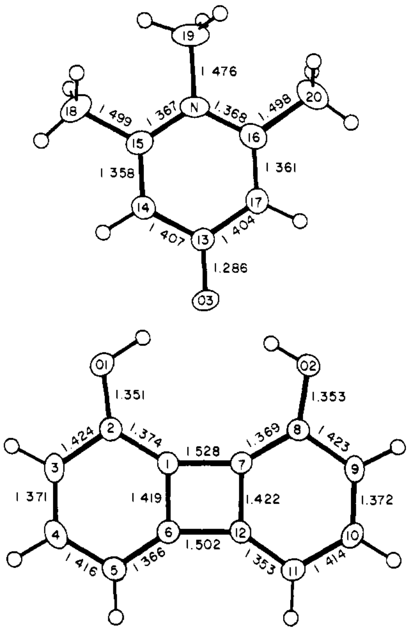

Figure 1. ORTEP drawing[13] displaying the labeling scheme and bond distances (Å) for the 1,8-biphenylenediol–1,2,6-trimethyl-4-pyridone complex with non-hydrogen atoms drawn at the 50% probability level and hydrogen atoms drawn with an artificial radius. The estimated standard deviations on the bond distances are 0.003–0.004 Å.

An ORTEP drawing of the structure of the 1,2,6-trimethyl-4-pyridone adduct is shown in Figure 1.[6] The two components are almost coplanar.[7] The O–H···O distances are 2.545 (3) and 2.548 (3) Å and the angles are 177 (3)° and 174 (3)°. Those of the pyrone adduct are 2.585 (2) and 2.589 (2) Å and 176 (3)° and 178 (3)°; those for the HMPA adduct are 2.601 (5) and 2.613 (5) Å and 168 (5)° and 172 (5)°. In his review of strong hydrogen bonds[8] Emsley lists one property of strong A–H···B hydrogen bonds as an overall bond length that is smaller than the summed van der Waals radii of A and B by at least 0.3 Å. This sum minus 0.3 Å is 2.70 Å for O–H···O and 2.75 Å for N–H···O.

The existence of the complexes in solution is established by vapor pressure osmometry determinations of molecular weight in toluene at 56.7 °C. Calcd for 1, 363.4; found; 374. Calcd for the pyrone complex, 308.3; found; 293. The pyridone complex was not soluble enough for its molecular weight to be determined.

There are other crystal structures known in which one molecule forms two hydrogen bonds to a given basic atom of a second molecule, but we know of no case in which these are two *strong* hydrogen bonds. The stronger pair in a crown ether–guanidinium ion complex, for example, are 2.90 and 2.94 Å[9] and in the case of urea are 2.98 and 3.04 Å.[10] A search of the Cambridge Crystallographic Data File by Murray-Rust and Glusker for precise data on hydrogen bonding to ketones and esters with O···X distances less than 3 Å yielded about 500 structures, of which 24 had two hydrogen bonds to the oxygen atoms.[11] Only two of these involved a diacid forming two hydrogen bonds to a given basic atom in another molecule. In the stronger of these two double hydrogen bonds, a urea derivative formed N–H···O hydrogen bonds of length 2.871 and 2.919 Å to the oxygen atom of acetone.[12] It is possible that 1,8-biphenylenediol is unique in having been shown to form two strong hydrogen bonds to a given basic atom in another molecule, with neither the acid nor the base being electrically charged. However, in view of the ubiquity of hydrogen bonds in nature, it is likely that unrecognized multiple hydrogen bonding acids are active as complexing agents and as catalysts in natural systems.

We are currently engaged in preparing additional adducts of the diol and its derivatives, in studying the catalytic activity of such diols in reactions subject to catalysis by hydrogen bonding, and in measuring equilibrium constants for hydrogen bonding of such diols to bases in poorly hydrogen bonding media and in aqueous solution.

Acknowledgment. We are greatly indebted to Dr. Jenny P. Glusker for additional details on her research,[11] to Dr. C.-S. Wu of Ashland Chemical Co. for molecular weight determinations, and to the National Science Foundation for Grant CHE-8114770.

Registry No. 1, 93136-30-2; (1,2,6-trimethyl-4-pyridone)(1,8-biphenylenediol) adduct, 93136-31-3; (2,6-dimethyl-α-pyrone)(1,8-biphenylenediol) adduct, 93184-34-0.

Supplementary Material Available: Positional and thermal parameters and structure factors (13 pages). Ordering information is given on any current masthead page.

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(6) All data sets were measured by the ω–2θ scan method on a Syntex $P\bar{1}$ diffractometer equipped with graphite monochromated MoKα radiation and an LT-1 low-temperature system. The 1,8-biphenylenediol–hexamethylphosphoramide adduct crystallizes with $Z = 4$ in $P2_1/n$ in a cell of dimensions $a = 8.527$ (1) Å, $b = 15.099$ (4) Å, $c = 15.354$ (3) Å, and $\beta = 95.17$ (1)° at −56 °C. At lower temperatures these crystals appear to undergo a destructive phase transition. The final refinement on the 2351 F_o values $[F_o^2 > 2\sigma(F_o^2)]$ yielded R (on F) of 0.077 for 234 variables (anisotropic non-hydrogen atoms, isotropic hydroxyl hydrogens, remainder of hydrogen atoms fixed). The rather high R index for this adduct results from large thermal motion for both molecules and/or positional disorder of the diol. The 1,8-biphenylenediol–1,2,6-trimethyl-4-pyridone adduct crystallizes with $Z = 4$ in $P2_1/n$ in a cell of dimensions $a = 7.639$ (1) Å, $b = 22.130$ (4) Å, $c = 9.411$ (1) Å, and $\beta = 90.66$ (1)° at −123 °C. The final refinement on the 2188 F_o values $[F_o^2 > 3\sigma(F_o^2)]$ yielded R (on F) of 0.048 for 225 variables (anisotropic non-hydrogen atoms, isotropic hydroxyl hydrogens, remainder of hydrogen atoms fixed). The 1,8-biphenylenediol–2,6-dimethyl-γ-pyrone adduct crystallizes with $Z = 2$ in $P\bar{1}$ in a cell of dimensions $a = 8.983$ (1) Å, $b = 13.450$ (2) Å, $c = 6.926$ (1) Å, $\alpha = 85.15$ (1)°, $\beta = 106.19$ (1)°, and $\gamma = 109.72$ (1)° at −125 °C. The final refinement on the 2592 F_o values $[F_o^2 > 1.5\sigma(F_o^2)]$ yielded R (on F) of 0.048 for 240 variables (anisotropic non-hydrogen atoms, isotropic methyl and hydroxyl hydrogens, remainder of hydrogen atoms fixed).

(7) The dihedral angle between the best least-squares planes for the two components is 3.2 (1)° for the pyridone adduct and 4.8 (1)° for the pyrone adduct.

(8) Emsley, J. *Chem. Soc. Rev.* **1980**, *9*, 91–124.

(9) de Boer, J. A. A.; Uitewijk, J. W. H. M.; Geevers, J.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1983**, *48*, 4821–4830.

(10) Pryor, A. W.; Sanger, P. L. *Acta Crystallogr., Sect. A* **1970**, *A26*, 543–558.

(11) Murray-Rust, P.; Glusker, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 1018–1025.

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(13) Johnson, C. K. Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN 1965.

An Unprecedented Triisocyano Diterpenoid Antibiotic from a Sponge

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Received August 20, 1984

We recently reported the structure of kalihinol A (**1**), a highly functionalized diisocyano diterpenoid antibiotic from a Guam sponge, *Acanthella* sp.[3] The Bio-Sil A fraction from the isolation of **1** was resolved on HPLC (RP-18, MeOH/water, 3:1) into

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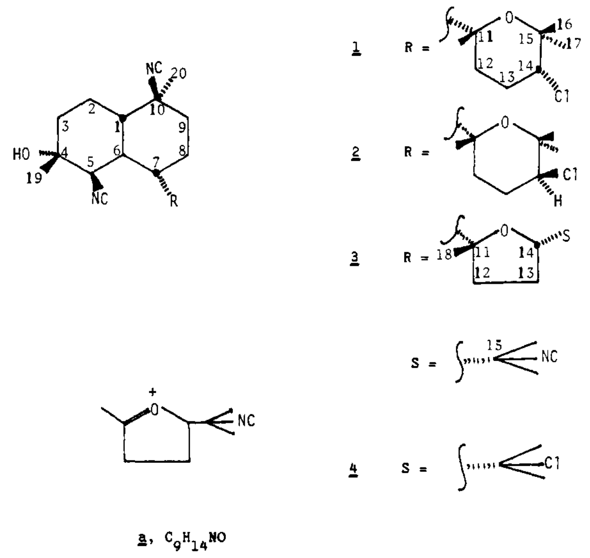
(1) UNESCO Fellow from the University of Calcutta, 1983.

(2) On sabbatical leave from the University of West Florida, Pensacola, FL, 1983.

(3) Chang, C. W. J.; Patra, A.; Roll, D. M.; Scheuer, P. J.; Matsumoto, G. K.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 4644–4646.

0002-7863/84/1506-7981$01.50/0

kalihinol E (**2**, 5 mg)[4] a C-14 epimer of **1**, and an unprecedented triisocyano diterpenoid, kalihinol F (**3**, 20 mg), which shows in vitro activity against *Bacillus subtilis*, *Staphylococcus aureus*, and *Candida albicans*.



Kalihinol F (**3**), colorless plates from hexanes plus a trace of EtOAc, or from MeCN–water, mp 176–178 °C, $[\alpha]_D$ +8° (*c* 1.0, $CHCl_3$), had IR and ^1H NMR spectra similar to those of **1**,[5] but the ^{13}C NMR data[6] (δ 63.2, 59.9, and 59.8) strongly suggested a triisocyano compound. Two carbon resonances, a singlet at 87.3 and a doublet at 82.8 ppm, suggested that the tetrahydropyranyl moiety in **1** was replaced by an oxetane or a tetrahydrofuran. Absence of the diagnostic mass spectral fragments at *m/z* 161/163,[3] replaced in **3** by a substantial peak at *m/z* 152 assignable to fragment **a** argued for lack of chlorine and for a tetrahydrofuranyl moiety. A mass spectral peak at *m/z* 315 ($M^+ - C_4H_6N$) is compatible with loss of an isocyanoisopropyl fragment. Single-crystal X-ray diffraction of kalihinol F confirmed these features and revealed cis stereochemistry of H-14 and Me-18.

After the mother liquors from the crystallization of kalihinol A were concentrated, the residue, despite its identical R_F on silica TLC, was separable by reversed-phase HPLC (same conditions as above) into kalihinol B (**4**, 1 mg)[6] and C (**5**, 2 mg).[7] Their structures are compatible with the spectral data. This remarkable trio of compounds, kalihinol F (**3**), B (**4**), and C (**5**), where the diterpenoid tail appears as an isopropenyl (**5**), a chloroisopropyl (**4**), or an isocyanoisopropyl (**3**) function, may well indicate a biogenetic sequence of events, which will have to be tested by experiment.

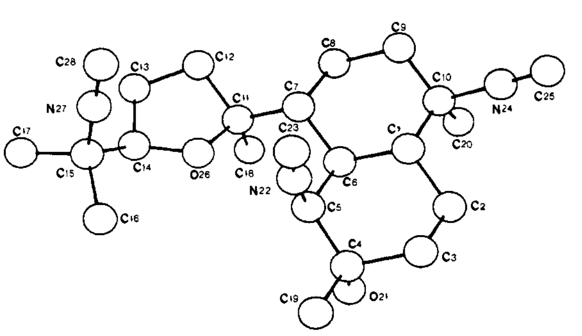


Figure 1. Computer-generated perspective drawing of the final X-ray model of kalihinol F. No absolute configuration is implied, and hydrogens are omitted for clarity.

Kalihinol F crystallized in the monoclinic space group $P2_1$ with $a = 6.5835$ (7) Å, $b = 35.676$ (6) Å, $c = 10.363$ (1) Å, and $\beta = 108.02$ (1)°. An estimated crystal density indicated that two molecules of composition $C_{23}H_{33}N_3O_2$ formed the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using a variable speed, 1° ω-scan and graphite monochromated Cu Kα radiation (1.54178 Å). A total of 3188 unique reflections were collected, and after correction for Lorentz, polarization, and background effects, 2834 (89%) were judged observed ($|F_o| \geq 3\sigma(F_o)$). A phasing model was found after considerable difficulty by extending a plausible fragment with the program DIRDIF.[8] Hydrogen atoms were located on a difference synthesis after partial refinement. Block-diagonal least-squares refinements with anisotropic heavy atoms and hydrogens with fixed isotropic thermal parameters have converged to a standard crystallographic residual of 0.078 for the observed reflections.[9] Additional crystallographic data are available and are described in the supplementary material.

Figure 1 is a computer-generated drawing of the final X-ray model of kalihinol F. Hydrogens are omitted for clarity, and no absolute configuration is implied. The *trans*-decalin system is adequately described as two boats with an axial isocyano substituent at C-5, an axial hydroxy at C-4, and an axial methyl at C-10. The tetrahydrofuran substituent at C-7 is equatorial, as is the methyl group at C-4 and the isocyano moiety at C-10. The

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(4) Kalihinol E (**2**); colorless needles from hexanes–acetone, mp 197–199 °C, $[\alpha]_D$ +4°, (*c* 1.0, $CHCl_3$); HREIMS for $C_{22}H_{33}ClN_2O_2$, *m/z* 357.2522 (calcd for $M^+ - Cl$, 357.2542); EIMS, *m/z* 377 (2%, $M^+ - Me$), 357 (6, $M^+ - Cl$), 330 (4, $M^+ - Cl - HCN$), 202 (11), 164 (25), 163 (70), 162 (61), 161 (100), 125 (75), 107 (70), 105 (51), 93 (42), 91 (45), 81 (48), 79 (43), 71 (54), 67 (59), 55 (57), 43 (64), 41 (65); IR ($CHCl_3$) ν_{max} 3400 (br), 2130 (br), 1380 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.58 (1 H, br s, H-5), 3.95 (1 H, t, *J* = 3.5 Hz, H-14), 1.40 (3 H, s, Me-19), 1.34 (3 H, s, Me-16), 1.33 (3 H, s, Me-17), 1.30 (3 H, br t, *J* = 1.2 Hz, Me-20), 1.13 (3 H, s, Me-18), 2.4–0.8 (complex). Cf. kalihinol A: H-14, δ 3.72 (dd, *J* = 12.5 Hz).

(5) Kalihinol F (**3**): HREIMS, *m/z* 383.2533 (M^+) (calcd for $C_{23}H_{33}N_3O_2$, 383.2572); EIMS, *m/z* 383 (0.1%, M^+), 368 (0.1, $M^+ - Me$), 356 (0.2, $M^+ - HCN$), 341 (0.2, $M^+ - Me - HCN$), 315 (2, $M^+ - C_4H_6N$), 288 (3, $M^+ - HCN - C_4H_6N$), 199 (6), 152 (49, $C_9H_{14}NO$), 125 (32), 85 (61), 83 (95), 43 (100); IR ($CHCl_3$) ν_{max} 3540–3240 (br), 2140, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.35 (1 H, br s, H-5), 3.95 (1 H, dd, *J* = 8.6, 3.3 Hz, H-14), 1.39 (6 H, br t, Me-16, Me-17), 1.38 (3 H, s, Me-19), 1.32 (3 H, t, *J* = 1.5 Hz, Me-20), 1.03 (3 H, s, Me-18), 2.1–0.9 (complex); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.2 (br t), 153.2 (br t), 87.3 (s, C-11), 82.8 (d, C-14), 70.4 (s, C-4), 63.2 (d, C-5), 59.9, 59.8 (br m, C-10, C-15), 46.3 (d, C-6), 42.1 (d, C-1), 39.8 (t), 38.2 (t), 35.9 (d, C-7), 32.6 (t), 28.7 (q, C-19), 25.9 (C-16 or C-17), 25.0 (t), 24.1 (t), 23.9 (C-17 or C-16), 21.5 (t), 20.7 (q, C-20), 17.7 (q, C-18), the third NC was not observed.

(6) Kalihinol B (**4**): ^1H NMR ($CDCl_3$) δ 4.40 (1 H, br s, H-5), 4.03 (1 H, dd, *J* = 9, 4 Hz), 1.58 (3 H, s, Me-16 or Me-17), 1.52 (3 H, s, Me-17 or Me-16), 1.4. (3 H, s, Me-19), 1.32 (3 H, br t, *J* ~ 1.5 Hz, Me-20), 1.02 (3 H, s, Me-18), 2.1–0.8 (complex); EIMS, *m/z* 356 (13%, M^+), 341 (12, $M^+ - Me$), 329 (28, $M^+ - HCN$), 314 (12), 313 (14), 285 (17), 245 (29), 204 (29), 163 (23), 162 (25), 161 (46), 152 (40), 145 (49), 126 (51), 125 (100), 107 (58), 93 (51), 79 (52), 43 (70).

(7) Kalihinol C (**5**): ^1H NMR ($CDCl_3$) δ 5.05 (1 H, s, H_A-16), 4.78 (1 H, s, H_B-16), 4.74 (1 H, m, H-14), 4.5 (1 H, br s, H-5), 1.72 (3 H, s, Me-17), 1.42 (3 H, s, Me-19), 1.33 (3 H, br t, *J* ~ 1.5 Hz, Me-20), 1.03 (3 H, s, Me-18), 2.4–0.8 (complex); EIMS, *m/z* 356 (14%, M^+), 341 (12, $M^+ - Me$), 329 (28, $M^+ - HCN$), 313 (14), 299 (10), 248 (29), 187 (25), 178 (35), 160 (51), 152 (40), 145 (49), 135 (41), 125 (100), 119 (49), 107 (58), 91 (51), 67 (54), 53 (48), 43 (70).

(8) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: Leonowicz, M. E., REDUCE and UNIQUE, data reduction programs, Cornell University, Ithaca, NY, 1978. Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M., MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patternson syntheses), University of York, England, 1978, 1980. Hirotsu, K.; Arnold, E., DIRDIF, Cornell University, Ithaca, NY, 1980. Motherwell, W. D. S., PLUTO78, a crystallographic illustration program, Cambridge Crystallographic Data Centre, MA, 1978. Hirotsu, K., BOND, a program to calculate molecular parameters and prepare tables, Cornell University, Ithaca, NY, 1978.

(9) The two independent molecules in the asymmetric unit are related by the following relation: $y' = -y + {}^1/_4$ and $z' = {}^1/_2 - z$. There is no such simple relation that relates the x' and x coordinates. There is a strong correlation between independent atoms related by this pseudosymmetry, and this has hampered refinement. There is a metrically attractive alternative unit cell where $a' = a$, $b' = a + 2c$, and $c' = b$. This cell appears to be orthorhombic with $b' = 19.710$ Å and would follow the systematic extinctions for $C222_1$ with an asymmetric unit containing only one triisocyano molecule. The diffraction data do not conform to this suggested orthorhombic symmetry.

tetrahydrofuran ring is in the envelope (C_s) conformation with C-11 as the flap. The molecular conformation observed in the solid state orients all of the isocyano groups on the same face of the molecule.

Acknowledgment. We thank Drs. C. Ireland and G. R. Schulte for collection of the sponge, Professor P. Bergquist for identification, and the National Science Foundation (CHE83-03912), NIH (CA 24487), and the Sea Grant College Program (HI and NY) for financial support. CWJC thanks the U. of West Florida for a Faculty Development Award.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, bond distances, bond angles, and torsional angles from the X-ray diffraction study of kalihinol F (11 pages). Ordering information is given on any current masthead page.

Zoanthamine: A Novel Alkaloid from a Marine Zoanthid

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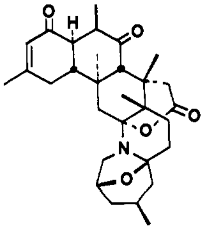
The chemical constituents of the colonial zoanthid *Zoanthus* sp.[1] were investigated as part of a program to study toxic marine organisms from the Visakhapatnam coast of India. The colonial zoanthids, which occur as dense mats on intertidal rocks, can eject jets of water when they are disturbed. If the spray comes in contact with a victim's eyes, it causes tears followed by prolonged redness and pain.[2] A preliminary investigation of extracts of the whole organism has revealed the presence of a series of novel alkaloids. In this communication we report the structural determination of zoanthamine (**1**), the first member of the new class of alkaloids.



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The ether-soluble material from an ethanolic extract of the homogenized animals was chromatographed on silica gel. The fractions eluted with 20% ethyl acetate in benzene contained zoanthamine (**1**, 9 × 10^{-4}% dry weight) that was crystallized from methanol. More polar fractions have yielded two additional alkaloids that will be reported elsewhere.

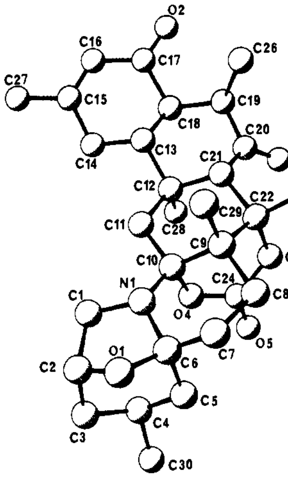

Figure 1. Computer-generated perspective drawing of zoanthamine (**1**).

Zoanthamine (**1**), $[\alpha]_D$ + 18° (*c* 0.48 $CHCl_3$), was obtained as a white crystalline solid, mp 306–308 °C. The molecular formula, $C_{30}H_{41}NO_5$, was indicated by mass measurement and by the off-resonance decoupled ^{13}C NMR spectrum.[3] An initial analysis of the ^{13}C NMR data of zoanthamine (**1**) revealed the presence of a ketone [δ 212.0 (s)], an α,β-unsaturated ketone [δ 197.2 (s), 159.9 (s), and 126.8 (d)], and an ester [δ 172.5 (s)]. The molecular formula required that zoanthamine (**1**) be heptacyclic and have both a fully substituted nitrogen atom and an ether linkage. The signal at δ 101.6 (s) in the ^{13}C NMR spectrum was assigned to a carbon atom bearing either two oxygen atoms or oxygen and nitrogen atoms. A search of the literature revealed that this molecule was unrelated to any known alkaloid structure.

Zoanthamine (**1**) crystallized in the orthorhombic crystal class with diffractometer-measured lattice constants of a = 11.775 (5) Å, b = 13.88 (1) Å, and c = 15.877 (6) Å. Systematic extinctions, crystal density, and optical activity were uniquely accommodated by space group $P2_12_12_1$ with one molecule of molecular weight 495 ($C_{30}H_{41}NO_5$) forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.541 78 Å) and variable-speed 1° ω-scans. Of the 2019 unique reflections measured in this fashion, 1677 (83%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[4] A phasing model was found using a multisolution tangent formula approach and tangent formula recycling of a plausible molecular fragment.[5] Eventually all 36 non-hydrogen atoms of zoanthamine were located. The attribution of atoms types was not a simple task. Initial assignments of heteroatoms were made on the basis of the behavior of the thermal parameters and consideration of molecular geometry. They were ultimately confirmed by refining several alternative models and location of hydrogen atoms in a difference synthesis. Block-diagonal least-squares refinements with aniso-

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[1] The animals may be a new species of *Zoanthus*. They were first identified as *Z. sociatus*, but this species is regarded as being restricted to the Caribbean. Specimens are available from either Andhra University or Scripps Institution of Oceanography.

[2] The effects can last up to a week. Several collectors have experienced these irritant effects, and they recommend caution when handling zoanthids from any location.

[3] $[\alpha]_D$ + 18° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 1720 (br), 1660 cm^{-1}; UV (CH_3CN) 233 nm (ϵ 11 000); ^1H NMR ($CDCl_3$) see text; ^{13}C NMR ($CDCl_3$) δ 212.0 (s), 197.2 (s), 172.5 (s), 159.9 (s), 126.8 (d), 101.6 (s), 89.9 (s), 74.2 (d), 53.8 (d), 48.0 (d), 48.0 (d), 47.2 (t), 45.8 (d), 44.4 (t), 41.9 (t), 40.1 (s), 39.5 (s), 38.8 (t), 35.9 (t), 35.9 (s), 30.6 (t), 29.9 (t), 24.5 (d), 23.7 (t), 22.9 (q), 21.8 (q), 20.7 (q), 18.4 (q), 18.3 (q), 13.8 (q); HRMS, obsd m/z = 495.2969, $C_{30}H_{41}NO_5$ requires 495.2985.

[4] All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: Leonowicz, M. E.; REDUCE and UNIQUE, data reduction programs, Cornell University, Ithaca, NY, 1978. Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M., MULTAN 78, a system of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses), University of York, England, 1978. Hirotsu, K.; Arnold, E., BLS78A, an anisotropic block diagonal least-squares refinement, Cornell University, Ithaca, NY, 1980. Motherwell, W. D. S., PLUTO78, a crystallographic illustration program, Cambridge Crystallographic Data Centre, 1978. Hirotsu, K., BOND, a program to calculate molecular parameters and prepare tables, Cornell University, Ithaca, NY, 1978.

[5] Karle, J. *Acta Crystallogr. Sect. B* 1968, *B24*, 182.