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TWO SESQUITERPENE LACTONES WITH AN ADDITIONAL PROPIOLACTONE RING FROM *DISYNAPHIA HALIMIFOLIA**

Ferdinand Bohlmann,† Autar K. Dhar,† Jasmin Jakupovic,† Robert M. King‡ qand Harold Robinson‡

†Institute for Organic Chemistry, Technical University of Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, West Germany;
‡Smithsonian Institution, Washington, DC 20560, U.S.A.

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Key Word Index—*Disynaphia halimifolia*; Compositae; Eupatorieae; sesquiterpene lactones; germacranolides; elemanolide; propiolactones; geranylgeraniol derivative; tremetone derivatives.

Abstract—The investigation of *D. halimifolia* afforded a new glaucolide and two sesquiterpene lactones with an additional propiolactone ring, one elemanolide and one modified germacranolide with an additional ring. Furthermore, two tremetone derivatives were present, a hydroxy-geranylgeraniol, also present in a *Kingianthus* species, and several known compounds.

INTRODUCTION

The Brazilian genus *Disynaphia* [1] is placed in one of the groups of the Eupatorieae [2] together with *Acanthostyles*, *Raulinoreitzia*, *Symphyopappus*, *Grazielia* and *Compovassouria*. While representatives of the latter three genera have been investigated chemically [3–6], nothing is known on the chemistry of the other three. We have now studied the constituents of *D. halimifolia*. The aerial parts afforded in addition to a new glaucolide two unusual sesquiterpene lactones and a new diterpene, while the roots gave two new toxol derivatives and several known compounds.

RESULTS AND DISCUSSION

The aerial parts afforded germacrene D, bicyclogermacrene and the diol **1** (F. Bohlmann *et al.*, unpublished results). The polar fractions further contained several sesquiterpene lactones. Only three of them could be isolated in the pure state, the lactones **2**, **3** and **5**. The structure of the main constituent **2** followed from the ^{1}H NMR data (Table 1). Spin decoupling allowed the assignment of nearly all the signals. The configuration at C-5 and C-6 followed from the chemical shifts, the coupling $J_{5,6}$ and the shift of 15-H, which obviously was deshielded by the lactone oxygen. The configuration at C-8 and C-10 was assigned by analogy to the glaucolides [7]. Only the signals of 2-H and 3-H were broadened, while usually in glaucolides all signals are broad at room temperature. The signals of 2-H in the spectrum of **2** in C_6D_6 at 75° were clearer but still a few signals were multiplets. We have named compound **2** disyfolide.

The presence of an elemanolide clearly followed from the ^{1}H NMR data of **3** (Table 1) by the characteristic signals of 1-H, 2-H and 3-H (usual sesquiterpene numbering), while the singlet at δ 9.56 must be assigned to an aldehyde proton, obviously at C-4 as could be seen by the downfield shifts of the 3-H signals. Furthermore, typical signals from a tiglate residue could be recognized. Spin decoupling showed that this group must be placed at C-8. Inspection of models indicated an 8α-H, while in the IR spectrum the presence of a β-lactone ring could be recognized. An IR-band at 1835 cm^{-1} would be extremely unlikely for an isomeric γ-lactone as models show that such a lactone would not be especially strained. Again a model showed that the 9-H must be α-orientated while a 6,12-*trans*-lactone was indicated by the couplings $J_{5,6}$ and $J_{6,7}$. We have named compound **3** disynaphiolide. Compound **3** was closely related to the dilactones isolated from *Grazielia* species [5], if an oxidation at C-15 and a Cope rearrangement was assumed.

The structure of **5** also followed from the ^{1}H NMR data (Table 1) and from the results of spin decouplings, which allowed the assignment of all signals, though even at 400 MHz some signals were unclear. Again the presence of a β-lactone was indicated by the corresponding IR band at 1835 cm^{-1}. The nature of the ester residue directly followed from the typical ^{1}H NMR signals. The stereochemistry at C-15 was deduced from the observed downfield shifts of 1β-H and 3β-H, caused by the deshielding effect of the OH group, while the α-position of 8-H and 9-H followed from the observed couplings in connection with inspection of a model. Compound **5** most probably was formed by an internal aldol condensation of **4**, which would be the dihydro compound of the precursor of **3**. We have named compound **5** disyhamifolide.

The roots afforded β-amyrin, lupeyl' acetate, the heliangolide **6** [8], the euparine derivative **7** [9] and three tremetone derivatives, the isomeric angelates **8** [10] and **9**, as well as the methyl ether **10**. The structure of the last two compounds clearly followed from the ^{1}H NMR data (Table 2), especially if compared with those of similar compounds. The configurations at C-2 and C-3 could be

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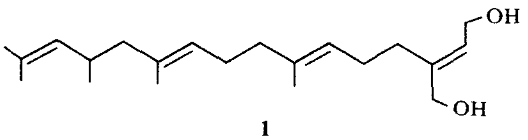
* Part 324 in the series "Naturally Occurring Terpene Derivatives". For Part 323 see Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, (in press).



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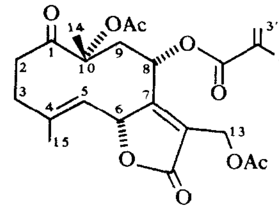

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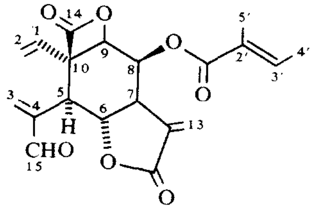

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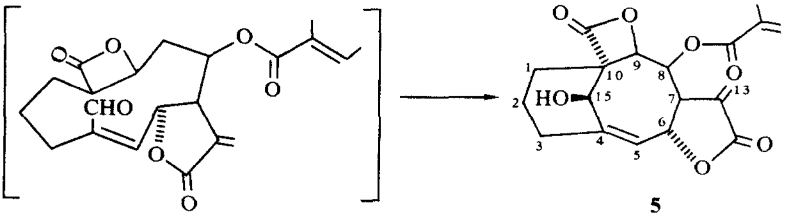
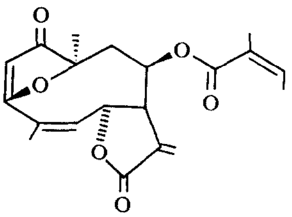


4 **5**



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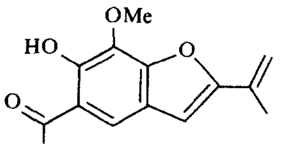

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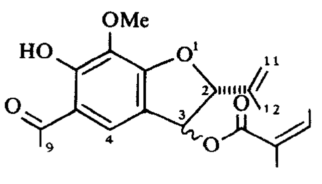

8 3α-H **9** 3β-H

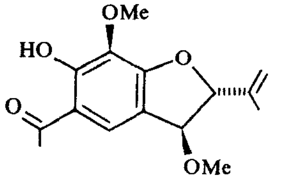

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Table 1. ^{1}H NMR spectral data of compounds **2**, **3** and **5** ($CDCl_3$, TMS as int. stand.)

	2	C_6D_6, 75°	**3***	**5†**
1α-H	—	—	5.95 *dd*	1.88 *brdd*
1β-H	—	—		2.62 *ddd*
2α-H	3.11 *m*	2.67 *ddd*	5.30 *d*(*t*)	1.49 *ddddd*
2β-H	2.2–2.0 *m*	2.00 *m*	5.32 *d*(*c*)	2.11 *brd*
3α-H		1.75 *m*	6.64 *brs*	2.16 *brd*
3β-H	2.47 *m*	2.14 *m*	6.48 *brs*	2.74 *ddd*
5-H	4.97 *brd*	4.53 *dq*	3.38 *brd*	5.78 *brd*
6-H	6.78 *brd*	5.63 *brd*	4.88 *dd*	5.41 *brdd*
7-H	—	—	3.03 *dddd*	2.92 *dddd*
8-H	4.56 *brd*	4.73 *dd*	5.87 *dd*	6.32 *dd*
9-H	2.61 *dd*	2.43 *dd*	4.82 *d*	4.43 *d*
9′-H	2.30 *brd*	1.94 *brd*		—
13-H	4.81 *brd*	4.99 *dd*	6.35 *d*	6.36 *d*
13′-H	4.75 *brd*	4.84 *dd*	5.60 *d*	5.84 *d*
14-H	1.48 *s*	1.48 *s*	—	—
15-H	2.02 *brs*	1.78 *brs*	9.56 *s*	5.56 *brs*
OH	—	—	—	2.33 *brs*
OCOR	6.14 *dq*	6.04 *dq*	6.92 *qq*	6.88 *brq*
	5.69 *dq*	5.27 *dq*	1.84 *dq*	1.85 *brd*
	1.94 *s*	1.78 *brs*	1.86 *brs*	1.87 *brs*
OAc	2.09 *s*	1.76 *s*	—	—
	2.05 *s*	1.71 *s*	—	—

* 270 MHz.

† 400 MHz.

J (Hz): Compound **2**: 5, 6 = 10; 2α, 2β = 15.5; 2α, 3β = 11.5; 2α, 3α = 6; 5, 15 = 6, 16 ≈ 1; 6, 13 = 1; 8, 9 = 7; 8, 9′ = 1.5; 9, 9′ = 16; 13, 13′ = 12; 3′, 4′ = $3'_1 3'_2$ ≈ 1.3; compound **3**: 1, 2*t* = 17.5; 1, 2*c* = 10.5; 5, 6 = 12; 6, 7 = 11; 7, 8 = 3.5; 8, 9 = 7; 7, 13 = 3.5; 7, 13′ = 3; 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1; compound **5**: 1α, 1β = 1β, 2α = 14; 1α, 2α = 4; 1β, 2β = 4.5; 2α, 2β = 13; 2α, 3α = 4; 2α, 3β = 13; 2β, 3β = 3.5; 3α, 3β = 13; 5, 6 = 7.5; 6, 7 = 10; 7, 8 ≈ 1; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 3; 3′, 4′ = 6.

Table 2. ^{1}H NMR spectral data of compounds **9** and **10**

	9	**10**
2-H	5.21 *brd*	5.14 *brd*
3-H	6.35 *d*	4.73 *d*
4-H	7.64 *s*	7.52 *s*
9-H	2.57 *s*	2.59 *s*
11-H	5.26 *brs*	5.09 *brs*
11′-H	5.12 *brs*	4.96 *brs*
12-H	1.82 *brs*	1.73 *brs*
OCOR	6.11 *qq*	—
	1.96 *dq*	—
	1.82 *brs*	—
OMe	4.01 *s*	3.99 *s*
		3.43 *s*
OH	12.57	13.08

J (Hz): Compound **9**: 2, 3 = 6.5; 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.5; compound **10**: 2, 3 = 2.5.

assigned by the typical difference in the coupling $J_{2,3}$. These results showed that *Disynaphia* is closely related to *Grazielia* by the occurrence of β-lactones, while the presence of **2** demonstrated a distinct difference from this genus. The absence of kolavane derivatives, typical for *Symphiopappus* [3, 4] indicated that the latter genus is not very close chemically to *Disynaphia*. Obviously more species have to be studied to get a clear picture of the whole group, which is botanically related to the Eupatorioid and Gyptoid groups [2].

EXPERIMENTAL

The air-dried plant material of *Disynaphia halimifolia* (DC) K. et R. (voucher RMK 8227) was extracted with Et_2O–petrol (1:2) and the resulting extracts first were separated by CC (Si gel) and further by repeated TLC (Si gel). Compound **5** could only be separated by HPLC (reversed phase, MeOH–H_2O, 7:3). Known compounds were identified by comparing the IR and ^{1}H NMR spectra with those of authentic material. The roots (140 g) afforded 65 mg β-amyrin, 65 mg lupeyl acetate, 15 mg **6**, 10 mg **7**, 170 mg **8**, 10 mg **9** (Et_2O–petrol, 1:1) and 140 mg (Et_2O–petrol, 1:1), while the aerial parts (400 g) gave 25 mg germacrene D, 60 mg bicyclogermacrene, 1 g **1** (Et_2O), 1 g **2** (CH_2Cl_2–C_6H_6–Et_2O, 5:5:1), 5 mg **3** (CH_2Cl_2–C_6H_6–Et_2O, 5:5:1) and 3.5 mg **5** (HPLC. MeOH–H_2O, 7:3).

Disyfolide (**2**). Colourless gum IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1775 (γ-lactone), 1750, 1240 (PhOAc), 1725, 1640 (C=CCO$_2$R); MS m/z (rel. int.): 448.173 (M^+, 3) ($C_{23}H_{28}O_9$), 406 (M − ketene, 1), 388 (M − AcOH, 1), 346 (388 − ketene, 1), 328 (388 − AcOH, 1), 260 (346 − RCO_2H, 10), 232 (260 − H_2O, 14), 69 ($C_3H_5CO^+$, 100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{-6.0}\quad\frac{578}{-7.0}\quad\frac{546\,\text{nm}}{-9.0}\;(c = 1.0,\ \text{CHCl}_3).$$

Disynaphiolide (**3**). Colourless crystals, mp 161° (Et_2O–petrol), IR $\nu_{max}^{CCl_4}$, cm^{-1}: 2710, 1685 (C=CCHO), 1835 (β-lactone), 1775 (γ-lactone), 1730 (C=CCO$_2$R); MS m/z (rel. int.): 372.127 (M^+, 0.2), 83 ($C_4H_7CO^+$, 100); CI (isobutane): 373 (M + 1, 100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{-58.6}\quad\frac{578}{-61.4}\quad\frac{546\,\text{nm}}{-70.9}\;(c = 0.35,\ \text{CHCl}_3).$$

Disyhamifolide (**5**). Colourless crystals, mp 270° (Et_2O), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1835 (β-lactone), 1777 (γ-lactone), 1730, 1655 (C=CCO$_2$R); MS m/z (rel. int.): 374.136 (M^+, 0.3) ($C_{20}H_{22}O_7$), 356 (M − H_2O. 0.5), 328 (356 − CO. 0.3). 274 (M − RCO_2H, 0.5), 230 (274 − CO_2, 5), 201 (230 − CHO, 5), 83 ($C_4H_7CO^+$. 100), 55 (83 − CO. 42).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{+27.0}\quad\frac{578}{+30.0}\quad\frac{546}{+36.0}\quad\frac{436\,\text{nm}}{+71.0}\;(c = 0.2,\ \text{CHCl}_3).$$

3α-Angeloyloxy-6-hydroxy-7-methoxytrementone (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3500–2600, 1640 (hydrogen bonded PhCO), 1725 (C=CCO$_2$R); MS m/z (rel. int.): 346.142 (M^+, 6) ($C_{19}H_{22}O_6$), 246 (M − RCO_2H, 100), 231 (246 − Me, 54), 213 (231 − CO, 9). 83 ($C_4H_7CO^+$. 35).

3β,7-Dimethoxy-6-hydroxytremetone (**10**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3500–2600, 1640 (hydrogen bonded PhCO); MS m/z (rel. int.): 278.115 (M^+, 100), 263 (M − Me, 35), 247 (M − OMe, 33), 246 (M − MeOH, 33).

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