Two New Cleavages of Hexahydroindolopyrrocoline leading to Systems containing a Nine-membered Ring

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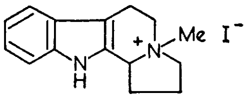
REDUCTION[1] of the hexahydroindolopyrrocoline methiodide[2] (I) with lithium in liquid ammonia leads to cleavage of the central carbon–nitrogen bond giving an indoloazanonane. Very recently this reaction has been applied to more complex quaternary salts leading to the total synthesis of quebrachamine[3] and the dihydrocleavamines.[4] We now report two non-reductive cleavages each of which introduces a functional group, and which have considerable potential value in alkaloid synthesis.

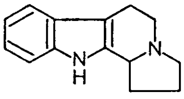
Treatment of the hexahydroindolopyrrocoline[2] (II) with cold acetic anhydride gives in high yield a neutral crystalline product (III; R = Ac) whose composition shows that the addition of one mole of acetic anhydride has occurred. The i.r. spectrum (ν_{max} 1740 and 1625 cm.$^{-1}$) indicates the presence of ester and amide carbonyl functions. Mild alkaline hydrolysis removes the ester function giving an alcohol (III; R = H) oxidised by manganese dioxide to a ketone (IV) whose u.v. spectrum (λ_{max} 238 and 312 mμ; ϵ, 11,610 and 17,350) is characteristic of a 2-acylindole. This reaction is somewhat similar to one described by Dolby and Sakai,[5] and probably proceeds by a similar mechanism.

Treatment of the methiodide (I) with potassium cyanide in diethylene glycol readily yields a crystalline base (V) containing a cyano-group (ν_{max} 2250 cm.$^{-1}$). Hydrolysis and esterification then gives the ester (VI). This reaction resembles an earlier reported synthesis of 2-cyanomethylindole.[6]

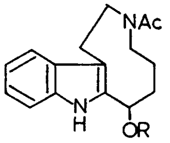
Application of these cleavages to indole alkaloid synthesis is now in hand.



(I)



(II)



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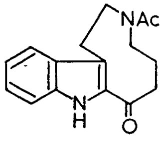

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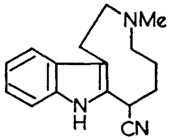
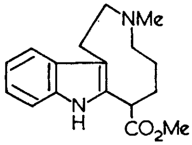


(V)



(VI)

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