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NITROPOLYZONAMINE: A SPIROCYCLIC NITRO COMPOUND FROM THE DEFENSIVE GLANDS OF A MILLIPED (*POLYZONIUM ROSALBUM*)[1]

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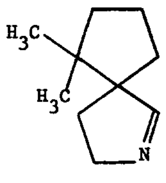
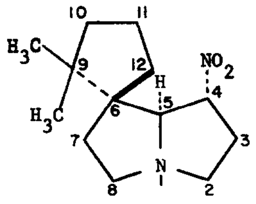
We have reported recently that polyzonimine (I) is the component in the defensive secretion of the milliped *Polyzonium rosalbum* which imparts a characteristic "camphoraceous" (or to some "earthy") odor to this animal.[2] Polyzonimine is accompanied in this secretion by a smaller amount (*ca.* 15%) of a less volatile, crystalline component which, in addition to the same spirocyclic nucleus, has another unusual feature not often found among animal metabolites, an aliphatic nitro group. We first isolated this compound, subsequently named nitropolyzonamine, from an ethereal solution of the crude defensive secretion as its crystalline perchlorate. Its structure and stereochemistry, based on an X-ray crystallographic study of the salt, are represented below in formula II.



I



II

Nitropolyzonammonium perchlorate, M=338.8, crystallizes in the orthorhombic system, space group $P2_12_12_1$, a=13.89(1), b=17.42(1), c=13.27(1) Å, U=3211 Å^3, D_m (flotation)=1.39 g.cm.$^{-3}$, Z=8, D_c=1.401 g.cm.$^{-3}$ With eight formula weights per unit cell, the asymmetric crystal unit comprises two independent pairs of nitropolyzonammonium cations and perchlorate anions. One octant of three-dimensional intensity data recorded on an Enraf-Nonius automated diffractometer (Zr-filtered Mo-$\underline{K}_\alpha$ radiation, λ=0.7107 Å) operating in the Θ-2Θ scanning mode yielded 1435 statistically significant [$I>2.0\sigma(I)$] reflections. The structure was solved by the heavy-atom method; atomic positional and anisotropic thermal parameters of the C, N, O, and Cl atoms were refined by full-matrix least-squares calculations to $\underline{R}$ 0.0820. For each of the crystallographically independent cations, the identity of the quaternary nitrogen atom was established by the relatively low thermal parameter assumed when treated as a carbon atom during the refinement cycles and supported by the presence of N-H...O (perchlorate) hydrogen bonding. The planar nitro group was distinguished from a carboxyl group on the basis of the equality of the refined N-O bond lengths and the absence of involvement of these oxygen atoms in any hydrogen bonds. Allowance for the anomalous dispersion effect[3] of the chlorine atoms in the structure-factor calculations established the absolute configuration to be as represented by II.

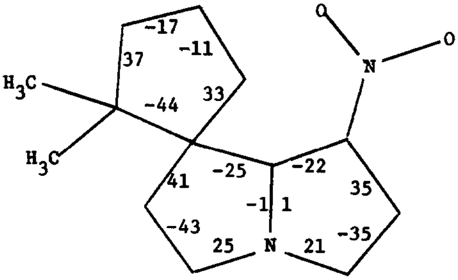
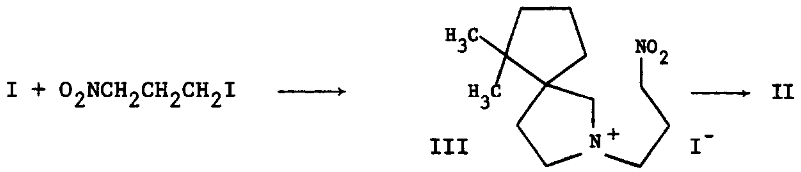


Figure: Mean endocyclic torsion angles (deg.) of the two crystallographically independent cations

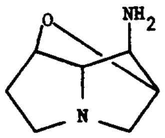
Bond lengths and valency angles agree with normal values. Although there is a small difference in the orientation of the nitro group in each of the crystallographically independent cations, the corresponding ring conformations are the same. The mean values of the endocyclic torsion angles,[4] shown in the Figure, indicate that rings A and B both adopt envelope ($\underline{C}_s$) forms with C(3) and C(7) the out-of-plane atoms. Ring C approximates a half-chair ($\underline{C}_2$) form in which symmetry axis passes through C(11) and bisects the C(6)-C(9) bond.

Nitropolyzonamine can be isolated directly as colorless crystals [m.p. 65.5-66.5°, $[\alpha]_D^{20}$ + 12° ($CHCl_3$)] from the milliped secretion by preparative gas chromatography (6' 10% SE-30 on Chromosorb W at 200°). Clear spectral evidence for the presence of the nitro group was provided both by its infrared absorption spectrum [($CDCl_3$) 6.52 and 7.31μ] and by its mass spectrum [*m/e* (rel. abundance) 238(2), 192(8), 191(12), 151(2), 150(6), 136(5), 135(9), 122(32), 108(35), 95(13), and 82(100)].

The close structural relationship between I and II suggested that it should be possible to synthesize the latter from the former in some direct way, and this hope has been realized. Treatment of synthetic I[2] with β-nitroiodopropane gives a crystalline salt (III) which is readily cyclized to (±)-nitropolyzonamine in boiling pyridine, as outlined below.



At least two entirely different biosynthetic hypotheses for II can be envisioned. It is conceivable that a β-nitropropionic acid unit[5] or its equivalent condenses with I (itself derived from geranyl pyrophosphate) in a scheme resembling the laboratory synthesis we have just described. Alternatively, it may be speculated that II may be a transformation product of an as yet unknown pyrrolizidine alkaloid of plant origin. In this context, it is intriguing to note that there are a small number of alkaloids, such as norloline (IV), which possess a second nitrogen atom in a position analogous to that occupied by the nitro function of II.[6] Were this the case, it would appear likely that II would then be the precursor of I in the milliped.



IV

We hope to present a fuller discussion of both the chemistry and biology of these novel natural products in the near future.[7]

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References and Notes

1. Paper No. 46 of the series "Defense Mechanisms of Arthropods."
2. J. Smolanoff, A. F. Kluge, J. Meinwald, A. McPhail, R. W. Miller, K. Hicks, and T. Eisner, *Science*, **188**, in press (1975).
3. "International Tables for *X*-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, 1968.
4. For a definition of the sign convention used, see W. Klyne and V. Prelog, *Experientia*, **16**, 521 (1960).
5. For a leading reference, see M. Luckner, "Secondary Metabolism in Plants and Animals," Academic Press, New York, 1972.
6. L. B. Bull, C. C. J. Culvenor, and A. T. Dick, "The Pyrrolizidine Alkaloids," North Holland Publishing Co., Amsterdam, 1968.
7. These results were presented at the "Symposium on the Chemical Senses" at the 169th Annual Meeting of the American Chemical Society, April 7, 1975, in Philadelphia, Pennsylvania.