Phytochemistry, 1981, Vol. 20, pp. 518–519. © Pergamon Press Ltd. Printed in England. 0031-9422/81/030518-02 $02.00/0

TWO HIRSUTINOLIDES AND A GERMACRANOLIDE FROM *CHRESTA SPHAEROCEPHALA**

FERDINAND BOHLMANN,† CHRISTA ZDERO,† ROBERT M. KING‡ and HAROLD ROBINSON‡

†Institute for Organic Chemistry, Technical University Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, West Germany; ‡Smithsonian Institution, Washington, DC 20650, U.S.A.

(*Received* 30 *May* 1980)

Key Word Index—*Chresta sphaeroceph ala*; Compositae; sesquiterpene lactones; hirsutinolides, germacranolides.

So far no representatives of the resurrected genus *Chresta* (Compositae, tribe Vernonieae) [1] have been investigated chemically. We therefore have collected material of the lectotype *C. sphaerocephala* DC. (= *C. cordata* Vell. = *C. intermedia* Gardn. = *Eremanthus sphaerocephalus* (DC.) Baker). The aerial parts afforded germacrene D, bicyclogermacrene, spathulenol, stigmasterol, lupeol, its acetate and the isomeric acetates **1** and **2** [2]. The polar fractions yielded a mixture of minute amounts of sesquiterpene lactones. The less polar ones obviously are further hirsutinolides, the isomeric tiglates **3** and **4**, which could be separated. The ^{1}H NMR data are very similar to those of the corresponding 1-epimeric 8-*O*-acetates [2]. The relative position of the tiglate group, however, followed only from the chemical shifts of 13-H, being slightly different from those in the spectrum of the corresponding acetates [2] (Table 1). A clear decision which isomer is which was not possible. On heating with

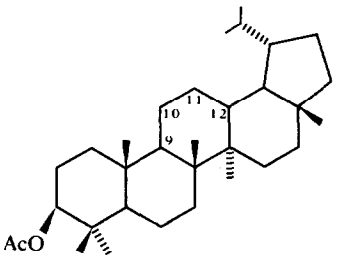
Table 1. ^{1}H NMR spectral data of compounds **3**–**5** and **7** (270 MHz, TMS as internal standard)

	3*	**4***	**5** ($CDCl_3$)	(C_6D_6)	+Eu(fod)$_3$, 77°	**7** (C_6D_6, 80°)
1-H	—	—	4.55 *br. d*	4.72 *br. d*	5.09 *br. d*	—
2-H			2.60 *dd*	2.30 *dd*	2.78 *dd*	4.10 *br. s*
2′-H	2.30 *m*		2.15 *br. d*	1.70 *br. d*	2.31 *br. d*	2.10 *m*
3-H			—	—	—	1.80 *m*
5-H	6.06 *s*	6.07 *s*	4.97 *br. d*	4.35 *br. d*	4.79 *br. d*	5.57 *s*
6-H	—	—	5.78 *d*	5.68 *d*	6.07 *d*	—
8-H	5.56 *dd*	5.55 *dd*	3.10 *ddd*	2.57 *ddd*	2.86 *ddd*	6.44 *br. d*
8′-H	—	—	2.29 *br. d*	2.10 *m*	2.12 *m*	—
9-H	2.63 *m*		2.47 *m*	1.91 *m*	2.22 *m*	2.33 *dd*
9′-H				1.70 *m*	2.05 *m*	1.81 *dd*
13-H	4.87 *br. s*		4.77 *br. s*	5.02 *br. d*	6.36 *br. d*	5.23 *br. d*
13′-H				4.89 *br. d*	6.00 *br. d*	5.05 *d*
14-H	1.30 *br. s*	1.35 *br. s*	1.48 *br. s*	1.51 *br. s*	1.72 *br. s*	1.07 *s*
15-H	1.57 *s*	1.54 *s*	2.02 *br. s*	1.77 *br. s*	1.87 *br. s*	1.33 *s*
OAc	2.03 *s*	2.04 *s*	2.04 *s*	1.67 *s*	2.34 *s*	1.68 *s*
			2.08 *s*	1.66 *s*	1.87 *s*	—
OTigl	6.94 *qq*		6.89 *qq*	6.86 *qq*	7.07 *qq*	6.95 *qq*
	1.85 *br. d*		1.84 *br. d*	1.40 *dq*	1.54 *dq*	1.41 *dq*
	1.83 *br. s*		1.82 *br. s*	1.70 *dq*	1.92 *dq*	1.70 *dq*
OMe	3.28 *s*	3.27 *s*	—	—	—	—

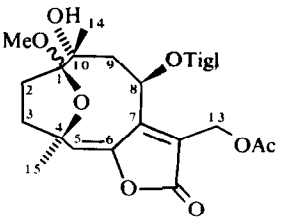
* May be interchangeable.

J (Hz): Compounds **3**/**4**: 8, 9 = 8, 9′ = 3.5; 3′, 4′ = 7; compound **5**: 1, 2 = 7; 1, 14 ~ 1; 2, 2′ = 16; 5, 6 = 10; 8, 8′ = 15; 8, 9 = 11; 8, 9′ = 5; 13, 13′ = 12; 3′, 4′ = 7; 3′, 5′ = 4′, 5′ ~ 1; compound **7**: 8, 9 = 8.5; 8, 9′ = 1.5; 9, 9′ = 15.5; 13, 13′ = 12.5.

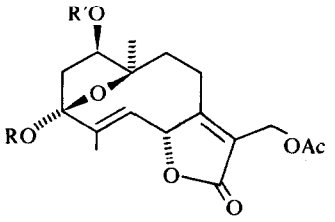
* Part 310 in the series 'Naturally Occurring Terpene Derivatives'. For Part 309 see: Mahmoud, Z. F., Abdel Salam, N. A., Sarg, T. M. and Bohlmann, F. (1981) *Phytochemistry* **20** (in press).



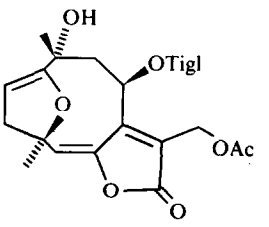
1 Δ9, 10
2 Δ11, 12



3 1α OMe
4 1β OMe



5 R = Ac, R′ = Tigl
6 R = Tigl, R′ = Ac



7

acetic anhydride both isomers afforded by elimination of methanol the lactone **7**, indicating that **3** and **4** differed only in the stereochemistry at C-1. The ^{1}H NMR signals of **7** (Table 1) were very broad at room temperature, but sharpened at 80° in benzene. As could be deduced from the ^{1}H NMR spectra and from models the conformations of **3**/**4** and **7** were different. The observed downfield shift of the 8-H signal in the spectrum of **7** could be explained only if this proton is deshielded by the 10-hydroxy group, which supported the 10α-orientation.

A further lactone most probably is **5**. The ^{1}H NMR data (Table 1) indicated the presence of an isomerized lactone, while spin decoupling clearly showed that a second oxygen function had to be placed at C-1, as irradiation at the 14-H signal caused a sharpening of the broadened doublet at $\delta = 4.55$ (W-coupling), which was further coupled with signals at 2.60 (*dd*) and 2.15 (*br. d*). The *trans*-configuration of the 5,6-double bond followed from the coupling $J_{5,6} = 10$ Hz, which in heliangolides is always very small. The other signals could be assigned by further decoupling experiments and from Eu(fod)$_3$ induced shifts, which clearly showed that one of the acetate groups was placed at C-13 (largest shifts of the 13-H and of one acetate methyl signals). The second one most probably was at C-3, though a C-1 position could not be excluded, as partial saponification was unsuccessful. Structure **5** therefore is not absolutely established, but is the more likely one since similar compounds have acetate groups at C-3 and no other ester groups [3]. We have named **5** chrestanolide.

EXPERIMENTAL

The air dried aerial parts (600 g) (voucher RMK 8251) were extracted with Et_2O–petrol and the resulting extract after treatment with MeOH (to remove long chain saturated hydrocarbons) was first separated by column chromatography and further by repeated TLC (SiO_2, GF 254). With petrol, 10 mg germacrene D and 80 mg bicyclogermacrene were obtained. Fractions with Et_2O–petrol, 1:10 afforded 200 mg lupeol acetate, 100 mg **1** and 100 mg **2**; those with Et_2O–petrol, 1:1 50 mg spathulenol, 100 mg lupeol and 10 mg stigmasterol; while the fractions obtained with Et_2O finally gave 8 mg **3** and **4** (*ca.* 3:2) and 6 mg **5** (purified by HPLC, reversed phase, MeOH–H_2O, 7:3).

10β-Hydroxy-8β-tiglinoyloxy-1α respectively 1β-O-methyl-hirsutinolide-13-O-acetate (**3** *and* **4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1780 (lactone), 1745, 1235 (OAc), 1710, 1640 (C=CCO_2R); UV (λ_{max}, Et_2O): 280 nm; MS *m/e* (rel. int.): 450.189 (M^+, 0.2) ($C_{23}H_{30}O_9$), 350 (M − RCO_2H, 2), 83 ($C_4H_7CO^+$, 100). 5 mg **3** and **4** were heated with 0.1 ml Ac_2O 1 hr at 70°. TLC (Et_2O–petrol, 1:1) afforded 3 mg **7**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3550 (OH), 1780 (lactone), 1750, 1235 (OAc), 1720 (C=CCO_2R), 1650 (C=COR); MS *m/e* (rel. int.): 418 (M^+, 0.5), 319 (M − OTigl, 2), 275 (315 − CO_2, 6), 234 (18), 216 (234 − H_2O, 9), 83 ($C_4H_7CO^+$, 100).

Chrestanolide (**5**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (lactone), 1745, 1240 (OAc), 1720, 1646 (C=CCO_2R); MS *m/e* (rel. int.): 462.189 (M^+, 2) ($C_{24}H_{30}O_9$), 420 (M − ketene, 1, 392 (420 − CO, 1), 362 (M − RCO_2H, 1), 332 (392 − AcOH, 3), 302 (362 − AcOH, 5), 232 (332 − RCO_2H, 13), 83 ($C_4H_7CO^+$, 100).

$[\alpha]_{24}^{\lambda}$ =	589	578	546	436	365 nm
	−2.4	−2.7	−2.7	+1.2	+22.0

($c = 0.5$, $CHCl_3$).

Acknowledgements—We thank Drs. Scott A. Mori and P. Alvim, Centro de Pesquisas at Itabanu, Bahia, Brazil, for their help during plant collection and the Deutsche Forschungsgemeinschaft for financial support.

REFERENCES

1. Robinson, H. (1980) *Phytologia* **45**, 89.
2. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1979) *Phytochemistry* **18**, 987.
3. Fischer, N. H., Olivier, E. J. and Fischer, H. D. (1979) *Prog. Chem. Nat. Org. Prod.* **38**, 47.