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1,2-DEHYDROASPIDOSPERMIDINE-*N*-OXIDE, AN ALKALOID FROM *RHAZYA STRICTA*

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Key Word Index—*Rhazya stricta*; Apocynaceae; alkaloids; 1,2-dehydroaspidospermidine-*N*-oxide; FAB-MS.

Abstract—A new alkaloid, 1,2-dehydroaspidospermidine-*N*-oxide, has been isolated from the roots of *Rhazya stricta*.

INTRODUCTION

Rhazya stricta (Apocynaceae) is a medicinal plant found in several regions of Pakistan. The plant is reputed in the indigenous system of medicine to be a cure for boils, eruptions, sore throat [1–3; Baquar, S. R., unpublished], syphilis [1, 2, 4], a bitter tonic for fever [1–3; Baquar, S. R., unpublished] and for chronic rheumatism [5, 6]. The leaves have anticancer properties [5, 6; Baquar, S. R., unpublished]. We have previously reported a number of new alkaloids from the plant [7–11]. In continuation of our studies on the isolation and structure elucidation of new chemical constituents from the roots of *R. stricta*, we have isolated a new alkaloid which has been shown to be the *N*-oxide of 1,2-dehydroaspidospermidine (**1**).

RESULTS AND DISCUSSION

The crude alkaloids were obtained from the ethanolic extract of the roots by the conventional procedures [11]. The crude extract was fractionated by extraction into chloroform at different pH values. The new alkaloid was obtained from the extract at pH 8 by repeated chromatographic purification on silica gel GF-254, $[\alpha]_D$ +120° ($CHCl_3$). The substance gave a UV spectrum characteristic of the indolenine system, showing absorption maxima at 206, 222, 260 nm and minima at 217 and 245 nm. The IR spectrum showed a peak at 1710 cm^{-1} and minima at 217 and 245 nm. The IR spectrum showed a peak at 1710 cm^{-1} indicating the presence of a C=N group. The substance afforded a mass spectrum with a strong peak at m/z 280.1434 and a very small $[M]^+$ peak at m/z 296 ($C_{19}H_{24}N_2O$). The exact mass of the molecule could be obtained by fast atom bombardment mass spectrometry which showed a $[M+H]^+$ peak at m/z 297.1927 ($C_{19}H_{25}N_2O$ requires 297.1967). Exact mass measurement with an EI source gave the mass of the molecular ion to be 296.1849 in agreement with the formula $C_{19}H_{24}N_2O$. Other significant peaks (by EI) were at m/z 280 $[M-O]^+$, 251 $[280-C_2H_5]^+$, 210, 194, 169, 168, 156, 149, 125, 97, 83 and 56. The fragmentation pattern was remarkably similar to that reported for 1,2-dehydroaspidospermidine suggesting that the substance was the corresponding *N*-oxide.

The ^1H NMR spectrum of **1** (300 MHz) showed the presence of a triplet at δ0.49 (J = 7.5 Hz) which is assigned to the methyl protons of the ethyl chain. The methylene protons of the ethyl group resonated as a quartet at δ1.71 (J = 7 Hz). A sharp singlet at δ3.74 is assigned to the C-19 proton. The downfield position of this signal as compared to its usual position in aspidosperma alkaloids [12] is consistent with the presence of a quaternary adjacent nitrogen. The aromatic protons resonated as complex multiplets in the range of δ7.13–7.52.

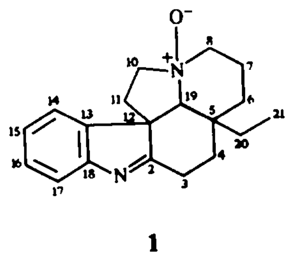
Attempted deoxygenation by reduction with $NaBH_4$ in methanol, or by treatment with PCl_3 [13], led to the formation of an indolic compound which showed an $[M]^+$ peak at m/z 298 and other fragment peaks at m/z 297, 251, 225, 197, 170, 169, 124 and 97. The structure of this product is presently under investigation.

On the basis of the above spectral studies the new alkaloid is identified as 1,2-dehydroaspidospermidine-*N*-oxide.

EXPERIMENTAL

FABMS were measured in glycerol–H_2O (1 : 1) in the presence of KI. Accurate mass measurement with the FAB source were made using glycerol as int. standard. ^1H NMR spectra were recorded in $CDCl_3$ at 300 MHz, UV in MeOH and IR in $CHCl_3$.

Isolation of **1**. Roots (75 kg) of *R. stricta* Decaisne were crushed with an Ultra-Turrax in EtOH (120 l). The material was filtered and evapd under vacuum to a gummy mass (900 g). The gum was



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acidified with 10% HOAc to pH 3 and extracted with $CHCl_3$ (2 l.).

The aq. layer was basified with NH_3 to pH 14 and washed with $CHCl_3$ (2 l.) and EtOAc (2 l.). The organic extracts were combined, dried (Na_2SO_4), filtered, evapd and treated with 2% aq. tartaric acid (3 l.) and then extracted with $CHCl_3$ (1.5 l.) at different pH values. The extract at pH 8 was dried (Na_2SO_4), filtered and concd to a crude alkaloidal gum (7.5 g). The gum was then subjected to repeated prep. TLC which afforded a pure compound (10 mg) in hexane–Me_2CO (7:3) + NH_3 (5 drops); $[\alpha]_D$ 120° ($CHCl_3$); UV MeOH λ_{max} nm: 206, 222, 260; λ_{min} nm: 217, 245; IR $\nu_{max}^{CHCl_3}$: 1710 cm^{-1}; ^1H NMR ($CDCl_3$): δ0.49 (3H, *t*, $J_{21,20} = 7.0$ Hz, CH_2–$\underline{Me}$), 1.71 (2H, *q*, $J_{20,21} = 7.0$ Hz, $C\underline{H}_2$-Me), 3.74 (1H, *s*, H-19), 7.13–7.52 (4H, *m*, aromatic protons); MS *m/z* (rel. int.): 296 $[M]^+$ (1), 280 (46), 251 (23), 210 (37), 194 (21), 169 (9), 168 (12), 156 (12), 149 (33), 125 (32), 97 (42), 83 (48), 56 (100). Peak matching measurements (EI): 296.1849 ($C_{19}H_{24}N_2O$, requires 296.1888), 280.1934 ($C_{19}H_{24}N_2$, requires 280.1939); FAB: 297.1927 ($C_{19}H_{25}N_2O$, requires 297.1967).

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