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AN EPOXYGERMACRANOLIDE AND FURTHER CONSTITUENTS FROM *MIKANIA* SPECIES*

FERDINAND BOHLMANN, PAHUP SINGH, JASMIN JAKUPOVIC, HAROLD ROBINSON† and ROBERT M. KING†

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

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Key Word Index—*Mikania purpurascens*; *M. arrojadoi*; Compositae; sesquiterpene lactone; epoxygermacranolide; thymol derivative; *ent*-kaurene derivatives.

Abstract—*Mikania purpurascens* afforded in addition to known compounds a 5,10-epoxygermacranolide, while *M. arrojadoi* gave only known *ent*-kaurene derivatives.

Out of the large genus *Mikania* (Compositae, tribe Eupatorieae, subtribe Mikaniinae [1]), which contains more than 300 taxa, several species have been investigated chemically. While some species afforded highly oxygenated sesquiterpene lactones [2] others mainly contain diterpenes of different types [3]. The roots of *M. purpurascens* Sch. Bip. ex Baker afforded the new thymol derivative **3**, and its structure clearly followed from the ^{1}H NMR spectral data (Table 1). The presence of a tiglate was obvious from the characteristic signals (7.09 *qq*, 1.89 *dq* and 1.95 *dq*). Also, the other oxygen functions could be deduced from the ^{1}H NMR spectral data to be an acetate, a methoxy and an epoxide group. The relative positions of these groups followed from the chemical shifts. The acetate was not a phenol acetate (2.01 *s*), while the chemical shift of the olefinic proton of the tiglate residue (7.09 *qq*) indicated a phenolic ester. The signals of H-9 and H-10 were nearly the same as those of similar compounds and the chemical shifts of the aromatic proton signals also agreed with the proposed substitution pattern. The aerial parts afforded germacrene D, 12-hydroxynerolidol (**4**) [4], the flavanone **5** [5] and a sesquiterpene lactone, its structure being **1**. From the IR spectrum of **1** the presence of a γ-lactone and a hydroxyl group could be deduced, while the molecular formula, $C_{15}H_{20}O_4$, indicated an additional oxygen function. Careful ^{1}H NMR investigation, including extensive decoupling experiments, allowed the assignment of all signals (Table 2). Irradiation of the signal at δ 2.52 collapsed the doublets of the exo-methylene protons to singlets, indicating that we were dealing with the H-7 signal. Furthermore, the signals at δ 1.95, 2.12 and 4.71 were altered. The latter could only be the signal of the proton under the lactone oxygen. As this proton was further coupled with signals at 1.98 and 2.17, which showed no further couplings, and a doublet at 4.45

Table 1. ^{1}H NMR spectral data of compound **3** (400 MHz, $CDCl_3$, TMS as internal standard)

H-3	6.90 *s*	OMe	3.83 *s*
H-6	6.85 *s*	OAc	2.01 *s*
H-7	2.18 *br s*	OTigl	7.09 *qq*
H-9	4.56 *d*		1.89 *dq*
H-9′	4.16 *d*		1.95 *dq*
H-10	3.02 *d*		
H-10′	2.82 *d*		

J(Hz): 9,9′ = 12.5; 10,10′ = 5; 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5.

Table 2. ^{1}H NMR spectral data of compounds **1** and **2** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	2
H-1β	3.72 *dd*	4.69 *dd*
H-2α	1.90 *m*	1.9 *m*
H-2β	2.40 *ddd*	2.35 *ddd*
H-3	5.72 *br d*	5.70 *br d*
H-5α	4.45 *br d*	4.40 *br d*
H-6α	1.95 *dd*	1.93 *br d*
H-6β	2.12 *ddd*	2.16 *ddd*
H-7α	2.52 *ddddd*	2.57 *m*
H-8β	4.71 *ddd*	4.89 *br dd*
H-9α	1.98 *dd*	1.97 *dd*
H-9β	2.17 *br d*	2.49 *br d*
H-13	6.27 *d*	6.27 *d*
H-13′	5.44 *d*	5.46 *d*
H-14	1.10 *s*	1.44 *s*
H-15	1.73 *br s*	1.71 *br s*
OAc	—	2.06 *s*
OH	3.24 *s*	—

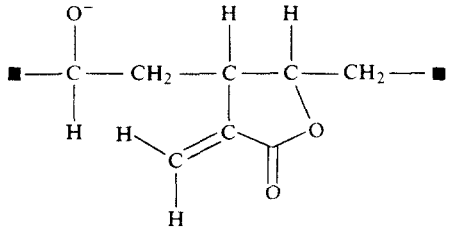
J(Hz): 1β,2α = 1β,2β = 8; 2α,2β = 17; 2β,3 = 6; 5α,6β = 6.5; 6α,6β = 13; 6α,7α = 3; 6β,7α = 10; 7α,8β = 6.5; 7α,13 = 3.5; 7α,13′ = 3; 8β,9α = 11; 8β,9β = 1.8; 9α,9β = 14.

*Part 377 in the series "Naturally Occurring Terpene Derivatives". For Part 376, see Bohlmann, F., Gupta, R. K. and Jakupovic, J. (1982) *Phytochemistry* **21**, 460.

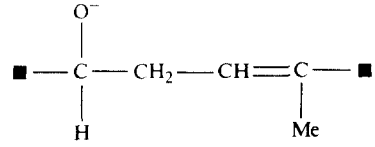
was coupled with the threefold doublet at 2.12, the sequence **A** was established.

Further decouplings starting with the double doublet at δ 3.72 led to the sequence **B**. A methyl singlet at 1.10 indicated the presence of a tertiary methyl which could be placed only at an oxygen-bearing carbon. These facts led to two possible structures, a germacranolide with a 1,5- or 5,10-oxygen bridge. However, acetylation clearly showed that a secondary hydroxyl group was present, as the double doublet at 3.72 was shifted to 4.69, thus indicating that a 5,10-oxygen bridge must be present. Inspection of models showed that the stereochemistry at C-1, C-5 and C-8 was in good agreement with the couplings observed. Furthermore, the shift differences in the spectra of the alcohol and the acetate supported the proposed stereochemistry. The downfield shift of H-14 required a *cis*-relationship of the C-1 hydroxyl and the C-10 methyl group. A 6,12-lactone with a 9,10-epoxide grouping could be ruled out due to the chemical shift of the proton under the ether oxygen. Compound **1** is most probably formed via the diepoxide C. Germacranolides with a 5,10-oxygen bridge have so far only been reported from *Liatris* spp. [6]. However, these compounds are 6,12-lactones. We have named compound **1** purpurascenolide.

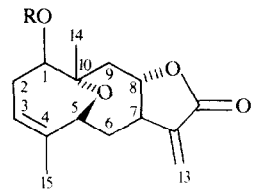
The roots of *M. arrojadoi* Mattf. afforded germacrene D, isocomene (**20**) [7], β-isocomene (**21**) [8], modhephene (**22**) [9, 10] and the *ent*-kaurene derivatives **6** [11], **10–12**, **14** [12] and **16** [13], while the aerial



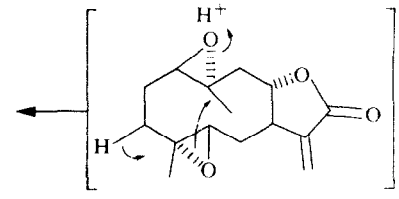
A



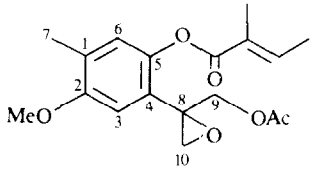
B



1 R = H
2 R = Ac



C



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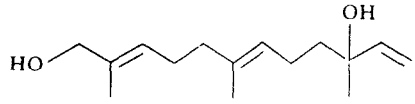

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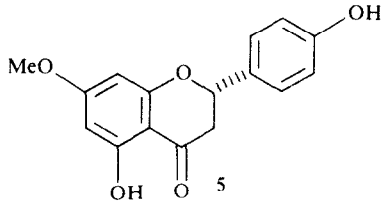

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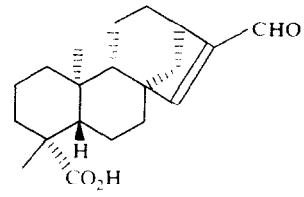

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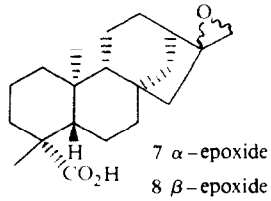
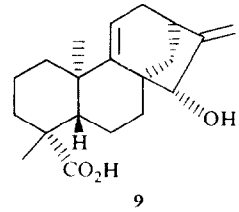


7 α-epoxide
8 β-epoxide



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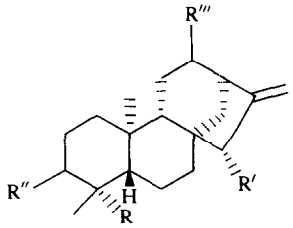
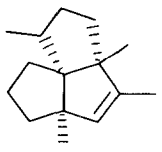


	10	11	12	13	14	15	16	17	18	19
R	CO_2H	CHO	CH_2OH	CO_2H	CO_2H	CO_2H	CO_2H	CO_2H	CO_2H	CO_2H
R′	H	H	H	OH	OCinn	OAc	OMeacr	β-OH	H	H
R″	H	H	H	H	H	H	H	H	H	OAc
R‴	H	H	H	H	H	H	H	H	OAc	H



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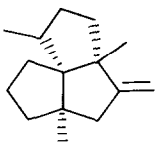

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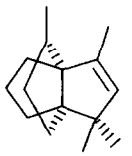

22

parts gave germacrene D, isocomene (**20**) and the *ent*-kaurene derivatives **6**, **7** [13], **8** [13], **9** [13], **10–16**, **17** [14], **18** [15] and **19** [16].

The investigation of two further *Mikania* species again shows that species of different chemistry are combined in this genus. Further taxonomic studies may show whether this large genus should be divided into smaller ones or not.

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil, was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by column chromatography (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing their IR and ^1H NMR spectra with those of authentic material. Vouchers are deposited in the U.S. National Herbarium.

Mikania purpurascens (*voucher RMK* 8376). The roots (20 g) afforded 6 mg **3** (Et_2O–petrol, 1:1) and the aerial parts (130 g) gave 10 mg germacrene D, 10 mg **1** (Et_2O–petrol, 3:1), 6 mg **4** and 5 mg **5**.

Mikania arrojadoi (*voucher RMK* 8071). The roots (250 g) afforded 20 mg germacrene D, 7 mg **6**, 2.3 g **10**, 700 mg **11**, 15 mg **12**, 500 mg **14**, 16 mg **16** and 90 mg **20–22** (*ca* 2:1:1), while the aerial parts (330 g) gave 20 mg germacrene D, 5 mg **6**, 5 mg **7**, 1 mg **8**, 5 mg **9**, 1 g **10**, 200 mg **11**, 10 mg **12**, 5 mg **13**, 100 mg **14**, 16 mg **15**, 6 mg **16**, 15 mg **17**, 10 mg **18**, 15 mg **19** and 15 mg **20**.

Purpurascenolide (**1**). Colourless crystals, mp 171–172°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560 (OH), 1760 (γ-lactone); MS *m/z* (rel. int.): 264.136 $[M]^+$ (9) ($C_{15}H_{20}O_4$), 246$[M-H_2O]^+$ (2), 236$[M-CO]^+$ (2), 221 $[236-Me]^+$ (10), 206 $[221-Me]^+$ (18), 188 $[206-H_2O]^+$ (10), 95 (73), 81 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-14.3 \quad -14.7 \quad -16.9 \quad -32.7} (CHCl_3;\ c0.7).$$

9 - *Acetoxy* - 2 - *methoxy* - 8,10 - *epoxythymol tiglate* (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R, OAc); MS *m/z* (rel. int.): 334.142$[M]^+$ (3) ($C_{18}H_{22}O_6$), 274$[M-AcOH]^+$ (1), 192 $[274-O{=}C{=}C(Me)CH{=}CH_2)^+$ (21), 177$[192-Me]^+$ (18), 83$[C_5H_7CO]^+$ (100).

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