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CONSTITUENTS OF BATHYAL MARINE ORGANISMS: A NEW ZOANTHOXANTHIN FROM A COELENTERATE

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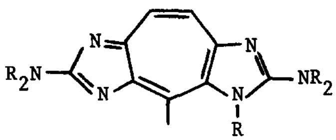
Our rapidly expanding knowledge of marine natural products[2] has been based almost entirely on a study of organisms accessible by snorkel or SCUBA. Some precious corals which are fashioned into jewelry are harvested in Hawaii by minisubmarine at depths of 350 m.[3] Thanks to this operation we have been able to examine the metabolites of gold coral,[4] Parazoanthus sp. (Coelenterata, Anthozoa, Zoantharia ≡ Hexacorallia).

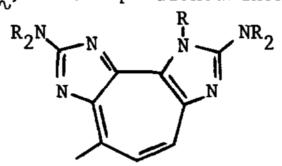
Steeping the freshly collected animals (320 g) in EtOH overnight produced a strongly fluorescent extract, which after concentration and acidification to pH 1 was purified successively by cation exchange (Dowex 50W-4X), basification of the fluorescent fraction, extraction of the aq base with n-BuOH, then $CHCl_3$/MeOH (4:3), and chromatography of the combined organic extracts, first on silica gel ($CHCl_3$/MeOH/25% NH_4OH, 80:20:2), then on Sephadex LH-20 ($CHCl_3$/MeOH, 4:3), resulting in an amorphous yellow powder, dec near 200°C (900 mg), $C_{13}H_{16}N_6$,[5] further characterized as an orange monoacetate, mp 125-129°C, $C_{15}H_{18}N_6O$.

The fluorescent nature of this compound and its biological origin from a zoantharian led us to suspect a structural relationship with a group of compounds first isolated from shallow water zoanthids by Prota and coworkers[6a-e] and later by a Japanese group.[7] These compounds are tetrazacyclopentazulenes that have either the zoanthoxanthin (**1**) or the pseudoxoanthoxanthin (**2**) skeleton. The zoanthoxanthins are further differentiated into para- and epizoanthoxanthins depending on the N-methylation pattern. One of the pseudozoanthoxanthins is also known as paragracine.[7,8] A representative of **1** and of **2** has been synthesized by Braun and Büchi.[9]



1

R = H, Me



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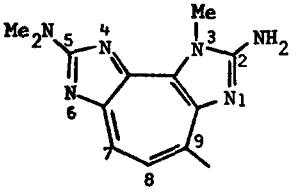
Comparison of our (**3**) uv spectral data with those reported for **1** and **2** (Table 1) suggests the gold coral metabolite to be a new compound. The ^1H nmr spectrum of **3** [CF_3CO_2D,[10] 100 MHz: δ 8.29 (1 Hd, J = 10 Hz), 8.04 (1 Hd, J = 10 Hz), 4.63 (3 Hs), 3.55 (6 Hs), 2.96 (3 Hs)]

Table 1. UV Spectral Comparison (MeOH) of the Zoanthoxanthins

1	427 (4.35), 293 (4.52)[6b]
2	421 (3.93), 367 (4.07), 307 (4.67), 281 (4.48)[6e]
3	416 (4.18), 377 (4.00), 317 sh (4.49), 306 (4.59), 261 (4.02), 226 (4.02).

further substantiated that **3** differed from the known zoanthoxanthins.[6e] Inspection of the tetrazacyclopentazulene skeleton shows that alkylation at any of the four nuclear nitrogens introduces subtle dissymmetry in the molecule.

Compound **3** was crystallized from EtOH/H_2O (80:20) and its structure was shown to be 2-amino-3,9-dimethyl-5-dimethylamino-3*H*-1,3,4,6-tetrazacyclopent[e]azulene monohydrate by single crystal x-ray techniques.



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The crystallographic structure determination was based on 757 reflections above background level (I > 2σ(I)) collected by counter methods.

Crystal data are as follows: Space group $P2_1/c$, a = 11.111(5) Å, b = 16.567(12) Å, c = 7.368(2) Å, β = 98.32°(3), V = 1342.0(12) Å^3, Z = 4, F(000) = 584.

A structure model was found by use of the MULTAN-77 program assembly[11] and refined to a conventional R of 0.096 ($R = \Sigma|kF_{obs}-|F_{calc}||/\Sigma kF_{obs}$, where k is the scale factor). The positions of the 18 hydrogen atoms were found in a difference Fourier synthesis, and these were included in the structure factor calculations with estimated isotropic temperature factors. Full-matrix least-squares refinement of positional and anisotropic thermal parameters of all nonhydrogen atoms converged to an R of 0.075 and an R_w of 0.058. ($R_w = \Sigma w(kF_{obs}-|F_{calc}|)^2/\Sigma w(kF_{obs})^2$).

The molecular structure and atomic numbering is shown in Fig. 1, where also bond lengths and bond angles are listed. The molecule is planar, the maximum deviation from a least-squares plane through all 19 nonhydrogen atoms is only 0.1 Å for N17. The bond lengths and this planarity imply a totally aromatic system. The water molecule participates in three hydrogen bonds, as a hydrogen donor in bonds to two different N5 atoms and as an acceptor in a bond to N17.

A full account of the crystallographic structure determination will be published elsewhere.

Acknowledgment -- We thank Richard W. Grigg for identifying the animal, Debra Hamburg for her valiant assistance with animal procurement, and the National Science Foundation for financial support.

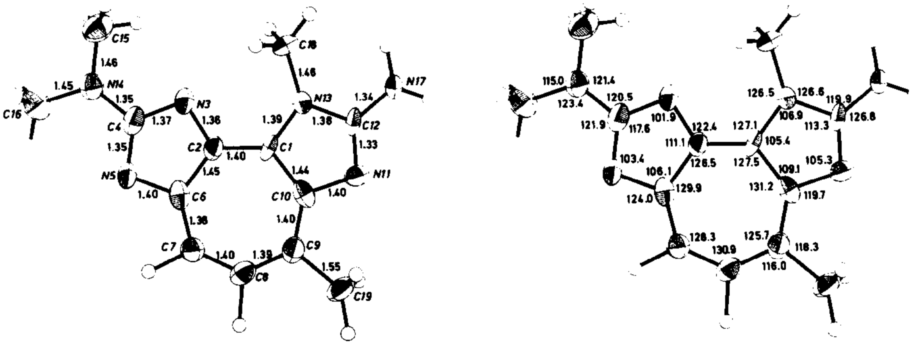

Fig. 1. Bond lengths (Å) and bond angles (°). The estimated standard deviations in bond lengths are 0.01 Å and in angles 0.8-1.0°. The ellipsoids are given for 50% probability, the hydrogens are drawn artificially small.

References and Notes

(1) NRCC Postdoctoral Fellow, 1975-1977.

(2) See *e.g.* "Marine Natural Products: Chemical and Biological Perspectives," Vol. 1, P. J. Scheuer, Ed., Academic Press, NY, 1978.

(3) We are indebted to Maui Divers, Inc. and to Mr. Bo Bartko for collecting the animals.

(4) The name is derived from the golden luster of the polished endoskeleton of the animal.

(5) By high resolution mass spectrometry.

(6) (a) L. Cariello, S. Crescenzi, G. Prota, F. Giordano, and L. Mazzarella, *J. Chem. Soc. Chem. Commun.* 99, 1973; (b) L. Cariello, S. Crescenzi, G. Prota, S. Capasso, F. Giordano, and L. Mazzarella, *Tetrahedron* **30**, 3281 (1974); (c) L. Cariello, S. Crescenzi, G. Prota, and L. Zanetti, *Tetrahedron* **30**, 3611 (1974); (d) L. Cariello, S. Crescenzi, G. Prota, and L. Zanetti, *Experientia* **30**, 849 (1974); (e) L. Cariello, S. Crescenzi, G. Prota, and L. Zanetti, *Tetrahedron* **30**, 4191 (1974).

(7) Y. Komoda, S. Kaneko, M. Yamamoto, M. Ishikawa, A. Itai, and Y. Iitaka, *Chem. Pharm. Bull* **23**, 2464 (1975).

(8) We should like to suggest a simplification of the existing nomenclature by using the generic name zoanthoxanthin for all tetrazacyclopentazulenes and replacing the prefixes (para, epi, pseudo) by uniform numbering.

(9) M. Braun and G. Büchi, *J. Am. Chem. Soc.* **98**, 3049 (1976).

(10) Superior resolution is achieved in DMSO-d_6.

(11) G. Germain, P. Main, and M. M. Woolfson, Acta Crystallogr. A27, 368 (1971).