Tetrahedron Letters No.60, pp. 5335-5336, 1969. Pergamon Press. Printed in Great Britain.

THE CHARACTERIZATION AND BIOGENESIS OF DELNUDINE

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(Received in the USA 17 November 1969; received in the UK for publication 29 November 1969)

Some time ago we examined the seeds of Delphinium denudatum. Chromatography of the basic fraction on alumina gave besides denudatine (1) a second alkaloid, m.p. 235-237°C., $C_{20}H_{25}NO_3$ which we call delnudine. [pK_a (methylcellosolve) = 7.8; I.R. (KBr): 3420, 1710, 900 cm^{-1}; U.V. (ethanol): λ_{max} = 300 mμ (log ε = 1.76); N.M.R.: singlet (3H) τ = 8.37 p.p.m. (), doublet (2H) τ = 5.04, 5.28 p.p.m. ().] The spectral data of delnudine were compatible with the presence of two hydroxyls, a ketone in a six-membered ring and an exocyclic methylenic group in the proximity of the ketone (exaltation of the extinction coefficient in the ultraviolet). In view of this functional group analysis the molecular formula indicated a heptacyclic compound. Oxidation of delnudine with chromic acid in pyridine yielded a hydroxy diketone $C_{20}H_{23}NO_3$, m.p. 264-266°C. [I.R. (KBr): 3400, 1720, 900 cm^{-1}; m/e 325; pK_a = 5.65.] Judging from the fact that the basicity decreased by more than two pK units it was clear that the new keto group must be located in the proximity of the nitrogen. The carbinolamine nature of the hydroxyl which resisted oxidation became clear on acetylation of delnudine with acetic anhydride in pyridine. This reaction yielded two crystalline isomeric diacetates $C_{24}H_{29}NO_5$. Basic diacetate--m.p. 141-143°C.; I.R. (KBr): 1735, 1710, 900 cm^{-1}. Neutral diacetate--m.p. 282°C.; I.R. (KBr): 1720-1715, 1700, 1625, 900 cm^{-1}. The neutral diacetate was clearly a derivative of the keto form of the carbinol-

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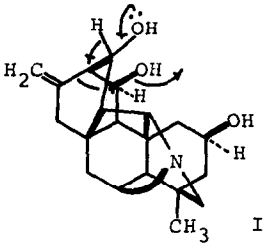
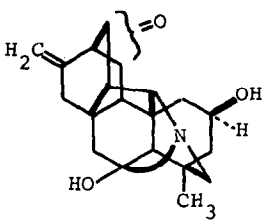
amine and was thus a N,O-diacetyl diketone. It showed in the N.M.R. a doublet (2H) τ = 5.03, 5.26 p.p.m. (), two singlets (3H) each at τ = 7.95, 8.03 p.p.m. (), and a singlet (3H) at τ = 8.74 p.p.m. (). The strong shift of this singlet as compared to its position in delnudine clearly demonstrates the proximity of the carbinolamine hydroxyl and the carbon methyl group in the alkaloid.

At this stage we have discontinued the investigation and we considered it probable that delnudine is based on the hetisine skeleton (2,3) and may possibly be a derivative of hetisine I itself (3). Thus, for instance, the formula II which may be derived from I by the introduction of the carbinolamine hydroxyl, deletion of one hydroxyl in the C/D ring system, and oxidation of the second hydroxyl to a ketone was compatible with all our data.

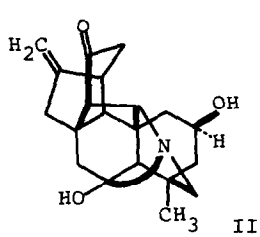
In the belief that we were dealing with a trivial derivative of hetisine, it was with some misgivings that we sent the crystals of delnudine to Dr. Maria Przybylska (N.R.C., Ottawa). The structure was solved recently by Dr. Karin B. Birnbaum and is given in formula III(4).It is clear that the structure of delnudine III may be biogenetically derived from hetisine I (3) by the concerted rearrangement portrayed by the arrows in formula I and by the introduction of the carbinolamine hydroxyl.



I



II



III

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