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SYNTHESIS OF HASUBANAN FROM MORPHINAN

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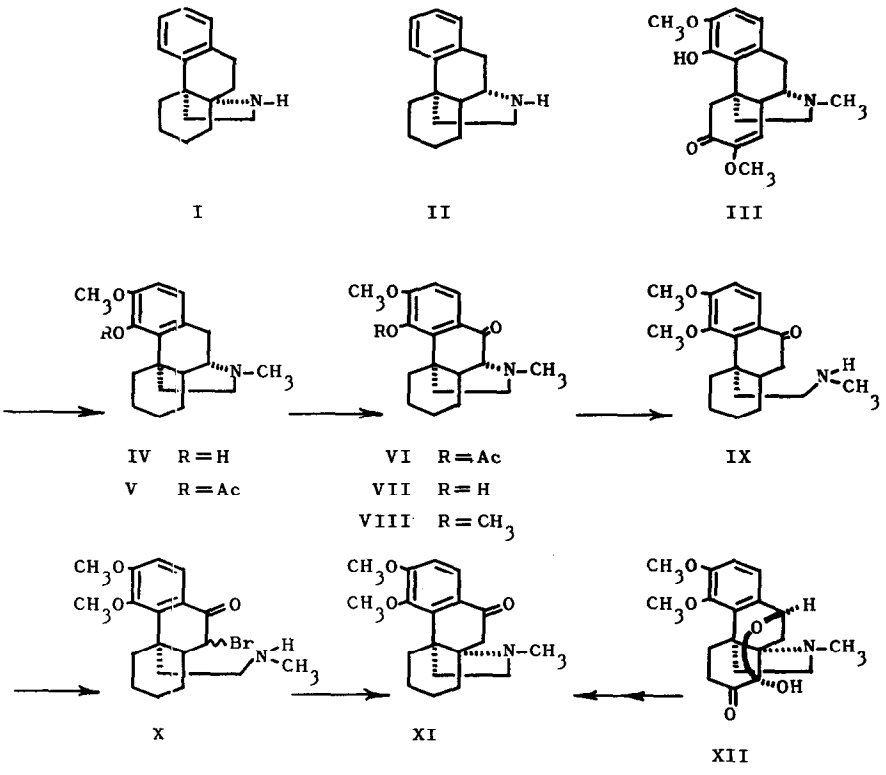
The hasubanan skeleton (I) of hasubanonine[1], metaphanine[2], prometaphanine[3], homostephanoline[4] and cepharamine[5] is closely related to morphinan (II), and the difference between two groups is that the ethanamine chain of hasubanan forms five membered ring, whereas of morphinan forms six membered one. In this communication the authors wish to communicate the transformation of morphinan derivative to hasubanan alkaloid*.

The starting material for the transformation was demethoxy-deoxodihydrosinomenine (IV)[6] obtained from Clemmensen reduction of sinomenine (III). Acetylation of (IV) with acetic anhydride in dry pyridine afforded the acetate (V), IR $\nu_{max.}^{CHCl_3}$ 1755 cm^{-1} (OAc), which was oxidized with chromium trioxide in aq. acetic acid[7] to give the keto-acetate(VI), m.p. 195°, $C_{20}H_{25}O_4N$, IR $\nu_{max.}^{CHCl_3}$ 1769 (OAc) and 1672 cm^{-1}(conj. CO). Saponification of the keto-acetate (VI) with potassium hydroxide in aq. ethylene glycol afforded the hydroxy-ketone (VII)[7], m.p. 214°, $C_{18}H_{23}O_3N$,

* All compounds reported in this communication gave satisfactory NMR spectra.



IR $\nu_{max.}^{CHCl_3}$ 1670 (CO) and 3500 cm^{-1}(OH), which was methylated with Rodionov reagent[8] in boiling toluene to give the ketone (VIII) as an oily substance, IR $\nu_{max.}^{CHCl_3}$ 1669 cm^{-1}(CO), MS: M^+ 315, which was characterized as its methiodide, m.p. 267~268°, $C_{20}H_{28}O_3NI$.

Reduction of the ketone (VIII) with zinc in boiling acetic acid gave rise to the ketone (IX), IR $\nu_{max.}^{CHCl_3}$ 1672 cm^{-1}. Bromination of the ketone (IX) in acetic acid gave the bromoketone (X), which was not purified or analyzed, but was

immediately treated with the mixture of lithium chloride and lithium carbonate in N,N-dimethylformamide at 120° to give the desired 3,4-dimethoxy-10-oxo-N-methylhasubanan (XI), m.p. 143~144°, IR $\nu_{max.}^{CHCl_3}$ 1678 cm^{-1}, MS: M^+ 315, $[\alpha]_D^{30} = -38°(CHCl_3)$. The compound (XI) thus obtained from sinomenine (III) and the hasubanan derivative (XI) derived from metaphanine (XII)[2] were found to be quite identical in terms of their IR spectra, NMR spectra, MS spectra[9], signs of specific rotation, and the mixed melting point did not depress.

The synthesis of the hasubanan alkaloid from morphinan derivative by the above route points to the accessibility of similar hasubanan derivatives.

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