Phytochemistry, Vol. 25, No. 5, pp. 1240–1242, 1986.
Printed in Great Britain.

0031-9422/86 $3.00 + 0.00

PIMARADIENE DITERPENES FROM *MIKANIA TRIANGULARIS**

FERNANDA S. KNUDSEN, WAGNER VILEGAS, FERNANDO OLIVEIRA† and NIDIA F. ROQUE‡

Instituto de Química, Universidade de São Paulo, 05508 São Paulo, SP, Brazil; †Faculdade de Ciências Farmacêuticas, Universidade de São Paulo, SP, Brazil

(*Revised received* 24 *September* 1985)

Key Word Index—*Mikania triangularis*; Compositae; pimaradiene diterpenes.

Abstract—The aerial parts of the species *Mikania triangularis* afforded one known and three new pimaradiene diterpenes besides friedelin and stigmasterol. Their structures were deduced on the basis of spectral data and chemical modifications.

INTRODUCTION

The genus *Mikania* (tribe Eupatoriae, subtribe Miikanae) is widespread in Brazil, 150 of its 300 species occurring in this country [2]. Some species of the genus, known as guaco, are used in popular medicine against a variety of diseases [3, 4].

We are presently investigating the chemical composition of Brazilian guaco belonging to the genus *Mikania*. As part of this work we report here the isolation and structural determination of some constituents from the aerial parts of *Mikania triangularis* Baker.

RESULTS AND DISCUSSION

The methylated hexane extract of the aerial parts of *M. triangularis* contained predominantly the compound **1a**. This substance was accompanied by very small quantities of the alcohol **1b**, the hydrocarbon **1c**, friedelin and stigmasterol, as well as by the ester **2** [5] which could not be obtained pure. The identification of **2** was achieved by ^{13}C NMR spectroscopy (Table 1) of the compound contaminated with **1a** and by its oxidation product **4**.

The IR, mass and ^1H NMR (Table 2) spectra of **1a** suggested that it was a pimaradiene methyl ester with a trisubstituted double bond and a terminal vinyl group. Hydrogenation of **1a** afforded **3** in 100% yield whereas lithium aluminium hydride reduction under vigorous conditions gave only 5% of **1b** suggesting that the ester function was axial [6]. The ^{13}C NMR spectra of **1a** (Table 1) agreed with this assumption. It also established the position $\Delta^{8(11)}$ for the endocyclic double bond and the relative stereochemistry of the molecule. The *cis* localization of H-8 and H-5 was inferred by the protection of C-5 by C-8 [7]. The configuration of C-13 was suggested by the chemical shift of C-17 (δ22.3) which was only compatible with an axial methyl group having one γ gauche interaction [8]. This interaction could only be due to C-8. Thus H-8 had to be located on the same side of the molecule as the methyl group at C-13. This situation placed the vinyl group at an equatorial position as expected by the normal quartet of the X part of the ABX system shown in the ^1H NMR spectrum [9].

Oxidation of the mixture of **1a** and **2** with Sarret reagent [10] furnished four main products, **4**–**7**. The UV and IR spectra of these compounds contained absorptions typical of α,β-unsaturated carbonyl groups. The spectral data of compound **4**, the oxidation product of **2**, was identical, including the sign of the CD curve, with those of the compound isolated from *Helianthus hirsutus* [5]. The

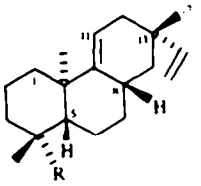
Table 1. ^{13}C NMR data (20 MHz, $CDCl_3$, δ)

C	1a	2	3	5	6	7
1	42.1	36.8	42.5	35.5	40.2	35.3
2	19.3	19.7	19.1	19.9	18.7	19.1
3	38.5	39.9	38.3	37.7	38.0	37.2
4	44.5	43.7	44.3	43.7	44.0	43.3
5	48.3	51.6	48.1	54.3	46.7	50.6
6	20.6	24.4	20.5	19.5	20.1*	36.9
7	28.5	120.0	28.4	36.3	26.6	200.6
8	28.8	134.4	28.8	153.7	30.1	142.3
9	150.1	53.1	150.1	140.6	177.4	153.5
10	38.5	†	38.3	38.2	39.6	39.7
11	116.8	21.2	117.1	197.6	121.9	200.1
12	37.7	35.3	37.8	51.0	202.9	51.9
13	35.0	37.1	31.4	38.0	46.4	38.5
14	42.1	45.6	42.0	43.9	41.3	36.8
15	150.3	144.1	36.9	145.6	142.7	143.5
16	109.2	112.2	7.5	111.5	112.7	112.8
17	22.3*	29.4	21.8	24.9	21.5*	27.0
18	28.1	†	28.0	28.7	28.2	28.1
19	178.0	177.0	177.9	175.9	177.4	176.8
20	22.4*	13.8	22.1	16.8	21.7*	15.3
OMe	51.1	51.2	51.0	51.2	51.4	51.5

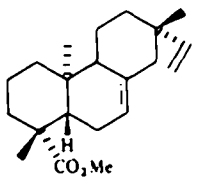
*Signals interchangeable.
†The assignment of C-10 and C-18 could not be made

* Part 3 in the series "The Chemistry of Brazilian Compositae". For part 2 see ref. [1]. Based on part of the M.S. Thesis submitted by F.S.K. to the Universidade de São Paulo (1984).

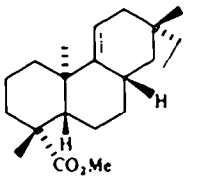
‡Author to whom correspondence should be addressed.



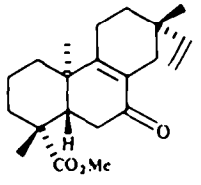
	R
1a	CO_2Me
1b	CH_2OH
1c	Me



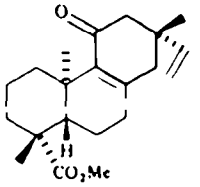
2



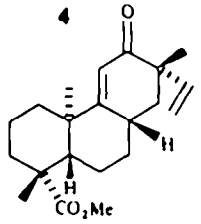
3



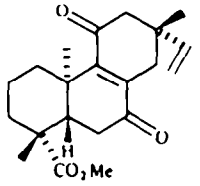
4



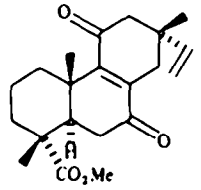
5



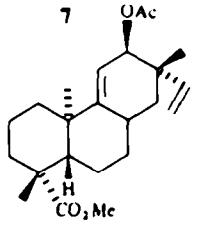
6



7



8



9

structure of **4** confirmed that of **2** proposed on the basis of ^{13}C NMR data of the original mixture. In **5** also the double bond had migrated to Δ^8 and the carbonyl group was now located at C-11. This information was given by the ^{13}C NMR spectra (Table 1). The chemical shift of the methyl group at C-13 was δ 24.9, the loss of the C-8 γ effect explained the paramagnetic shift of the absorption of this carbon in relation to **1a** in agreement with the proposed stereochemistry. The ^1H NMR data of **6** (Table 2) indicated that the double bond had not migrated, thus the carbonyl group should still be at C-12. The ^{13}C NMR data (Table 1) and the mass spectrum (retro Diels–Alder fragment, m/z 262, 100%) agreed with the proposed structure. Compound **7** had a cross conjugated O=C–C=C–C=O of the transoid type. The ^{13}C NMR data of **7** was comparable with those of **8** [11] except, as expected for the chemical shifts of the ring A carbons.

The negative $[\alpha]_D$ sign of **1a**, the CD curve of **4** and the application of the octante rule for **5** and **6** established the absolute configurations of **1a**, **2** and their derivatives. The structural determination of **1b** and **1c** was based on the similarities of the IR, MS and ^1H NMR (Table 2) data of these compounds with the analogous data of **1a** and confirmed by the lithium aluminium hydride reduction product **1b**. The localization of the trisubstituted double bond is unusual. The only $\Delta^{9(11)}$ pimaradiene diterpenes described are the C-13 epimeric compounds of **1a** and **1b** [12] and **9** [5].

EXPERIMENTAL

The air dried aerial parts (2.5 kg) of *M. triangularis* collected in São Paulo, SP, Brazil (Voucher RB 188769 deposited in the herbarium of Jardim Botânico, Rio de Janeiro) were extracted with hexane at room temp. After methylation with CH_2N_2 the extract (30.0 g) was chromatographed on a silica gel (600 g) column using a petrol–CH_2Cl_2 gradient. The mixture (0.13 g) eluted with 5% CH_2Cl_2 was submitted to flash chromatography (petrol–CH_2Cl_2) to give **1c** (3 mg); elution with petrol–CH_2Cl_2 (7:3) gave on further purification by repeated CC **1a** and **2** (10 g). Repeated prep. TLC gave **1a** (500 mg). The fractions eluted with petrol–CH_2Cl_2 (1:1) gave after prep. TLC (silica gel, petrol–EtOAc, 4:1) friedelin (15 mg) and **1b** (10 mg). CH_2Cl_2

Table 2. ^1H NMR data of compounds **1a**, **1b**, **1c**, **3**, **5**, **6** and **7** (60 MHz, $CDCl_3$, δ)

H	1a	1b	1c*	3	5*	6	7
11	5.42 *m*	5.38 *m*	5.32 *m*	5.37 *m*	—	5.92 *d*	—
15	5.83	5.85 *dd*	5.80 *dd*	—	5.83	6.22 *sext*	5.75 *sext*
16 *trans*	4.92 *dd*	4.91 *dd*	4.87 *dd*	0.83 *m*	4.92 *dd*	5.05 *dd*	4.90 *dd*
16 *cis*	4.85 *dd*	4.85 *dd*	4.82 *dd*		4.95 *dd*	5.12 *dd*	4.97 *dd*
17	0.97 *s*	0.98 *s*	0.98 *s*	0.80 *s*	1.07 *s*	1.20 *s*	1.13 *s*
18	1.20 *s*	1.05 *s*	0.87 *s*	1.20 *s*	1.22 *s*	1.23 *s*	1.23 *s*
19a	—	3.85 *d*	0.87 *s*	—	—	—	—
19b	—	3.52 *d*		—	—	—	—
20	0.90 *s*	1.05 *s*	1.05 *s*	0.90 *s*	1.00 *s*	1.00 *s*	1.13 *s*
OMe	3.65 *s*	—	—	3.63 *s*	3.63 *s*	3.67 *s*	3.67 *s*

*80 MHz.

J (Hz)—H-15: 18 and 11; H-16 *trans*: 18 and 2; H-16 *cis*: 11 and 2; H-19: 11.

eluted a mixture which after purification by prep. TLC (silica gel, C_6H_6–EtOAc, 7:3) gave stigmasterol (10 mg). All the fractions before purification were contaminated with **1a**.

Methyl-ent-*pimara*-9(11),15-*dien*-19-*oate* (**1a**). Colourless oil; IR ν_{max}^{KRS-5} cm^{-1}: 2920, 1730, 1635, 1460, 1220, 1150, 910; MS *m/z* (rel. int.): 316, $[M]^+$ (29), 301 (66), 257 (55), 248 (37), 241 (82), 189 (53), 188 (74), 173 (56), 134 (43), 133 (57), 121 (77), 119 (76), 43 (100); 316.2412 ($C_{21}H_{32}O_2$); $[\alpha]_D^{20} - 55°$ ($CHCl_3$); ^{13}C and ^1H NMR: see Tables 1 and 2.

ent-*Pimara*-9(11),15-*dien*-19-*ol* (**1b**). Colourless oil; IR ν_{max}^{KRS-5} cm^{-1}: 3380, 3080, 2920, 1635, 1450, 1370, 1025, 910; MS *m/z* (rel. int.): 288 $[M]^+$ (5), 273 (57), 257 (62), 241 (17), 220 (26), 189 (78), 173 (32), 134 (51), 133 (63), 121 (65), 119 (80), 107 (100); 288.2440 ($C_{20}H_{32}O$), ^1H NMR: see Table 2.

ent-*Pimara*-9(11),15-*dien* (**1c**). Colourless oil; IR ν_{max}^{KRS-5} cm^{-1}: 3080, 2940, 1635, 1470, 1370, 910; MS *m/z* (rel. int.): 272 $[M]^+$ (1), 257 (3), 243 (4), 201 (2), 189 (4), 175 (6), 161 (9), 134 (11), 133 (12), 121 (6), 120 (9), 119 (21), 41 (100); 272.2529 ($C_{20}H_{32}$). ^1H NMR: see Table 2.

Methyl-ent-*pimar*-9(11)en-19-*oate* (**3**). A soln of **1a** (0.1 g) in MeOH (10 ml) was hydrogenated with 10% Pd–C to give 0.1 g of **3**, colourless oil; IR ν_{max}^{KRS-5} cm^{-1}: 2960, 1730, 1460, 1380, 1225, 1150; ^{13}C and ^1H NMR: see Tables 1 and 2.

Reduction of **1a**. $LiAlH_4$ (0.60 g) was added to a soln of **1a** (0.4 g) in THF (30 ml) and the mixture refluxed for 6 days. After which usual work up and purification by prep. TLC ($CHCl_3$) gave **1b** (0.018 g).

Oxidation of the mixture **1a** *and* **2**. CrO_3 (1 g) was added to a soln of pyridine (9 ml) and CH_2Cl_2 (100 ml), to this suspension the mixture (1 g) was added and the reaction mixture left for 5 days at room temp. After removal of the solvents the ppt was washed with Et_2O. The organic extract was washed with a soln of $NaHCO_3$ and H_2O, dried, and the solvent evaporated to give a residue (0.6 g). Repeated prep. TLC, C_6H_6–EtOAc (4:1) gave **4** (25 mg), **5** (70 mg), **6** (80 mg) and **7** (70 mg).

Methyl-ent-11-*oxopimara*-8,15-*dien*-19-*oate* (**5**). Colourless gum; IR ν_{max}^{KRS-5} cm^{-1}: 2960, 1725, 1660, 1610, 1460, 1230, 1150, 915; UV λ_{max}^{MeOH} nm: 244 (log ε 3.93); CD (MeOH) nm: $[\theta]_{321} + 1450$, $[\theta]_{240} - 10\,100$; MS *m/z* (rel. int.): 330 $[M]^+$ (11), 315 (1), 271 (6), 262 (2), 255 (9), 202 (4), 188 (4), 161 (5), 160 (5), 121 (20), 41 (100); ^1H and ^{13}C NMR: see Tables 1 and 2.

Methyl-ent-12-*oxopimara*-9(11),15-*dien*-19-*oate* (**6**). Colourless gum; IR ν_{max}^{KRS-5} cm^{-1}: 2930, 1720, 1665, 1610, 1460, 1225, 1130, 910; UV λ_{max}^{MeOH} nm: 245 (log ε 4.05); CD (MeOH) nm: $[\theta]_{330} + 1250$, $[\theta]_{257} - 5000$; MS *m/z* (rel. int.): 330 $[M]^+$ (4), 315 (2), 289 (3), 271 (2), 262 (100), 247 (3), 202 (9), 188 (59), 187 (15), 161 (20), 160 (27), 159 (39), 145 (26), 121 (31); ^1H and ^{13}C NMR: see Tables 1 and 2.

Methyl-ent-7,11-*dioxopimara*-8,15-*dien*-19-*oate* (**7**). Colourless gum; IR ν_{max}^{KRS-5} cm^{-1}: 2990, 2950, 2860, 2850, 1720, 1685, 1675, 1580, 1460, 1235, 930; UV λ_{max}^{MeOH} nm: 263 (log ε 3.96); CD (MeOH) nm: $[\theta]_{271} - 26\,950$; $[\theta]_{239} - 24\,060$; MS *m/z* (rel. int.): 334 $[M]^+$ (17), 329 (1), 285 (4), 284 (5), 276 (2), 269 (3), 217 (3), 216 (4), 201 (7), 188 (13), 173 (13), 149 (16), 145 (16), 121 (20), 41 (100); ^1H and ^{13}C NMR: see Tables 1 and 2.

Acknowledgements—We thank Conselho Nacional de Desenvolvimento Cientffico e Tecnológico (CNPq) and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for financial aid and a graduate fellowship to F.S.K.

REFERENCES

1. Lourenço, T. O., Akisue, G. and Roque, N. F. (1981) *Phytochemistry* **20**, 773.
2. Barroso, G. M. (1960) *Arq. Jard. Bot. Rio de Janeiro* **16**, 239.
3. Cattorinni, D. P. E. (1961) *Fitoterapia* **32** 7.
4. Cattorinni, D. P. E. (1961) *Fitoterapia* **33**, 10.
5. Herz, W. and Kulanthaivel, P. (1984) *Phytochemistry* **23**, 1453.
6. Bory, S. and Fetizon, M. (1964) *Bull Sol. Chim. Fr.* 570.
7. Blunt, J. W. and Munro, M. H. G. (1980) *Org. Magn. Reson.* **13**, 26.
8. Bier, R. (1978) *Org. Magn. Reson.* **11**, 586.
9. Wenkert, E. and Beak, P. (1961) *J. Am. Chem. Soc.* **83**, 998.
10. Dauben, W. G., Lorder, M. and Fullerton, D. S. (1969) *J. Org. Chem.* **34**, 3587.
11. Alvarez, M. C. G., Paternostro, M., Peozzi, F., Rodrigues, B. and Savana, G. (1979) *Phytochemistry* **18**, 1835.
12. Bohlmann, F. and Knoll, K.-H. (1976) *Phytochemistry* **15**, 1072.