

RHAZINILAM, A NEUTRAL ALKALOIDAL ARTEFACT FROM  
RHAZYA STRICTA DECAISNE.

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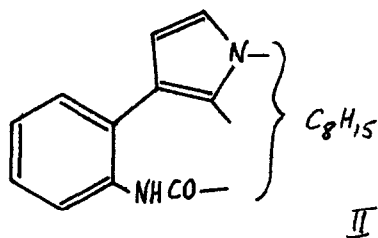
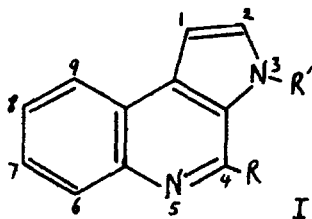
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Rhazinilam,  $C_{19}H_{22}N_2O$ , (to which we assign structure V), is a neutral compound first studied by A. Chatterjee *et al.*<sup>1</sup> who isolated it from Rhazya stricta Decaisne and found it to contain a  $\cdot CONH \cdot$  function and a C·Et group. Some years previously, H.A.A. Linde<sup>2</sup> had isolated a compound, Ld 82, from Melodinus australis (F. Mueller) Pierre, which we have recently shown to be identical with Rhazinilam.<sup>3</sup>

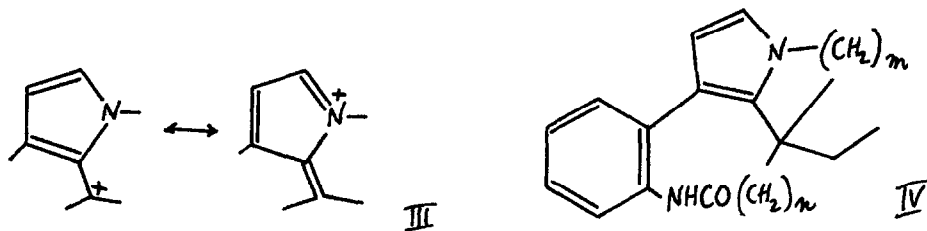
We have found Rhazinilam to gradually accumulate *in vitro* in the basic fractions of R. stricta, in which it must arise from an alkaloidal precursor.

Rhazinilam is converted by acid into a mixture of closely related bases  $C_{19}H_{20}N_2$ , the electronic absorption and fluorescence spectra of which are very closely similar to those of 3H-3,4-dimethylpyrrolo(2,3-c)quinoline (I,  $R = R' = Me$ ):<sup>4</sup> the N.M.R. spectrum of the bases shows six aromatic protons in three groups of two centred at  $\tau$  2.1, 2.65, and 3.15 which very closely parallel the corresponding groups of two protons in I ( $R = R' = Me$ ), centred at  $\tau$  1.95, 2.55, and 3.0. Since a hydrogen at C4 in the pyrroloquinoline system would be expected to resonate at or below  $\tau$  1, part-structure I ( $R + R' = C_8H_{14}$ ) follows for the bases derived from Rhazinilam.

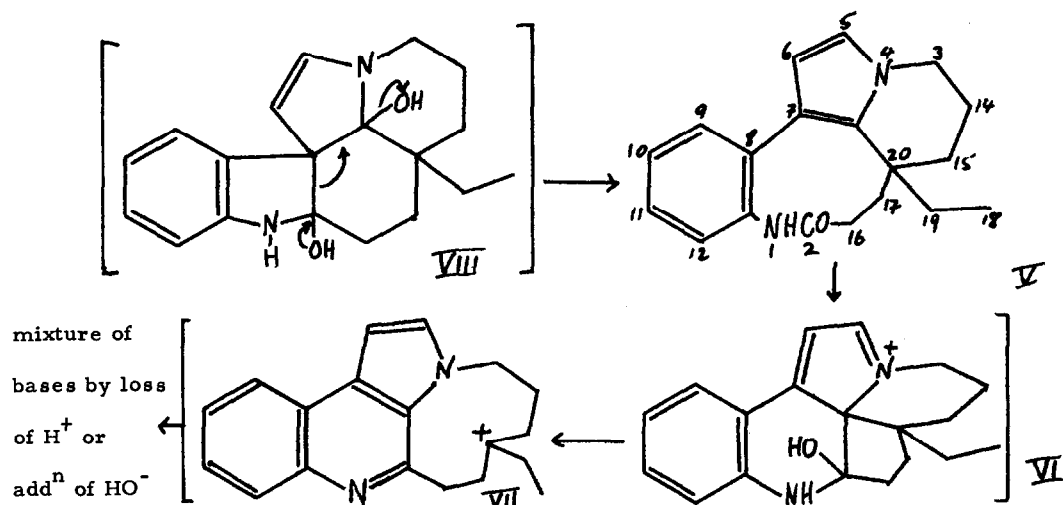
It then becomes evident that Rhazinilam must possess part-structure II in which the amide group is almost certainly part of a medium ring: this structure accounts for its non-basic character, for the sharp AB system ( $\tau$  3.54, 4.27,  $j = 1.5$  cps in  $CDCl_3$ )



corresponding to the two pyrrolic hydrogens,<sup>5</sup> for the smooth formylation ( $\text{Ac}_2\text{O}-\text{HCO}_2\text{H}$ ) to  $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_2$  the electronic absorption of which ( $\lambda_{\text{max}} 303 \text{ nm}$ ,  $\epsilon 16200 \text{ MeOH}$ ) corresponds to that of a 2-formylpyrrole, for the positive Ehrlich test, and above all for the weak electronic absorption which shows no maxima and which becomes explicable in terms of steric inhibition of conjugation of all three chromophores (amide, benzene, and pyrrole), the consequence of the conformation of the medium ring they form a part of. The N.M.R. spectrum of Rhazinilam further shows only one  $\text{CH}_3$  group as part of a  $-\overset{\text{C}}{\text{C}}-\text{CH}_2\text{CH}_3$  group (triplet  $\tau 9.3$ ,  $j = 7.0 \text{ cps}$ ; loss of  $\text{C}_2\text{H}_5$  in mass spectrum) attached to a fully substituted carbon (double irradiation at  $\tau 9.3$  brings out a 2H singlet at  $\tau 8.7$ ), and a complex multiplet (2H) centred at  $\tau 6.15$  which is shown to be a  $\text{CH}_2$  group (by its change to an AB system,  $\tau 6.0, 6.2$ ,  $j = 10.5 \text{ cps}$ , by double irradiation at  $\tau 7.8$ ) which from its chemical shift must be attached to the pyrrolic nitrogen (corresponding N- $\text{CH}_2$  in cyclohexano(a)-pyrrole =  $\tau 6.20$ <sup>6</sup>). The fact that M- $\text{C}_2\text{H}_5$  is by far the most intense peak in the mass spectrum of Rhazinilam strongly suggests stabilisation involving the pyrrolic nitrogen, as shown in III. The partial structure for Rhazinilam can now be extended to IV ( $m+n=5$ ).



Treatment of Rhazinilam with aq. NaOH yields an aminoacid (not isolated) which is not reconvertible into rhazinilam on heating, but which is converted by  $\text{Ac}_2\text{O}$  into a carboxylic acid  $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_3$  the base peak in the mass spectrum of which corresponds to M- $\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$  (observed 281.164, calc. for  $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O} - 281.165$ ): this is only compatible with attachment of the propionyl residue to the same quaternary atom as the ethyl group (this is supported by the absence of fragments corresponding to M- $\text{CH}_2\text{CO}_2\text{H}$  or M- $\text{C}_3\text{H}_6\text{CO}_2\text{H}$ ). The assignment of structure V to Rhazinilam then follows<sup>7,8</sup>.



The formation of pyrroloquinolines by acid catalysis is a transannular electrophilic addition of the protonated amide group to C21 to give cation VI, which loses  $\text{H}_2\text{O}$  and undergoes C20 - C21 bond fission to give cation VII, which finally can lose proton in four ways to give two endocyclic olefins and two (syn and anti) ethylidene compounds, and can add water to give a tertiary alcohol (only partial separation of these five compounds has so far been achieved by t.l.c.).

In conclusion one can postulate the derivation of Rhazinilam from an aspidosperma precursor such as VIII by the fragmentation reaction shown, a reaction hitherto not yet observed in this field. A search for this precursor is under way.

#### References and Footnotes

1. A. Banerji, P.L. Majumder, and A. Chatterjee, Phytochemistry, **9**, 1491, (1970).
2. H.A.A. Linde, Helv. Chim. Acta, **48**, 1822, (1965).
3. We are indebted to Dr. Linde for sending us a sample of his compound Ld82 which was identical with Rhazinilam by mixed m.p. and t.l.c. behaviour in six systems.
4. H.F. Hodson, Ph.D. thesis, University of Manchester, 1957.
5. H. Suhr, Anwendungen der Kernmagnetischen Resonanz in der Organischen Chemie, p. 224 (Springer Verlag, Berlin, 1965).
6. J.M. Patterson and S. Svedigdo, J. Org. Chem., **32**, 2969, (1967).

7. The numbering follows the biogenetic system of J. Le Men and W.I. Taylor, Experientia, 21, 508, (1965).
8. After conclusion of the work described in this paper we learned of the structure elucidation of Rhazinilam by X-ray crystallographic analysis by D.J. Abraham et.al. (see accompanying publication).