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DAPHNIPHYLLUM ALKALOIDS. PART V (1). THE REVISED STRUCTURE OF MACRODAPHNINE

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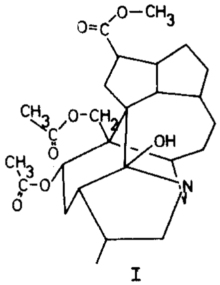
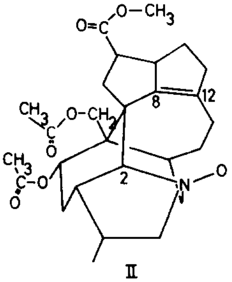
In part II (2) of this Series, one of the authors (T.N.) tentatively formulated macrodaphnine, one of the alkaloids isolated from the bark of Daphniphyllum macropodum Miquel (Euphorbiaceae), as a dihydro-derivative (I) of macrodaphnidine on the basis of the elemental analysis, infrared, n.m.r., and mass spectral data. The most characteristic feature of this alkaloid was that the mass spectrum gave main peaks at m/e 471, 412, and 398, which were all two mass units higher than the corresponding ions in the mass spectrum of macrodaphnidine. In order to confirm that these ions actually resulted from the same fragmentation pattern as in the case of macrodaphnidine, it was necessary to establish the structure of this alkaloid by an X-ray analysis.

Macrodaphnine hydrobromide, $C_{27}H_{37}O_7N\cdot HBr$, formed from acetone - methanol small colourless crystals, m.p. 249-252°. The crystals are monoclinic, spacegroup $P2_1$, with a=8.76±0.02, b=10.11±0.02, c=16.17±0.03Å, β=102.4° ± 0.2° (λ for CuKα = 1.5418Å). With Ni-filtered CuKα radiation three-dimensional film data were collected around the [100] and [010] axes. The films were photometered automatically, giving a set of 987 independent reflexions. The x and z coordinates of the bromine were obtained from a three-dimensional Patterson synthesis, its y coordinate was arbitrarily chosen = 0.5. False symmetry then occurred across the plane y = 0.5, but the molecule could be identified by several successive Fourier syntheses. By least-squares block diagonal techniques the bromine was refined with anisotropic, the remainder of the atoms with isotropic thermal parameters, giving a final conventional R factor of 0.099. The nitrogen and oxygen atoms were initially undistinguished and treated as carbon atoms, but could be identified by their low isotropic B values after some cycles of refinement. The absolute configuration of the molecule is not determined.

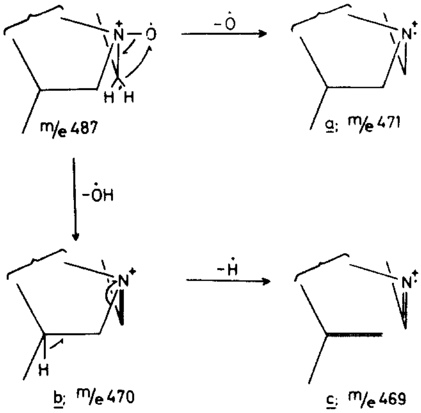
The X-ray analysis (to be published in full extent elsewhere) disclosed the N-oxide structure (II) for macrodaphnine which possesses a double bond between C-8 and C-12, as in macrodaphnidine (2), but no hydroxyl group at C-2. This revised structure thus deserved re-investigation of the mass spectrometric fragmentation of this alkaloid. Careful re-determination (3) of its spectrum gave fragment peaks as well as the molecular ion: *m/e* 487 ($M^{\dagger}$) (intensity, 5 %), 471 (*a*) (base peak, 100 %), 470 (*b*) (53 %), 469 (*c*) (65 %), 428 (*a*-CH_3CO) (59 %), 412 (*a*-CO_2CH_3) (87 %), 410 (*c*-CO_2CH_3 (81 %), 398 (*a*-$CH_3CO_2CH_2$) (15 %), and 396 (*c*-$CH_3CO_2CH_2$) (6 %). A possible rationalization for the formation of the fragment ions, *a*, *b*, and *c*, may be shown below.



I



II



The X-ray structure is also consistent with the elemental analysis and all other spectroscopic data (i.r. and n.m.r.) (2) reported previously for macrodaphnine and its hydrobromide.

References

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(2) T. Nakano and Y. Saeki, Tetrahedron Letters, No. 48, 4791 (1967).

(3) For the mass spectra of N-oxides, see O. Buchardt, A.M. Duffield, and R.H. Shapiro, Tetrahedron **24**, 3139 (1968) and references cited therein. We are indebted to Drs. C. Djerassi and A.M. Duffield of Stanford University for the mass spectra determination.