

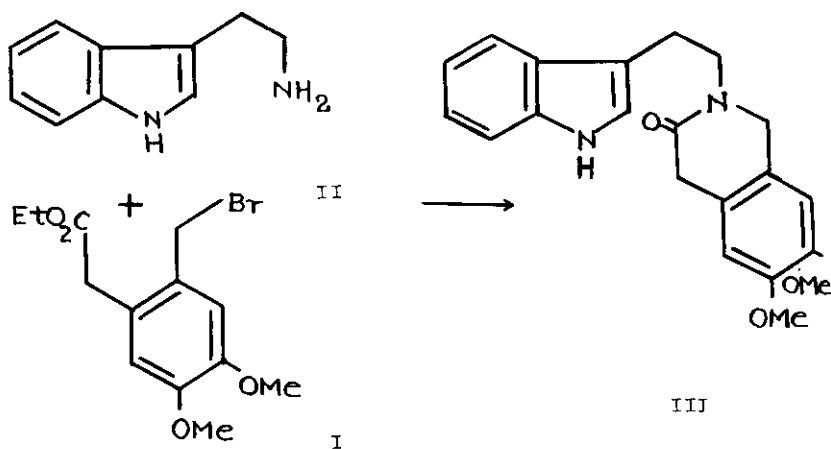
SYNTHESIS OF HETEROCYCLES VIA LACTONES. PART XI¹.

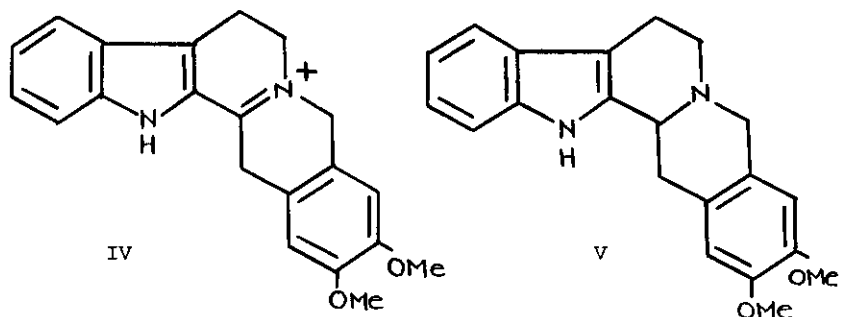
A NEW ROUTE TO YOHIMBANE SKELETON—SYNTHESIS OF 17,18-DIMETHOXY-15,16,17,18,19,20-HEXADEHYDROYOHIMBANE

Ganesh D. Pandey and Kamla P. Tiwari²
 Department of Chemistry, University of Allahabad,
 Allahabad-211002, India

Abstract - A new synthesis of the yohimbane skeleton has been described. Condensation of the bromo ester (I) with tryptamine (II) gave the lactam (III) which was cyclized and reduced to get the title compound (V).

In the recent past we have particularly been interested in the field of tetrahydroisoquinoline³ and berbine alkaloids⁴ and very recently have reported a new method for their syntheses^{5,6} by the intermediacy of a bromo ester essentially like (I). We have now further extended our approach successfully to synthesize the yohimbane alkaloids and in this present communication wish to report a new synthesis of the yohimbane skeleton, as exemplified by the synthesis of the title compound (V). The approach as outlined in scheme 1 is much to our belief, the first report of the use of the bromo ester (I) for the synthesis of the yohimbane skeleton.





(Scheme 1)

6,7-dimethoxy-3-isochromanone⁷ was dissolved in ethanolic hydrobromic acid at 0-5°. After 24 h the solvent and excess reagent was removed at 3-4 mm Hg and 20° to get ethyl 2-bromomethyl-4,5-dimethoxyphenylacetate⁸(I) in 78% yield, IR(CHCl₃) 1713 cm⁻¹, which was condensed with tryptamine⁹(II) in DMF at 100° for 48 h to get the tetracyclic lactam⁸ (III), C₂₁H₂₁N₂O₃ in 65% yield, IR (CHCl₃) 1640 (six membered lactam), 3330 cm⁻¹; MS m/e 349 (M⁺), 207, 206, 143, 117. Cyclization of the lactam (III) in toluene with phosphoryl chloride afforded the iminium salt(IV) as an oil. Sodium borohydride reduction of the iminium salt (IV) in methanol gave 17,18-dimethoxy-15,16,17,18,19,20-hexadehydroyohimbane (V), C₂₁H₂₂N₂O₂, m.p. 251-253° (lit.¹⁰, 249-250°; lit.¹¹, 294-295°; lit.¹², 248-250°); IR (KBr) 3335 cm⁻¹; UV: λ_{max} (log ε) 216 (4.48), 225 (4.56), 284 (3.99), 291 nm (3.94); NMR (CD₃)₂SO δ: 10.7 (broad, 1H, -NH), 7.5-6.8 (m, 4H, C-9H, C-10H, C-11H and C-12H), 6.75 (s, 2H, C-16H and C-19H), 4.2-4.0 (m, 1H, C-3H), 3.86 (broad, 2H, C-21H), 3.75 and 3.74 (2s, 6H, -OCH₃), 3.8-2.8 (m, 6H, C-5H, C-6H and C-14H).

Thus, utilization of the bromo ester(I) has successfully been shown to lead to the synthesis of the yohimbane skeleton.

ACKNOWLEDGEMENTS We thank Dr. K. Nagarajan, Ciba-Geigy Research Centre, Bombay for spectral facilities and

Dr. S.Teitel, Hoffmann La-Roche Inc., Nutley, New Jersey, U.S.A. for an authentic specimen of 6,7-dimethoxy-3-isochromanone. The award of a J.R.F. to one of us (G.D.P.) from U.G.C., New Delhi, India, is gratefully acknowledged.

REFERENCES

1. Part X. G.D.Pandey and K.P.Tiwari, Indian J. Chem., submitted.
2. Present address : DANIDA Fellow, Institut for Hygiejne OG Socialmedicin, Odense Universitet, J.B.Winsl vsvej 19. DK-5000, Odense, Denmark.
3. M.Shamma, "The isoquinoline alkaloids-Chemistry & Pharmacology", Academic Press, New York & London, 1972, p.1.
4. Ref. 3. P. 268 ; T.Kanetani, "The Chemistry of the isoquinoline alkaloids", Hirokawa Publishing Company, Tokyo, 1968, 2, 109 ; The Sendai Institute of Heterocyclic Chemistry, Sendai, 1974, 2, 191.
5. G.D.Pandey and K.P.Tiwari, Indian J.Chem., in press ; G.D.Pandey and K.P.Tiwari, Polish J.Chem., in press.
6. G.D.Pandey and K.P.Tiwari, Heterocycles, in press.
7. G.D.Pandey and K.P.Tiwari, Curr. Sci., 1979, 48, 724, J.Finkelstein and A. Brossi, J.Heterocyclic Chem., 1967, 4, 315 ; S.N.Rastogi, J.S.Bindra and N.Anand, Indian J. Chem., 1976, 19, 882.
8. All new compounds gave correct elemental analysis and spectral data.
9. E.H.P.Young, J.Chem.Soc., 1958, 3493.
10. G.Hahn and A.Hansel, Ber.Dtsch.Chem.Ges., 1938, 71, 2192.
11. J.Harley-Mason and W.R.Waterfield, Tetrahedron, 1963, 19, 65.
12. K.T.Potts and R.Robinson, J.Chem.Soc., 1955, 2675.

Received, 14th August, 1979