

AN INDOLE ALKALOID FROM *STRYCHNOS ERICHSONII*

P. FORGACS, A. JEHANNO, J. PROVOST, C. THAL*, J. GUILHEM*, C. PASCARD* and C. MORETTI†

Centre de Recherches, Laboratoire Roger Bellon, 90, rue Marcel Bourdarias, 94140 Alfortville, France; *Institut de Chimie des Substances Naturelles (C.N.R.S.), 91190 Gif-sur-Yvette, France; †Centre O.R.S.T.O.M., B.P. 165, 97305 Cayenne, French Guiana

Key Word Index—*Strychnos erichsonii*; Loganiaceae; indole alkaloids; erichsonine.

Abstract—Erichsonine is a new indole alkaloid isolated from the stem bark of *Strychnos erichsonii*. Its structure has been established by spectral means and confirmed by X-ray crystallographic analysis. This is the first report of a vobasine-type alkaloid from the Loganiaceae.

INTRODUCTION

Strychnos erichsonii [1, 2], *S. urbanii* [3] and *S. bovetiana* [4] comprise the various species used for the preparation of curare in Columbia [5, 6]. However, King has shown that the former plant had no curarizing effect but was rich in alkaloids which resinify easily [7, 8]. During our detailed study of total alkaloids in stem barks, we have isolated from *S. erichsonii* a main alkaloid, with an unknown structure, which is the subject of this paper. We have called it erichsonine.

RESULTS AND DISCUSSION

The major compound (1), was isolated as yellow needles, mp 250° (decomp.), crystallized from methanol, $[\alpha]_D^{20} -166^\circ$. The IR (KBr) spectrum demonstrated the presence of a conjugated C=O at 1630 cm^{-1} , as well as a large band at 3300 cm^{-1} (NH and OH). The UV spectrum [λ_{max} nm (log ϵ): 237 (4.05) and 318 (4.19)] is also characteristic of a 2-acyl indole [9], non-shifted in an acid or alkaline medium. The $^1\text{H NMR}$ spectrum (Table 1) of 1 showed at $\delta 11.40$ the presence of a proton singlet, disappearing on deuteration, attributable to the indolic NH. Two other proton singlets are exchangeable by D_2O at $\delta 4.25$ and 4.30 proving the existence of two hydroxyl groups in the molecule. A doublet of three protons at $\delta 1.05$ ($J = 6\text{ Hz}$) supports the hypothesis of a substitution of the C-19 by a hydroxyl. In the mass spectrum, we observe next to the $[\text{M}]^+ m/z 342$ ($\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_3$), characteristic peaks at $m/z 166$ and 152 shifted to 208 and 194 in the diacetylated derivative 2.

Acetylation of 1 (pyridine- Ac_2O) at room temperature provided the di-*O*-acetylated derivative 2, crystallized from ethanol, mp 210° , $[\alpha]_D^{20} -115^\circ$. The IR (KBr) spectrum exhibited bands for NH at 3430 cm^{-1} and *O*-acetyls at 1730 and 1745 cm^{-1} . The $^1\text{H NMR}$ spectrum confirmed the existence of two acetyl groups at $\delta 1.85$ (s, 3H) and 2.00 (s, 3H) (Table 1). Hot acetylation of 1 provides the tri-*O,O,N*-acetyl derivative 3, crystallized from isopropyl oxide, mp $133-135^\circ$, $[\alpha]_D^{20} -70^\circ$. The disappearance of the NH band in the IR (KBr) spectrum was observed. The mass spectrum of 3 indicated the molecular formula $\text{C}_{26}\text{H}_{32}\text{N}_2\text{O}_6$, $[\text{M}]^+ m/z 468$. Comparison of the $^1\text{H NMR}$ spectra of erichsonine (1) and its acetylated derivative 2 with those of 16-epi-affinine

(4) and its acetylated homologue [10] 5 also revealed certain similarities.

Final confirmation of the structure of 1 was obtained by single crystal X-ray diffraction studies. Crystal data: crystals are monoclinic, space group $\text{P}2_1$, $Z = 4$, with $a = 19.073$ (12), $b = 12.386$ (8), $c = 7.789$ (5) Å, $\beta = 93.4$ (2)°. The data were collected with a 4-circle automatic diffractometer using $\text{Cu-K}\alpha$ ($\lambda = 1.5418$ Å). From 3516 independent collected data, 2802 [$I > 3\sigma(I)$] were used. The structure was solved by direct methods [11] and

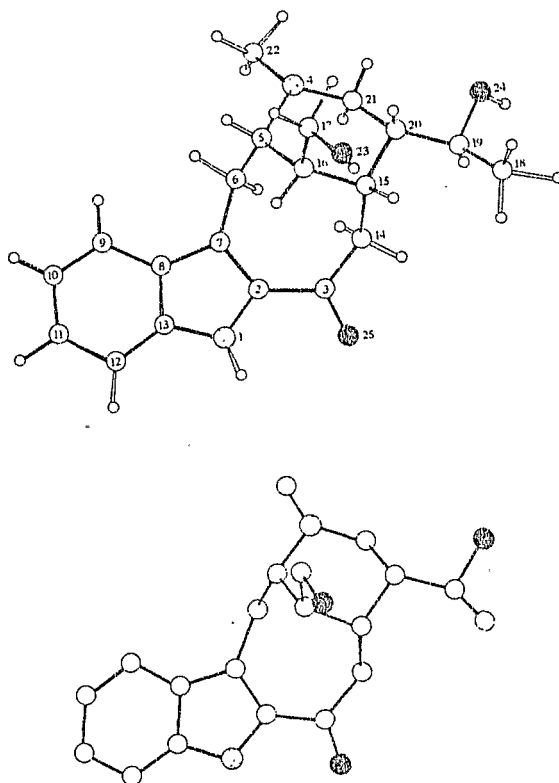
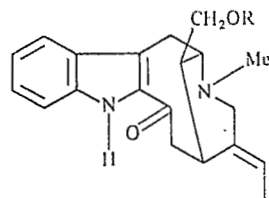
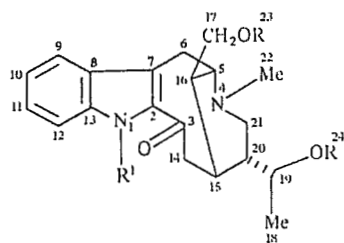


Fig. 1. Molecular structure of erichsonine (1).

ORSTOM Fonds Documentaire



- 1** R = R¹ = H, erichsonine
The stereochemistry at
C - 19 is configuration S
- 2** R = Ac, R¹ = H
- 3** R = R¹ = Ac

- 4** R = H, 16 - epi-affinine
- 5** R = Ac

Table 1. ¹H NMR spectral data of **1**, **2**, **4** and **5** (80 MHz, CDCl₃, TMS as internal standard)

	Erichsonine (1)	Di-O-acetyl- erichsonine (2)	16-Epi affinine (4)	O-Acetyl- 16-epi affinine (5)
NH-1	11.40 s	9.37 s	9.79 s	9.37 s
	exchange D ₂ O			
NMe-4	2.37 s	2.40 s	2.47 s	2.50 s
H-9	7.67 d (J = 8)	7.60 d (J = 8)	7.64 d (J = 8)	7.61 d
H-10 } H-11 } H-12 }	6.80–7.50 m	7.00–7.40 m	6.95–7.45 m	7.0–7.5 m
H-16	1.67 m	1.60 m	1.85 m	2.15 m
H-17	3.40 d	4.02 m	3.47 d (J = 5)	4.02 m
OH-17	4.25 s exchange D ₂ O	—	3.93 s exchange D ₂ O	—
OAc-17	—	1.85 s	—	1.9 s
H-18	1.05 d (J = 6)	1.20 d (J = 6)	1.62 dd (J ₁ = 7, J ₂ = 1.5)	1.64 dd (J ₁ = 7, J ₂ = 1.5)
H-19	—	4.75 m*	5.42 q (J = 7)	5.53 q (J = 7)
OH-19	4.30 s exchange D ₂ O	—	—	—
OAc-19	—	2.00 s	—	—

*Assignments were confirmed by decoupling experiments.
Coupling constants (J in parentheses) are given in Hz.

refined by the least-squares method [12]. One water molecule and all the hydrogen atoms of both independent molecules of **1** were located on a Fourier difference map and included in the calculations. The final R-factor was 0.071. A perspective view of one of the molecules (nitrogen shaded, oxygen blackened) is illustrated in Fig. 1. Full crystal data are deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

EXPERIMENTAL

UV spectra were recorded in MeOH and IR spectra in KCl disks. ¹H NMR spectra were determined at 80 MHz in CDCl₃ or in DMSO-*d*₆ using TMS or HMDS as int. standard. TLC was generally performed on silica gel (Merck 60 F 254) using CHCl₃-MeOH-NH₄OH (79:20:1) for development and Ce(SO₄)₂-H₂SO₄ as spray reagent. Mps are uncorr. MS were obtained at 70 eV.

Plant material. *Strychnos erichsonii* Rich. Schomb. was collected in April 1979, from la Montagne des Chevaux, French Guiana. Voucher specimens of these plants are deposited in the herbarium of the Museum National d'Histoire Naturelle de Paris (reference CM 1079).

Extraction. Dried and powdered stem bark (7.6 kg) was moistened with 20% Na₂CO₃ soln (5 l) and extracted exhaustively by percolation with CHCl₃ (100 l). After concn of CHCl₃ by distillation (8 l) the extract was triturated with 1 N H₂SO₄ (20 l). The aq. layer was alkalized to pH 9.5 with satd Na₂CO₃ soln (240 g/l) and extracted with CHCl₃ (ca 5 l) until a negative Mayer reaction was obtained. The CHCl₃ extracts when pooled were washed with H₂O until neutral, the CHCl₃ soln dried (Na₂SO₄), filtered and evapd *in vacuo*. The total bases yielded 58.5 g (7.7 g/kg).

Isolation of compounds. Crude alkaloids (58.5 g) were dissolved in CHCl₃ and separated by CC on silica gel (Merck 7734, diameter 0.06–0.2 mm, 1 kg). Fractions of 200 ml vol. were collected. For elution CHCl₃ was used first (1000 ml, fractions 1–5), then CHCl₃–EtOAc (4:1, 1400 ml, fractions 6–12), then EtOAc–Me₂CO (3:2, 2000 ml, fractions 13–22). After evapn of fractions 13–22, 15 g were obtained.

The amorphous residue (15 g) was dissolved in EtOAc–Me₂CO (3:2) and separated by CC on silica gel (Merck 7734; 150 g). Fractions of 100 ml were collected. For elution EtOAc–Me₂CO (3:2, 500 ml, fractions 1–5; then 1:1, 500 ml, fractions 6–10). Separation with EtOAc–Me₂CO (2:3) was carried on and 1000 ml (fractions 11–20) were used. The composition of the fractions was monitored by TLC.

After evapn of fraction 11–20, 9.1 g were obtained. After recrystallization from MeOH, 8.0 g (1.05 g/kg) of erichsonine were obtained.

Erichsonine (1). Yellow prisms, mp 250° (decomp.), $[\alpha]_D^{20}$ –166° (MeOH; *c* 1.0). IR ν_{\max}^{KBr} cm⁻¹: 3300 (OH and NH), 1630 (C=O). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 318 (4.19), 237 (4.05). Not shifted in acid or alkaline medium. MS *m/z*: 342 [M]⁺, 166, 152. ¹H NMR: Table 1. ¹³C NMR: Table 2. (Found: C, 69.95; H, 7.88; N, 8.08. C₂₀H₂₆N₂O₃ requires: C, 70.15; H, 7.65; N, 8.18%.) Crystal data: Fig. 1. X-ray crystal structure of erichsonine (1), with crystallographic numbering scheme. HPLC has extensively been applied in the analysis of indole alkaloids [13]. TLC: CHCl₃–MeOH–NH₄OH (79:20:1), Ce(SO₄)₂, R_f 0.45.

Di-O-acetylerichsonine (2). Compound 1 (50 mg) was treated with Ac₂O–pyridine (1:1, 10 ml) at 27° for 24 hr, and usual work up followed by prep. TLC (CHCl₃–MeOH, 4:1) afforded a white solid which on crystallization in EtOH gave 2 (40 mg), mp 210°, $[\alpha]_D^{20}$ –115° (MeOH; *c* 0.4). IR ν_{\max}^{KBr} cm⁻¹: 3430 (NH), 1730 and 1745 (OAc), 1635 (C=O). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 319 (4.25), 238 (4.11). MS *m/z*: 426 [M]⁺. ¹H NMR: Table 1. (Found: C, 67.58; H, 7.16; N, 6.54. C₂₄H₃₀N₂O₅ requires: C, 67.58; H, 7.09; N, 6.57%.) TLC: CHCl₃–MeOH–NH₄OH (79:20:1), Ce(SO₄)₂, R_f 0.60.

Tri-O,O,N-acetylerichsonine (3). Compound 1 (50 mg) was treated with Ac₂O (10 ml) at 105° for 3 hr and evapd *in vacuo*. After recrystallization from isopropyl oxide (50 mg) of compound 3 were obtained, mp 133–135°, $[\alpha]_D^{20}$ –70° (CHCl₃; *c* 0.5). IR ν_{\max}^{KBr} cm⁻¹: 1725 (OAc), 1650 (C=O). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 238 (4.19), 318 (4.35). MS *m/z*: 468 [M]⁺. (Found: C, 66.43; H, 7.00; N, 5.71. C₂₆H₃₂O₆N₂ requires: C, 66.65; H, 6.88; N, 5.98%.) TLC: CHCl₃–MeOH–NH₄OH (79:20:1), Ce(SO₄)₂, R_f 0.77.

Table 2. ¹³C NMR spectral data of 1 (22.63 MHz, CDCl₃, TMS as internal standard)

Carbon	ppm	Carbon	ppm
2	135.1	13	136.7
3	192.5	14	39.0
5	54.7	15	29.9
6	19.4	16	38.6
7	120.6	17	64.7
8	127.8	18	20.0
9	120.0	19	66.7
10	119.6	20	41.4
11	126.0	21	45.2
12	111.9	22	42.6

16-Epiaffinine (4) [9, 10]. Mp 152–154°, picrate 187–189°, $[\alpha]_D^{20}$ –190° ± 2° (CHCl₃; *c* 1.0). IR $\nu_{\max}^{\text{CHCl}_3}$ cm⁻¹: 3413, 3289 (NH) and 1642 (C=O). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 209 (4.35), 238 (4.19), 318 (4.26), not shifted in acid or alkaline medium. MS *m/z* (rel. int.): 324 [M]⁺, 306 (33), 265 (5), 172 (7), 166 (7), 152 (100), 122 (14). ¹H NMR: Table 1. (Found: C, 73.90; H, 7.50; N, 8.70. Calc. for C₂₀H₂₄N₂O₂: C, 74.04; H, 7.46; N, 8.64%.)

O-Acetyl-16-epiaffinine (5) [10]. Colourless oil. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 212 (4.27), 238 (4.17), 318 (4.32), not shifted in acid or alkaline medium. IR ν_{\max}^{KBr} cm⁻¹: 3436 (NH), 3290, 2778 (NCH₃), 1727 (OAc), 1639 (conj. C=O). MS *m/z* (rel. int.): 366 [M]⁺, 322 (3), 306 (44), 263 (5), 208 (6), 194 (100), 172 (9). ¹H NMR: Table 1. (Found: C, 72.02; H, 7.10; N, 7.80. Calc. for C₂₂H₂₆N₂O₃: C, 72.10; H, 7.15; N, 7.65%.)

REFERENCES

- Krukoff, B. A. (1972) *Lloydia* 35, 193.
- Schomburgk, R. P. (1868) *Mart. Fl. Bras.* 6, 274.
- Barbosa Rodrigues, J. (1891) *Vellosia* Sec. 2, 1:38, pl. 4, fig. A.
- Pires, J. M. (1960) *Bol. Tech. Inst. Agron. Norte* 38, 40.
- Krukoff, B. A. and Monachino, J. (1947) *Bol. Tech. Inst. Agron. Norte* 12, 5.
- Krukoff, B. A. and Monachino, J. (1950) *Bol. Tech. Inst. Agron. Norte* 20, 3.
- King, H. (1949) *J. Chem. Soc.* 955.
- King, H. (1935) *Nature* 135, 469.
- Renner, U., Prins, D. A., Burlingame, A. L. and Biemann, K. (1963) *Helv. Chim. Acta* 46, 2186.
- Naranjo, J., Pinar, M., Hesse, M. and Schmid, H. (1972) *Helv. Chim. Acta* 55, 752.
- Riche, C. 7th European Crystallographic Meeting (Jerusalem). (1982) *Coll. Abstr.* 25.
- Sheldrick, G. M. (1976) *Program for Crystal Structure Determination*. University of Cambridge, U.K.
- Perera, P., Van Beek, T. A. and Verpoorte, R. (1984) *J. Chromatogr.* 285, 214.