

NEW ALKALOID FROM *SCHULTESIA GUIANENSIS*

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Schultesia guianensis Malme is a wild shrub of the Gentianaceae family, occurring in Africa and tropical America. In northeastern Brazil it has the popular name of "mata zombando," because it is considered to be highly toxic toward cattle (1).

The aerial part of the plant was brought to our laboratory by a farmer who reported cattle poisoning on his farm in the county of Quixadá, Ceará. Earlier reports in the literature showed that the plant is toxic to cows when fresh plant is administered in the amount of 30 g/kg (2).

A positive Dragendorff's test suggested the presence of alkaloids and stimulated a detailed chemical screening of the basic fraction of the plant extracts.

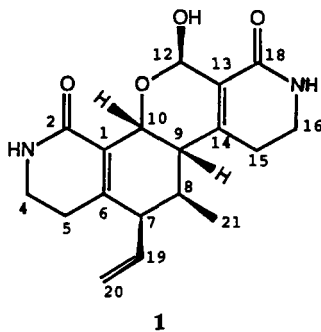
An EtOH extract from the dry plant (6.1 kg) was concentrated and extracted with 1 N HCl, giving, after traditional workup (see Experimental section), the crude bases (23.0 g). Si gel chromatography of the basic fraction (20.0 g) allowed the isolation of four pure substances.

Three compounds were shown to be the well-known alkaloids gentianine [4-(2-hydroxyethyl)-5-vinylnicotinic acid lactone], gentiocrucine (3-aminomethylene-dihydropyran-2,4-dione), and gentianidine [4-(2-hydroxyethyl)-6-methylnicotinic acid lactone], by spectroscopic studies and, in the case of gentianine and gentianidine, by comparison of melting points with those recorded in the literature (3). This is the first report of the presence of gentianine, gentiocrucine, and gentianidine in the *Schultesia* genus; they may be artifacts formed from the

reaction of terpenoids with the NH₃ used in isolation, as indicated earlier (3).

The fourth compound was isolated as white crystals, mp 192.0–193.0°. Its ir spectrum showed absorptions for hydroxyl (3550 cm⁻¹) amide (3300, 770 cm⁻¹), vinyl 930 (cm⁻¹) and lactam carbonyl groups (1680 cm⁻¹). Its ¹H-nmr spectrum (Table 1) showed the presence of methyl, methylene, and methine protons, together with an unconjugated vinyl group and a hydroxyl group. The mass spectrum showed a molecular ion at *m/z* 330, in agreement with the composition C₁₈H₂₂N₂O₄.

The structure of the compound was shown to be that of the novel dilactam alkaloid **1** by X-ray crystallography corresponding to (4*bS*, 5*S*, 6*R*, 10*bR*, 12*R*)-3,4,4*b*,5,6,7,8,9,10*b*,12-decahydro-12-hydroxy-5-methyl-6-vinyl-1*H*-pyrido[4',3':4,5]pyrano[3,2-*b*]isoquinoline-1,10(2*H*)-dione.¹ An ORTEP diagram of **1** is shown in Figure 1, and atomic coordinates are given in Table 2. The structure **1** is supported by its 2D



¹We are grateful to Dr. Kurt Loening, Director of Nomenclature of the Chemical Abstract Service, for naming this structure.

TABLE 1. 2D ^1H nmr (300 MHz) for Compound 1 in CD_2Cl_2 .

Proton	δ	Coupling Observed [Proton and Coupling Constant (Hz)]
H-4	4.4 (m)	H-5
H-5 ^a	2.2 (m)	H-4
H-7	2.3 (m)	H-19
H-8	2.9 (dd)	H-21, $J_{8,21} = 7.2$
H-9	2.1 (dd)	H-9, $J_{8,9} = 8.0$
H-10	5.0 (d)	H-8, $J_{9,8} = 8.0$
H-12	5.7 (d)	H-10, $J_{9,10} = 0.8$
H-15 ^a	2.6 (m)	H-9, $J_{10,9} = 0.8$
H-16	2.7 (m)	OH
H-19	4.4 (m)	H-16
H-20	5.6 (m)	H-15
H-20'	5.3 (dd)	H-7
H-21	5.2 (dd)	H-20, $J_{19,20} = 10.2$
OH	1.0 (d)	H-20', $J_{19,20'} = 17.8$
NH	3.8 (d)	H-19, $J_{20,19} = 10.2$
	1.9 (m)	H-20', $J_{20,20'} = 0.8$
		H-19, $J_{20',19} = 17.8$
		H-20, $J_{20',20} = 0.8$
		H-8, $J_{21,8} = 7.2$
		H-12
		—

^aAssignments may be interchanged.

^1H -nmr spectrum (Table 1); in particular, the coupling constant of the vicinal H-7 and H-8 protons suggests a dihedral angle of 90° and shows that both are on the same side of the molecule.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded as KBr pellets on a Perkin-Elmer 720 spectrometer. ^1H -nmr spectra were performed on a Varian EM-360 (60 MHz) or

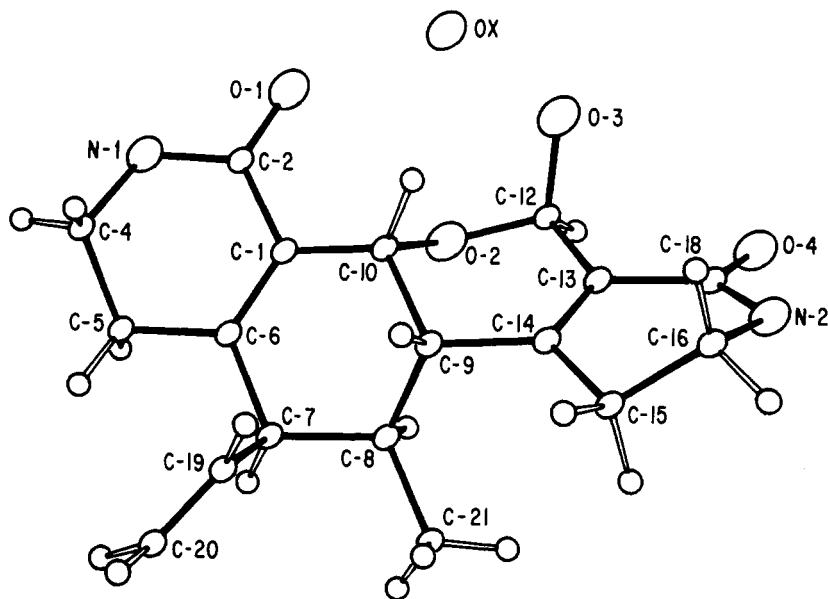


FIGURE 1. ORTEP diagram of compound 1.

TABLE 2. Atomic Coordinates ($\times 10$) and Temperature Factors ($A \times 10$) for Compound 1.

Atom	x	y	z	U
Ox	9388(6)	2351(3)	401(4)	88(2)
C-1	7980(5)	-303(3)	973(4)	32(2)
O-1	9661(4)	834(2)	1677(3)	49(2)
C-2	9036(5)	200(3)	1897(5)	41(2)
N-1	9320(4)	-12(2)	3028(3)	28(1)
C-4	8851(7)	-852(4)	3271(5)	58(3)
C-5	7291(7)	-1020(4)	2561(5)	49(2)
C-6	7128(5)	-872(3)	1273(4)	37(2)
C-7	5960(5)	-1391(3)	384(4)	37(2)
C-8	5595(5)	-997(3)	-859(4)	37(2)
C-9	7016(5)	-813(3)	-1136(4)	31(2)
C-10	7909(5)	-139(3)	-283(4)	30(2)
O-2	7228(4)	700(2)	-603(3)	37(1)
C-12	7387(6)	1012(3)	-1679(5)	42(2)
O-3	8818(4)	1280(2)	-1527(3)	53(2)
C-13	6999(5)	323(3)	-2607(4)	38(2)
C-14	6822(5)	-502(3)	-2379(4)	36(2)
C-15	6508(6)	-1144(4)	-3380(5)	51(2)
C-16	7224(6)	-835(4)	-4261(5)	55(3)
N-2	6782(4)	29(3)	-4663(3)	36(2)
C-18	6768(6)	596(4)	-3853(5)	54(3)
O-4	6533(5)	1365(3)	-4130(4)	72(2)
C-19	6455(6)	-2324(3)	446(5)	53(2)
C-20	5883(8)	-2951(4)	882(6)	77(3)
C-21	4490(6)	-1553(4)	-1767(5)	55(3)

on a Varian XL-300 (300 MHz). The latter was also used for 2D nmr experiments. Mass spectra were recorded on a Hewlett-Packard HP 5995 gc-ms operating in the electron impact mode at 70 eV or on a Finnigan 4000 gc-ms.

ISOLATION PROCEDURE.—*S. guianensis* (20.0 kg fresh whole plant) was collected in Itapiúna-Ce, northeastern Brazil. Voucher specimens are registered under numbers 12.711 and 13.214 in the Herbarium Prisco Bezerra of Universidade Federal do Ceará. Ground material (6.1 kg), after air-fanned oven drying at 50°, was extracted in a semi-industrial Soxhlet system with EtOH at approximately 70°. The EtOH extract, after solvent evaporation, was treated with 1 N HCl solution, filtered, and extracted with CHCl₃ to yield 47.4 g after concentration. The acid aqueous phase was neutralized with NH₄OH and extracted with CHCl₃ to provide 23.0 g of free bases after low pressure distillation at approximately 60°. The latter 20.0 g was coarsely partitioned on Si gel by elution with CHCl₃ followed by EtOAc, Me₂CO, and finally MeOH. Rechromatography of these fractions on a Si gel column yielded 400.0 mg of gentianine (white crystals, mp 79.5–80.5°), 78.0 mg of gentiocrucine (white crystals, mp 144.4–145.6°), 245.0 mg of gentianidine (pale yellow crystals, mp 129.0–130.0°), and 31.0 mg of compound 1.

Compound 1.—Ir (KBr) 3550, 3300, 3030, 3080, 2970, 1680, 1650, 1640, 1445, 1375, 1405, 1285, 1050, 1000, 930, 770 cm⁻¹; ¹H nmr (300 MHz) δ 1.0 (d, 3H), 1.9 (m, 2H), 2.1 (dd, 1H), 2.2 (m, 1H), 2.3 (m, 1H), 2.6 (m, 1H), 2.7 (m, 1H), 2.3 (m, 1H), 2.9 (dd, 1H), 3.8 (d, 1H), 4.4 (m, 4H), 5.0 (d, 1H), 5.2 (dd, 1H), 5.3 (dd, 1H), 5.6 (m, 1H), 5.7 (d, 1H); ms *m/z* (rel. int.) [M]⁺ 330, [M-OH]⁺ 313, [M-H₂O]⁺ 312, [312-OH]⁺ 295, [313-HNCH₂-2H₂]⁺ 280, [280-CO]⁺ 252, [252-C₂H₄]⁺ 224, [312-CO-H₂O]⁺ 266, [M-C₉H₉NO₂]⁺ 167, [167-H₂O]⁺ 149.

X-RAY STRUCTURAL DETERMINATION OF COMPOUND 1.²—A single crystal of 1 was obtained by recrystallization from CHCl₃. X-ray data collection was performed with a Nicolet R3m automated diffractometer equipped with MoK α target tube (λ 0.710730) and a graphite-crystal monochromator. The crystal data are space group P2₁/n; *a* = 9.7183(30), *b* = 15.5216(50),

²Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.

and $c = 11.9797(30) \text{ \AA}$; $\alpha = 90.00^\circ$, $\beta = 108.164^\circ$, and $Z = 4$. The absorption coefficient was $\mu(\text{Mo}) = 1.55 \text{ cm}^{-1}$. The X-ray intensity data were measured for a total of 1235 reflections with $F \geq 6\sigma(F_o)$. The structure was solved by direct methods which revealed the locations of all hydrogen atoms on the initial E map. The structure was refined to a final value of $R_1 = 4.85\%$ and $R_2 = 4.85\%$ by full matrix, least squares techniques with anisotropic-thermal parameters for all non-hydrogen atoms. Hydrogen atoms were placed in idealized positions with isotropic thermal parameters set to 1.2 times the attached carbon thermal parameter. All structural determinations and refinement calculations were carried out with the SHELXTL package on the Nicolet R3m Nova 3 crystallographic system (4). On the basis of 4 molecules of $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_4$ in a unit cell of volume 1715.72 \AA^3 , the calculated density was 1.20 g/cm^3 . The final difference map revealed no abnormal features (final difference-Fourier, map

peak equals $0.27 \text{ electrons/\AA}^3$). The final atomic parameters are given in Table 2.

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