Tetrahedron Letters No.47, pp. 4229-4232, 1965. Pergamon Press Ltd.
Printed in Great Britain.

ALKALOIDS OF NUPHAR VARIEGATUM

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(Received 10 September 1965)

A new alkaloid, nuphenine, has been isolated from the yellow water lily, Nuphar variegatum Engelm. Chromatography on alumina of a chloroform extract of air-dried rhizomes yielded nupharidine(2), deoxynupharidine(2), nuphenine and several other uncharacterized alkaloids. This paper reports on the structure and stereochemistry of nuphenine.

A mass spectrum of nuphenine showed a molecular ion peak of 233, consistent with the molecular formula $C_{15}H_{23}NO$. The I.R. spectrum indicated N-H absorption at 3310 cm^{-1}, Bohlmann bands at 2800 and 2730 cm^{-1} and furan peaks at 1505 and 880 cm^{-1}. The U.V. showed only end absorption. Specific rotation $[\alpha]^{25}_{Hg} = -23$ (methanol). The N-H was confirmed by formation of a monoacetate with acetic anhydride-pyridine (I.R., 1650 cm^{-1}, no N-H, N.M.R. methyl at 7.83 τ).

The presence and substitution of a double bond is indicated by the signal centered at 4.88 τ in the N.M.R. spectrum (Fig.1). The signal is split by the adjacent methylene group into a triplet (J = 7 cps), which is further split by the two methyl groups (J = 1 cps). Hydrogenation of nuphenine over 10% palladium-charcoal yielded dihydronuphenine, in the N.M.R. of which the 4.88 τ signal is not present and the peak at 8.3 τ in nuphenine has shifted to 8.75 τ (6H doublet, J = 6 cps). The presence of the $^{CH_3}_{CH_3}\!\!>\!C{=}C\!<^{CH_2}_{H}$ group is confirmed by the large (100%) peak in the mass spectrum at 164, equivalent to the loss of this group. The strength of the peak indicates that the group is α to the nitrogen, this position giving easiest fragmentation. This arrangement was confirmed by decoupling Hc from Ha and Hb, the six peaks of Hc collapsing almost completely to a doublet (J = 2.5 cps).

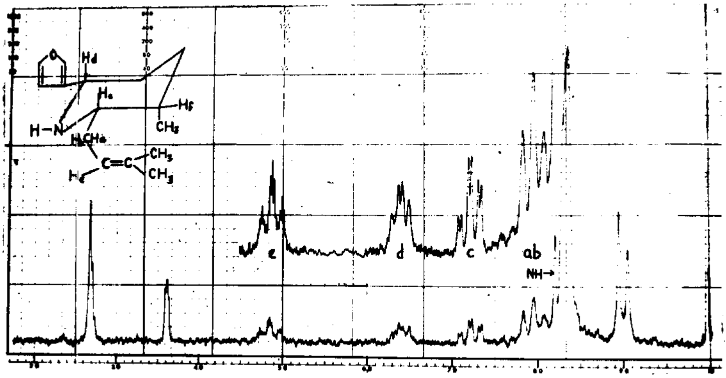
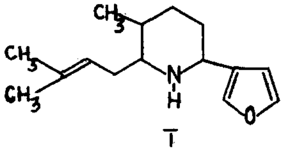
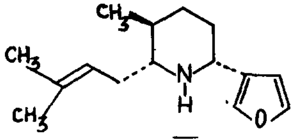


FIG. 1 N.M.R. Spectrum of Nuphenine

Prolonged hydrogenation of nuphenine over platinum gave a hexahydro derivative, indicating the presence of only one double bond other than those of the furan ring. A mass spectrum of the perhydrogenated compound gave a parent peak of 238 and a 100% peak of 168, equivalent to the loss of an isopentyl or tetrahydrofuryl radical from the position adjacent to the nitrogen. From the molecular formula it is apparent that the compound has one ring other than the furan ring. Since ten carbons are required to account for the other groups seen in the N.M.R., the other ring must be a piperidine ring. The other carbon attached to the nitrogen has one proton (Hc, quartet, 7.20 τ, peaks broadened by coupling to the furan protons). Since Hc is split by only one ring proton, the methyl group must be on the adjacent carbon. The only possible structure for nuphenine is I, which is isomeric to anhydronupharamine(3).



I



II

The stereochemistry of nuphenine is not the same as that reported for anhydronupharamine(3). The protons Hc and Hf, with a coupling constant of 2.5 cps, must be in an axial-equatorial or equatorial-equatorial relation to one another(4,5). The reported stereochemistry of anhydronupharamine (II) would require both Hc and Hf to be axial in the most stable conformation of the ring. The presence of bands in the I.R. of nuphenine at 2800 and 2730 cm^{-1} may be taken as evidence for two axial hydrogens α to the nitrogen(6). Of the several substituted piperidines that we have examined, all which had two axial hydrogens α to the nitrogen showed a strong peak at 2800-2810 cm^{-1} and a weaker peak at 2725-2730 cm^{-1}. No peaks in the 2700-2800 region were seen in 2,2,4,6-tetramethylpiperidine or 2,2,6,6-tetramethylpiperidine. The most probable configuration of nuphenine is that shown in Fig. 1.

Nuphenine could be an artifact of nupharamine, but it is unlikely that dehydration would occur under the mild conditions used in the isolation. If it is derived from nupharamine, a revision would be required in the stereochemistry of all of the nuphar alkaloids which have been directly related to nupharamine(3).

Acknowledgements: We are indebted to the National Research Council of Canada for financial aid, to D. G. Smith for determining the N.M.R. spectra and to Dr. R. D. G. Cooper for determining and interpreting the mass spectra.

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