STRICTINE - A NEW MAVACURINE TYPE ALKALOID FROM THE LEAVES OF RHAZYA STRICTA

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Abstract - A new alkaloid strictine (1) has been isolated from the leaves of R.stricta. The structure has been confirmed by ^{13}C-NMR studies and ^{1}H-NMR homodecoupling experiments.

INTRODUCTION

Rhazya stricta (Decaisne) is a small glabrous erect shrub, abundantly distributed in Pakistan[1-3]. The plant is well reputed in the indigenous system of medicine for the treatment of various diseases[4-7]. Extracts of R.stricta showed anticancer activity[8-10] and antineoplastic activity.[11] We have previously reported a number of new alkaloids from Rhazya stricta[4,12-19].

On reinvestigation of the alkaloidal constituents of the plant R.stricta, a new alkaloid strictine (1) has been isolated and structure (1) has been confirmed by spectroscopic studies.

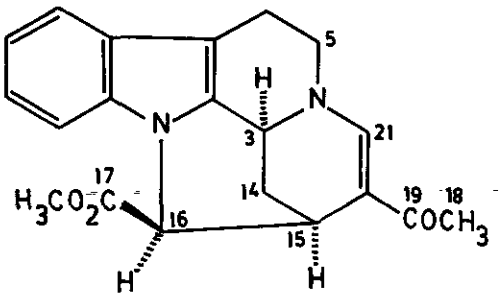
RESULTS AND DISCUSSION

The crude alkaloidal material isolated by previously described procedures[12,13] was subjected to column chromatography over neutral alumina. Elution with pure $CHCl_3$ afforded a white amorphous alkaloidal material, named strictine. The UV spectrum showed absorption maxima at 222 nm (log ε : 4.30), 295 nm (log ε : 4.05) and absorption minimum at 241 nm (log ε: 3.89). The high UV absorption indicated the presence of a vinylogous enamide function, as reported earlier for vallesiachotamine[20,21]. The IR spectrum showed absorptions at 1738 cm^{-1} (ester C=O), 1670 cm^{-1} (>N-C=C-C=O). The low value of the carbonyl absorption at 1670 cm^{-1} indicated that it was in conjugation. High resolution mass measurements for strictine afforded the molecular ion peak at m/z 336.1462 leading to the molecular formula $C_{20}H_{20}N_2O_3$. Other significant peaks were found at m/z 277.1337 (100%, $C_{18}H_{17}N_2O$), 165.0763 (30%, $C_{11}H_{19}N$) and 123.1167 (20%, C_9H_{15}). The ^{1}H-NMR

spectrum ($CDCl_3$, 300 MHz) showed the presence of 20 protons, each of which was identified by a series of homodecoupling experiments and further substantiated by recording its COSY-45° spectra[22]. A three-proton singlet at δ2.29 was assigned to the methyl protons of the acetyl group. The absence of any signal for the methyl group, normally found in mavacurine type alkaloids suggested that oxidation had occurred at C-19 in strictine. Another three proton singlet at δ 3.57 was consistent with the presence of methyl protons of the carbomethoxy group. A downfield doublet at δ4.60 ($J_{16_\alpha,15_\alpha}$ = 4.5Hz) was assigned to C-16H , which is characteristic for compounds bearing a mavacurine type skeleton[23]. A rather downfield one proton broad singlet at δ 7.10 was assigned to the olefinic proton at C-21, its lowfield value being consistent with the presence of an adjacent nitrogen atom. The ^{1}H-NMR spectral assignments for other protons of strictine (1) are presented in Table-I.

The ^{13}C-NMR spectrum ($CDCl_3$, 75 MHz, DEPT) of the compound showed an upfield signal resonating at δ 24.74 which was assigned to the methyl carbon of the acetyl group. Another signal at δ 51.76 was assigned to the methyl carbon of the ester methyl group. Two downfield signals for C-3 and C-5 were observed in the DEPT spectrum at δ56.01 as a -CH group and δ50.23 as a $-CH_2$ group respectively. The signal for the C-16 carbon resonated at δ 53.23 as a -CH group. A downfield signal at δ150.31 was assigned to the C-21 CH carbon atom. The quaternary carbon atoms gave very weak signals. Other ^{13}C-NMR assignments are presented in Table II.

On the basis of the above spectal data, the structure of strictine was assigned as (1).



(1)

EXPERIMETNAL

The ethanolic extracts of the fresh leaves (35 kg) of Rhazya stricta were concentrated to a gum. This gummy material was dissolved in 10% acetic acid (1 lit.). The non-alkaloidal part was removed by extraction with ethyl acetate (25 lit.), the aqueous acidic solution was basified with aqueous ammonia (500 ml) to pH 11 and extracted with ethyl acetate (36 lit.) to afford the crude

alkaloids (350 gm). This alkaloidal material was subjected to flash chromatography (alkaloids: silica gel, 1:40) for preliminary fractionation. Elution with chloroform-ethyl acetate (9:1-6:4) afforded a fraction of crude alkaloids (30 gm). This crude alkaloidal fraction was further subjected to column chromatography over neutral alumina (Merck, 90 active). Elution with $CHCl_3$ afforded a white amorphous alkaloidal material (6 mg).

Spectral Data of Strictine (1)

UV (MeOH) : λ_{max} nm, 222, 295; λ_{min} nm, 241. IR ($CHCl_3$) : ν_{max} cm^{-1}, 1738 (ester CO) 1670 (N-CH=$\overset{1}{C}$-CO-) and 1620 (>C=CH). HRMS : observed MS (%, formula, calculated MS), 336.1462 (80%, $C_{20}H_{20}N_2O_3$: 336.1472), 277.1337 (100%, $C_{18}H_{17}N_2O$: 277.1340), 165.0763 (30%, $C_{11}H_{19}N$: 165.0763), 123.1167 (20%, C_9H_{15} : 123.1167), ^{1}H-NMR ($CDCl_3$, 300 MHz) : Table-1. ^{13}C-NMR ($CDCl_3$, 75 MHz, DEPT): Table II.

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

Proton	Chemical shift (δ)	Proton	Chemical shift (δ)
C-3Hα	3.60 (d, 1H, $J_{3\alpha,14\alpha}$=6Hz)	C-11H	7.31 (m, 1H)
C-5Hα	3.70 (m,1H)	C-12H	7.60 (d, 1H, $J_{12,11}$ = 7.0Hz).
C-5Hβ	3.20 (dd,1H, $J_{5\beta,5\alpha}$=13Hz) $J_{5\beta,6\beta}$=4Hz)	C-14Hα C-14Hβ	2.10 (m,1H) 2.39 (m, 1H)
C-6Hα	2.83(ddd, 1H, $J_{6\alpha,6\beta}$=13Hz, $J_{6\alpha,5\alpha}$=4Hz , $J_{6\alpha,5\beta}$=4Hz)	C-15Hα	2.33 (m,1H)
C-6Hβ	1.70 (dd, 1H, $J_{6\beta,6\alpha}$= 13Hz $J_{6\beta,5\beta}$=4Hz)	C-16Hα C-21H	4.60(d, 1H, $J_{16\alpha,15\alpha}$= 4.5Hz) 7.10 (s, 1H)
C-9	7.20 (d, 1H, $J_{9,10}$ = 7Hz)	$\underline{CH_3}$-OCO	3.57 (s, 3H)
C-10H	7.35 (m, 1H)	$\underline{CH_3}$-CO	2.29 (s, 3H)

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

Carbon	(δ)	Multiplicity	Carbon	(δ)	Multiplicity
3	56.01	-CH	14	39.14	$-CH_2$
5	50.23	$-CH_2$	15	27.13	-CH
6	29.59	$-CH_2$	16	53.23	-CH
9	122.74	-CH	21	150.31	-CH
10	125.75	-CH	$\underline{CH_3}$OCO	51.76	$-CH_3$
11	128.17	-CH	$C\underline{H_3}$CO	25.74	$-CH_3$
12	121.22	-CH			

Note: Signals for quaternary carbon atoms were too weak to be detected.

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