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STRICTICINE - A NEW ALKALOID FROM THE LEAVES OF RHAZYA STRICTA

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Summary: On reinvestigation of the chemical constituents of a medicinal plant Rhazya stricta, a new alkaloid stricticine (1) has been isolated. The stereochemistry was elucidated with the help of ^1H-NMR (homodecoupling, COSY-45°, NOE difference) and ^{13}C-NMR (DEPT) spectra.

The crude alkaloids (350 gm) isolated by conventional procedures[1,2] from 90 kg of leaves of Rhazya stricta (Decaisne)[3-11] were subjected to column chromatography over silica gel. Elution with EtOAc - MeOH (9:1-2:8) afforded a mixture of alkaloids (70 mg) which was chromatographed over silica gel. Elution with EtOAc-MeOH (9:1) yielded a mixture of three alkaloids which was further purified, by preparative TLC (Al_2O_3, Merck, F-254) to afford 17 mg of a new alkaloid named "stricticine" as a white amorphous material. The substance gave a light orange colouration with Dragendorff's reagent and a deep blue colouration with $Ce(SO_4)_2$ $4H_2O$ solution, $[\alpha]_D$ $CHCl_3$ = 515.0. Its UV spectrum (MeOH) gave absorptions at λ_{max} 208 nm, 228 nm, 292 nm and 327 nm; λ_{min} 220 nm and 305 nm, characteristic of the anilinoacrylate chromophore. The IR spectrum showed absorption at 1690 cm^{-1} and 3400 cm^{-1} (NH). HRMS afforded M^+ at m/z 338.1615 (26%) in agreement with the formula $C_{20}H_{22}N_2O_3$. Other fragments were present at m/z 293.1272 (22%, $C_{18}H_{17}N_2O_2$), 269.1038 (6%, $C_{19}H_{13}N_2$), 254.0806 (8%, $C_{18}H_{10}N_2$), 235.1221 (24%, $C_{16}H_{15}N_2$), 223.0623 (10%, $C_{14}H_9NO_2$), 208.0756 (8%, $C_{14}H_{10}NO$), 194.0593 (14%, $C_{13}H_8NO$) and 180.0817 (15%, $C_{13}H_{10}N$).

The ^1H-NMR spectrum ($CDCl_3$, 300 MHz) indicated the presence of 22 protons. The coupling interactions between coupled protons were confirmed by spin decoupling and COSY - 45° experiment[12] (Fig. 1). An upfield three proton doublet at δ 0.99 ($J_{18,19}$ = 5.5Hz) was assigned to the C-18 methyl protons. A one proton multiplet at δ 2.83 was assigned to the C-19 proton while a one proton broad singlet at δ 3.62 was assigned to C-3H. A three proton singlet for the ester methyl group appeared at δ3.75. Other ^1H-NMR assignments are presented in Table 1.

The ^{13}C-NMR spectrum of stricticine ($CDCl_3$, 75 MHz, DEPT)[12] is presented in Table II. A signal at δ 14.59 was assigned to the C-18 methyl protons while two downfield signals (CH groups) at δ 61.49 and δ 39.35 were assigned to C-3 and C-19 carbon atoms respectively. The C-5 and C-21 carbons (CH_2) resonated at δ 44.91 and δ 53.59 respectively.

The stereochemistry at the various asymmetric centres of stricticine (1) was established by carrying out NOE difference studies. Irradiation at δ 0.99 (18-CH_3) resulted in 17.2% NOE at δ 2.83 (19-H), 17.0% NOE at δ 2.01 (6-H_b) and 10.0% NOE at δ3.75 (21-Hα). Irradiation at δ 2.01 (6-H_b), on the other hand resulted in 17.2% NOE at δ 0.99 (18-CH_3). These NOE interactions established that the epoxide bearing carbons C-19 and C-20 possessed S configuration These NOE effects establish that the C-18 methyl group overlying the cyclohexene ring system possesses cis configuration, The positive value for the optical rotation indicates that it belongs to the same enantiomeric series of strychnos alkaloids as (+)-20-epilochneridine[13,14].

Notably, both enantiomeric forms of strychnos alkaloids have been isolated.[14,15] Stricticine (1) may arise in nature by oxidation of (+)-akuammicine and it may be a biogenetic precursor of (+)-20-epilochneridine. In the light of these studies structure (1) is assigned to stricticine Stricticine is not an artifact since (a) it is present in the fresh extracts and (b) it is not formed from akuammicine under the isolation conditions.

Table-1: ^{1}H-NMR ($CDCl_3$, 300 MHz)

Proton	(δ)		Proton	(δ)	
C-3 Hβ	3.62	(bs,1H)	C-14 Hβ	1.82	(m,1H)
C-5 H_b	3.04	(m,1H)	C-14 Hα	2.44	(m,1H)
C-5 H_a	2.75	(d, 1H, $J_{5a\ 6a}$=6Hz)	C-15 H β	2.15	(m,1H)
C-6 H_b	2.01	(m,1H)	C-18 H	0.99	(d,3H, $J_{18,19}$=5.5Hz)
C-6 H_a	1.94	(m,1H)	C-19 H	2.83	(m, 1H)
C-9 H	7.13	(d, 1H, $J_{9,10}$ = 7.3Hz)	C-21 Hα	3.25	(m,1H)
C-10 H	6.69	(m,1H)	C-21 H β	3.75	(m,1H)
C-11 H	6.67	(m, 1H)	N-H	8.76	(s,1H)
C-12 H	6.80	(d,1H,$J_{12\ ,11}$=7.3Hz)	$COOCH_3$	3.57	(s,3H)

Table-II : ^{13}C-NMR ($CDCl_3$, 75MHz)

Carbon	2	3	5	6	7	8	9
(δ)	169.39	61.49	44.91	24.13	57.35	134.00	120.23
Carbon	10	11	12	13	14	15	16
(δ)	121.26	127.87	109.10	144.84	29.74	35.35	98.70
Carbon	18	19	20	21	COO<u>Me</u>	<u>C</u>OOMe	
(δ)	14.59	59.35	66.50	53.59	51.30	169.39	

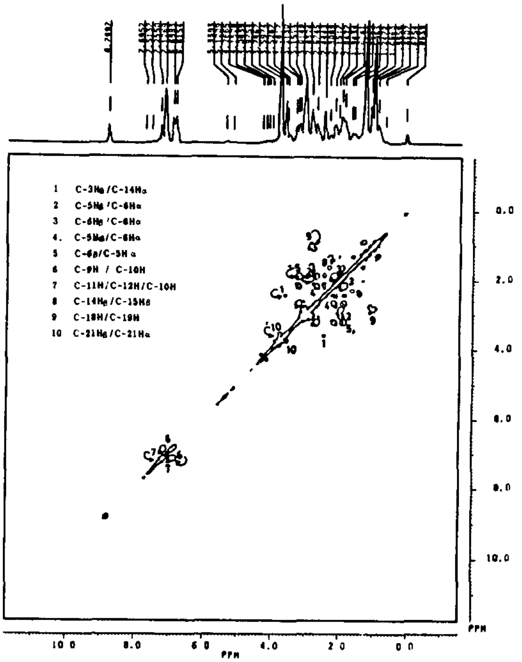
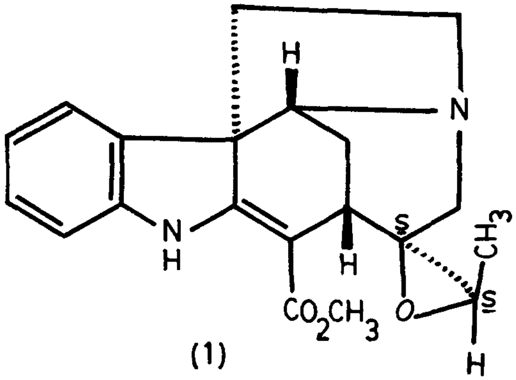
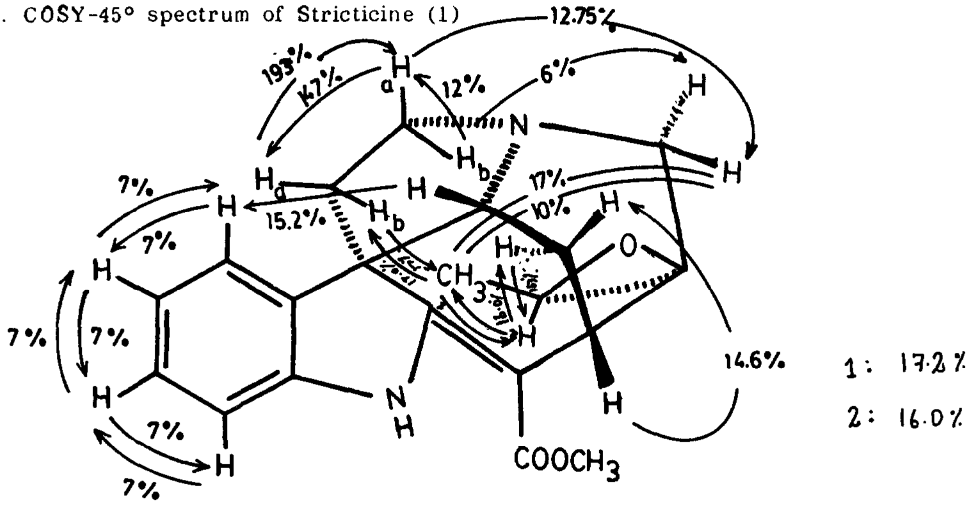


Fig.1. COSY-45° spectrum of Stricticine (1)



(1)

Stricticine (1)



NOE difference interactions of Stricticine (1).

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