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VINCADINE FROM THE LEGUMES OF *RHAZYA STRICTA*

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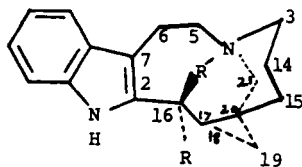
Rhazya stricta Decsne. (Apocynaceae) (1) is a small glabrous, erect shrub, widely distributed in Western Asia and abundantly found in Pakistan. It has long been used in the indigenous system of medicine for the treatment of various diseases (2-4). Some of its alkaloids also possess anticancer activity (5,6). In our continuing chemical analysis of the legumes of *R. stricta* (7), we report here the isolation of vincadine, identified on the basis of spectral studies. Vincadine has not previously been reported from this plant.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Spectra were recorded on JASCO A-302 ir spectrophotometer, Shimadzu UV-240 spectrophotometer, Finnigan MAT 312 mass spectrometer, and Bruker WP-100 SY nmr spectrometer.

PLANT MATERIAL.—The plant material was collected in the month of July 1982, from a small village near Karachi and was identified by the Botany Department of Karachi University where a voucher specimen is deposited.

The crude alkaloids (40 g) isolated by conventional procedures (8) from (10 kg) dried legumes (without seeds) were dissolved in 10% HOAc solution and subjected to selective pH separations after the stepwise basification with NH_3 . The fraction which was extracted into CHCl_3 at pH 2.7 (2 g) was subjected (0.7 g) to preparative tlc and afforded a faster running alkaloid (~10 mg) on silica gel (GF-254) plates (0.2 mm) with light petroleum (40°-60°): Me_2CO (8:2) as the solvent system, with an overall yield of $2.85 \times 10^{-4}\%$. The R_f value calculated was 0.80. The alkaloid thus obtained was crystallized with MeOH, mp 125°, $[\alpha]^{23}_{\text{D}} \pm 0$ (EtOH). The structure of this alkaloid was confirmed as vincadine (1) by comparison of its spectral data with those reported in the literature (9-13).



1

R=H
R'=COOCH₃

It showed a characteristic indolic uv with λ max (MeOH) 228 (log ϵ 4.59), 284 (log ϵ 3.94) and 292 nm (infl., log ϵ 3.89), λ min 255 nm (log ϵ 3.46). The ir spectrum (CHCl_3) showed prominent peaks at 3448 cm^{-1} (N-H), 1726 cm^{-1} (ester carbonyl) and 1602 cm^{-1} (C=C). Its hrms afforded the molecular ion peak (M^+ at m/z 340.214, calc. 340.215 ($\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_2$). Other prominent peaks occurred at m/z 325.191 ($\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_2$), 311.175 ($\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_2$), 309.196 ($\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}$), 281.201 ($\text{C}_{19}\text{H}_{25}\text{N}_2$), 215.093 ($\text{C}_{13}\text{H}_{13}\text{NO}_2$), 210.149 ($\text{C}_{12}\text{H}_{20}\text{NO}_2$), 138.128 ($\text{C}_9\text{H}_{16}\text{N}$), 124.114 ($\text{C}_8\text{H}_{14}\text{N}$), and 110.096 ($\text{C}_7\text{H}_{12}\text{N}$). The ^1H nmr (CDCl_3 , 100 MHz, internal standard TMS, δ ppm) showed resonances at 8.99 (brs, 1H, N-H), 7.26 (m, 4H, aromatic protons), 3.83 (m, 1H, C-16 H), 3.75 (s, 3H, COOCH_3), and 0.87 (t, 3H, $J=6.9\text{Hz}$, $-\text{CH}_2-\text{CH}_3$). The C-16 proton resonated at characteristic upfield position of δ 3.83 indicating that the compound was vincadine rather than the C-16 epimer, epivincadine, in which the C-16 H is known to resonate farther downfield at δ 5.59 due to its proximity with the nitrogen lone pair. The assignment was further supported by the relatively low field value of the ester methyl at δ 3.75 (in epivincadine it resonates at δ 3.65). The downfield shift (δ 0.87) of the methyl group of the ethyl side chain in vincadine in comparison to epivincadine (δ 0.67) reflects its proximity to the ester carbonyl group.

The isolation of vincadine from *R. stricta* provides a useful link in the hypothetical biosynthetic route (14, 15) to the various Aspidosperma alkaloids present in this plant.

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