Phytochemistry, Vol. 21, No. 1, pp. 173–176, 1982.
Printed in Great Britain.

0031-9422/82/010173-04 $03.00/0

ENT-LABDANES FROM *MIKANIA ALVIMII**

FERDINAND BOHLMANN, ALFONS ADLER, ROBERT M. KING† and HAROLD ROBINSON†

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

(*Received* 27 *March* 1981)

Key Word Index—*Mikania alvimii*; Compositae; diterpenes; *ent*-labdane derivatives; norditerpene.

Abstract—The aerial parts of *Mikania alvimii* afforded in addition to known compounds seven new *ent*-labdane derivatives and a 15-nor compound. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation of this large genus is discussed briefly.

INTRODUCTION

From the large genus *Mikania* containing about 300 taxa, several species have already been investigated chemically. While some species contain highly oxygenated sesquiterpene lactones [1] others afforded various diterpenes [2]. We have now investigated a new species from north-eastern Brazil, *Mikania alvimii*. Again the aerial parts afforded diterpenes, mainly belonging to the *ent*-labdane series.

RESULTS AND DISCUSSION

The aerial parts of *M. alvimii* gave γ-humulene, β-selinene, isocomene [3], β-isocomene [4], phytol and its linolenoate, methyl linolenoate, the thymol derivative **13** [5], rudbeckianone (**14**) [6], the chromone **15** as well as several diterpenes, the laevorotatory pimarenic acid **12** [7], the *ent*-labdanes ozic acid (**1**) [8], **4** [9], **5** [8], the α- and β-epoxides **10a** and **11a** [10], and the epimers **8a** and **9a**. The diol **2**, its diacetate **3**, the diol **6a** and the norditerpene **7a** were also present. The ^{1}H NMR spectral data of **1** and its methyl ester were identical with those of authentic samples. Also the optical rotation was the same. Therefore most probably all compounds were *ent*-labdanes. The epoxides **8a**–**11a** could be separated as their methyl esters into two pairs. One pair contained the α-epoxides **8b** and **10b**, while the other was a mixture of **9b** and **11b**. As **10b** and **11b** had been isolated before [11], the ^{1}H NMR signals of **8b** and **9b** could be assigned (Table 1). Though the stereochemistry could not be established with certainty, the proposed assignments were likely, as typical differences in the ^{1}H NMR signals of H-12 and H-17 could be observed. The downfield shift of H-17′ was most probably caused by the deshielding effect of the β-epoxide, as this seemed to be the only explanation of the differences. The identical stereochemistry at C-4, C-5, C-9 and C-10 was deduced from the similarity of the ^{1}H NMR data with those of the methyl ester of ozic acid and the typical IR band for an equatorial C-4 carboalkoxy group [8]. The ^{1}H NMR spectral data of **2** and **3** (Table 1) showed that both C-18 and C-19 were oxygenated. As the other signals were similar to those of **1**, the same stereochemistry had to be assumed. The ^{1}H NMR spectrum of **6a** (Table 1) showed that a derivative of **4** with an additional hydroxyl group was present. The corresponding signal (3.68) was a double doublet indicating a C-1 or C-3 position. Transformation of **6a** to the acetonide **6b** established the C-3 position of this hydroxyl. Therefore, compound **6a** was most probably *ent*-3β,19-dihydroxylabda-12,14-diene, though the absolute configuration was not determined. Compound **7a**, which after addition of diazomethane afforded **7b**, was a norditerpene, as could be deduced from the molecular formula. The ^{1}H NMR spectral data (Table 1) showed that the side-chain was degraded. The presence of an *E*-configuration double bond clearly followed from the chemical shifts of H-12 and H-14. As all the other signals were close to those of **1** and the aldehyde was laevorotatory, identical stereochemistry was very likely.

EXPERIMENTAL

The air-dried aerial part of *Mikania alvimii* K. et R. (voucher RMK 8126, deposited in the U.S. National Herbarium) was extrd with Et_2O–petrol (1:2) and the extract obtained first sepd by CC (Si gel) and further by repeated TLC (Si gel). The nonpolar fractions afforded 8 mg γ-humulene, 21 mg isocomene, 3.5 mg β-isocomene, 7 mg β-selinene, 5 mg methyl linolenoate, 15 mg phytyl linolenoate, 3 mg **13** and 3 mg **14**, while more polar fractions gave 6 mg **15**, 15 mg **1**, 1 mg **4** and 0.5 mg **5**. Repeated TLC of the methyl esters of the acids (Et_2O–CH_2Cl_2–petrol, 1:6:10) afforded two pairs of isomers containing **8b** and **10b** (3 mg, *ca* 1:2) and **9b** and **11b** (4.5 mg, *ca* 2:1), which could not be sepd further. Compound **8b**: Colourless oil containing **10b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1731, 1248 (equatorial CO_2R), 1649 ($C{=}CH_2$); MS *m/z* (rel. int.): 332.235 $[M]^+$ (2) ($C_{21}H_{32}O_3$), 317 $[M - Me]^+$ (17), 273 $[M - CO_2Me]^+$ (4), 121 $[C_9H_{13}]^+$ (100). Compound **9b**: Colourless oil containing **11b**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1726, 1244 (equatorial CO_2R), 1640 ($C{=}CH_2$); MS *m/z* (rel. int.): 332.235 $[M]^+$ (2)($C_{21}H_{32}O_3$), 317 $[M - Me]^+$ (3), 121 $[C_9H_{13}]^+$ (100). Furthermore, the polar fractions afforded 3 mg **2**, 4 mg **6a** and 6 mg **7a** (Et_2O–C_6H_6, 9:1, 3 ×).

---

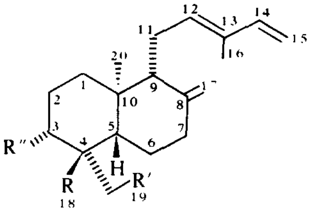
*Part 374 in the series "Naturally Occurring Terpene Derivatives". For Part 373, see Bohlmann, F. and Zdero, C. (1981) *Phytochemistry* **20**, 2431.

Table 1. ^{1}H NMR spectral data of compounds **2**, **3**, **6a**, **6b**, **7a**, **7b** and **8b** **11b** (400 MHz, $CDCl_3$, TMS as internal standard)

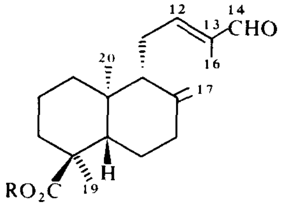
	2	**3**	**6a**	**6b***	**7a**	**7b**	**8b**	**9b**	**10b**	**11b**
H-3			3.68 *dd*	3.54 *dd*						
H-11	2.36 *br dd*	2.38 *br dd*	2.36 *m*							
H-12	5.39 *br t*	5.40 *br t*	5.38 *br t*		6.42 *br t*		2.89 *dd*	2.92 *dd*	2.80 *dd*	2.82 *dd*
H-14	6.32 *dd*	6.32 *dd*	6.32 *dd*		9.34 *s*		5.81 *dd*	5.81 *dd*	5.62 *dd*	5.62 *dd*
H-15	5.04 *br d*	5.04 *br d*	5.04 *br d*	5.03 *br d*	—		5.32 *dd*	5.34 *dd*	5.28 *dd*	5.28 *dd*
H-15′	4.88 *br d*	4.89 *br d*	4.88 *br d*		—		5.30 *dd*	5.31 *dd*	5.14 *dd*	5.15 *dd*
H-16	1.75 *br s*	1.75 *br s*	1.74 *br s*		1.77 *br s*		1.38 *s*	1.39 *s*	1.41 *s*	1.41 *s*
H-17	4.81 *br s*	4.83 *br s*	4.83 *br s*	4.83 *br s*	4.85 *br s*		4.83 *br s*	4.89 *br s*	4.85 *br s*	4.90 *br s*
H-17′	4.46 *br s*	4.48 *br s*	4.47 *br s*	4.48 *br s*	4.41 *br s*		4.46 *br s*	4.76 *br s*	4.48 *br s*	4.76 *br s*
H-18	3.90 *d*	4.04 *d*	0.88 *s*	1.04 *s*	1.18 *s*	1.16 *s*	—	—	—	
H-18′	3.42 *d*	3.93 *d*					—	—	—	—
H-19	3.94 *br d*	4.32 *d*	3.42 *d*	3.45 *d*	0.79 *s*		1.13 *s*	1.14 *s*	1.14 *s*	1.15 *s*
H-19′	3.73 *br d*	3.99 *br*	3.71 *d*	3.51 *d*						
H-20	0.68 *s*	0.76 *s*	0.77 *s*	0.86 *s*			0.68 *s*	0.69 *s*	0.71 *s*	0.72 *s*
OAc	—	2.08 *s* 2.03 *s*	—	—	—	—	—	—	—	—
OMe		—	—		—	3.67 *s*	3.66 *s*	3.66 *s*	3.66 *s*	3.67 *s*

* H-22 1.44 *s*, H-23 1.41 *s*.

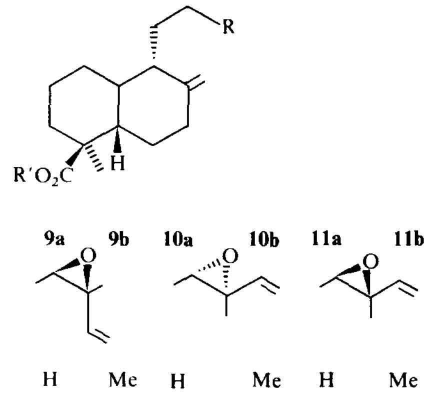
J(Hz): compounds **2**, **3**, **6a** and **6b**: 11,11′ = 13.5; 11,12 = 6.5; 14,15 = 17.5; 14,15′ = 11; 18,18′ = 19,19′ = 10.5; (**6a**: 2,3 = 11; 2′,3 = 5; **6b**: 2,3 = 12; 2′,3 = 4); compounds **7a** **7b**: 11,12 = 6.5; compounds **8b**–**11b**: 14,15 = 17; 14,15′ = 11; 15,15′ = 1 (**8b**: 11,12 = 4; 11′,12 = 6; **9b**: 11,12 = 8; 11′,12 = 3.5; **10b**: 11,12 = 3.5; 11′,12 = 6.5; **11b**: 11,12 = 7; 11′,12 = 4).



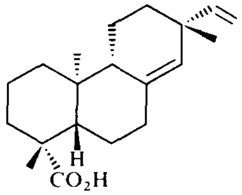
	1	2	3	4	5	6a	6b
R	CO_2H	CH_2OH	CH_2OAc	Me	CH_2OH	Me	Me
R'	H	OH	OAc	OH	H	OH	–O 22
R''	H	H	H	H	H	OH	–O 23



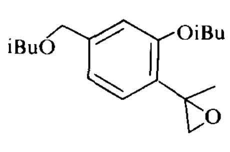
7a R = H
7b R = Me



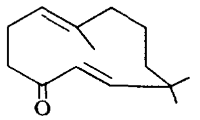
	8a	**8b**	**9a**	**9b**	**10a**	**10b**	**11a**	**11b**
R'	H	Me	H	Me	H	Me	H	Me



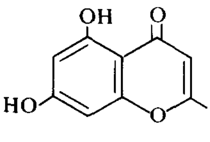
12



13



14



15

Compound **2**: colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3622 (OH), 897 (C $=CH_2$); MS m/z (rel. int.): 304.240 $[M]^+$ (4)($C_{20}H_{32}O_2$), 286 $[M - H_2O]^+$ (16), 255 $[286 - CH_2OH]^+$ (14), 81 $[C_6H_9]^+$ (100). $[\alpha]_D = -7 (c = 0.2, CHCl_3)$. Compound **6a**: Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS m/z (rel. int.): 304.240 $[M]^+$ (8), ($C_{20}H_{32}O_2$), 286 $[M - H_2O]^+$ (16), 255 $[286 - CH_2OH]^+$ (24), 81 $[C_6H_9]^+$ (100), $[\alpha]_D = -14°$ ($c = 0.3$, $CHCl_3$). To 4 mg **6a** in 1 ml Me_2CO 10 mg *p*-toluene sulfonic acid was added. After 24 hr, TLC (Et_2O–petrol, 1:10) afforded 3 mg **6b**, colourless gum, MS m/z (rel. int.): 344.272 $[M]^+$ (23)($C_{23}H_{36}O_2$), 329 $[M - Me]^+$ (38), 81 $[C_6H_9]^+$ (100). Compound **7a**: Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1727 (CO_2H), 2710, 1689, 1646 (C $=CCHO$), 895 ($C=CH_2$) $[\alpha]_D = -13°$ ($c = 0.6$, $CHCl_3$). Compound **7a** (6 mg) on addition of CH_2N_2 afforded **7b**, colourless gum, MS m/z (rel. int.): 318.220 $[M]^+$ (9) ($C_{20}H_{30}O_3$), 121 $[C_9H_{13}]^+$ (100). From the less polar fractions (Et_2O–petrol, 3:7), 1 mg **3** was obtained, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1230 (OAc), 895 ($C=CH_2$): MS m/z (rel. int.): 388. 261 $[M]^+$ (8) ($C_{24}H_{36}O_4$), 328 $[M - AcOH]^+$ (23), 268 $[328 - AcOH]^+$ (42), 81 $[C_6H_9]^+$ (100). $[\alpha]_D = -4°$ ($c = 0.3$, $CHCl_3$).

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

REFERENCES

1. Herz, W., Subramaniam, P. S., Murari, K., Dennis, N. and Blouret, J. F. (1977) *J. Org. Chem.* **42**, 1720.
2. Bohlmann, F., Adler, A., Schuster, A., Gupta, R. K., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1899.
3. Zalkow, L. H., Harris, N. R., III, Van Derveer, D. and Bertrand, J. A. (1977) *J. Chem. Soc. Chem. Commun*, 456.

4. Bohlmann, F., Le Van, N., Cuong Pham, T. V., Jakupovic, J., Schuster, A., Zabel, V. and Watson, H. W. (1979) *Phytochemistry* **18**, 1831.
5. Bohlmann, F., Niedballa, V. and Schulz, J. (1969) *Chem. Ber.* **102**, 864.
6. Bohlmann, F., Jakupovic, J. and Zdero, C. (1978) *Phytochemistry* **17**, 2034.
7. Shibata, S., Mihashi, S. and Tanaka, O. (1967) *Tetrahedron Letters* 5241.
8. Bevan, C. W. L., Ekong, D. E. V. and Okogun, S. I. (1968) *J. Chem. Soc.* 1063.
9. Thomas, B. K. (1966) *Acta Chem. Scand.* **20**, 1074.
10. Bohlmann, F., Natu, A. A. and Mahanta, P. K. (1978) *Phytochemistry* **17**, 483.