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STAPFININE, AN INDOLE ALKALOID FROM *ERVATAMIA CORONARIA*

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Key Word Index—*Ervatamia coronaria*; Apocynaceae; indole alkaloid; stapfinine; structural determination.

Abstract—A new indole alkaloid, stapfinine, was isolated from the leaves of *Ervatamia coronaria* and its structure determined by spectroscopic means.

INTRODUCTION

Ervatamia coronaria (Apocynaceae) is a glabrous, evergreen tree commonly grown in the gardens of West Pakistan. Various parts of the plant are used in the indigenous system of medicine for the treatment of opthalmia, for application on wounds and inflamed parts of the body, as an anthelmintic, etc. Anticancer activity has also been reported from the crude extracts of the plant [1]. A number of indole alkaloids have previously been reported by us from its leaves [2–5].

RESULTS AND DISCUSSION

The crude alkaloids obtained from the ethanolic extract of the fresh leaves of the plant were subjected to pH fractionation. The fraction obtained at pH 7 afforded a mixture of alkaloids which was further purified by prep. TLC to afford a new alkaloid named stapfinine, as a yellow amorphous material $[\alpha]_D = 25°$ ($CHCl_3$).

The compound afforded a typically indolic UV spectrum showing absorption maxima at 222 (log ε 4.58), 275 (log ε 3.84) and 292 nm (log ε 3.83) and minima at 253 (log ε 3.50), 278 (log ε 3.84) and 288 nm (log ε 3.80). The IR spectrum (chloroform) afforded peaks at 3450 (OH), 3300 (NH), 2900 (CH), 1460, 1360, 1240 (C–O–C of epoxide), 1140, 980, 900, 850 and 730 cm^{-1} but did not show any peaks in the olefinic or carbonyl region.

In the mass spectrum of stapfinine, the $[M]^+$ appeared at *m/z* 312.1821 which was consistent with the molecular formula $C_{19}H_{24}N_2O_2$, indicating nine double bond equivalents. Since six of these were accounted for by the presence of an indole chromophore and since the IR and NMR spectrum did not show the presence of any additional olefinic linkages or carbonyl groups, it seemed plausible that one of the oxygen atoms was in the form of an epoxide or an ether linkage. Stapfinine showed the following major peaks in its mass spectrum: 312.1821 ($[M]^+$, $C_{19}H_{24}N_2O_2$, 18.3%), 294.1728 ($[M-H_2O]^+$, $C_{19}H_{22}N_2O$, 2.4%), 265.1345 ($C_{17}H_{17}N_2O$, 98%), 243.1132 ($C_{14}H_{15}N_2O_2$, 2.1%), 158.0602 ($C_{10}H_8NO$, 4.3%), 156.0813 ($C_{11}H_{10}N$, 13.1%), 144.0805 ($C_{10}H_{10}N$, 9.4%), 138.0917 ($C_8H_{12}NO$, 3.4%), 130.0659 (C_9H_8N, 7.2%), 124.0761 ($C_7H_{10}NO$, 3.0%), 110.0967 ($C_7H_{12}N$, 2.7%), 108.0811 ($C_7H_{10}N$, 4.2%) and 96.0577 ($C_6H_{10}N$, 3%). The formulae of the ions were determined by computer monitored high resolution mass measurements and confirmed by peak matching experiments on important ions.

Linked scan measurements of metastable transitions on the $[M]^+$ at *m/z* 312 showed that the ions at *m/z* 294, 243, 158, 156, 144, 138 and 124 arise directly from it. Similarly it was demonstrated that the ion at *m/z* 294 fragments directly to the ion at *m/z* 265 indicating the presence of an ethyl group in the molecule. The ion at *m/z* 130 was also seen to arise directly from the ion at *m/z* 158 and also from the ion at *m/z* 156. The fragmentation pathway of the ion at *m/z* 138 showed that the ions at *m/z* 110, 108 and 96 arise directly from it. The peaks at *m/z* 156, 144 and 130 gave support to the presence of a quebrachamine skeleton [6] and the mass fragments at *m/z* 138 and 124 indicated that only one oxygen is present on the piperidine ring.

The ^1H NMR spectrum (300 MHz, $CDCl_3$) showed the presence of a triplet centred at δ0.74 (J = 7.4 Hz) and a quartet centred at δ1.22 (J = 7.4 Hz) which were assigned to the methyl and methylene protons of the ethyl group, respectively. The C-15 proton resonated as a doublet at δ3.25 (J = 3.0 Hz) and the C-14 proton as a multiplet centred at δ2.90. The C-5 proton appeared as a doublet of double doublets centred at δ5.2 ($J_{5,6\beta}$ = 2.4 Hz, $J_{5,6\alpha}$ = 5.0 Hz, $J_{5,OH}$ = 11.4 Hz) which collapsed to a double doublet ($J_{5,6\beta}$ = 2.4 Hz, $J_{5,6\alpha}$ = 5.0 Hz) on shaking with D_2O indicating the presence of a hydroxyl group on this carbon. The C-6β proton resonated as a double doublet centred at δ2.49 ($J_{6\beta,5}$ = 2.4 Hz, $J_{6\beta,6\alpha}$ = 14.0 Hz) while the C-6α proton appeared as another double doublet at

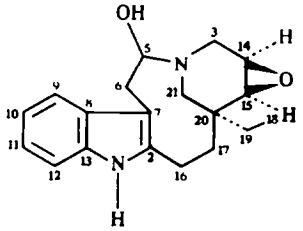

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Table 1. ^{13}C NMR spectral data of stapfinine

Carbon no.	Chemical shift	Multiplicity	Carbon no.	Chemical shift	Multiplicity
2	139.0	*s*	14	53.1	*d*
2	54.9	*t*	15	58.6	*d*
5	68.9	*d*	16	24.4	*t*
6	42.4	*t*	17	29.7	*t*
7	103.0	*s*	18	32.6	*t*
8	129.0	*s*	19	7.5	*q*
9	117.9	*d*	20	29.3	*s*
10	119.1	*d*	21	52.8	*t*
11	121.4	*d*			
12	110.3	*d*			
13	137.0	*s*			

δ1.95 ($J_{6\alpha,5}$ = 5.0 Hz, $J_{6\alpha,6\beta}$ = 14.0 Hz). The triplet centred at δ7.08 ($J_{10,9} = J_{10,11}$ = 6.0 Hz) was assigned to the C-10 proton while another triplet centred at δ7.13 ($J_{11,10} = J_{11,12}$ = 6.0 Hz) was attributed to the C-11 proton. The C-12 proton resonated as a doublet at δ7.29 ($J_{12,11}$ = 6.0 Hz) and the C-9 proton appeared as a doublet at δ7.47 ($J_{9,10}$ = 6.0 Hz). The broad singlet at δ7.73 was assigned to the NH proton. These assignments were confirmed by homodecoupling and 2-D NMR (COSY-45°) experiments. The upfield chemical shifts for the C-14 and C-15 protons indicated that the epoxide has a β-configuration [7]. The ethyl group is assigned as having an α-configuration in view of the known stereochemistry at this centre in aspidosperma alkaloids [7].

The ^{13}C NMR (75 MHz) of stapfinine recorded in $CDCl_3$ showed the presence of an epoxide group by the signals at δ53.1 and δ58.6 which were assigned to the oxygen bearing C-14 and C-15 carbons. The other signals were consistent with structure **1** for stapfinine. The assignments to various carbon atoms were confirmed by performing DEPT (Distortionless Enhancement by Polarization Transfer) experiments [8] and are shown in Table 1.

On the basis of these spectral data, structure **1** (relative stereochemistry shown) is proposed for stapfinine. The stereochemical configuration of the hydroxyl group at C-5 is not known.

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