

## STEREOCHEMISTRY AND DEGRADATION OF THIONUPHUTINE S-METHIODIDE

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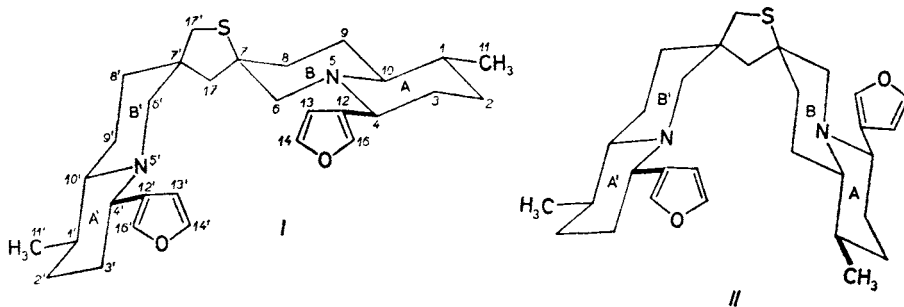
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The structure of thionuphutine S-methiodide is presented, based on the  $^{13}\text{C}$  NMR spectra analysis. The S-methiodide was degraded under the conditions of Hofmann degradation.

Thionuphutine *I* is a sulfur containing *Nuphar* alkaloid isomeric with thiobinupharydine *II* (sulfur equatorial) in respect of the configuration on the atom C(7) in the AB quinolizidine ring (sulfur atom axial)<sup>1</sup>.

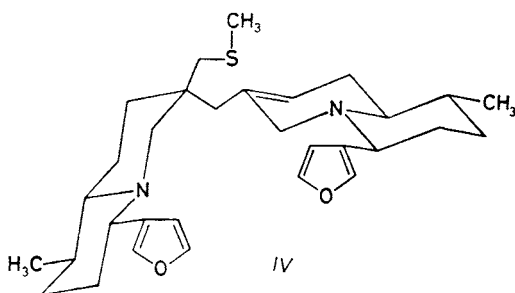
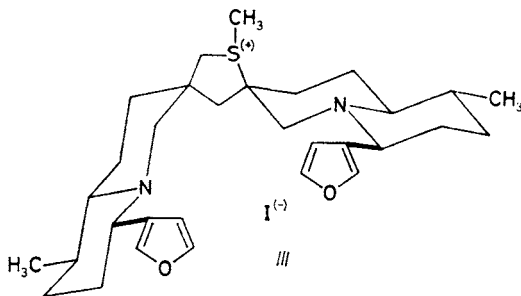
Methylation of *I* at room temperature, contrary to the results obtained<sup>2-4</sup> with *II*, afforded S-methiodide *III* in a reasonably good yield. Compound *III* was accompanied by some N-methylated products. This reaction is the first example in the group of *Nuphar* alkaloids of methylation which takes place on the sulfur atom. This phenomenon could be explained in terms of lesser steric hindrance while sulfur is axial.



The structure of *III* was established by  $^{13}\text{C}$  NMR spectroscopy. To identify the carbon atoms the SFORD technique was used (Table I). Chemical shifts for carbon atoms in both quinolizidine and furan rings were similar to those of the corresponding carbon atoms of thionuphutine *I* (ref.<sup>5</sup>). Paramagnetic shifts were observed for carbon atoms  $\alpha$  to sulfur. In addition, the paramagnetic shift for the quaternary

C(7) atom was larger ( $+14.8$  ppm) than that of C(17') ( $+2.4$  ppm), thus pointing out the presence of the S—CH<sub>3</sub> group<sup>6</sup>.

S-Methiodide *III* was degraded under the conditions used for Hofmann degradation. The sole product *IV* was obtained in a good yield. Breaking of the C(7)—S<sup>(+)</sup> bond must be interpreted in terms of  $\beta$ -*trans* elimination due to the presence of the sulfonium fragment and axial hydrogen atom on  $\beta$  C(8).



The structure of *IV* was determined by <sup>13</sup>C NMR spectroscopy (Table I). Both quinolizidine rings save the *trans* conformation and the atom C(7') retains its configuration, *i.e.* the —CH<sub>2</sub>—S—CH<sub>3</sub> group remains equatorial and the C(17) atom axial in the A'B' ring. The double bond is present between the C(7)—C(8) atoms.

The above findings are based on the following observations: (i) Diagnostics for the *trans* configuration of the quinolizidine rings: C(6) atom appears at 58.18 ppm (compare with *trans*- $\Delta^7$ -dehydronupharolutine<sup>7</sup>; C(6) at 56.99 ppm), C(6') at 62.47 ppm (compare with *I*). (ii) Chemical shift for C(17) was 38.14 ppm (axial) and for C(17') 46.11 ppm (equatorial)<sup>5</sup>. (iii) Chemical shifts for the C(7) and C(8) were 132.90 ppm and 122.34 ppm, respectively, placing the double bond between these atoms (compare with *trans*- $\Delta^7$ -dehydronupharolutine; C(7) = 133.80 ppm, C(8) = 118.54 ppm).

## EXPERIMENTAL

The results of elemental analyses were within permissible error. The  $^1\text{H}$  NMR spectra were recorded on a Jeol 100 MHz spectrometer and the  $^{13}\text{C}$  NMR spectra on a Jeol FX 90Q spectrometer using tetramethylsilane as an internal reference. Mass spectrum was registered on a LKB 2 091 spectrometer. Optical rotation was measured in chloroform solution on a Perkin-Elmer polarimeter (type 241) using a 1-dm cell.

Quaternization of Thionuphlutine *I*

To 988 mg (0.002 mol) *I* in 20 cm<sup>3</sup> acetone, methyl iodide (0.01 mol) was added and the mixture was kept at room temperature for two weeks. Upon removal of the solvent and excess methyl iodide, the mixture was chromatographed on a column packed with  $\text{Al}_2\text{O}_3$  (Fluka 506 C, pH  $6.0 \pm 0.5$ , grade III). Thin-layer chromatography was carried out on glass plates coated with the alumina Woelm acid TLC. From reaction mixture, compound *III* was obtained from the chloroform-methanol 97 : 3 fraction; 521 mg, 41% yield, yellow oil.  $^1\text{H}$  NMR spectrum ( $\text{C}^2\text{HCl}_3$ ): 0.92 d, 6 H ( $\text{C}(1')\text{-CH}_3$ ,  $\text{C}(1)\text{-CH}_3$ ); 1.00–3.06 m, 28 H; 3.20 s, 3 H ( $\text{S-CH}_3$ ); 3.94 d, 2 H ( $\text{S-CH}_2\text{-C}(7')$ ,  $J = 15$  Hz); 6.36 m, 2 H ( $\beta$ -furanyl); 7.30 m, 4 H ( $\alpha$ -furanyl). TLC (benzene-ethyl acetate-n-propanol 1 : 1 : 0.5)  $R_F = 0.18$ .

TABLE I

$^{13}\text{C}$  Chemical shifts and splittings of compounds *I*, *III*, and *IV*

Atoms <sup>a</sup>	<i>I</i> <sup>b</sup> (see ref. <sup>5</sup> )	<i>III</i> <sup>b</sup>	<i>IV</i> <sup>b</sup>
1,1'	35.91 <sup>c</sup> , 36.07 <sup>c</sup> (d, d)	36.13, 36.13 (d, d)	35.22, 36.35 (d, d)
2,2'	33.74, 33.74 (t, t)	32.39 <sup>d</sup> , 33.59 <sup>d</sup> (t, t)	32.51, 33.48 <sup>d</sup> (t, t)
3,3'	35.55 <sup>c</sup> , 36.42 <sup>c</sup> (t, t)	34.80, 35.51 (t, t)	33.70 <sup>e</sup> , 34.35 (t, t)
4,4'	60.09, 60.09 (d, d)	58.48, 59.71 (d, d)	61.22, 60.09 (d, d)
6,6'	64.13, 64.33 <sup>e</sup> (t, t)	62.75, 63.73 (t, t)	58.18, 62.47 (t, t)
7,7'	59.56, 46.74 (s, s)	74.41, 46.23 (s, s)	132.90, 38.63 (s, s)
8,8'	39.30, 37.78 (t, t)	41.71, 38.90 (t, t)	122.34, 37.44 (d, t)
9,9'	28.42, 29.11 (t, t)	27.74, 29.12 (t, t)	32.13, 26.82 (t, t)
10,10'	69.02, 69.41 (d, d)	67.00 <sup>d</sup> , 67.86 <sup>d</sup> (d, d)	64.53, 69.30 (d, d)
11,11'	19.20, 19.20 (q, q)	18.85, 19.04 (q, q)	18.85, 19.07 (q, q)
12,12'	128.71, 128.71 (s, s)	127.53, 128.77 (s, s)	128.52, 129.43 (s, s)
13,13'	109.26, 110.04 (d, d)	108.36, 109.53 (d, d)	109.55, 109.71 (d, d)
14,14'	142.97, 143.38 (d, d)	142.90, 144.06 (d, d)	142.60, 142.80 (d, d)
16,16'	139.50, 139.50 (d, d)	138.93, 139.51 (d, d)	139.30, 139.51 (d, d)
17,17'	50.59, 42.77 (t, t)	50.20, 45.20 (t, t)	38.14, 46.11 (t, t)
(+)			
S-CH <sub>3</sub>	—	20.00 (q)	—
S-CH <sub>3</sub>	—	—	17.50 (q)

<sup>a</sup> In ppm from tetramethylsilane, s singlet, d doublet, t triplet, q quartet; <sup>b</sup> in  $\text{C}^2\text{HCl}_3$ ; <sup>c</sup> these four peaks may be interchanged; most likely assignment is given; <sup>d</sup> assignments may be reversed;

<sup>e</sup> one of these values can be assigned to C(6), the other to C(6').

### Degradation of *III*.

To a solution of 0.2 mmol *III* in 6 ml methanol, moist silver oxide (prepared from 500 mg of silver nitrate) was added and the mixture was shaken for 1 h. After filtration, the solvent was removed *in vacuo*, sodium hydroxide (5 g), water (5 ml), and methanol (5 ml) were added and the mixture was heated under reflux for 2 h. After dilution with water, the crude product was extracted with chloroform, dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. The residue was chromatographed on alumina (Fluka 506 C, grade III) using benzene as eluent; *IV*, 60 mg, 61% yield, TLC (aluminium oxide)  $\text{CHCl}_3$   $R_F = 0.3$ ,  $[\alpha]_D^{25} = -190^\circ$ .  $^1\text{H}$  NMR spectrum, ( $\text{C}^2\text{HCl}_3$ ): 0.98 d, 6 H (C(1)— $\text{CH}_3$ , C(1')— $\text{CH}_3$ ); 1.92 s, 3 H (S— $\text{CH}_3$ ); 1.00—3.10 m, 28 H; 5.56 m, 1 H (C=CH); 6.38 s, 1 H ( $\beta$ -furanyl); 6.52 s, 1 H ( $\beta$ -furanyl); 7.42 m, 4 H ( $\alpha$ -furanyl). Mass spectrum,  $m/z$  (relative intensity): 508 ( $\text{M}^+$  9.9), 493 (1.7), 461 (2), 447 (1.3), 278 (1.8), 230 (100), 178 (2.6), 136 (2.9), 110 (1.3), 107 (7.1), 94 (14.6), 81 (5.5).

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