Tetrahedron Letters No.30, pp. 2625-2628, 1970. Pergamon Press. Printed in Great Britain.

AN ALTERNATE MODEL FOR THE BIOGENESIS OF THE SPIROBENZYLISOQUINOLINE ALKALOIDS

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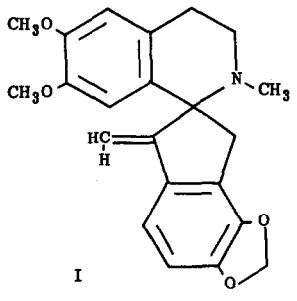
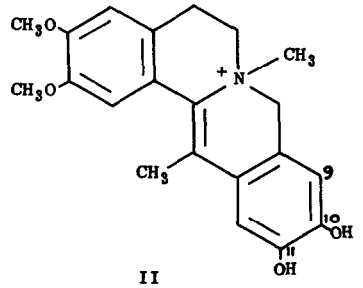
(Received in USA 6 May 1970; received in UK for publication 29 May 1970)

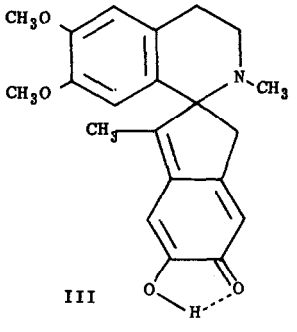
In an in vitro study of the biogenesis of the spirobenzylisoquinoline alkaloid ochotensimine (I), it was demonstrated that base catalyzed rearrangement of the enamine N-metho salt II gives the quinone methide III which in DMSO tautomerizes to the spiro structure IV.[1, 2a-2f]



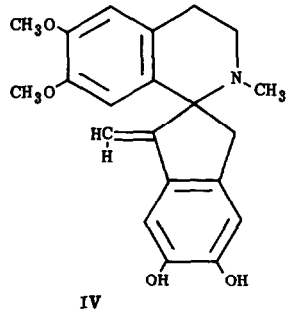
I



II

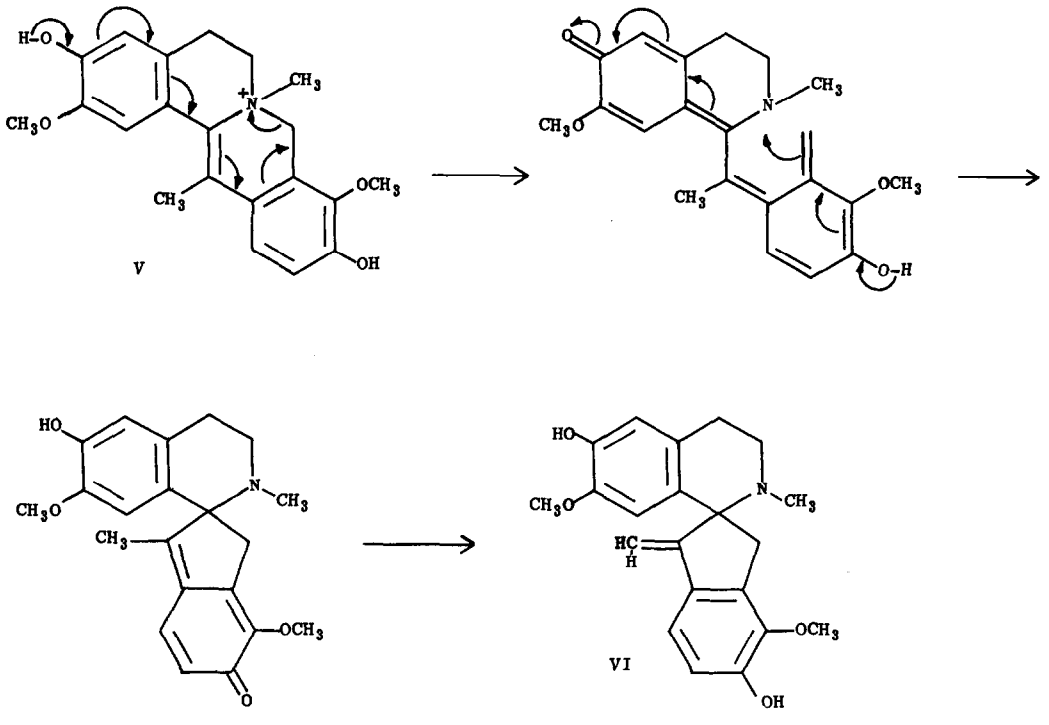


III

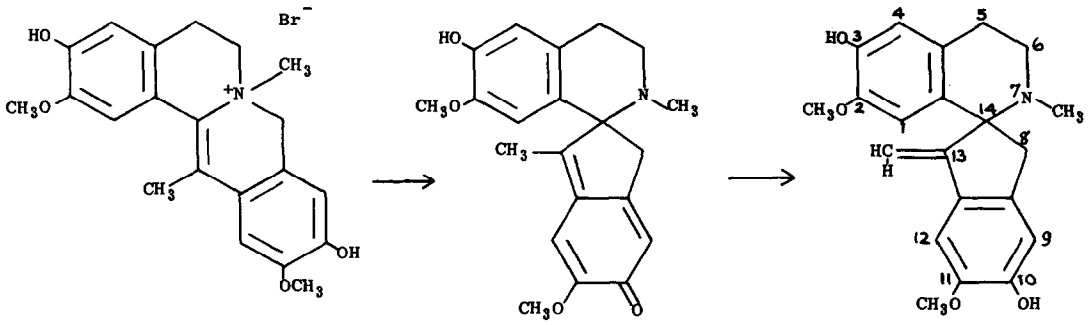


IV

There is a possibility, however, that the plant does not use an enamine N-metho salt with two phenolic groups in the same ring as a precursor for ochotensimine (I), and may prefer instead to proceed through the intermediacy of the diphenolic salt V in which the phenolic groups are placed in different rings. Base induced rearrangement of V would lead to the spirane VI which can then be transformed into ochotensimine (I).



In order to test this hypothesis, the diphenolic N-metho salt VII was prepared, $C_{21}H_{24}NO_4Br$, mp 234-236°,[3,4] and submitted to prolonged refluxing in aqueous ethanolic sodium hydroxide under a nitrogen atmosphere. The product was the required spirane IX, $C_{21}H_{23}NO_4$, obtained as an oil in 50% yield; nmr spectrum in $CDCl_3$, $N\text{-}CH_3$ (3H singlet, δ2.23), C-2 OCH_3 (3H singlet, δ3.64), C-11 OCH_3 (3H singlet δ3.95), two vinylic protons (2H singlets, δ4.96 and 5.62), four aromatic protons (4H singlets, δ6.29, 6.63, 6.83 and 7.03).



VII VIII IX

The quinone methide VIII could not be isolated because it lacks the stability imparted by internal hydrogen bonding which is present in the analogous compound III. Additionally, whereas the salt II rearranged to a spiro structure by heating overnight in base, it was necessary for the salt VII to be refluxed for four days to obtain satisfactory yields of the spiro product IX.

Experimental data therefore so far indicate that either N-metho salts II (with OH groups at C-9,10 rather than 10,11) or V can act as precursors for ochotensimine. The question as to which of these two systems is the true precursor for ochotensimine can be answered conclusively only by in vivo experiments using labeled precursors.[5]

Acknowledgments:- The authors wish to thank the National Science Foundation for a research grant, and the Hoffmann-La Roche Foundation for an unrestricted grant. JFN is the recipient of National Institutes of Health predoctoral fellowship 5-FO1-GM-42,430-02.

References

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2. For the structural elucidation of the spirobenzylisoquinoline alkaloids see:

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   (f) R.H.F. Manske, R.G.A. Rodrigo, D.B. MacLean, D.E.F. Gracey and J.K. Saunders, Can. J. Chem., 47, 3589 (1969).

3. This 10,11-substituted system is much more readily prepared than the 9,10 analog, and lends itself equally well to the aims of this investigation. Similarly, salt II was used in the work described in Ref. 1 above, rather than its 9,10-dihydroxy analog.

4. The details of the synthesis of the salt VII, λ_{max}^{EtOH} 230 and 331 mμ (log e 4.45 and 4.55), will be reported at a later date.

5. Satisfactory elemental analyses were obtained for all key intermediates.