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ALKALOID METABOLITES OF THE MARINE TUNICATE EUDISTOMA SP.: SEGOLINE A, ISOSEGOLINE A AND NOR-SEGOLINE

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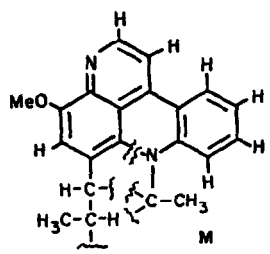
Abstract - Three alkaloid constituents of the marine tunicate Eudistoma sp. have been shown to be segoline A(1), isosegoline A(2) and norsegoline (3)

Eudistoma sp is a purple tunicate found in the straits of the Gulf of Suez the Red Sea. In the course of a survey of chemical constituents of tunicates we have isolated from this organism by chromatography of the concentrated CH_2Cl_2 extract several new alkaloids The structure of three, segoline A(1)(0 4%), isosegoline A(2)(0.01%), and norsegoline (3)(0.001%) follows[1]

Detailed analysis of the NMR spectral data (1D and 2D COSY[2] and HETCOSY[3] experiments) for segoline A[4], $C_{23}H_{19}N_3O_3$, m p >300° $[\alpha]_D^{25}$-322°(C=0 01), ν_{max} 1710cm^{-1}, indicated partial structure M The full structure was established unequivocally by single crystal X-ray methods All data were collected on an Enraf-Nonius CAD4-diffractometer with MoKα radiation The structure was solved by direct methods (SHELX-86)[5] Its refinement was carried out by large-block least-squares (SHELX-76)[6] The final refinement was based on 806 intensity data above the intensity threshold of 36 At convergence, R=0 056, wR=0 054, goodness-of-fit=1 14e, $[\varrho_{max}]$=0 27e Å^{-3} An ORTEP projection is shown below



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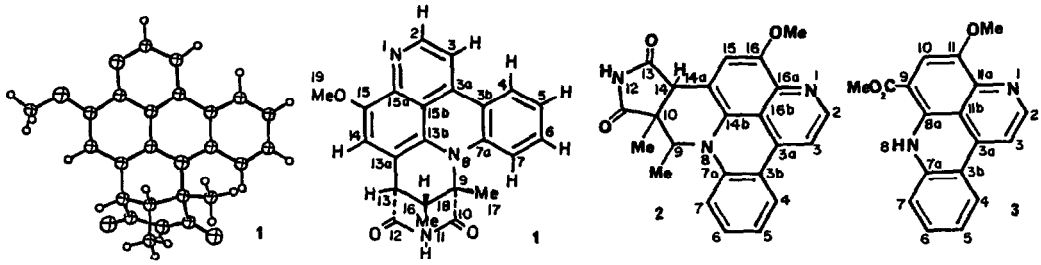
Most characteristic for the aromatic portion in all three new alkaloids (1-3) was the UV spectrum which changes with pH from orange in neutral solution to deep purple in acid media[7] In addition to the UV spectrum, the aromatic portion was also characterised by the proton and carbon chemical shifts and more specifically by correlation spectroscopy[2,3] and NOE's of the aromatic protons among themselves and with their neighbour groups

Isosegoline A(2), $C_{23}H_{19}N_3O_3$[8] possesses in addition to the same aromatic portion as in 1, a mono methyl succinimide moiety; ν_{max}1730cm^{-1}, δ_C180 5 & 175 2ppm and a NH group (δ_H11 2 d_6-DMSO) which is readily methylated with CH_2N_2 The linkages of the succinimide to C-14a and N-8 through a CH(Me) group (δ_{CH}=5 06 & δ_{Me}=1 04ppm) were unequivocally established by correlation spectroscopy and NOE's

Nor-segoline (3), $C_{18}H_{14}N_2O_3$.[9] ν_{max} 1670cm^{-1}, embodies in its structure the above mentioned diaza heterocyclic ring system which is substituted, in addition to the OCH_3 group common to



compounds 1-3, by a carbomethoxy function (δ_{OMe} 3 99ppm). The N(8)H, in contrast to the imide-NH's of 1 & 2 is methylated only with CH_3I, K_2CO_3 in acetone(3b, δ_{NMe} 3 70ppm) Nuclear Overhauser enhancements of the original NH in 3 and of the newly formed NMe in 3b determined unequivocally the position of the N(8) atom NOE's and ^{13}C chemical shifts established also the C-9 position of the carbomethoxy group (enhancement of H-10 while irradiating the OMe)

All three alkaloids are new types, compounds 1 & 2 possesses the naturally rare imide group Interesting biogenetically is the aromatic portion of 1-3 which is similar to part of the penta cyclic heterocycle system of amphimedin[10], petrosamine[11] and ascididemin[12]

References and Notes

1 The name segoline comes from segole the Hebrew word for purple

2 K Nagayama et al J Mag Res , 40, 321 (1980)

3 Y Sato, M Geckle and S J Gould, Tetrahedron Lett , 26, 4019 (1985)

4 δ_H($CDCl_3$ & 50λ of TFA) 8 73d, 8 02d, 7.94d, 7 66d, 7 55t, 7 47s, 7 25t, 4 09s (3H), 3 96d, 2 20dq, 1 87s (3H) and 1 36d (3H)

5 G M Sheldrick, in "Crystallographic Computing 3" Eds G.M Sheldrick, C Kruger and R Goddard, Oxford University Press, 1985, pp 175-189

6 G M Sheldrick, Program for Crystal Structure Determination, University of Cambridge, England, 1976

7 1, λ_{max} MeOH 460(3100), 383(2600), 368(1600), 320(5600),308(5100),274(16200),236(9000s), λ_{max} MeOH,H^+ 545(2500), 382(2500), 366(1400), 298(21300), 278(15600s), 245(7400)mn

8 2, δ_H(d_6-DMSO, 360MHz) 11 2bs, 8 57d, 8 08d, 7 63d, 7 48t, 7.18s, 7 06t, 5 06q, 3 89s (3H), 3 88s, 1.45s (3H), 1.04d (3H), δ_C($CDCl_3$) 180 5s, 175.2s, 150 9d, 147.8s, 143 1s, 140 5s, 138.9s, 132 4d, 127 0s, 124 4d, 121 4d, 120 4s, 118 9s, 114 5d, 109 9d, 108 8d, 107 4s, 56 5q, 52 7s, 51 1d, 49 3d, 23 6q & 12 3q.

9 Compound 3, δ_H 11 66s, 8.86d, 8.03d, 7.61d, 7.51s, 7.48dt, 7 18dd, 7 17t, 4 06s (3H), 3 99s (3H), δ_C ($CDCl_3$) 168.8s, 151 9d, 145 2s, 141 1s, 137 9s, 137 3s, 132 3d, 130 8d, 123 9d, 123 5s, 122.3d, 119 3s, 117 1d, 116.5s, 109 1d, 108 7d, 56 2q & 51 9q

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