

TWO NEW NUPHAR ALKALOIDS
6,6'-DIHYDROXYTHIONUPHUTINE-A AND -B

Robert T. LaLonde, C. F. Wong and W. P. Cullen
Department of Chemistry, State University College
of Forestry at Syracuse University, Syracuse, New York 13210

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Over the years various C-30 alkaloids have been isolated from Nuphar (1-5). Of these, only the structure of one, neothiobinupharidine, has been secured and this on the basis of an x-ray study. We report here evidence for the gross structures of 6,6'-dihydroxythionuphlutine-A and -B, C₃₀ alkaloids isolated* from Nuphar luteum subsp. macrophyllum (Beal) (6).

6,6'-Dihydroxythionuphlutine-A, C₃₀H₄₂N₂O₄S^{**} (A), obtained as a glass-like solid, possessed physical properties as follows: $[\alpha]_D^{25} +44.5^\circ$ (CH₂Cl₂, c 1.2); λ (EtOH, neutral) 208 nm (ϵ 12,200); λ_{\max} (EtOH, H⁺) 291 nm (ϵ 1850); μ^t 2.78 and 2.85 (OH), 6.67 and 11.49 (furan); m/e (% rel. int.) 526(0.3), 509(0.3), 508(0.7)(M⁺-H₂O)^{tt}, 507(0.4)(M⁺-H₃O), 490(0.5)(M⁺-H₄O₂), 447(1.9), 446(1.9)(M⁺-CH₄O₂S), 445(0.6)(M⁺-CH₅O₂S), 262(9), 245(5), 230(39), 176(36), 107(46), 94(82); δ 0.92(d, 5.5Hz, 6H, CHCH₃), 2.49(AB q, 2H, CH₂S), 3.61(q, 1H, HC-4 or -4'), 3.74(q, 1H, HC-4 or -4'), 4.1(wide s, $w_{H1/2}$ 3Hz, 1H, HCOH), 4.33(d, 5Hz, 1H, HC6OH), 6.50(m, 2H, furan β -H), 7.48(m, 4H, furan α -H); δ (CDCl₃-D₂O)

* Details of the isolation procedure and a description of biological properties will be published elsewhere.

** Satisfactory elemental analyses were obtained for all new compounds whose molecular formulas are given.

t Unless otherwise noted, ir were run in CCl₄ and nmr in CDCl₃, TMS 0.0 δ . Ms were determined at 20 and 70 eV using a direct inlet system.

tt Where ions are assigned, the mass of the assigned ion is within three millimass units of the mass of the observed ion.

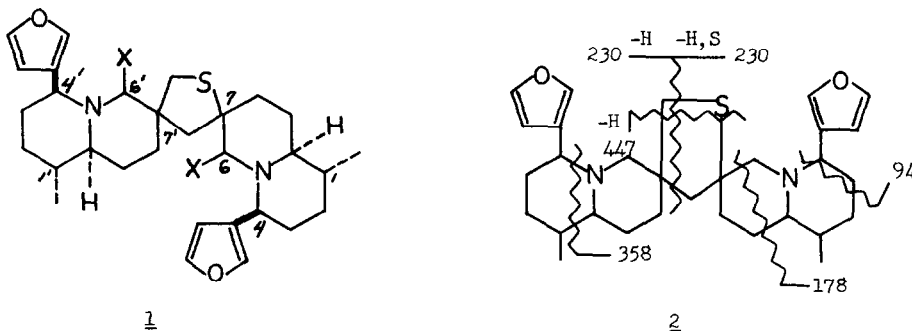
4.1 (sharp s, 1H, HCO_D), 4.33 (s, 1H, HCO_D). A was converted to its bisimmonium diperchlorate salt ($\text{C}_{30}\text{H}_{40}\text{N}_2\text{O}_{10}\text{SCl}_2$): mp (powder) 226-228°; $[\alpha]_D^{25} +184(\text{CH}_3\text{OH}-\text{CH}_3\text{COCH}_3, 16.5:3.5, c 0.5)$, $\lambda_{\text{max}}(\text{EtOH}) 291 \text{ nm } (\epsilon 2300)$; μ (KBr) 6.00 ($>\text{N}^+=\text{C}$).

6,6'-Dihydroxythionuphlutine-B, $\text{C}_{30}\text{H}_{42}\text{N}_2\text{O}_4\text{S}$ (B), also a glass-like solid, possessed physical properties somewhat like those of A. These properties are as follows: $[\alpha]_D^{25} -69^\circ$ ($\text{CH}_2\text{Cl}_2, c 0.1$); μ 2.76 and 2.89 (OH), 6.69 and 11.49 (furan); m/e (% rel. int.) 509(0.4), 508(0.4) ($\text{M}^+-\text{H}_2\text{O}$), 507(0.2) ($\text{M}^+-\text{H}_2\text{O}$), 490(0.5), 447(1.0), 446(1.0), 445(2.5), 262(5.5), 245(3), 230(66), 176(100), 107(22), 94(22); δ 0.88 (m, $w_{\text{H}_1/2}$ 9Hz, 6H, HCC_3H_3), 2.49 (AB q, 2H, CH_2S), 2.86 (m, 1H, $\text{HC}-4$ or $-4'$), 3.56 (q, 1H, $\text{HC}-4$ or $-4'$), 3.92 (d of m, 1H, HCOH), 4.10 (d, 5Hz, 1H, HCOH), 6.27 (m, 1H, furan $\beta\text{-H}$), 6.47 (m, 1H, furan $\beta\text{-H}$), 7.27 (m, 2H, furan $\alpha\text{-H}$), 7.37 (m, 2H, furan $\alpha\text{-H}$); δ ($\text{CDCl}_3\text{-D}_2\text{O}$) 3.92 (s, 1H, HCO_D), 4.10 (s, 1H, HCO_D).

The dicarbinolamine character of A, manifested in bisimmonium salt formation, was revealed in both alkaloids by the conversion with sodium borohydride in methanol of A to liquid thionuphlutine-A ($[\alpha]_D^{25} +7.8^\circ$ (MeOH, $c 0.18$): m/e 494 (M^+); $\lambda_{\text{sh}}(\text{EtOH, neutral}) 215 \text{ nm } (\epsilon 13,000)$, $\lambda_{\text{sh}}(\text{EtOH}-\text{H}^+) 215 \text{ nm } (\epsilon 13,000)$; μ 3.6 (s, Bohlmann bands), 6.69 and 11.47 (furan); δ 0.93 (d, 6H, HCC_3H_3), 1.42 (m), 2.32 (AB q, 2H, CH_2S), 2.75-3.1 (m, 4H, $\text{HC}-4$ and $-4'$ and $\text{HC}-6$ -equatorial and $-6'$ -equatorial), 6.39 (m, 2H, furan $\beta\text{-H}$), 7.30 (m, 4H, furan $\alpha\text{-H}$); monoperchlorate monohydrate ($\text{C}_{30}\text{H}_{42}\text{N}_2\text{O}_2\text{S} \cdot \text{HClO}_4 \cdot \text{H}_2\text{O}$) mp (decomp.) 266-267° and B to liquid thionuphlutine-B, $\text{C}_{30}\text{H}_{42}\text{N}_2\text{O}_2\text{S}$ ($[\alpha]_D^{25} -131^\circ$ (MeOH, $c 0.8$): m/e 494 (M^+); μ 3.7 (s, Bohlmann bands), 6.69 and 11.49 (furan); δ 0.91 (d, 6H, HCC_3H_3), 1.42 (m), 2.33 (AB q, 2H, CH_2S), 2.42-3.15 (m, 4H, $\text{HC}-4$ and $-4'$ and $\text{HC}-6$ -equatorial and $-6'$ -equatorial), 6.23 (m, 1H, furan $\beta\text{-H}$), 6.43 (m, 1H, furan $\beta\text{-H}$), 7.22 (m, 2H, furan $\alpha\text{-H}$), 7.31 (m, 2H, furan $\alpha\text{-H}$).

The mass spectra of thionuphlutines-A and -B both were very much like that reported (7) for neothiobinupharidine, although the various other properties of the thionuphlutines were unlike those of neothiobinupharidine, $\underline{1}(\text{X} = \text{H})^*$ (8), and thus showed that no two of these three alkaloids were identical. However the properties of the thionuphlutines are uniquely

* The x-ray study on which this structural assignment is based did not settle the problem of absolute configuration (G. I. Birnbaum, private communication). We tentatively assume in representing neothiobinupharidine in terms of $\underline{1}$ that deoxynupharidine moieties belong to the same configurational series as deoxynupharidine itself (9).



consistent with structures stereoisomeric with 1 ($R = H$). Firstly the symmetrical nature of the thionuphlutines, as well as A and B, is indicated in m/e 230, always intense, attributable to cleavage through the thiaspirane ring as shown in 2 with loss of hydrogen and sulfur or hydrogen, sulfur and C-6,6'-oxygen from A and B. M/e 230 is shifted to 231 in thionuphlutines prepared by reduction of the parent alkaloids with sodium borodeuteride. Secondly thionuphlutines-A and -B both give m/e 178 shifted to 179 in the spectrum of the labelled alkaloids. Peaks in the 357-359 region are shifted two mass units higher in the labelled thionuphlutines. The last observation is consistent with the loss of 136 from deoxynupharidine to give m/e 97 and m/e 99 from deoxynupharidine-6 β ,7 β -d₂ (10). The fragments assigned to m/e 358, 447 ($M^+ - SCH_3$), 463 ($M^+ - SH$) are consistent with high resolution ms.

Incorporation of carbinolamine functions at C-6 and -6' follows from the ms data and the singlet resonance of the carbonyl protons when measured in $CDCl_3 - D_2O$. The two proton, thiomethylene AB-quartet demonstrates that only two protons are adjacent to sulfur. Therefore the thiaspirane ring which embodies the thiomethylene group and the remaining methylene, must be incorporated so as to include C-7 and -7'. It follows that A and B must be the C-6,6'-dicarbinolamines (1, $X = OH$) corresponding to structures stereoisomeric with the neothiobinupharidine skeleton, 1 ($X = H$).

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