SYNTHESIS OF ALKALOID, ZEPHYRANTHINE

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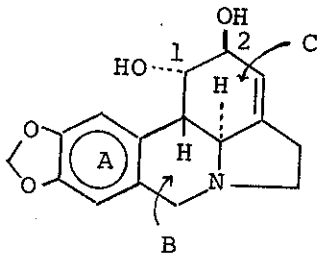
Synthesis of zephyranthine, which is an alkaloid isolated from Zephyranthes candida Nerb., was described.

Recently[1], we reported the synthesis of lycorine (I) which is a main alkaloid occurring in a variety of Amaryllidaceae plants. In continuation of our synthetic work on the alkaloids of this family, we report here the synthesis of zephyranthine (II)[2] which has been isolated from Zephyranthes candida Nerb. (Amaryllidaceae) and characterized by a vicinal cis-glycol on ring C different from lycorine (I).

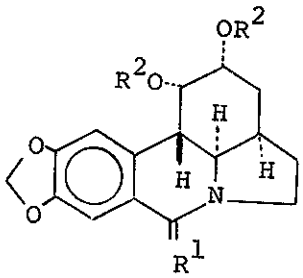
Starting from the imide (III)[1], an attempt was made to introduce the cis-glycol system by oxidation with osmium tetroxide followed by hydrogen sulfide but the oxidation product was a serious mixture and treatment of the mixture with acetic

anhyride in pyridine gave the dehydro-acetoxy-imide (IV), m.p. 254-258°, $\nu_{max.}$(KBr); 1750, 1730, and 1660cm^{-1}: δ ($CDCl_3$); 2.09 (3H, s, $OCOCH_3$), 5.38 (1H, m, C_2-H), 6.08 (2H, s, O-CH_2-O), 6.48 (1H, d of d, J=2 and 4Hz., C_1-H), 6.94 and 7.58 (1H each, s, aromatic H), as a sole isolable product in poor yield. The fact suggested us to modify the imide system into the lactam one which would be more stable under reductive hydrolysis condition for the osmate ester.

Reduction of the imide (III) with lithium aluminum hydride in ether at 0° for 1 hr. gave the lactam (V), m.p. 126-128°, $\nu_{max.}$($CHCl_3$); 1650cm^{-1}: δ ($CDCl_3$); 6.00 (2H, s, O-CH_2-O), 6.18 (2H, m, olefinic H), 6.88 and 7.50 (1H each, s, aromatic H) in 80% yield. Treatment of the lactam (V) with osmium tetroxide in pyridine followed by sodium bisulfite in aqueous pyridine[3] furnished a mixture of two constituents (thin layer chromatographic examination) which was, without further purification, treated with acetic anhydride and pyridine to give the lactam diacetate (VI), m.p. >300°, $\nu_{max.}$($CHCl_3$); 1740 and 1640cm^{-1}: δ ($CDCl_3$); 2.03 and 2.07 (3H each, s, $OCOCH_3$), 5.07 and 5.86 (1H each, m, C_1-H and C_2-H), 5.96 (2H, s, O-CH_2-O), 6.53 and 7.38 (1H each, s, aromatic H) and its isomer (VII), m.p. 243-245° in 10 and 1% yield, respectively. Infrared and n.m.r. spectra of the former was identical with those of the optical active one (VI)[2] derived from natural sources. Mass spectrum (M^+ m/e 378) of the latter was virtually identical with that of the



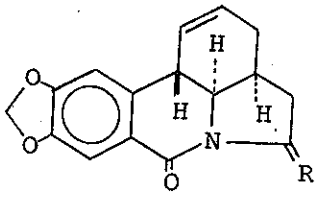
(I)



(II) $R^1=H_2$; $R^2=H$

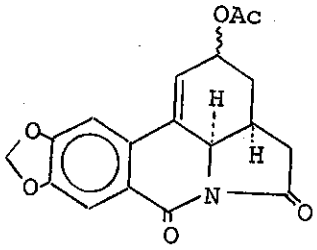
(VI) $R^1=O$; $R^2=Ac$

(VIII) $R^1=H_2$; $R^2=Ac$

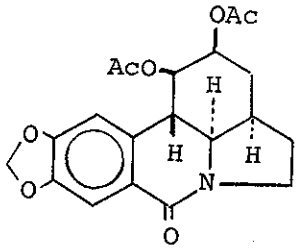


(III) R=O

(V) $R=H_2$



(IV)



(VII)

former, indicating that the latter was a stereoisomer (VII) of the former.

Lithium aluminum hydride reduction of the synthetic lactam diacetate (VI) gave (±)-zephyranthine, m.p. 224-225°, n.m.r. spectrum of which was also identical with that of zephyranthine in d_6-dimethyl sulfoxide. Furthermore, (±)-diacetylzephyranthine (VIII), m.p. 143-145° was identical with diacetylzephyranthine in ir ($CHCl_3$) and n.m.r. ($CDCl_3$) spectra and thin layer chromatographic comparison.

References

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