Registry No. 1, 673-32-5; 2, 766-90-5; 3, 35216-11-6; 4, 1002-36-4; 5, 95387-57-8; 6, 95387-58-9; 7, 930-68-7; 10, 79734-43-3; 11, 74233-41-3; 12, 623-70-1; 13, 105-54-4; 14, 141-97-9; 15, 5405-41-4; 16, 95387-59-0; 17, 95387-60-3; 18, 32820-47-6; 19, 10108-56-2; 20, 2623-87-2; 21, 822-02-6; 22, 54298-99-6; 23, 95387-61-4; 24, 95387-62-5; 25, 54844-65-4; 28, 124-19-6; (*Z*)-$CH_3(CH_2)_5CH$=$CH(CH_2)_5CH_3$, 41446-60-0; (*Z*)-$CH_3(CH_2)_3CH$=$CHCH_2OH$, 55454-22-3; $CH_3(CH_2)_4C{\equiv}CLi$, 42017-07-2; $(CH_3O)_2P(O)CH_2Li$, 34939-91-8; naphthalenetricarbonylchromium, 57220-00-5; 1-heptyne, 628-71-7; (methyl benzoate)tricarbonylchromium, 12125-87-0.

Mikiko Sodeoka, Masakatsu Shibasaki*

Sagami Chemical Research Center
Nishi-Ohnuma, Sagamihara
Kanagawa 229, Japan

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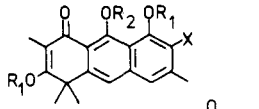
Garveatin A, an Antimicrobial 1(4*H*)-Anthracenone Derivative from the Hydroid *Garveia annulata*

Summary: The structure of garveatin A (1), an antimicrobial metabolite from the hydroid *Garveia annulata*, was inferred from its spectral data and confirmed via X-ray diffraction analysis of its triacetate 4.

Sir: Coelenterates belonging to the class Hydrozoa are small, often inconspicuous, marine invertebrates that have received very little attention from natural product chemists.[1] We report herein the structure of garveatin A (1), the major antimicrobial[2] metabolite present in the extracts of the hydroid *Garveia annulata* collected in Barkley Sound, British Columbia.

Pure garveatin A (1) (orange needles, mp 236–240 °C, acetone) was obtained by LH20 ($MeOH/CH_2Cl_2$, 9:1) and silica gel (EtOAc/hexane, 1:1) purification of the ethyl acetate soluble portion of crude methanol extracts of the hydroid. A molecular formula of $C_{20}H_{20}O_5$ was established



1 $R_1 = R_2 = H$ X = 
2 $R_1 = R_2 = Ac$ X = 
3 $R_1 = R_2 = Me$ X = 
4 $R_1 = Ac$ $R_2 = H$ X = 

by mass spectrometry (M^+ m/z obsd 340.1317, calcd 340.1311). The highly aromatic nature of garveatin A (1) was indicated by ^1H NMR ($CDCl_3$, 80 MHz) resonances at δ 7.10 (bs, 1 H) and 7.15 (s, 1 H), by its UV chromophore (MeOH, λ_{max} 232, 282, 323 (sh) and 432 nm), and by the observation of ten aromatic carbon resonances in the ^{13}C NMR ($CDCl_3$) 106.3 (s), 110.9 (s), 114.1 (d), 119.6 (d), 127.3 (s), 138.0 (s), 138.4 (s), 146.3 (s), 155.8 (s), 161.5 (s) ppm). Three additional deshielded carbon resonances at 189.3 (s), 106.7 (s), and 181.5 (s) ppm were assigned to an enolized β-diketone system which had to be alkylated at the central carbon.[3] The remaining resonances in the ^1H NMR spectrum of garveatin A (1) could be assigned to five methyl groups as follows: δ 1.63 (s, 6 H) to a pair of geminal methyls attached to a carbon which appears at 40.8 (s) in the ^{13}C NMR; 2.68 (s, 3 H) to an acetyl side chain (^{13}C NMR, 204.7 (s), 32.0 (q)); 2.40 (bs, 3 H) to an aromatic methyl; and 1.98 (s, 3 H) to the alkyl substituent on the central carbon of the β-diketone.

Garveatin A (1) forms a triacetate (2)[4] (Ac_2O, pyridine: ^1H NMR ($CDCl_3$) δ 2.35, 2.54, 2.55 all s, 3 H) which demonstrated that the three remaining protons required by the molecular formula but not observed in the ^1H NMR of 1 belonged to two phenolic and one enolic functionalities. The substituted 1(4*H*)-anthracenone derivative 1 was a biogenetically reasonable structure for garveatin A that successfully accounted for all the observed spectral data. Support for this structure came from (i) demonstration of ^1H difference NOE's between H5 and H10, between H10 and the C12 and C13 methyl protons, and between the C11 methyl and the C3 methoxy protons in the trimethoxy derivative 3, (ii) demonstration of spin coupling between H5 and the C14 methyl protons, (iii) the chemical shift of the acetyl carbonyl (δ 204.7) which requires that it be ortho to a phenol, and (iv) the similarity of the UV chromophore and the chemical shifts of H5 and H10 in garveatin A (1) and the known metabolite ferruginin A.[5]

Attempted crystallization of triacetate 2 by slow evaporation of a chloroform/hexane solution gave a 3:1 mixture of triacetates 2 and 4. We have shown that 2 can be quantitatively converted to 4 by heating with TsOH in benzene. The structure of garveatin (1) was verified by a single-crystal X-ray diffraction analysis on triacetate 4.

Preliminary X-ray photographs of garveatin A triacetate (4) displayed monoclinic symmetry. Accurate lattice constants of a = 8.1755 (15) Å, b = 18.0988 (15) Å, c = 16.0627 (22) Å, and β = 86.079 (13)° were determined from a least-squares fit of 15 diffractometer-measured 2θ values. Systematic extinctions and crystal density were uniquely accommodated by space group $P2_1/n$ with one molecule of composition $C_{26}H_{26}O_8$ as the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using variable speed, 1° ω-scans, and graphite monochromated Cu K$\bar{\alpha}$ radiation (1.541 78 Å). A total of 3200 unique reflections were collected and, after correction for Lorentz, polarization, and background effects, 2057 (64%) were judged observed.[6] A phasing model was found routinely using direct methods, and hydrogen atoms were located in difference electron density syntheses following partial refinement. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of

(1) Cimino et al. have isolated a highly oxygenated steroid from *Eudendrium sp.*, see: Cimino, G.; De Rosa, S.; De Stephano, S.; Sodano, G. *Tetrahedron Lett.* **1980**, *21*, 3303. We are not aware of any other natural products reported from hydroids.

(2) In a disk bioassay, garveatin A shows in vitro activity against *Staphylococcus aureus* (MIC; 2 μg/disk), *Bacillus subtilis* (MIC; 2 μg/disk), *Pythium ultimum* (MIC; 20 μg/disk), and *Rhizoctonia solani* (MIC; 20 μg/disk).

(3) Our tentative ^{13}C NMR assignments are 189.3 (C1), 106.7 (C2 or C8a), 181.5 (C3), 40.8 (C4), 119.6 (C5 or C10), 138.4 (C6 or C10a), 138.0 (C6 or C10a), 127.3 (C7), 155.8 (C8), 106.2 (C8a or C2), 106.7 (C8a or C2), 161.5 (C9), 110.9 (C9a), 114.1 (C10 or C5), 146.3 (C4a), 7.1 (C11), 28.9 (C12 and C13), 19.8 (C14), 204.7 (C15), 32.0 (C16).

(4) Triacetate 2 shows MS, M^+ m/z 466, 424, 382, 340 (base peak), 325; ^1H NMR ($CDCl_3$) δ 1.60 (s, 6 H), 1.80 (s, 3 H), 2.35 (s, 3 H), 2.38 (s, 3 H), 2.43 (bs, 3 H), 2.54 (s, 3 H), 2.55 (s, 3 H), 7.59 (bs, 1 H), 7.84 (s, 1 H). Triacetate 4 shows MS, M^+ m/z 466; ^1H NMR ($CDCl_3$) δ 1.53 (s, 6 H), 1.90 (s, 3 H), 2.05 (s, 3 H), 2.33 (s, 3 H), 2.38 (s, 3 H), 2.55 (bs, 3 H), 5.00 (d, J = 2 Hz, 1 H), 5.38 (d, J = 2 Hz, 1 H), 7.24 (s, 1 H), 7.45 (bs, 1 H), 15.33 (s, 1 H).

(5) Monache, F. D.; McQuhae, M. M.; Ferrari, F.; Marini-Bettolo, G. B. *Tetrahedron* **1979**, *35*, 2143.

0022-3263/85/1950-1149$01.50/0

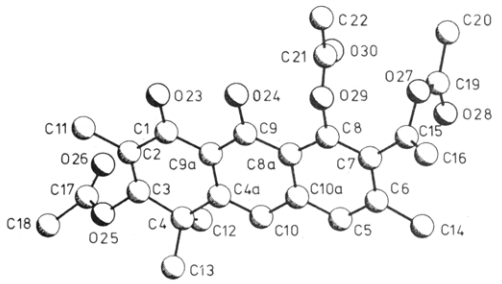


Figure 1. Computer-generated perspective drawing of garveatin A triacetate. Hydrogens are omitted for clarity.

0.0511 for the observed reflections. Additional crystallographic parameters are available and are described in the paragraph headed Supplementary Material Available at the end of this paper.

Figure 1 is a computer-generated perspective drawing of the final X-ray model of garveatin A triacetate (**4**). The tricyclic array is essentially planar, and the two *O*-acetates attached directly to a ring are rotated roughly perpendicular to the rings to avoid serious steric repulsions. The third *O*-acetate is attached to the *enolized* methyl ketone substituent. Bond distances and angles agree well with generally accepted values.

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Registry No. 1, 95388-04-8; 2, 95388-05-9; 3, 95388-06-0; 4, 95388-07-1.

Supplementary Material Available: Experimental details of isolation and characterization and tables of fractional coordinates, thermal parameters, bond distances, and bond angles (8 pages). Ordering information is given on any current masthead page.

Eoin Fahy, Raymond J. Andersen*

Departments of Chemistry and Oceanography
University of British Columbia
Vancouver, British Columbia, Canada, V6T 1W5

He Cun-heng, Jon Clardy*

Department of Chemistry
Baker Laboratory, Cornell University
Ithaca, New York 14853
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(6) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures of X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P. T. Beruskens et al., University of Nijmegen, Netherlands, 1981; MITHRIL, an automatic solution package written by C. J. Gilmore, University of Glasgow, Scotland, 1983; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.