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THE STRUCTURE ELUCIDATION OF RHAZINILAM, A NEW CLASS OF ALKALOIDS FROM THE APOCYNACEAE, BY X-RAY ANALYSIS

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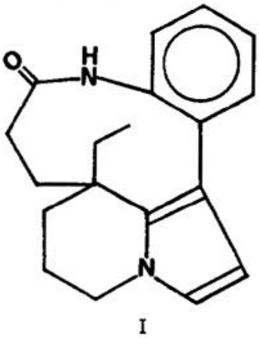
Rhazinilam, first isolated from the leaves of Rhazya stricta Decaisne by Banergi et al.[1] in 1970, has recently been isolated in our laboratories from the leaves of Aspidosperma quebracho-blanco in a yield of 0.002 per cent.[2] At this time we wish to report the structure of rhazinilam (I) by single crystal X-ray diffraction studies. The elemental formula for rhazinilam ($C_{19}H_{22}N_2O$) isolated in this study was obtained from high resolution mass spectral measurements, and is in agreement with that found for I isolated from Rhazya stricta[1]. Single crystals (m.p. 214-215°) of I were grown from methanol, and one such crystal was mounted on a Picker FACS-1 automatic diffractometer. The following lattice parameters were recorded: a = 7.589, b = 8.524, c = 24.342 Å, and the space group was determined as $P2_12_12_1$ from systematic absences.



I

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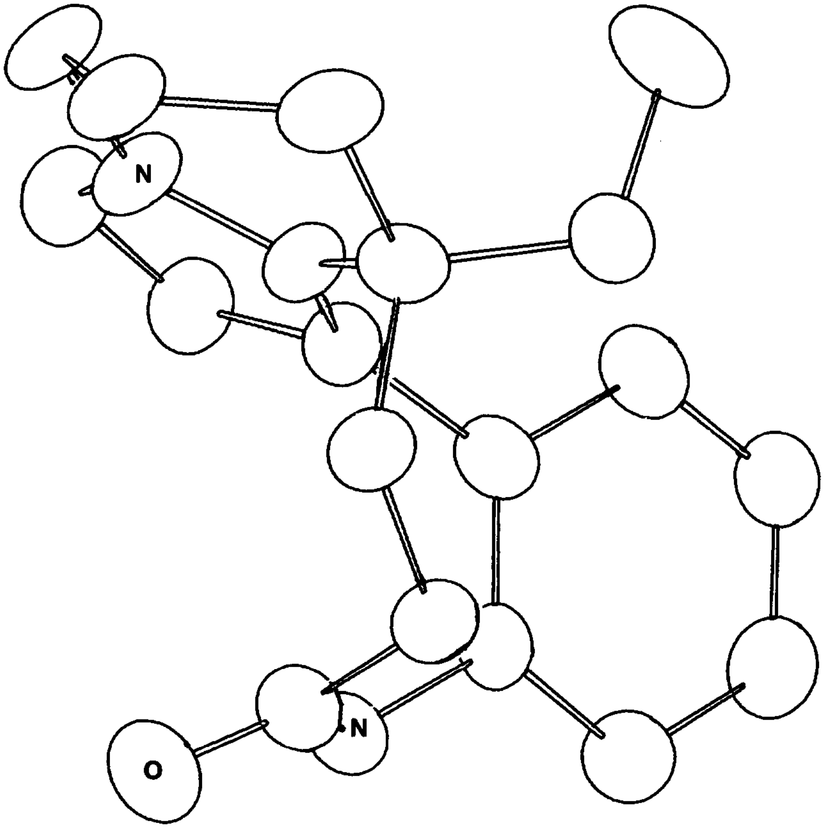
These data were then processed in the usual manner to give relative structure factors. These were normalized using Wilson statistics and renormalized to give average values of E^2 close to unity in classes of indices, parity, and sin θ. Values of E greater than 1.35 were used in determining a set of phases by the direct method, using Syd Hall tangent refinement and extension programs[3], starting with three origin phases and one enantiomorph phase. The phases from the above calculations were next used to make an E synthesis and this map revealed the entire molecule.

The structure was refined initially by placing carbon atoms at all atomic positions (excluding hydrogens). The temperature factors of three atoms dropped below 2.0 after two cycles of isotropic least squares. One oxygen and the two nitrogens were then placed at the appropriate positions and several cycles of isotropic least squares, followed by three cycles of anisotropic least squares, produced a conventional R factor of 12.5% for all reflections (1537 excluding systematic absences).

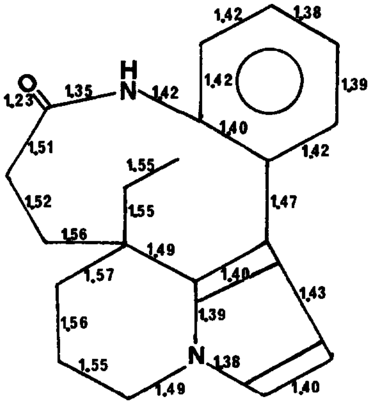
The available physical data could then be easily correlated with the resulting structure I. The NMR showed the vinyl protons on the pyrrole nucleus at 5.9 and 6.65 δ (J = 3 Hz), which correlates well with those similar protons on other 1,2,3-substituted pyrroles (the vinyl proton next to the nitrogen atom is deshielded to 6.65 δ by the ring nitrogen). The four aromatic protons were found as a multiplet from 7.36 to 7.69 δ; the CH_2 protons next to the carbonyl as a distorted triplet at 3.75 to 4.20 δ; the terminal methyl as a distorted triplet at 0.46 to 0.89 δ (partially shielded by the phenyl ring); and the NH proton at 6.84 δ .

An amide NH absorption at 3230 cm^{-1}, as well as the amide carbonyl absorption at 1672 cm^{-1}, were evident in the infrared spectrum. In addition, the ultraviolet spectrum displayed an ϵ_{max} at 224 nm, with a shoulder at 264 nm.

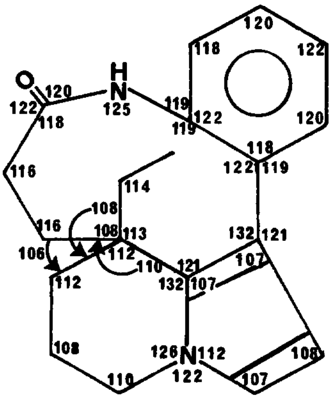
An interesting feature of the structure is the theoretical existence of four optical isomers in the solid state. One d-l pair would obviously arise from the one asymmetric carbon atom and the other pair arises because of the frozen conformation (in the crystal) around the phenyl and pyrrole rings. Model building confirms the above and clearly shows the asymmetry around the aromatic rings. Crystallization of the conformation (if possible) containing the phenyl ring rotated 180° to that found in this study would produce a diastereoisomer.[4] The absolute configuration of this enantiomer was not determined in this X-ray structural analysis. A figure of the molecule derived from the electron density map, using the coordinates at R = 12.5%, is given below.



The bond distances and angles are summarized in the following diagrams. The pyrrole distances are similar to those pyrroles which have been determined previously by single crystal X-ray analysis.



Distances in Angstroms



Angles in Degrees

COORDINATES FOR RHAZINILAM

	X	Y	Z		X	Y	Z
1 O	-.0368	.1528	.4969	12 C	-.1993	-.0159	.3958
2 N	.1891	.1950	.4399	13 C	.3601	.3178	.3664
3 N	.0843	-.3166	.4232	14 C	.2518	-.3259	.4451
4 C	.3794	.0253	.3119	15 C	.4510	.3024	.3157
5 C	.0192	.1574	.4494	16 C	.2304	-.1084	.3900
6 C	.4590	.1583	.2900	17 C	-.2305	-.2935	.3626
7 C	-.1046	.1409	.4011	18 C	-.1037	-.1482	.3629
8 C	.2757	.1832	.3881	19 C	-.2332	-.3836	.4185
9 C	.2892	.0364	.3630	20 C	-.0450	-.4464	.4289
10 C	.3440	-.1945	.4259	21 C	-.0793	-.0899	.3031
11 C	.0673	-.1859	.3896	22 C	.0083	-.2093	.2638

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REFERENCES AND FOOTNOTES

1. A. Banerji, P.L. Majumder and A. Chatterjee, Phytochemistry, 9, 1491 (1970).
2. While this study was in progress, we learned of the structure elucidation studies of rhazinilam by Dr. G.F. Smith and co-workers at the University of Manchester, in which they arrived at structure I for rhazinilam by chemical degradative and spectroscopic methods. The latter work is described in the preceding communication of this issue of Tetrahedron Letters.
3. S.R. Hall (1967), adapted to the IBM 7090 by H. Berman (1969), and revised by R. Shiono, University of Pittsburgh, unpublished report (1970).
4. Model building indicates that placing the aromatic rings in the same plane is quite unfavorable. The amide group is held in the syn conformation because of the ring and this influences other conformational perturbations in the molecule. Because the aromatic rings are approximately perpendicular, little or no resonance between the two moieties should be possible.