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AN INDOLE ALKALOID FROM *STRYCHNOS ERICHSONII*

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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°. 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}H NMR spectrum (Table 1) of **1** showed at δ11.40 the presence of a proton singlet, disappearing on deuteration, attributable to the indolic NH. Two other proton singlets are exchangeable by D_2O at δ4.25 and 4.30 proving the existence of two hydroxyl groups in the molecule. A doublet of three protons at δ1.05 (J = 6 Hz) supports the hypothesis of a substitution of the C-19 by a hydroxyl. In the mass spectrum, we observe next to the $[M]^+$ m/z 342 ($C_{20}H_{26}N_2O_3$), 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°. The IR (KBr) spectrum exhibited bands for NH at 3430 cm^{-1} and *O*-acetyls at 1730 and 1745 cm^{-1}. The ^{1}H NMR spectrum confirmed the existence of two acetyl groups at δ1.85 (*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°, $[\alpha]_D^{20}$ −70°. The disappearance of the NH band in the IR (KBr) spectrum was observed. The mass spectrum of **3** indicated the molecular formula $C_{26}H_{32}N_2O_6$, $[M]^+$ m/z 468. Comparison of the ^{1}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 $P2_1$, Z = 4, with a = 19.073 (12), b = 12.386 (8), c = 7.789 (5) Å, β = 93.4 (2)°. The data were collected with a 4-circle automatic diffractometer using Cu-K_α (λ = 1.5418 Å). From 3516 independent collected data, 2802 [$I > 3\sigma(I)$] were used. The structure was solved by direct methods [11] and

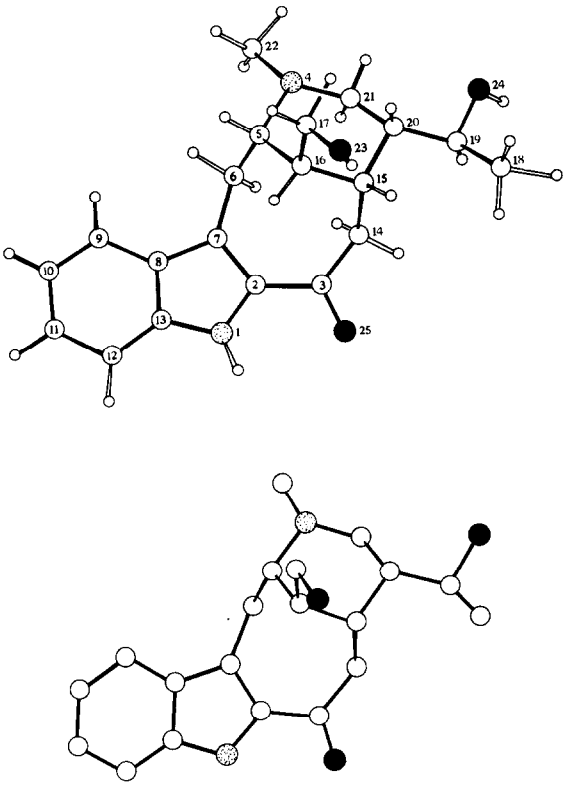
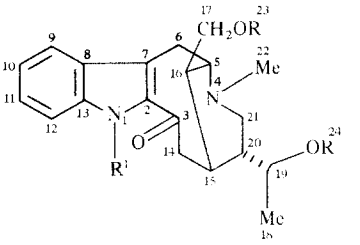
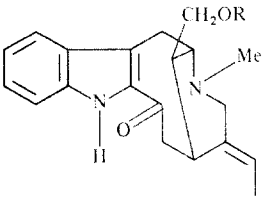


Fig. 1. Molecular structure of erichsonine (**1**).





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

4 R = H, 16 - epiaffinine
5 R = Ac

Table 1. ^{1}H NMR spectral data of **1**, **2**, **4** and **5** (80 MHz, $CDCl_3$, 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* exchange D_2O	9.37 *s*	9.79 *s*	9.37 *s*
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_2O	—	3.93 *s* exchange D_2O	—
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_2O	—	—	—
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. ^{1}H NMR spectra were determined at 80 MHz in $CDCl_3$ or in DMSO-d_6 using TMS or HMDS as int. standard. TLC was generally performed on silica gel (Merck 60 F 254) using $CHCl_3$–MeOH–NH_4OH (79:20:1) for development and $Ce(SO_4)_2$–H_2SO_4 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% Na_2CO_3 soln (5 l.) and extracted exhaustively by percolation with $CHCl_3$ (100 l.). After concn of $CHCl_3$ by distillation (8 l.) the extract was triturated with 1 N H_2SO_4 (20 l.). The aq. layer was alkalinized to pH 9.5 with satd Na_2CO_3 soln (240 g/l.) and extracted with $CHCl_3$ (*ca* 5 l.) until a negative Mayer reaction was obtained. The $CHCl_3$ extracts when pooled were washed with H_2O until neutral, the $CHCl_3$ soln dried (Na_2SO_4), 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 $CHCl_3$ 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 $CHCl_3$ was used first (1000 ml, fractions 1–5), then $CHCl_3$–EtOAc (4:1, 1400 ml, fractions 6–12), then EtOAc–Me_2CO (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–Me_2CO (3:2) and separated by CC on silica gel (Merck 7734; 150 g). Fractions of 100 ml were collected. For elution EtOAc–Me_2CO (3:2, 500 ml, fractions 1–5; then 1:1, 500 ml, fractions 6–10). Separation with EtOAc–Me_2CO (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 λ_{max}^{EtOH} (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. ^{13}C NMR: Table 2. (Found: C, 69.95; H, 7.88; N, 8.08. $C_{20}H_{26}N_2O_3$ 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: $CHCl_3$–MeOH–NH_4OH (79:20:1), $Ce(SO_4)_2$, R_f 0.45.

Di-O-acetylerichsonine (**2**). Compound **1** (50 mg) was treated with Ac_2O–pyridine (1:1, 10 ml) at 27° for 24 hr, and usual work up followed by prep. TLC ($CHCl_3$–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 λ_{max}^{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. $C_{24}H_{30}N_2O_5$ requires: C, 67.58; H, 7.09; N, 6.57%.) TLC: $CHCl_3$–MeOH–NH_4OH (79:20:1), $Ce(SO_4)_2$, R_f 0.60.

Tri-O,O,N-acetylerichsonine (**3**). Compound **1** (50 mg) was treated with Ac_2O (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° ($CHCl_3$; *c* 0.5). IR ν_{max}^{KBr} cm^{-1}: 1725 (OAc), 1650 (C=O). UV λ_{max}^{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. $C_{26}H_{32}O_6N_2$ requires: C, 66.65; H, 6.88; N, 5.98%.) TLC: $CHCl_3$–MeOH–NH_4OH (79:20:1), $Ce(SO_4)_2$, R_f 0.77.

Table 2. ^{13}C NMR spectral data of **1** (22.63 MHz, $CDCl_3$, 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° ($CHCl_3$; *c* 1.0). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3413, 3289 (NH) and 1642 (C=O). UV λ_{max}^{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 $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64%.)

O-Acetyl-16 epiaffinine (**5**) [10]. Colourless oil. UV λ_{max}^{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 (NCH_3), 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 $C_{22}H_{26}N_2O_3$: C, 72.10; H, 7.15; N, 7.65%.)

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