Phytochemistry, Vol 23, No 1, pp 125–127, 1984
Printed in Great Britain

0031–9422/84 $3 00 + 0 00

ZOAPATANOLIDES C AND D, TWO GUAIANOLIDES FROM *MONTANOA TOMENTOSA**

LEOVIGILDO QUIJANO, FEDERICO GOMEZ G, JOSÉ S CALDERÓN, JESUS LÓPEZ P and TIRSO RIOS

Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, 04510 México, D F

(*Received* 13 *May* 1983)

Key Word Index—*Montanoa tomentosa*, Asteraceae, guaianolides, sesquiterpene lactones

Abstract—Further investigation of *Montanoa tomentosa* afforded two new guaianolides as well as the known pumilin and the previously isolated heliangolide zoapatanolide A The structures were established on the basis of spectroscopic studies and chemical evidence

INTRODUCTION

In our previous papers we have described the isolation and structure elucidation of sesquiterpene lactones of the germacrolide type from *Montanoa frutescens* [1] and of the heliangolide type from *M tomentosa* [2] Recently, we have re-investigated *M tomentosa* and isolated, besides zoapatanolide A [2], three guaianolides, the known pumilin (**2**) with established X-ray structure, previously isolated from *Berlandiera pumila* [3], and two new compounds which we have named zoapatanolides C and D These represent the first guaianolides isolated from the genus *Montanoa* The close structural relationship of the guaianolides present in *M tomentosa* and those isolated from *Berlandiera pumila* [3] and *B subacaulis* [4] might have taxonomic implications

RESULTS AND DISCUSSION

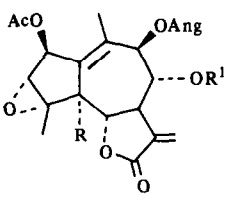
The structures of zoapatanolides C (**1a**) and D (**1b**) were established by extensive ^{1}H NMR studies and spin–spin decoupling as well as some chemical evidence

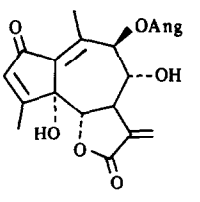
Zoapatanolide C (**1a**), $C_{22}H_{26}O_9$, mp 130–132°, showed a UV end absorption at 207 nm (ε 11 544) and typical IR bands at 1762, 1630 and 3430 cm^{-1} indicating the presence of a γ-lactone moiety, an α,β-unsaturated ester and hydroxyl groups, respectively The unsaturated ester was shown to be an angelate by the typical mass spectral peaks at m/z 83 and 55 as well as the vinyl proton signal at δ 6 2 and the vinyl methyl signals at δ 2 03 and 1 96 in the ^{1}H NMR spectrum (Table 1), which also showed the presence of an acetate signal at δ 2 12 The ^{1}H NMR spectrum of **1a**, when determined in $CDCl_3$, only showed overlapping signals at δ 6 1–6 3 due to the exocyclic methylene protons, the side-chain vinyl proton and H-9 A complex signal at δ 3 8–3 9 was resolved into a triplet of triplets (H-7), a triplet (H-8) and a doublet (H-6) when the spectrum was run in C_6D_6 A broad singlet at δ 5 63 was assigned to H-2 on the carbon bearing the acetate group, since this signal shifted upfield after hydrolysis A doublet at δ 3 77 (J = 2 0 Hz) was assigned to H-3 on the carbon bearing the epoxy-function Finally, the methyl groups on C-10 and C-4 appeared as singlets at δ 1 66 and 1 60, respectively

The acetylation product of **1a** contained one more acetate signal in the ^{1}H NMR spectrum and showed a hydroxyl absorption (3440 cm^{-1}) in the IR spectrum suggesting the presence of a tertiary hydroxyl group and a secondary one in zoapatanolide C (**1a**) which can be placed at C-5 and C-8, respectively, since the H-6 signal appeared as a doublet and H-8 as a triplet that shifted downfield upon acetylation

All proton signals of the basic skeletal arrangement of zoapatanolide C (**1a**) were mainly assigned by extensive ^{1}H NMR spin-decoupling experiments of the acetate **1c** in C_6D_6 Irradiation of the triplet of triplets at δ 3 9 (H-7, J = 10 5 Hz, J = 3 0 Hz) collapsed the exocyclic methylene doublets at δ 5 17 (J = 3 0 Hz) and 6 06 (J = 3 1 Hz) to singlets, the triplet at δ 5 04 (H-8, J = 10 5 Hz) to a doublet, and the doublet at δ 2 81 (H-6, J = 10 3 Hz) to a singlet Thus these signals can be assigned to H-8 and H-6 Furthermore, since H-6 is a doublet, the tertiary hydroxyl group must be placed at the C-5 position of the guaianolide skeleton, as in pumilin [3]

Irradiation at the frequency of H-8 (δ 5 04) affected one of the C-13 protons and changed the H-7 triplet of triplets to a doublet of doublets (J = 10 5 Hz, J = 3 0 Hz), and the broad doublet at δ 6 37 (H-9, J = 10 2 Hz) to a broad singlet Saturation of the H-6 doublet at δ 2 81 changed





2

1a R = OH, R^1 = H
1b R = R^1 = H
1c R = OH, R^1 = Ac
1d R = H, R^1 = Ac

*Contribution No 630 from Instituto de Quimica, U N A M

Table 1 ^{1}H NMR data* of zoapatanolides C (**1a**) and D (**1b**) and acetates **1c** and **1d** (80 MHz, $CDCl_3$, TMS as internal standard)

H	1a	1b	1c	1d
2	5 62 (5 4)† *s* (*br*)	5 77 (5 57 *s* (*br*)	5 65 (5 42) *s* (*br*)	5 76 (5 58) *s* (*br*)
3	3 75 (3 43 (*d*	3 66 (3 37) *d*	3 77 (3 39) *d*	3 65 (3 35) *d*
5	—	3 36 (2 74) *d*	—	3 39 (2 3–2 6) *d*
6	3 8–4 0 (2 9) *d*	3 64 (2 5) *t*	3 95 (2 81) *d*	3 76 (2 3–2 6) *d*
7	3 8–4 0 (3 72) *tt*	3 06 (2 11) *tt*	4 12 (3 9) *tt*	3 27 (2 3–2 6) *tt*
8	3 8–4 0 (3 32) *t*	3 76 (3 13) *td*	5 2 (5 04) *t*	5 12 (4 89) *t*
9	6 0–6 2 (6 0–6 2) *obs*	5 44 (5 15) *d* (*br*)	6 35 (6 37) *d* (*br*)	5 62 (5 46) *d* (*br*)
13a	6 2 (6 05) *s* (*br*)	6 23 (5 96) *dd*	5 45 (5 17) *d*	5 43 (5 12) *d*
13b	6 2 (6 24) *s* (*br*)	6 23 (6 18) *dd*	6 15 (6 06) *d*	6 15 (6 02) *d*
14	1 6 (1 47) *s* (*br*)	1 65 (1 46) *s* (*br*)	1 60 (1 52) *s* (*br*)	1 68 (1 54) *s* (*br*)
15	1 67 (1 5) *s*	1 69 (1 52) *s*	1 65 (1 46) *s*	1 68 (1 47) *s*
3′	6 1–6 3 (5 73) *q* (*br*)	6 15 (5 72) *qq*	6 2 (5 75) *qq*	6 17 (5 76) *q* (*br*)
4′	2 0 (1 93) *dq*	2 04 (1 91) *dq*	2 00 (1 94) *dq*	2 02 (1 95) *dq*
5′	1 97 (1 8) *s* (*br*)	1 99 (1 76) *quint*	1 85 (1 8) *quint*	1 86 (1 79) *quint*
AcO	2 1 (1 7) *s*	2 14 (1 64) *s*	2 03, 2 1 (1 63, 1 64) *s*	2 04, 2 11 (1 6, 1 63) *s*
OH	1 52 *d*, 2 92 *s*	2 54 *d*	3 07 *s* (*br*)	

J (Hz) 2, 3 = 1 9, 5, 6 = 10 2, 6, 7 = 10 3, 7, 8 = 10 5, 8, 9 = 10 2, 7, 13a = 3 0, 7, 13b = 3 1, 13a, 13b = 1 2, 3′, 4′ = 7 1, 3′, 5′ = 1 5, 4′, 5′ = 1 5

Numbers in parentheses are chemical shifts in C_6D_6

the H-7 signal to a doublet of triplets (J = 10 5 Hz, J = 3 0 Hz) and irradiation at the frequency of H-9 collapsed the H-8 triplet to a doublet and the broad C-14 methyl singlet to a doublet ($J \sim$ 1 0 Hz) Saturation of the broad H-2 signal at δ 5 42 changed the doublet at δ 3 39 (H-3, J = 1 9 Hz) to a singlet and also sharpened the C-14 methyl signal These results indicated a long-range *W*-coupling between H-14 and H-9 and a homoallylic coupling between H-14 and H-2 Conversely, irradiation of the C-10 vinyl methyl signal changed the H-9 broad doublet to a doublet of doublets (J = 10 2 Hz, $J \sim$ 1 0 Hz) and the H-2 broad singlet to a triplet ($J \sim$ 1 0 Hz) indicating coupling not only between H-14 and H-9 and H-14 and H-2, but also a residual coupling between H-9 and H-2 of the same magnitude The above spectral data established structure of zoapatanolide C (**1a**)

Zoapatanolide D (**1b**), $C_{22}H_{20}O_8$, mp 205–207°, differed from zoapatanolide C (**1a**) by the lack of a hydroxyl group, most likely the hydroxyl group at C-5, since the ^{1}H NMR spectrum showed an extra proton signal as a broad doublet at δ 3 36 (J = 10 2 Hz) and the H-6 signal as a triplet Acetylation of **1b** corroborated the above assumption since the IR spectrum of the acetylation product **1d** did not show hydroxyl absorption The ^{1}H NMR data of **1b** indicated close similarities with **1a** It showed the presence of an acetate, an angelate and a secondary hydroxyl group as in zoapatanolide C (**1a**), but the H-9 and the H-7 signals were shifted upfield to δ 5 44 and 3 06, respectively These differences in the chemical shifts of H-9 and H-7 strongly suggested that the configuration of the hydroxyl group at C-5 in zoapatanolide C (**1a**) must be α, and strongly deshields the α-protons at C-7 and C-9

The stereochemistry at C-5 in zoapatanolide D (**1b**) and at C-6, C-7, C-8 and C-9 in both **1a** and **1b** was derived from the coupling constants, which indicated a *trans*-diaxial relationship between these protons The α-orientation of the hydroxyl group at C-8 is also strongly suggested by the deshielding effect on one of the exocyclic methylene protons and the splitting of these signals due to the geminal coupling [5], which was clearly observed when the ^{1}H NMR spectrum of **1b** was run in C_6D_6

The stereochemistry of the acetate at C-2 and the epoxy group at C-3, 4 was assumed to be β and α by comparison with analogues [4, 5]

EXPERIMENTAL

Montanoa tomentosa Cerv (2 9 kg), collected at the UNAM Campus, Mexico City in July 1980, was extracted and fractionated as described before [2] The $CHCl_3$ fractions were combined and percolated on a column packed with 300 g Tonsil optimum extra (supplied by Tonsil Mexicana) and eluted with petrol, $CHCl_3$–Me_2CO Fourteen fractions (500 ml) were collected

Zoapatanolide C (**1a**) From fractions 3–5, after repeated chromatography, **1a** was obtained as an amorphous solid (mp 110–115°), which was recrystallized from $CHCl_3$–Et_2O $C_{22}H_{26}O_9$, mp 117–118°, UV λ_{max}^{MeOH} nm (ε) 207 (11 544), IR ν_{max}^{KBr} cm^{-1} 3430, 1762, 1718, 1630, EIMS (probe) *m/z* (rel int) 256 [M – AngOH – HOAc – H_2O]$^+$ (1 1), 228 [256 – CO_2], (0 8), 83[C_7H_5O]$^+$ (100 0), 55 [C_4H_7]$^+$ (25 0), 43 [C_2H_3O] (9 7), CIMS (isobutane) *m/z* 435 [MH]$^+$ (1), 417 [MH – H_2O]$^+$ (5), 375 [MH – HOAc]$^+$ (10), 335 [MH – AngOH]$^+$ (3), 275 [MH – HOAc – AngOH]$^+$ (13), 257 [MH – HOAc – AngOH – H_2O]$^+$ (35), 239 [MH – HOAc – AngOH – $2H_2O$]$^+$ (18), 101 [AngOH + 1]$^+$ (100)

Zoapatanolide C acetate (**1c**) **1a** (35 mg) was acetylated with Ac_2O–pyridine and worked up as usual to give 20 mg **1c** as a gum UV λ_{max}^{MeOH} nm (ε) 206 (51 646), IR ν_{max}^{film} cm^{-1} 3440, 1783, 1740, 1670, 1650, EI MS (probe) *m/z* (rel int) 476 [M]$^+$ (0 3), 416 [M – 60]$^+$ (0 1), 376 [M – 100]$^+$ (0 3), 316 [M – 100 – 60]$^+$ (0 6), 83 [C_5H_7O]$^+$ (100 0), 55 [C_4H_7]$^+$ (16 2), 43 [C_2H_3O]$^+$ (12 1)

Zoapatanolide D (**1d**) Fraction 2 was rechromatographed on silica gel and eluted with petrol and mixtures of petrol–EtOAc From fractions eluted with petrol–EtOAc (4 1), **1b** was obtained as a solid which was crystallized from $CHCl_3$–Et_2O, $C_{22}H_{20}O_8$, mp 202–204°, UV λ_{max}^{MeOH} nm (ε) 205 (15965), IR ν_{max}^{KBr} cm^{-1} 3430, 1760, 1720, 1632, EIMS (probe) *m/z* (rel int) 418 $[M]^+$ (0 5), 358 $[M-60]^+$ (0 15), 318 $[M-100]^+$ (0 2), 83 $[C_5H_7O]^+$ (100 0), 55 $[C_4H_7]^+$ (23 4), 43 $[C_2H_3O]^+$ (10 1)

Zoapatanolide D acetate (**1d**) Acetylation of 14 5 mg **1b** gave the acetate **1d** as a gum after prep TLC UV λ_{max}^{MeOH} nm (ε) 205 (14048), IR ν_{max}^{film} cm^{-1} 1780, 1750, 1735, 1650, EIMS (probe) *m/z* (rel int) 460 $[M]^+$ (0 7), 401 $[M-59]^+$ (0 5), 361 $[M-99]^+$ (1 1), 340 $[M-120]^+$ (0 3), 83 $[C_5H_7O]^+$ (100 0), 55 $[C_4H_7]^+$ (20 3), 43 $[C_2H_3O]^+$ (11 6)

Acknowledgements—We thank Mrs T German and Mr F Ramos, Herbarium of the Instituto de Biologia (U N A M), for identification of the plant material and Messrs R Saucedo, J Cardenas, H Bojorquez, L Velasco, R Villena and A Toscano for ^1H NMR, IR, UV and mass spectra

REFERENCES

1 Quijano, L, Calderón, J S, Gómez, G F and Rios, T (1979) *Phytochemistry* **18**, 843
2 Quijano, L, Calderón, J S, Gómez, G F and Rios, T (1982) *Phytochemistry* **21**, 2041
3 Korp, J D, Bernal, I, Fischer, N H, Leonard, C, Lee, I Y and LeVan, N (1982) *J Heterocycl Chem* **19**, 181
4 Herz, W, Bhat, S W and Srinivasan, A (1972) *J Org Chem* **37**, 2532
5 Salmón, M, Diaz, E and Ortega, A (1973) *J Org Chem* 1759