Pergamon

0031-9422(95)00965-5

Phytochemistry, Vol. 42, No. 2, pp. 565–567, 1996

0031-9422/96 $15.00 + 0.00

MAURITINE J, A CYCLOPEPTIDE ALKALOID FROM *ZIZYPHUS MAURITIANA*

AKINO JOSSANG, ABDELLATIF ZAHIR and DANDIO DIAKITE

Laboratoire de Chimie, URA 401 CNRS, Muséum National d'Histoire Naturelle, 63 rue Buffon, 75005 Paris, France

(*Received* 6 *November* 1995)

Key Word Index—*Zizyphus mauritiana*; Rhamnaceae; root bark; cyclopeptide alkaloid; mauritines E and J; NMR.

Abstract—A new cyclopeptide alkaloid, mauritine J, besides known alkaloids, was isolated from the root bark of *Zizyphus mauritiana*. Its structure was established by homo- and hetero-nuclear 2D NMR analysis and compared with that of amphibine E.

INTRODUCTION

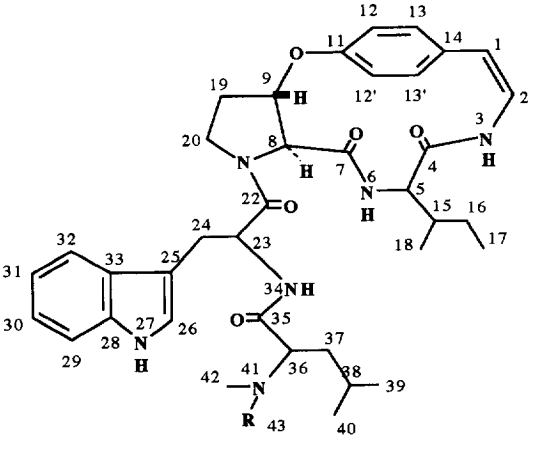
A number of *Zizyphus* species have been investigated due to the presence of cyclopeptide alkaloids, particularly common in rhamnaceous plants [1]. Some *Zizyphus* species have been found to possess sedative, analgesic, anti-inflammatory, hypoglycaemic [1, 2], antibacterial and antifungal activities [3]. Previous chemical studies of *Z. mauritiana* Lam. led to the isolation of the cyclopeptide alkaloids, mauritines A and B [4], C–F [5], G and H [6], frangufoline [4], amphibines D [4], E [5, 7], B and F [5]. Most of these alkaloids belong to the structural type with a 14-membered ring system containing *trans*-3-aryloxyproline, *p*-oxystyrylamine and one α-amino acid residues. In this paper, we describe the isolation and characterization of a new cyclopeptide, named mauritine J (**1**), from *Z. mauritiana*.

RESULTS AND DISCUSSION

Extensive chromatography on silica gel of the alkaloid extract of root bark and preparative TLC furnished minor amounts of **1**, in addition to other alkaloids found previously in this genus. Compound **1**, an amorphous solid displayed an intense pseudomolecular ion $[M+H]^+$ at *m/z*, 657 in its CI mass spectrum, allowing the deduction of the molecular formula $C_{37}H_{48}N_6O_5$, supported by ^1H and ^{13}C NMR spectra (Table 1).

The ^1H–^1H and ^1H–^{13}C COSY spectra displayed typical signals of *N*-methyl and spin systems of amino acid units of isoleucine, 3-oxygenated proline, leucine and tryptophan. The presence of a *para*-oxygenated *Z*-styrylamino group suggested that **1** was a 14-membered cyclopeptide alkaloid. These subgroups were connected by analysis of HMBC spectra (Fig. 1). The signal at δ 166.98 showed cross-peaks with δ 6.51 of *p*-oxystyrylamino-NH-3 and δ 4.20 of isoleucyl Hα-5. The carbonyl signal at δ 170.56 gave cross-peaks with isoleucyl NH-6 at δ 6.58 and Hα-8 at δ 4.25 and Hβ-9 at δ 5.43 of β-oxyproline; C-14 at δ 132.56 with H-2 at δ 6.73 and H-12′ at δ 122.32; C-11 at δ 157.40 with H-13 and H-13′ at δ 7.09 and 7.05, respectively. Hence, the 14-membered cyclopeptide feature was confirmed. The connection of the *N*-methyl at δ 2.38 with leucyl Hα-36 at δ 2.98 indicated that *N*-methylleucine was the terminal amino acid. The carbonyl at δ 174.81 also exhibited cross-peaks with leucyl H-36 and NH-34 at δ 7.73 of tryptophan. Thus, the tryptophyl carbonyl (C-22) was connected to the prolyl N in spite of the absence of a cross-peak between them.

Further evidence was provided by a NOESY spec-



Mauritine J **1**: **R** = H
Amphibine E **2**: **R** = CH_3

Table 1. ^1H and ^{13}C NMR data for compounds **1** and **2** ($CDCl_3$, 300 and 75 MHz)

	1		**2**	
No.	δ_C	δ_H *J* (Hz)	δ_C	δ_H *J* (Hz)
1	114.54	6.30 *d* 7.7	114.80	6.29 *d* 7.7
2	125.44	6.73 *dd* 7.7, 10.5	125.41	6.72 *dd* 7.7, 10.5
3	NH	6.51 *d* 10.5	NH	6.52 *d* 10.5
4	166.98	—	167.03	—
5	59.05	4.20 *dd* 8.5, 3.0	59.02	418 *dd* 8.5, 3.0
6	NH	6.58 *d* 8.5	NH	6.62 *d* 8.5
7	170.56	—	170.58	—
8	63.90	4.25 *d* 5.5	63.95	4.25 *d* 5.5
9	83.49	5.43 *m*	83.51	5.42 *m*
11	157.40	—	157.40	—
12	122.60	7.24 *m*	122.55	7.22 *m*
12′	122.32	7.18 *m*	122.28	7.20 *m*
13	130.17	7.09 *m*	132.38	7.08 *m*
13′	132.44	7.05 *m*	132.54	7.05 *m*
14	132.56	—	132.54	—
15	35.26	2.22 *m*	35.31	2.19 *m*
16	23.78	1.15 *m*	23.79	1.08 *m*
		1.30 *m*		1.29 *m*
17	12.24	0.88 *t* 6.5	12.19	0.89 *t* 6.5
18	16.09	0.82 *d* 7.0	16.06	0.80 *d* 7.0
19	31.82	2.00 *m*	32.05	2.02 *m*
		2.32 *m*		2.30 *m*
20	46.43	2.50 *m*	46.47	2.55 *m*
		3.79 *dd* 8.3, 11.5		3.90 *dd* 8.3, 11.5
22	171.46	—	171.64	—
23	50.00	5.00 *ddd* 6.2, 8.0, 8.5	50.18	5.05 *ddd* 6.2, 8.0, 8.5
24	29.34	2.90 *dd* 8.0, 14.5	29.06	2.90 *dd* 8.0, 14.5
		3.13 *dd* 6.2, 14.5		3.10 *dd* 6.2, 14.5
25	110.03	—	109.92	—
26	122.71	6.76 *d* 2.5	122.38	6.75 *d* 2.5
27	NH	8.12 *br s*	NH	8.41 *br s*
28	135.94	—	136.03	—
29	111.23	7.31 *d* 8.0	111.27	7.28 *d* 8.0
30	122.82	7.10 *m*	122.55	7.10 *m*
31	119.81	7.12 *m*	119.78	7.10 *m*
32	118.53	7.68 *d* 8.0	118.35	7.64 *d* 8.0
33	127.40	—	127.27	—
34	NH	7.73 *d* 8.5	NH	7.55 *d* 8.5
35	174.81	—	175.42	—
36	63.34	2.98 *dd* 5.0, 9.2	66.93	2.88 *dd* 5.0, 9.2
37	42.54	1.25 *m*	36.36	1.25 *m*
		1.42 *m*		1.48 *m*
38	25.04	1.59 *m*	25.94	1.59 *m*
39	21.82	0.87 *d* 6.5	22.12	0.85 *d* 6.5
40	23.16	0.89 *d* 6.5	23.16	0.85 *d* 6.5
42	35.43	2.38 *s*	41.96	2.15 *s*
43	NH	1.90 *br s*	41.96	2.15 *s*

trum (Fig. 1). The principle cross-peaks were observed between H-36 and NH-34, connecting *N*-methylleucine to tryptophan; between H-23 (δ 5.00) and H-20 (δ 3.79), bonding the tryptophan to proline; and between H-9 and H-12 (δ 7.24) confirming a C-9-O-C-11 ether linkage. H-8 was situated in proximity to NH-6 and H-12′ (δ 7.18); H-5 was close to CH_3-18 (δ 0.82). Noteworthy differences between ^1H and ^{13}C NMR assignments for the leucyl-tryptophyl side-chain were observed between **1** and its *N*-methyl derivative, amphibine E (**2**).

Rhamnaceous cyclopeptide alkaloids are generally composed of L-amino acids [1, 4] and 2*S*,3*S*-*trans*-3-hydroxy-L-proline [1, 7], as well as **2** [7], $[\alpha]_D$ −187.2° (methanol). Compound **1**, determined as *N*-demethylamphibine E and laevorotatory, $[\alpha]_D$ −175.9° (methanol), should have the same absolute configuration, and be built up by L-amino acids, just like **2**.

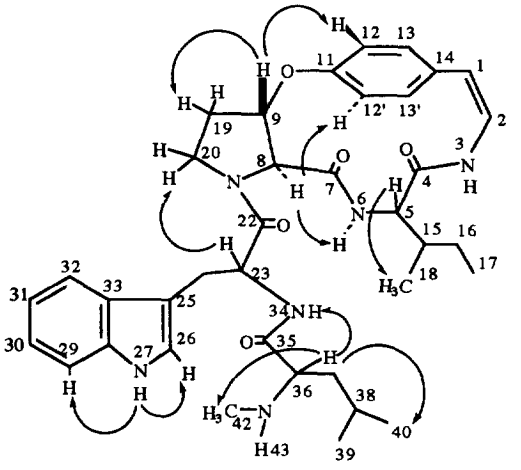


Fig. 1. Selected NOEs for compound **1**.

EXPERIMENTAL

General. ^1H and ^{13}C NMR spectra were recorded with δ (ppm) scale and TMS as int. standard. TLC was performed on Kieselgel GF254 plates (Merck). Alkaloids were detected with Dragendorff's reagent.

Extraction and isolation. Powdered root bark of *Z. mauritiana* Lam. (500 g), collected in Mali, was moistened with 10% NH_4OH and percolated by EtOAc. A 5% citric acid soln of the extract was rendered alkaline and extracted with CH_2Cl_2 furnishing crude alkaloids (1.15 g). The crude base was repeatedly fractionated on a silica gel column eluting with CH_2Cl_2–MeOH mixts of increasing polarity. Further prep. TLC purification (CH_2Cl_2–MeOH, 93:7) of the amphibin E-containing fr. afforded pure **1** (11 mg) and **2** (93 mg).

Mauritine J (**1**). Amorphous. $[\alpha]_D$ −175.9° (MeOH, *c* 1.0). UV, λ_{max}^{MeOH} nm: 220, 270, 281, 290. IR ν_{max}^{KBr} cm^{-1}: 3390 (NH), 1691 (CONH), 1235, 1040 (C-O-C). CIMS, *m/z* (rel. int.): 658 ($[M+H]^+ + 1$, 60), 657 ($[M+H]^+$, 100); $C_{37}H_{48}N_6O_5$.

Amphibine E (**2**). Amorphous. $[\alpha]_D$ −187.2° (MeOH, *c* 1.0), lit. −175° (MeOH, *c* 0.14) [7]. CIMS, *m/z* (rel. int.): 672 ($[M+H]^+ + 1$, 68), 671 ($[MH]^+$, 100); $C_{38}H_{50}N_6O_5$.

Acknowledgement—We are grateful to Dr J. P. Brouard for mass spectra.

REFERENCES

1. Tschesche, R. and Kaussmann, E. U. (1975) in *The Alkaloids* (Manske, R. H. F., ed.), Vol. XV, pp. 165–205. Academic Press, New York.
2. Anand, K. K., Singh, B., Chand, D., Chandan, B. K. and Gupta, V. N. (1989) *J. Ethnopharmacol.* **27**, 121.
3. Pandey, V. B. and Devi, S. (1990) *Planta Med.* **56**, 649.
4. Tschesche, R., Wilhelm, H. and Fehlhaber, H.-W. (1972) *Tetrahedron Letters* 2609.
5. Tschesche, R., Wilhelm, H., Kaussmann, E. U. and Eckhardt, G. (1974) *Liebigs Ann. Chem.* 1694.
6. Tschesche, R., Hillebrand, D., Wilhelm, H., Ammermann, E. and Eckhardt, G. (1977) *Phytochemistry* **16**, 1025.
7. Tschesche, R., Kaussmann, E. U. and Fehlhaber, H.-W. (1972) *Chem. Ber.* **105**, 3094.