

THE BIOGENESIS OF THE LYTHRACEAE ALKALOIDS (1)

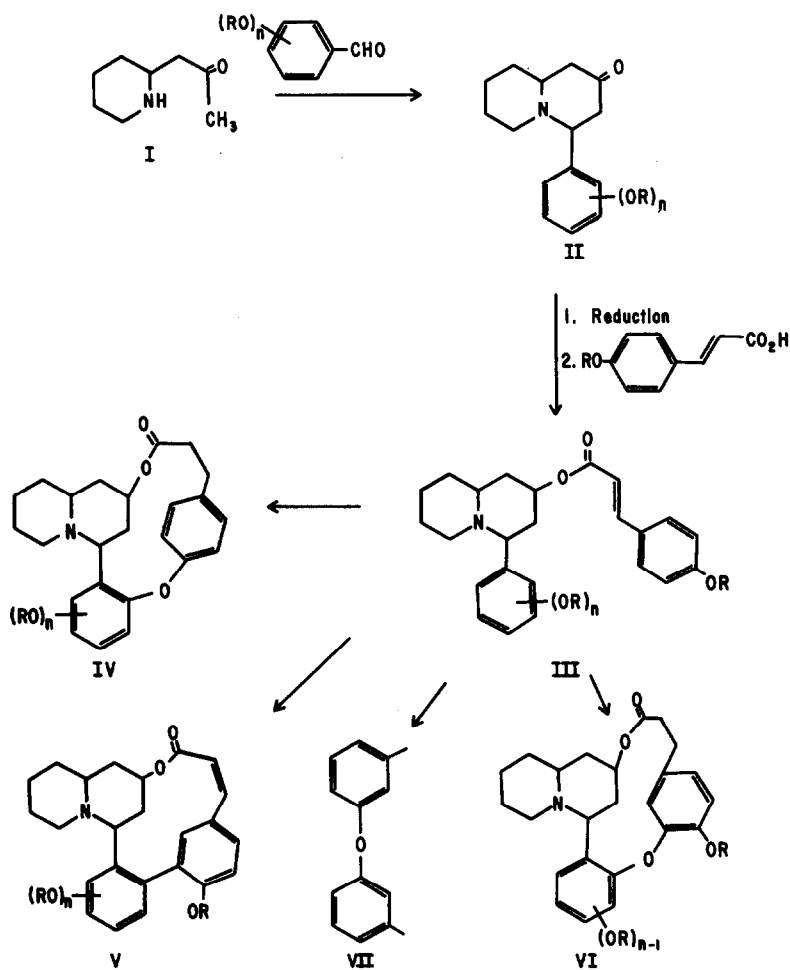
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A structural pattern is now apparent from the growing body of information available for the Lythraceae alkaloids. These bases differ in the following ways: the stereochemistry at the quinolizidine ring, the nature of the linkage between the phenyl rings and the oxygenation pattern of the phenyl rings. (2)

We wish to present a biogenetic scheme (Chart I) which accommodates the structural and stereochemical parameters of the Lythraceae alkaloids in a convincing manner. This scheme also outlines what appears to be a simple approach to synthesis of these alkaloids.

The conversion of lysine to  $\Delta^1$ -piperidine and the conversion of the latter to isopelleterine (I) is a well established biosynthetic path. (3) This condensation results in an asymmetric center next to the nitrogen as well as the introduction of the requisite oxygen substituent. Condensation of isopelleterine with an appropriately oxygenated benzaldehyde derivative yields II. Reduction of the keto group and esterification of the resulting alcohol gives III which on oxidative coupling results in the biphenyl and biphenyl ethers structures (IV-VI) that have been observed for the Lythraceae alkaloids. One might also expect the oxidative coupling of the type exhibited in VII but it has yet to be observed. It is possible that the more highly oxygenated Lythraceae alkaloids of unknown structure (4) (sinichuichine, sinine (6)) have this oxidation pattern or that in IV-VI with additional aromatic hydroxyl and/or methoxyl groups.

CHART I<sup>a</sup>

(a)  $R = H, CH_3$ . Cinnamic double bond may be hydrogenated or hydrated. (5)

- (1) Address correspondence to J. P. F. at The Salk Institute.
- (2) See accompanying communications; J. P. Ferris, C. B. Boyce, R. C. Briner, B. Douglas, J. L. Kirkpatrick and J. A. Weisbach, Tetrahedron Letters, in press (1966) and references therein.
- (3) These steps are in accord with current biogenetic theory. In view of the number of examples of the incorporation of lysine and its derivatives into quinolizidine alkaloids, an alternative scheme based on acetate  $\rightarrow$  poly- $\beta$ -keto acid  $\rightarrow$  quinolizidine seems less probable. For recent reviews, see E. Leete in "The Biogenesis of Natural Compounds" P. Bernfeld, Editor, Macmillan Co., N. Y., 1963, p. 739, K. Mothes and H. R. Schutte Ang. Chem. Internatl. Ed. 3, 341, 441 (1963), A. R. Battersby, Proc. Chem. Soc. 189 (1963), D. H. R. Barton, ibid. 293 (1963)
- (4) Lythridine (5) has been found to have the lythrine structure but with the double bond hydrated. B. Douglas, private communication.
- (5) B. Douglas, J. L. Kirkpatrick, R. F. Raffauf, O. Ribeiro and J. A. Weisbach, Lloydia 27, 25 (1964)
- (6) R. M. Blomster, A. E. Schwarting and J. M. Bobbitt, ibid. 27, 15 (1964)