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THE STRUCTURE OF NEOTHIOBINUPHARIDINE

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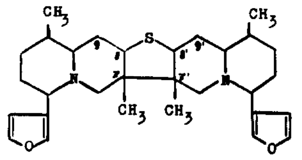
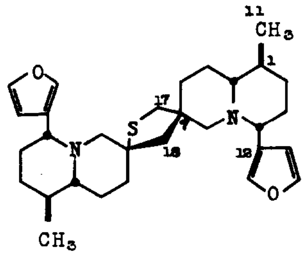
The structure of neothiobinupharidine, one of several sulfur-containing alkaloids from Nuphar Luteum, has recently been investigated by Achmatowicz and his co-workers(1,2). Based mostly on IR, NMR and mass spectra, they suggested I as the structure of this substance. An X-ray structure analysis revealed that the correct structure is as shown in II.



I



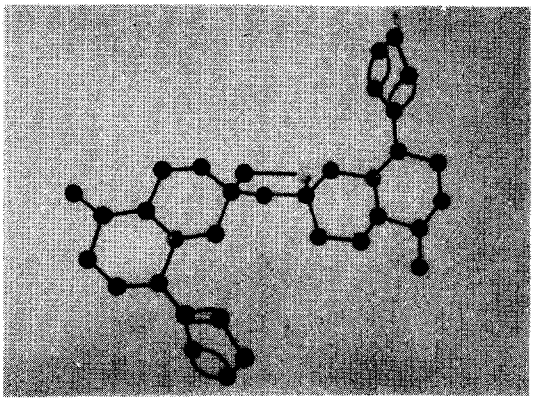
II

Structures I and II are very similar to each other, differing only in the linkage of the two quinolizidine systems. The incorrect linkage in I was based on a misinterpretation of a Kuhn-Roth determination. Its results corresponded to two $-\overset{|}{\underset{|}{C}}-CH_3$ groups which led Achmatowicz et al. to the conclusion that there are three or four such groups in the molecule(2). It is interesting to note that this is one of the rare instances in which the Kuhn-Roth determination gave exactly the right results.

Crystals of neothiobinupharidine dihydrobromide tetrahydrate, $C_{30}H_{42}O_2N_2S.2HBr.4H_2O$, which were kindly supplied by Prof. Achmatowicz, were recrystallized from aqueous ethanol, giving colorless prisms elongated in the direction of the a axis. Precession photographs showed the crystals to be orthorhombic, space group $P2_12_12_1$, with 4 molecules in the unit cell whose dimensions were a = 14.71 Å, b = 16.07 Å, c = 14.68 Å. Three-dimensional data were collected using an equi-inclination Weissenberg camera and the multiple film technique. The crystals were deteriorating as a result of X-ray exposure and, since long exposures were necessary, four crystals were used in succession. Intensities were estimated visually, and 50% of the reflections within the CuKα sphere were obtained.

A three-dimensional Patterson synthesis sharpened to point atoms at rest was calculated from which the positions of the two bromine atoms were obtained. The scattering power of a bromide ion corresponds to 30% of the average scattering factor of the asymmetric unit and there was no difficulty in locating these two positions. Using the phases thus obtained, structure factors were computed followed by a three-dimensional electron-density distribution. In addition to the sulfur atom, this first Fourier showed an almost flat five-membered ring, a six-membered ring in chair form and five other atoms within bonding distance of each other. Based on the contribution of these 17 atoms as well as the two bromines a second set of structure factors was calculated and subsequently a second Fourier synthesis. All atomic positions of structure II became apparent except the position of C-17 which remained ambiguous. This and the positions of the four water molecules were revealed by a difference Fourier synthesis computed with the contribution of 36 atoms. The structure is now being refined by the least-squares procedure. At the present time, the reliability factor R = 11.8%.

Both quinolizidine systems are trans-joined and all four six-membered rings are in chair conformation. The 20 atoms which form these rings all lie close to a plane. Perpendicular to this plane is the thiophane ring and the two furan rings. One of the furan rings lies almost parallel to the thiophane ring while the other is almost perpendicular to it. Both furan rings and both methyl groups are in equatorial positions. C-18 is equatorial with respect to both quinolizidine systems while C-17 and the sulfur are axial. A photograph of the molecular model is shown below.



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REFERENCES

1) O. Achmatowicz and J.T. Wrobel, *Tetrahedron Letters*, 129 (1964).
2) O. Achmatowicz, H. Banaszek, G. Spiteller and J.T. Wrobel, *ibid.*, 927 (1964).