SYNTHESIS OF HETEROCYCLES VIA LACTONES. PART XI[1]. A NEW ROUTE TO YOHIMBANE SKELETON-SYNTHESIS OF 17,18-DIMETHOXY-15,16,17,18,19,20-HEXADEHYDROYOHIMBANE

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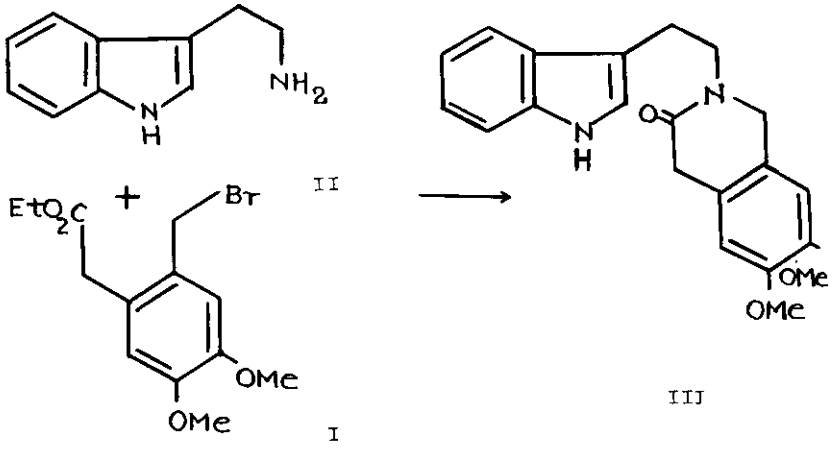
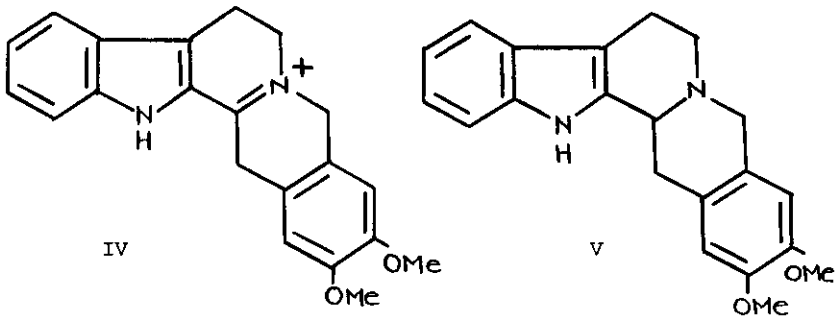
Abstract - A new synthesis of the yohimbane skeleton has been described. Condensation of the bromo ester(I) with tryptamine (II) gave the lactam (III) which was cyclized and reduced to get the title compound (V).

In the recent past we have particularly been interested in the field of tetrahydroisoquinoline[3] and berbine alkaloids[4] 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 examplified 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-isochromanone[7] 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-dimethoxyphenylacetate[8](I) in 78% yield, IR($CHCl_3$) 1713 cm^{-1}, which was condensed with tryptamine[9](II) in DMF at 100° for 48 h to get the tetracyclic lactam[8] (III), $C_{21}H_{21}N_2O_3$ in 65% yield, IR ($CHCl_3$) 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), $C_{21}H_{22}N_2O_2$, 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 $(CD_3)_2SO$ 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, $-OCH_3$), 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.

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