Phytochemistry, Vol. 26, No. 6, pp. 1847–1848, 1987.
Printed in Great Britain.

0031-9422/87 $3.00 + 0.00
Pergamon Journals Ltd.

LOESENERINE, AN ALKALOID FROM *MAYTENUS LOESENERI*

MARÍA DÍAZ, ALFRED PREISS* and HELMUT RIPPERGER*

Institute of Botany, Academy of Sciences of Cuba, Havana, Cuba; *Institute of Plant Biochemistry, Academy of Sciences of the GDR, Halle (Saale), G.D.R.

(*Received* 24 *September* 1986)

Key Word Index—*Maytenus loeseneri*; Celastraceae; spermidine alkaloid; loesenerine.

Abstract—Loesenerine has been isolated from *Maytenus loeseneri* and its structure has been elucidated as (*R*)-1-acetyl-8-[(*Z*)-1-heptenyl]-1,5,9-triazacyclotridecan-6-one.

From leaves of *Maytenus loeseneri* Urb. the alkaloid loesenerine has been isolated. Its structure of (*R*)-1-acetyl-8-[(*Z*)-1-heptenyl]-1,5,9-triazacyclotridecan-6-one (**1**) is in accordance with spectroscopic measurements as outlined below. Similar macrocyclic spermidine alkaloids, especially with regard to the incorporation of spermidine, also occur in other *Maytenus* species and other members of the Celastraceae [1–4].

The IR spectrum indicated a secondary amide group. The elemental composition was shown to be $C_{19}H_{35}N_3O_2$ by high resolution MS. The fragment **a** arose by α-cleavage (7,8-bond) followed by elimination of an amide. The appearance of **a** is in accordance with a 13-membered ring and four unsubstituted CH_2 groups between N-1 and N-9 (*cf.* [1, 3]). A 13-membered ring seemed to be very probable for biogenetic reasons. The 14,15-position of the double bond explained the relatively low intensity of the cleavage of the side chain (m/z = 240). **d** was very intense and could be understood by allyl rearrangement of the double bond to the 8,14-position followed by cleavage of the 14,15-bond to give a very stable ion. An alternative explanation for m/z = 266 could be a structure with a C_5-side chain and a 15-membered ring. But the expected fragment analogous to **a**, for this case at m/z = 154, had only a low intensity. **b** and **c** were formed by elimination to yield the acyclic derivative **2** and subsequent cleavage of the 4,5- (*cf.* [1, 3]) and 6,7- bond, respectively. Loss of NH_3 gave **e** from **c**.

In the ^{13}C NMR spectrum of **1** more than the expected number of signals were observed at room temperature (Table 1) as a consequence of a dynamic process, probably of the *cis*/*trans* isomerization around the partial C–N double bond of the lactam ring [5]. Thus, with the exception of C-8 for each carbon atom of the 13-membered ring, two signals were observed in toluene, whereas in chloroform and in 1,1,2,2-tetrachloroethane, respectively, some of these signal pairs coalesced or were already averaged. An inverse gated spectrum in chloroform indicated that the populations of the two isomers at room temperature were approximately equal. An averaged spectrum was observed at 140° in 1,1,2,2-tetrachloroethane. The assignment of the majority of the ring carbons could only be made in groups. C-6, C-7 and C-8 were identified by comparison with the ^{13}C NMR data of palustrine [6], furthermore C-7 by the large $\Delta\nu$ value (190 Hz) in the slow exchange limit (*cf.* [5]) and C-8 by its doublet structure in the SFORD spectrum. In the ^1H NMR spectrum the proton attached to C-8 was located at δ = 3.70 by selective $^{13}C\{^1H\}$ decoupling. On the other hand, the connectivity between H-8 and the high-field olefinic proton was proved by homonuclear spin decoupling, thus indicating the position of the double bond. The signals of the side chain carbons were assigned by selective $^{13}C\{^1H\}$ decoupling and comparison with the ^{13}C chemical shifts of *cis*- and *trans*-3-nonene, respectively [7]. From chemical shift comparison of C-16 in **1** with C-5 in *cis*- and *trans*-3-nonene, respectively, the *cis*-configuration at the double bond was probable. Further evidence for this followed from the vicinal $^1H,^1H$ coupling constant ($^3J_{14,15}$ = 10.5 Hz), which was de-

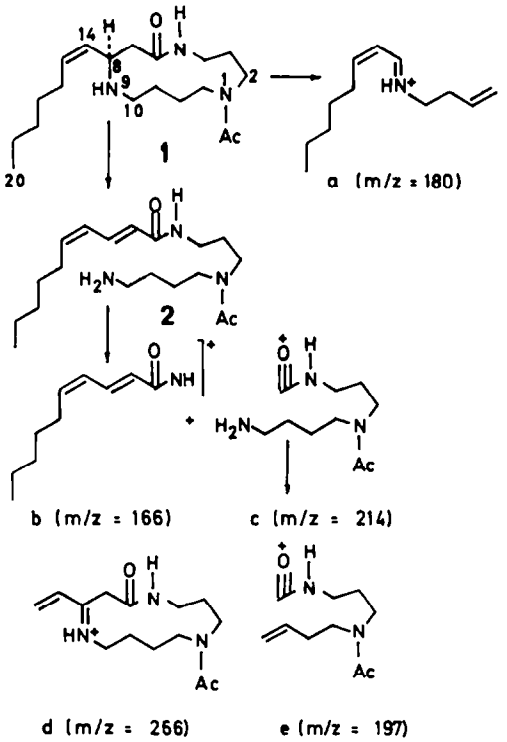

Table 1. ^{13}C NMR chemical shifts* of loesenerine (1)

Carbon	$CDCl_3$ 30°	1,1,2,2-Tetrachloroethane-d_2 30°	140°
C-$\underline{CH_2}$-C	23.0, 24.7	Coalescence	24.2 (*t*)
	24.1, 24.9	24.3	24.5 (*t*)
	27.7, 28.6	Coalescence	28.3 (*t*)
C-$\underline{CH_2}$-N	36.6, 36.9	36.9	37.0 (*t*)
	42.2	42.0	42.2 (*t*)
	42.9, 45.1	Coalescence	44.0 (*t*)
	44.7	44.8	45.3 (*t*)
C-6	171.9, 172.1	171.3	170.7 (*s*)
C-7	43.4, 47.2	Coalescence	45.6 (*t*)
C-8	52.9	53.1	53.5 (*d*)
C-14	130.7, 130.9	129.3	129.1 (*d*)
C-15	132.5, 132.7	133.3	133.5 (*d*)
C-16	27.7	27.6	27.5 (*t*)
C-17	29.4	29.2	29.0 (*t*)†
C-18	31.5	31.4	31.2 (*t*)†
C-19	22.5	22.4	22.2 (*t*)
C-20	14.0	14.0	13.5 (*q*)
Ac (Me)	21.3, 21.4	21.3	20.8 (*q*)
Ac (CO)	169.9	169.9	169.6 (*s*)

*In ppm downfield from internal TMS.
†Assignment may be interchanged.

termined by analysis of the olefinic signals by means of spin decoupling and spectrum simulation.

The positive optical rotation of 1 was compared with that of (*R*)-(+)-3-methoxybut-1-ene [8] and indicated the (*R*)-configuration of the alkaloid.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded at 200.13 and 50.33 MHz, respectively. The inverse gated ^{13}C NMR spectrum was run with a pulse flip angle of *ca* 30° and a relaxation delay of 7 sec using the DISNMRP microprogram INVGAT. For the selective $^{13}C\{^1H\}$ decoupling experiments the ^1H NMR spectrum was recorded over the decoupler channel. The power for selective decoupling was 10 dB below 0.2 W. The simulation of the ^1H partial spectrum of the olefinic protons was performed with the microprogram PANIC version 820601.

Plant material. M. loeseneri Urb. was collected in September in Mina vieja de la Melba, Moa, Province de Holguín, Cuba, and identified by Tec. Ramona Oviedo, Havana. A voucher specimen has been deposited at the Herbarium of the Institute of Botany, Academy of Sciences of Cuba, Havana.

Loesenerine (1). Dried (40°) and ground leaves were extracted with EtOH at room temp. Evapn of the EtOH *in vacuo* gave a residue which was partitioned between 0.5 M HCl and C_6H_6–Et_2O (1:1). After addition of $KHCO_3$ to the aq. layer, the latter was extracted with $CHCl_3$–EtOH (2:1). Evapn of the solvents gave raw material which was chromatographed over silica gel G using $CHCl_3$–MeOH (19:1) and later over silica gel G containing 9% $AgNO_3$ using $CHCl_3$–MeOH (9:1). The soln of 1 in $CHCl_3$ was treated with aq. $KHCO_3$ in order to eliminate silver ions. Crystallization from EtOAc afforded crystals; yield 0.03%; mp 117°, $[\alpha]_D^{22}$ + 45.4° ($CHCl_3$; *c* 0.52). ν_{max}^{KBr} cm^{-1}: 3356, 3277 (NHCO), 1630 (N–CO), 1560 (NHCO). MS 70 eV, *m/z* (rel. int.): 337.2723 $[M]^+$, calc. for $C_{19}H_{35}N_3O_2$ 337.2729 (100), 322 $[M-Me]^+$ (3), 308.2347 $[M-Et]^+$, calc. for $C_{17}H_{30}N_3O_2$ 308.2338 (12), 294.2552 $[M-Ac]^+$, calc. for $C_{17}H_{32}N_3O$ 294.2545 (30), 294.2199 $[M-C_3H_7]^+$, calc. for $C_{16}H_{28}N_3O_2$ 294.2181 (10), 266.1851 $[d]^+$, calc. for $C_{14}H_{24}N_3O_2$ 266.1868 (72), 240.1703 $[M-C_7H_{13}]^+$, calc. for $C_{12}H_{22}N_3O_2$ 240.1712 (14), 214.1546 $[c]^+$, calc. for $C_{10}H_{20}N_3O_2$ 214.1555 (17), 197.1265 $[e]^+$, calc. for $C_{10}H_{17}N_2O_2$ 197.1290 (24), 180.1744 $[a]^+$, calc. for $C_{12}H_{22}N$ 180.1752 (39), 166.1600, calc. for $C_{11}H_{20}N$ 166.1596 (17), 166.1233 $[b]^+$, calc. for $C_{10}H_{16}NO$ 166.1232 (17). ^1H NMR ($CDCl_3$, TMS): δ 0.90 (*t*, $^3J_{20,19}$ = 7.0 Hz, 3H, H_3-20), 2.10, 2.11 (two *s*, together 3H, N-Ac), 3.70 (*m*, 1H, H-8), 5.11 (*t*, $^3J_{14,8}$ = 10.0 Hz, $^3J_{14,15}$ = 10.5 Hz, 1H, H-14), 5.33 (*dt*, $^3J_{15,16a} + {}^3J_{15,16b}$ = 15.0 Hz, $^3J_{15,14}$ = 10.5 Hz, 1H, H-15), 7.62 (*br s*, 1H, NH), 8.16 (*br s*, 1H, NH).

Acknowledgement—We thank Dr. P. Franke, Berlin, for the high resolution MS.

REFERENCES

1. Kupchan, S. M., Hintz, H. P. J., Smith, R. M., Karim, A., Cass, M. W., Court, W. A. and Yatagai, M. (1977) *J. Org. Chem.* **42**, 3660.
2. Wagner, H., Burghart, J. and Hull, W. E. (1978) *Tetrahedron Letters* 3893.
3. Ripperger, H. (1980) *Phytochemistry* **19**, 162.
4. Diaz, M. and Ripperger, H. (1982) *Phytochemistry* **21**, 255, 1475.
5. Williamson, K. L. and Roberts, J. D. (1976) *J. Am. Chem. Soc.* **98**, 5082.
6. Rüedi, P. and Eugster, C. H. (1978) *Helv. Chim. Acta* **61**, 899.
7. Couperns, P. A., Clague, A. D. H. and van Dougen, J. P. C. M. (1976) *Org. Magn. Reson.* **8**, 426.
8. Klyne, W. and Buckingham, J. (1978) *Atlas of Stereochemistry. Absolute Configurations of Organic Molecules*, 2nd edn, Vol. 1, p. 5. Chapman and Hall, London.