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STRUCTURE OF NUPHLEINE – AN ALKALOID FROM Nuphar luteum

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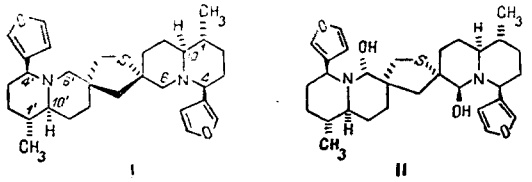
We have previously [1, 2] reported the isolation from the dry rhizomes of Nuphar luteum L. (European cowlily) of a new sulfur-containing alkaloid – nuphleine $C_{30}H_{42}O_4N_2S$. The preparation lutenurine, possessing protistocidal and antimicrobial activity has been created on the basis of this alkaloid.

It was shown that nuphleine contains two furan rings and two hydroxy groups present in the α positions to nitrogen atoms. The reduction of nuphleine with sodium tetrahydroborate gave a quantitative yield of thiobinupharidine, for which structure (I) has recently been established [4, 5].

We give the results of a spectroscopic study of nuphleine which permits structure (II) to be ascribed to it.



I

II

The thiobinupharidine molecule (I) has six carbon atoms in α positions to nitrogen atoms: 4, 4', 6, 6', 10, and 10'. In the NMR spectrum of nuphleine there are two one-proton singlets the half width of which change on the addition of D_2O (Table 1); these signals must be assigned to protons geminal to hydroxy groups.

Thus, positions 4 and 4', and 10 and 10', are excluded for the hydroxy groups and only positions 6 and 6' remain possible.

The NMR spectra also confirmed the equatorial orientation of the β-furyl groups (trans-diaxial coupling constants 8.0 and 8.5 Hz for the protons at C_4 and $C_{4'}$) and of the methyl groups at C_1 and $C_{1'}$ (upfield shift of the signals of these groups by 0.17 ppm on passing from $CDCl_3$ to C_6D_6 [5]).

One of the hydroxy groups forms an intramolecular hydrogen bond and the other is free; in the IR spectrum of a dilute solution of nuphleine in CCl_4 (0.001 M) there are two bands in the region of stretching vibrations of OH bonds – a narrow one at 3628 cm^{-1} and a broadened one at 3535 cm^{-1}. This is also shown by the NMR results – one of the HC–OH signals is broadened ($W_{1/2}$ 5.0 Hz) as the result of hindrance to exchange; on the addition of D_2O the signal narrows (see Table 1). A consideration of a model shows that the formation of an intramolecular hydrogen bond is impossible only for an axial OH group at $C_{6'}$. In the case of an equa-

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TABLE 1. Features of the NMR Spectra of Nuphleine*

Solvent	2 CH_3–CH	C–CH_2–S–	C_4–H C_4'–H	C_6–H	C_6'–H	Furan	
						β–H	α–H
$CDCl_3$	0,89; d; 5,0; 6H	2,18; d; 13,0; 1H 2,71; d; 13,0; 1H	3,58; q; 6,0; 8,0 3,70; g 6,5; 8,5	4,24; s; 1H $W_{\frac{1}{2}}$ 5,0 c D_2O $W_{\frac{1}{2}}$ 2,9	3,98; s; 3,5; 1H s D_2O $W_{\frac{1}{2}}$ 2,6	6,36; us; 2H	7,33; us; 4H
C_6D_6	0,72; d; 5,0; 6H	2,15; d; 13,0; 1H 2,66; d; 13,0; 1H	3,37; q; 5,5; 8,5	4,31; s; 5,0	4,18; s; 3,5	6,31; m; 1H 6,38; m; 1H	7,47; m; 1H 7,33; m; 1H

*s) singlet; d) doublet; q) quartet; m) multiplet; us) unresolved or weakly resolved signal appearing in the form of a singlet.

torial OH group at C_6, conversely, the formation of a fairly strong hydrogen bond with the sulfur atom is possible. This gives grounds for assuming that the hydroxy group at $C_{6'}$ is axial and that at C_6 is equatorial.

The following considerations can also be made to confirm the equatorial position of the C_6 hydroxy group. The formation of perchlorates of carbinolamine bases takes place with the splitting out of water; on subsequent alkalinization, the anhydro derivatives are rehydrated. Naturally, the reorientation of the hydroxyl in the α-carbinolamine form will be determined by the configuration of the substituent on the neighboring carbon atom – the attack of the OH^- ion will take place from the side opposite to that of the most voluminous substituent. Since the isolation of nuphleine includes a stage of passage through the perchlorate, on passing to the base the C_6 hydroxy group must occupy the trans position with respect to the sulfur atom, i.e., the equatorial position.

Similar results have been obtained in the reduction of similar systems with sodium tetradeuteroborate; the deuterium enters the trans position with respect to the sulfur atom [5].

Thus, the structure of nuphleine can be expressed by formula (II). The results that we have obtained show that the 6,6'-dihydroxythiobinupharidine (6,6'-dihydroxythionuphlutine-A) [6] is identical with nuphleine.

EXPERIMENTAL

The NMR spectra were taken on a Ha-100D instrument at 20°C; 0 – TMS. The IR spectra were taken on a UR-20 spectrophotometer.

SUMMARY

A structure is proposed for nuphleine – a sulfur-containing alkaloid isolated previously from the roots of the European cowlily.

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