)], 1.74 [*d*(*br*)] [*J* (Hz): 2,3 ~ 3; 5,6 = 11; 5,15 = 1.5; 7,13 = 2.5; 7,13′ = 2; 9,9′ = 15; 3′,4′ = 7].

Eucannabinolide diacetate (**2**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (γ-lactone), 1750 (OAc), 1720, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 504.200 $[M]^+$ (6) (calc. for $C_{26}H_{32}O_{10}$: 504.200), 462 $[M-ketene]^+$ (1), 445 $[M-OAc]^+$ (1), 444 $[M-HOAc]^+$ (0.4), 402 $[444-ketene]^+$ (2), 289 $[M-OCOR]^+$ (17), 246 $[462-ROC_2H]^+$ (74), 228 $[246-H_2O]^+$ (51), 157 $[RCO-ketene]^+$ (100), 115 $[157-ketene]^+$ (80); ^1H NMR ($CDCl_3$): δ5.20 (*m*, H-1), 2.70 and 2.28 (*m*, H-2), 5.25 (*t*, H-3), 5.18 [*d*(*br*), H-5], 5.86 [*d*(*br*), H-6], 2.97 [*s*(*br*), H-7], 5.32 [*s*(*br*), H-8], 2.72 and 2.45 [*d*(*br*), H-9], 6.36 and 5.76 (*d*, H-13), 1.74 [*s*(*br*), H-14], 1.78 [*s*(*br*), H-15]; OAc: 2.08, 2.03, 2.01 (*s*); OCOR: 6.92 (*t*), 4.36 (*d*) (2H), 4.79 and 4.73 (*d*) [*J* (Hz) as **1** except 3′,4′ = 6; 5′,5′ = 12].

2α-Hydroxy-8β-isobutyryloxycostunolide (**3**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 334.177 $[M]^+$ (0.7) (calc. for $C_{19}H_{26}O_5$: 334.178), 316 $[M-H_2O]^+$ (0.3), 264 $[M-O{=}C{=}CMe_2]^+$ (1.3), 246 $[M-RCO_2H]^+$ (19), 228 $[246-H_2O]^+$ (8), 71 $[C_3H_7CO]^+$ (100); ^1H NMR ($CDCl_3$): δ5.51 [*d*(*br*), H-1], 5.26 (*dddd*, H-2), 2.11 (*d*, H-3), 2.73 (*dd*, H-3β), 5.47 [*d*(*br*), H-5], 5.07 (*dd*, H-6), 2.94 (*dddd*, H-7), 5.74 [*d*(*br*), H-8], 2.34 (*dd*, H-9), 2.79 [*dd*(*br*), H-9β], 6.31 (*d*, H-13), 5.58 (*d*, H-13′), 1.53 [*s*(*br*), H-14], 1.79 (*d*, H-15); *Oi*Bu: 2.52 (*qq*), 1.11 (*d*), 1.09 (*d*) [*J* (Hz): 1,2 = 2,3 = 5,6 = 10; 2,OH = 3.5; 2,3β = 5.5; 3,3β = 11.5; 5,15 = 1.5; 6,7 = 8.5; 7,8 = 1; 7,13 = 3.5; 7,13′ = 3; 8,9 = 2.5; 8,9β = 5; 9,9′ = 15; 2′,3′ = 2′,4′ = 7].

Santhemoidin B epimers. ^1H NMR ($CDCl_3$, values of epimer in parentheses): δ5.20 (*m*, H-1) 2.73 and 2.28 (*m*, H-2), 5.27 (5.26) (*t*, H-3) 5.20 (5.19) (*t*, H-5), 5.86 [*d*(*br*), H-6], 2.97 [*s*(*br*), H-7], 5.32 (5.28) [*s*(*br*), H-8], 2.76 and 2.46 [*d*(*br*), H-9], 6.38 and 5.78 (*d*, H-13), 1.77 [*s*(*br*), H-14], 1.80 [*s*(*br*), H-15]; OAc: 2.09 (2.08) (*s*); OMe: 3.39 (3.38) (*s*); OCOR: 6.60 (6.53) [*s*(*br*), H-3′], 5.82 (5.81) [*s*(*br*), H-4′], 4.83 (4.82) (*dd*, H-5_1′), 4.66 [*d*(*br*), H-5_2′] [*J* (Hz) as **1** except 4′,5′ = 2; 5′,5′ = 14].

8β-[4′-Acetoxy-5′-hydroxytigloyloxy]-novanin (**4**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1760 (γ-lactone), 1745, 1235 (OAc), 1710 (C=CCO_2R); MS *m/z* (rel. int.): 462.188 $[M]^+$ (3) (calc. for $C_{24}H_{30}O_9$: 462.189), 402 $[M-HOAc]^+$ (2.5), 342 $[402-HOAc]^+$ (1), 288 $[M-RCO_2H]^+$ (8), 246 $[288-ketene]^+$ (70), 228 $[288-HOAc]^+$ (84), 157 $[RCO]^+$ (73), 115 $[157-ketene]^+$ (100); ^1H NMR ($CDCl_3$): δ4.95 (*m*, H-1, H-5), 5.26 (*dd*, H-3), 5.18 (*dd*, H-6), 2.95 (*dddd*, H-7), 5.82 [*d*(*br*), H-8], 2.86 (*dd*, H-9), 2.33 [*d*(*br*), H-9′], 6.34 and 5.64 (*d*, H-13), 1.52 [*s*(*br*), H-14], 1.78 [*s*(*br*), H-15]; OCOR: 6.72 (*t*), 4.86 (2H, *d*), 4.38 [*s*(*br*)] (2H); OAc: 2.13, 2.11 (*s*) [*J* (Hz): 2,3 = 5; 2′,3 = 10; 5,6 = 10; 6,7 = 8; 7,13 = 3.5; 7,13′ = 3; 8,9 = 5; 9,9′ = 14; 3′,4′ = 6.5].

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