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DITERPENES FROM *MIKANIA* SPECIES*

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Key Word Index—*Mikania officinalis*; *M. sessilifolia*; *M. luetzelburgii*; *M. belemii*; Compositae; Eupatorieae; diterpenes; geranylgeraniol derivatives; *ent*-kaurane derivatives.

Abstract—The investigation of four further *Mikania* species afforded several diterpenes, four geranylgeraniol derivatives and three kaurane epoxides. The structures were elucidated by spectroscopic methods and a few chemical transformations.

INTRODUCTION

The large genus *Mikania* (Compositae, tribe Eupatorieae) is mainly distributed throughout tropical America and placed in the subtribe Mikaniinae [1] as the only genus. So far about ten species have already been investigated chemically. While from some species highly oxygenated sesquiterpene lactones were reported [2–8], others afforded diterpenes, mainly *ent*-kaurene derivatives [3, 8, 9]. Also several flavones were isolated [10, 11]. We now have investigated some more species, all from north-eastern Brazil.

RESULTS AND DISCUSSION

The aerial parts of *M. officinalis* Mart. afforded germacrene D, γ-humulene, squalene, phytol, geranyl linalol (**1**), **22** and a further geranyl nerol derivative, the trihydroxy-aldehyde **2**. The structure of **2** followed from the ^{1}H NMR data and from those of the corresponding tetra-aldehyde **3** (Table 1). The stereochemistry of the 2,3-double bond could be assigned from the chemical shifts of H-1 and H-20 in the spectrum of **3**, while the position of the two additional aldehyde groups followed from the shift differences in the spectra of **2** and **3** and from the signals of H-14 in that of **2**. Spin decoupling further allowed the assignment of the H-5, H-9, H-12 and H-13 signals in the spectrum of **3**. From the chemical shifts of H-5 and H-9 the position of the last aldehyde group could be assigned.

The roots afforded γ-humulene and the thymol derivatives **22**–**24**. The aerial parts of *M. sessilifolia* DC. afforded germacrene D, α-humulene, squalene, the *ent*-kaurene derivatives **8** [13], **12** [14] and **13** [14] and four further diterpenes, the aldehydes **4**–**6** and the furan **7**. Again the structures could be deduced from the ^{1}H NMR data (Table 1). **4** and **5** obviously were 2,3-*E*/*Z*-isomers as could be deduced from the different chemical shifts of H-20. **4** has already been prepared from geranylgeraniol [15]. The stereochemistry of **6** and the position of the hydroxyl group also followed from the ^{1}H NMR data and the fragmentation pattern in the mass spectrum of **6**. The H-2 signal was a doublet doublet quartet, indicating the presence of only one allylic proton in addition to the H-20 protons. Furthermore, the usually downfield shifted H-4 signals were missing. In the mass spectrum a fragment at m/z 100 ($C_5H_8O_2$) also was in agreement with a 4-hydroxyl derivative of **4**. The stereochemistry of the 2,3-double bond followed from the chemical shift of H-20, while that of the other double bonds was assigned by comparing the corresponding shifts with those of geranylgeraniol and similar compounds. The structure of **7** clearly followed directly from the ^{1}H NMR data. The presence of a 2,3-disubstituted furan could be easily deduced from the signals of the two furan protons, their chemical shifts and couplings showed the presence of an α- and a vicinal β-proton. We have named **7** mikanifuran.

The roots afforded **8**, **9** [16], **10** [17], **11** [18], **12** [14], **14** [19] and small amounts of further kaurane derivatives, the epoxides **17a**, **18a** and **19**, the first two only isolated as their methyl esters (**17b** and **18b**). To establish the relative stereochemistry of **17a** and **18a** as well as that of **19**, we have prepared the epoxides **20a** [20] and **20b** from *ent*-kaurene. ^{1}H NMR investigations using shift reagent allowed the assignment of the H-15 signals, which, however, could only be assigned in the β-epoxide **20a**. However, the chemical shifts of H-17 and $J_{17,17'}$ allowed the assignment of the stereochemistry in all epoxides (Table 2).

The roots of *M. luetzelburgii* Mattf. afforded germacrene D, **8**, **10**, **12**, **13** [14], **15** [15], **16** [21], **17a** and **21**, while the aerial parts gave germacrene D, lupeyl acetate **8**, **10**, **12**, **13**, **15**, **16** and **21**. The aerial parts of *M. belemii* K. et R. afforded α-humulene, caryophyllene and its 5,6-epoxide, gurjunene, **8**, **10**, **12**, **13** and **16**.

The results of the investigation of four further *Mikania* species show again that the chemistry of this large genus is not very uniform, though taxonomically it is one of the most distinctive genera in the Compositae. As in other

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* Part 360 in the series "Naturally Occurring Terpene Derivatives". For Part 359 see Bohlmann, F., Kramp, W., Grenz, M., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 1907.

Table 1. ^{1}H NMR spectral data of compounds **2**–**7** (400 MHz, $CDCl_3$, TMS as internal standard)

	2	**3**	**4**	**5**	**6**	**7**
H-1	4.16 *d*	10.27 *d*	10.00 *d*	9.92 *d*	10.07 *d*	7.20 *d*
H-2	5.70 *br t*	6.64 *br d*	5.90 *br d*	5.88 *br d*	6.13 *ddq*	6.15 *d*
H-4	2.15 *m*	2.88 *br t*	2.24 *br s*	2.60 *br t*	4.15 *dd*	—
H-5		2.77 *br dt*		2.25 *br dt*	2.42 *br ddd* 2.30 *br ddd*	3.28 *br d*
H-6	5.30 *br t*	6.39 *br t*	5.10 *br t*	5.09 *br t*	5.12 *br t*	5.26 *br t*
H-8	2.15 *m*	2.19 *m*	2.05 *m*	2.04 *m*	2.08 *m*	2.09 *m*
H-9		2.07 *br dt*				
H-10	5.14 *br t*	5.13 *br t*	5.10 *br t*	5.09 *br t*	5.09 *br t*	5.10 *br t*
H-12	2.20 *br t*	2.16 *m*	2.05 *m*	2.04 *m*	2.02 *m*	2.05 *m*
H-13	2.45 *br dt*	2.45 *br dt*				
H-14	6.48 *br t*	6.46 *br t*	5.10 *br t*	5.09 *br t*	5.09 *br t*	5.08 *br t*
H-16	9.36 *s*	9.39 *s*	1.68 *br s*	1.68 *br s*	1.69 *br s*	1.67 *br s*
H-17	1.73 *br s*	1.75 *br s*	1.60 *br s*	1.60 *br s*	1.60 *br s*	1.59 *br s*
H-18	1.63 *br s*	1.62 *br s*			1.60 *br s*	1.60 *br s*
H-19	4.04 *br s*	10.00 *s*			1.65 *br s*	1.70 *br s*
H-20	4.05 *br s*	9.67 *s*	2.18 *d*	1.98 *d*	2.17 *d*	1.96 *br s*

J(Hz): compounds: **2**/**3**: 1,2 = 4,5 = 5,6 = 8,9 = 9,10 = 12,13 = 13,14 ~ 7; compounds **4**/**5**: 1,2 = 8; 2,20 = 1; 4,5 = 5,6 = 9,10 = 13,14 = 7; compound **6**: 1,2 = 8; 2,4 = 2,20 = 1; 4,5 = 8; 4,5′ = 4.5; 5,5′ = 14; 5,6 = 9,10 = 13,14 = 7; compound **7**: 1,2 = 1.5; 5,6 = 9,10 = 13,14 = 7.

Table 2. ^{1}H NMR spectral data of compounds **17b**, **18b**, **19** and **20** ($CDCl_3$, 400 MHz, TMS as internal standard)

	17b	**18b**	**19**	**20a**	**20a** + Eu(fod)$_3$	**20b**
H-13	2.03 *br d*	2.01 *br d*	2.02 *br d*	2.05 *dd*	3.12 *br s*	2.05 *dd*
H-14					2.44 *br d*	
H-15					2.89 *br d*	
H-15′					2.62 *br d*	
H-17	2.89 *d*	2.85 *d*	2.89 *d*	2.87 *d*	5.02 *br s*	2.85 *d*
H-17′	2.81 *d*	2.75 *d*	2.81 *d*	2.80 *d*	4.96 *br s*	2.76 *d*
H-18	1.19 *s*	1.17 *s*	1.00 *s*	1.02 *s*	1.21 *s*	0.99 *s*
H-19	—	—	9.75 *d*	0.80 *s*	0.87 *s*	0.79 *s*
H-20	0.85 *s*	0.85 *s*	0.89 *s*	0.84 *s*	0.90 *s*	0.85 *s*
OMe	3.65 *s*	3.65 *s*	—	—	—	—

J(Hz): compound **17b**: 13,14 = 1.5; 14,14′ = 12; 15,15′ = 14.5; 17,17′ = 4.5 (**18b** and **20b**: 5.5); compound **19**: 5,19 = 1.5.

large genera, however, different degrees of morphological development may be the reason for this diversity in chemistry.

EXPERIMENTAL

The air-dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by column chromatography (Si gel) and further by TLC (Si gel). Known compounds were identified by comparing the IR and ^{1}H NMR spectra with those of authentic material.

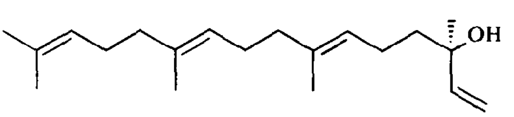
Mikania luetzelburgii (*voucher RMK* 8119). The roots (70 g) (150 g) afforded 1 mg γ-humulene, 1 mg **22**, 6 mg **23** and 4 mg **24**, while the aerial parts (300 g) gave 5 mg germacrene D, 60 mg γ-humulene, 2 mg squalene, 8 mg **1**, 6 mg phytol and 38 mg **2** (Et_2O).

Mikania sessilifolia (*voucher RMK* 8104). The roots (20 g) afforded 200 mg **8**, 6 mg **9**, 6 mg **10**, 2 mg **11**, 60 mg **12**, 1 mg **14** (Et_2O–petrol, 1:1), 3 mg **17a** (Et_2O–petrol, 1:1), 0.2 mg **18a** (Et_2O–petrol, 1:1) (both isolated as their methyl esters) and 1.2 mg **19** (Et_2O–petrol, 1:3), while the aerial parts (500 g) gave 25 mg germacrene D, 5 mg α-humulene, 50 mg squalene, 6 mg **4** (Et_2O–petrol, 1:10), 2 mg **5** (Et_2O–petrol, 1:10), 8 mg **6** (Et_2O–petrol, 1:1), 12 mg **7** (Et_2O–petrol, 1:50), 20 mg **8**, 6 mg **12** and 4 mg **13**.

Mikania luetzelburgii (*voucher RMK* 8119). The roots (70 g) afforded 50 mg germacrene D, 80 mg **8**, 25 mg **10**, 18 mg **12**, 40 mg **13**, 12 mg **15**, 30 mg **16**, 2 mg **17a** and 8 mg **21**, while the aerial parts (100 g) gave 10 mg germacrene D, 90 mg lupeyl acetate, 80 mg **8**, 5 mg **10**, 1 mg **12**, 1 mg **13**, 8 mg **15**, 40 mg **16** and 5 mg **21**.

Mikania belemii (*voucher RMK* 8007). The aerial parts (300 g) gave 50 mg α-humulene, 20 mg caryophyllene, 20 mg caryophyllene 5,6-epoxide, 5 mg gurjunene, 200 mg **8**, 100 mg **10**, 50 mg **12**, 5 mg **13** and 10 mg **16**.

19,20-*Dihydroxy*-16-*oxo-geranyl nerol* (**2**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3400 (OH), 2730, 1680 (C=CCHO); MS *m*/*z* (rel. int.): 308 $[M - CO]^+$ (0.2), 235.170 $[M - {}^{\cdot}CH_2C$-



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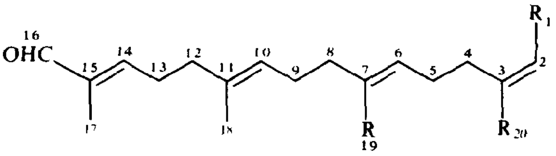
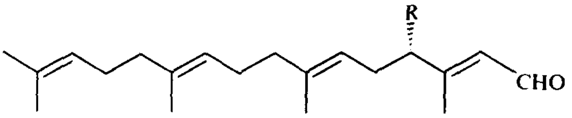
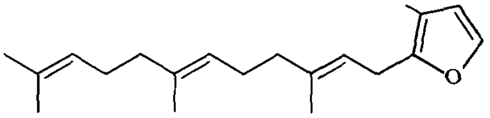


2 R = CH_2OH 3 R = CHO



4 R = H
5 R = H (2,3Z)
6 R = OH



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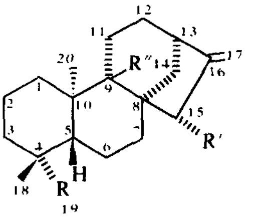
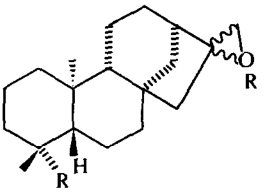
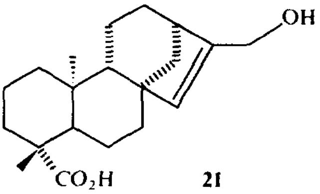


	8	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**
R	CO_2H	CO_2H	CO_2H	CO_2H	CH_2OH	CHO	$CO_2CH_2CH_2OH$	CO_2H	CO_2H
R′	H	OiVal	OCinn	OCinn	H	H	H	OH	OMeacr
R″	H	H	H	OH	H	H	H	H	H



17a	**17b**	**18a**	**18b**	**19**	**20a**	**20b**
CO_2H	CO_2Me	CO_2H	CO_2Me	CHO	Me	Me
16β-epoxide		16α-epoxide		16β-epoxide		16β



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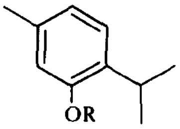
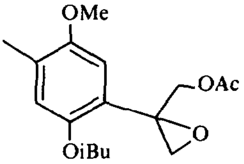


22 R = H
23 R = iBu



24

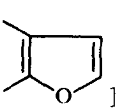
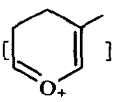
(CH_2OH)=$CHCH_2OH]^+$ (4) ($C_{15}H_{23}O_2$), 124 (61), 55 (100); CI (isobutane): 337 $[M + 1]^+$ (6), 319 $[337 - H_2O]^+$ (28), 301 $[319 - H_2O]^+$ (100), 283 $[301 - H_2O]^+$ (58), 253 $[283 - CH_2O]^+$ (33). 10 mg **2** in 2 ml $CHCl_3$ were stirred 12 hr with 300 mg MnO_2. TLC (Et_2O–petrol, 1:1) afforded 6 mg **3**, colourless gum; MS *m/z* (rel. int.): 247.133 [M − OCH(Me)= $CHCH_2^{\bullet}]^+$ (6) ($C_{15}H_{19}O_3$), 299 $[247 - H_2O]^+$ (5), 55 (100).

Geranylgeranal (**4**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2740, 1685, 1618 (C=CCHO), 1640 (C=C); MS *m/z* (rel. int.): 288.245 $[M]^+$ (6) ($C_{20}H_{32}O$), 69 $[C_5H_9]^+$ (100).

Geranyl neral (**5**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2740, 1686, 1620 (C=CCHO); MS *m/z* (rel. int.): 288.245 $[M]^+$ (6) ($C_{20}H_{32}O$), 204 $[M - MeC(=CH_2)CH_2CHO]^+$ (4), 136 $[C_{10}H_{16}]^+$ (13), 84 $[C_5H_8O]^+$ (32), 69 $[C_5H_9]^+$ (100).

4-Hydroxygeranylgeranial (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 2740, 1740, 1680, 1615 (C=CCHO); MS *m/z* (rel. int.): 304.240 $[M]^+$ (1.5) ($C_{20}H_{32}O_2$), 286 $[M - H_2O]^+$ (2.6), 100.052 $[C_5H_8O_2]^+$ (30), 69 $[C_5H_9]^+$ (100).

Mikanifuran (**7**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1505, 895 (furan); MS *m/z* (rel. int.): 286.230 $[M]^+$ (16) ($C_{20}H_{30}O$), 191.

[M − $H_2\dot{C}$  $]^+$ (9), 149 $[M - C_{10}H_{17}]^+$ (22), 95[] (58), 69 $[C_5H_9]^+$ (100).

Methyl ent-*kauranoate 16β,17-epoxide* (**17b**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (CO_2R); MS *m/z* (rel. int.): 332.235 $[M]^+$ (18) ($C_{21}H_{32}O_3$), 300 $[M - MeOH]^+$ (7), 273 $[M - CO_2Me]^+$ (80), 55 $[C_4H_7]^+$ (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-84 \quad -88 \quad -100 \quad -167} \; (c = 1.16, \text{CHCl}_3).$$

Identical with the epoxide obtained by epoxidation of methyl *ent*-kauranoate (*ca* 90%).

Methyl ent-*kauranoate*-16α,17-*epoxide* (**18b**). Colourless gum, IR $\nu^{\text{CCl}_4}_{\text{max}}$ cm^{-1}: 1730 (CO_2R); MS *m/z* (rel. int.): 332.235 $[M]^+$ (20) ($C_{21}H_{32}O_3$), 300 $[M - MeOH]^+$ (4), 273 $[M - CO_2Me]^+$ (100), identical with the epoxide from methyl *ent*-kaurenoate (*ca* 10%).

Ent-*kauran*-19-*al*-16β,17-*epoxide* (**19**). Colourless gum, IR $\nu^{\text{CCl}_4}_{\text{max}}$ cm^{-1}: 2720, 1720, (CHO); MS *m/z* (rel. int.): 302.225 $[M]^+$ (41) ($C_{20}H_{30}O_2$), 273 $[M - CHO]^+$ (36), 255 $[273 - H_2O]^+$ (15), 55 $[C_4H_7]^+$ (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-65 \quad -71 \quad -79 \quad -123} \; (c = 0.1, \text{CHCl}_3).$$

Preparation of **20a** *and* **20b**. 37 mg *ent*-kaurene in 2.5 ml $CHCl_3$ was stirred with 1.25 ml H_2O_2 and 1.25 ml HCO_2H for 5 hr at room temp. (see [20]). TLC afforded 5.2 mg **20a** and 0.2 mg **20b**.

$$\mathbf{20a}: [\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-69 \quad -72 \quad -82 \quad -140} \; (c = 0.89, \text{CHCl}_3).$$

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