substantial potential for the synthesis of highly functionalized target molecules.

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Petrosamine, a Novel Pigment from the Marine Sponge *Petrosia* sp.

Summary: Petrosamine (1) is an alkaloid isolated from the marine sponge *Petrosia* sp. collected at Belize. The colors of petrosamine solutions vary significantly with solvent.

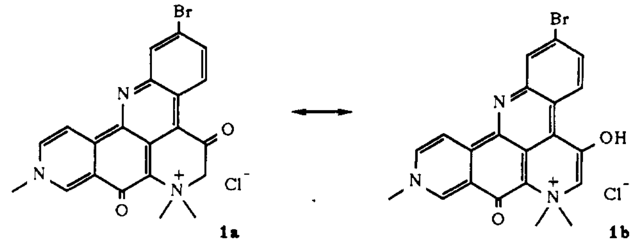
Sir: While attempting to purify an antimicrobial constituent from the marine sponge *Petrosia* sp., we isolated a new alkaloid, petrosamine (1), that has the same carbon skeleton as amphimedine (2), which is a cytotoxic constituent of the sponge *Amphimedon* sp.[1] Petrosamine (1) is remarkable because the colors exhibited by dilute organic or aqueous solutions of the compound are noticeably different. In this paper we report the isolation, spectral properties, and X-ray structure determination of petrosamine (1).

The marine sponge *Petrosia* sp. was collected in shallow water at Carrie Bow Cay, Belize. The deep blue colored methanol extracts of *Petrosia* sp. showed antimicrobial activity against *Staphylococcus aureus* and *Bacillus subtilis*. The methanol soluble material was partitioned to obtain ethyl acetate, *n*-butanol, and aqueous extracts. Both the blue color and the antimicrobial activity were concentrated in the *n*-butanol extract. Chromatography of the butanol-soluble material on Sephadex LH-20 (MeOH) resulted in separation of a blue band from a pale yellow band that contained the antimicrobial activity. Subsequent chromatography of the antimicrobial fraction on silica gel, Sephadex, or a variety of ion-exchange resins invariably led to partial loss of the antimicrobial activity and the isolation of tyramine.

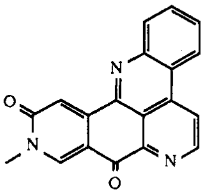
The blue material was rechromatographed on Sephadex LH-20 to obtain petrosamine (1, 0.1% dry weight) as dark green crystals, mp. >330 °C, from dichloromethane–methanol. The high-resolution mass spectrum of petrosamine (1) required a molecular formula of $C_{21}H_{17}BrN_3O_2$. The ^1H and ^{13}C NMR spectra[2] were both highly solvent-dependent and gave few clues for structural elucidation. Both the ^1H and ^{13}C NMR spectra indicated the presence of three *N*-methyl signals, two of which were always equivalent. The remaining signals were all in the aromatic region of the spectra, except for a ^{13}C NMR signal at δ 187.4 (s) that could be assigned to a single quinone-type carbonyl.

Petrosamine (1) crystallized in the triclinic crystal class with diffractometer-measured lattice constants of a = 10.894 (3) Å, b = 12.394 (4) Å, c = 9.210 (2) Å, α = 107.852 (19)°, β = 112.755 (18)°, and γ = 93.447 (22)°. All unique diffraction maxima with $2\theta < 110°$ were collected using variable speed, 1° ω-scans and graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å). Of the 2179 reflections surveyed, 1628 (75%) were judged observed after correction for Lorentz, polarization, and background effects.[3] Intensity statistics suggested the centrosymmetric space group $P\bar{1}$, and successful solution and refinement validated this choice. The structure was solved by a combination of heavy atom and tangent formula recycling techniques. Hydrogen atoms were located in a ΔF synthesis. Block-diagonal least-squares refinements have converged to the current residual of 0.082 for the observed data. Additional crystallographic details are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

Figure 1 is a computer-generated perspective drawing of the final X-ray model of petrosamine (1). Hydrogens are omitted for clarity, as are the chloride counterion and the three waters of crystallization. In the crystalline form, petrosamine (1) clearly exists as a diketone [i.e., **1a**] with a C5 carbonyl (C=O, 1.20 Å) and a C6 methylene group (C5–C6, 1.50 Å). In solution, however, the C5 carbonyl exists in the enol form [**1b**, ^{13}C NMR δ ca. 161 (s)] and the C6 protons exchange so rapidly in deuteriated solvents that they could not be observed in the ^1H NMR spectra of D_2O or MeOH-d_4 solutions.



1a **1b**



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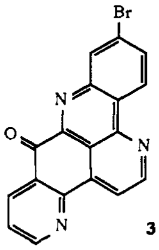

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The color of a dilute solution of petrosamine (1) varies according to the polarity of the solvent. An aqueous solution of petrosamine is purple (574 nm), a methanolic solution is blue (595 nm), and a very dilute tetrahydrofuran

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[1] Schmitz, F. J.; Agarwal, S. K.; Guunasekera, S. P.; Schmidt, P. G.; Shoolery, J. N. *J. Am. Chem. Soc.* **1983**, *105*, 4835.

[2] Petrosamine (1) mp >330 °C; IR (KBr) 3400 (br), 1670 (br), 1640, 1585, 1530 cm^{-1}; UV (MeOH) 289 nm (ϵ 42 600), 346 (12 400), 414 (sh, 6900), 595 (5300), (H_2O) 284 nm (ϵ 32 000), 345 (10 900), 574 (4700), (THF) 611 nm; ^1H NMR (MeOH-d_4) δ 3.93 (s, 6 H), 4.66 (s, 3 H), 7.90 (dd, 1 H, J = 8, 2 Hz), 8.46 (d, 1 H, J = 2 Hz), 9.05 (br d, 1 H, J = 6 Hz), 9.27 (d, 1 H, J = 8 Hz), 9.52 (d, 1 H, J = 6 Hz), 9.80 (br s, 1 H), (DMSO-d_6) δ 3.86 (s, 6 H), 4.62 (s, 3 H), 7.70 (s, 1 H), 7.94 (dd, 1 H, J = 8,2 Hz), 8.34 (d, 1 H, J = 2 Hz), 9.14 (d, 1 H, J = 8 Hz), 9.22 (br d, 1 H, J = 6 Hz), 9.27 (d, 1 H, J = 6 Hz), 9.89 (br s, 1 H), (D_2O) δ 3.70 (s, 6 H), 4.54 (s, 6 H), 7.02 (dd, 1 H, J = 8,2 Hz), 7.12 (d, 1 H, J = 2 Hz), 8.11 (d, 1 H, J = 8 Hz), 8.71 (d, J = 6 Hz), 8.82 (d, 1 H, J = 6 Hz), 9.49 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 187.4 (s), 161.4 (s), 145.6 (d), 142.6 (d), 142.3 (s), 141.7 (s), 140.1 (s), 135.3 (s), 132.1 (d), 131.7 (s), 128.9 (s), 126.4 (d), 123.0 (s), 122.1 (d), 120.4 (s), 114.6 (s), 114.5 (s), 53.4 (2 q), 48.6 (q), (D_2O) δ 187.3 (s), 160.3 (s), 144.6 (d), 142.0 (d), 141.6 (s), 140.9 (s), 138.5 (s), 134.5 (d), 131.1 (d), 127.1 (s), 125.0 (d), 122.4 (d), 120.9 (s), 114.9 (s), 54.4 (2 q), 48.6 (q); HRMS obsd m/z 422.0500, $C_{21}H_{17}\,{}^{79}BrN_3O_2$ requires m/z 422.0504.

[3] All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: FOBS a data reduction program by G. D. Van Duyne, Cornell University, 1987; 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 Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1980; BDLS, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu, E. Arnold, and G. D. Van Duyne, Cornell University, 1987; PLUTO78, a locally modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

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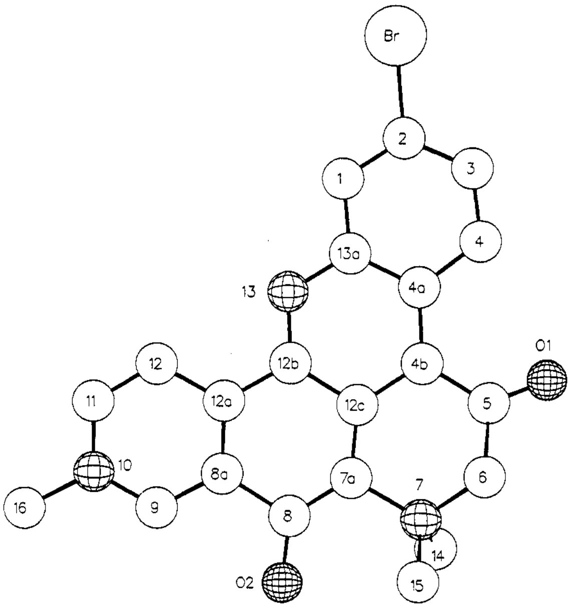

Figure 1. Computer-generated perspective drawing of the final X-ray model of petrosamine (1). Hydrogens, the chloride counterion, and waters of crystallization are omitted for clarity.

solution is green (611 nm). On treatment with base, both the aqueous and methanolic solutions turn green. The colors of the methanol and tetrahydrofuran solutions vary according to the amount of water added but the color change is not sufficient to allow detection of traces of water in the anhydrous solvents.

While preparing this paper, examples of related alkaloids have been described from a sea anemone[4] and an ascidian.[5] The sea anemone *Calliactis parasitica* produces a pigment, calliactine, that changes color from orange in acidic solution to blue in alkaline solution. While the structure of calliactine is not known with certainty, it appears to be based on a closely related carbon skeleton.[4] 2-Bromoleptoclinidinone (3) is a pentacyclic aromatic alkaloid from the ascidian *Leptoclinides* sp. that also has a closely related carbon skeleton.[5] With only four examples, it is not clear whether these metabolites should be classed together biosynthetically, but, if this is the case, the diversity of source organisms would suggest that the metabolites are produced by symbionts.

Acknowledgment. The sponge was identified by Dr. Klaus Rützler, Smithsonian Institution, and antimicrobial assays were performed by Mary Kay Harper. The research was generously supported by the National Institutes of Health (AI-11969) and the California Sea Grant College Program (NOAA, NA85AA-D-SG140, R/MP40).

Supplementary Material Available: Tables of fractional coordinates, interatomic distances, interatomic angles, and torsional angles for petrosamine (1) (5 pages). Ordering information is given on any current masthead page.

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(4) Cimino, G.; Crispino, A.; De Rosa, S.; De Stefano, S.; Gavagnin, M.; Sodano, G. *Tetrahedron* **1987**, *43*, 4023.

(5) Bloor, S. J.; Schmitz, F. J. *J. Am. Chem. Soc.* **1987**, *109*, 6134.

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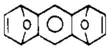
Bisannelation with a Benzo[1,2-*c*:4,5-*c*′]difuran Equivalent: A New Route to Linear Acene Derivatives

Summary: The bis adduct 4 of anthracene diendoxide 1 and tetraphenylcyclone is a synthetic equivalent for linear benzodifuran 2; it reacts thermally with dienophiles including some exceedingly weak ones to give linear acene derivatives (Table I).

Sir: syn- and *anti-***1**, both of which are readily available from 1,2,4,5-tetrabromobenzene (a 1,4-benzadiyne equivalent), furan, and butyllithium,[1,2] are excellent and useful bis dienophiles.[3,4] We observed that the base peak in the mass spectra of all the Diels–Alder bis adducts of **1** that we have prepared so far, as well as of tetrahydro-**1**, appears at m/e 158, corresponding to the radical cation of benzo[1,2-*c*:4,5-*c*′]difuran (BDF) **2**.[5,6] Unlike benzo[*c*]furan, one cannot draw a planar classical valence bond structure for **2**,[7] and as far as we are aware, no compound of this type has previously been reported.[8-10] We describe here a synthetic equivalent of **2** and demonstrate its utility for the construction of linear acene derivatives.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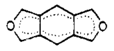
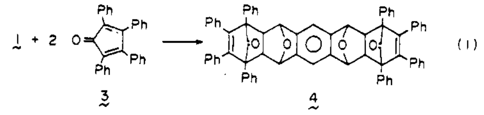

2

Following the lead of Fieser and Haddadin[11] (who first trapped isobenzofuran), either *syn-* or *anti-***1** was heated with tetracyclone **3** (2 equiv) in benzene at reflux (12 h) to give, in each case, a single bis adduct **4** in 90–92% yield.[12,13] Adduct **4** serves as a synthetic equivalent of **2**.



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(1) Hart, H.; Raju, N.; Meador, M. A.; Ward, D. L. *J. Org. Chem.* **1983**, *48*, 4357.

(2) Hart, H.; Lai, C.-Y.; Nwokogu, G. C.; Shamouilian, S. *Tetrahedron* **1987**, *43*, 5203.

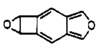
(3) Luo, J.; Hart, H. *J. Org. Chem.* **1987**, *52*, 4833.

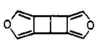
(4) Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 892.

(5) Unpublished results.

(6) The preparation of benzo[*c*]furans via analogous retro-Diels–Alder reactions is well-known; for reviews, see: Haddadin, M. J. *Heterocycles* **1978**, *9*, 865. Friedrichsen, W. *Adv. Heterocycl. Chem.* **1980**, *26*, 135. Wiersum, U. E. *Aldrichimica Acta* **1981**, *14*, 53. For more recent lead references to isobenzofurans, see: Rodrigo, R.; Knabe, S. M.; Taylor, N. J.; Rajapaksa, D.; Chernishenko, M. J. *J. Org. Chem.* **1986**, *51*, 3973. Yamaguchi, Y.; Yamada, H. *J. Org. Chem.* **1987**, *52*, 2611.

(7) Classical structures such as **2a–c** are nonplanar and have different bond angles and lengths than is implied by structure **2**; planar diradical structures such as **2d** and its many contributors are of course possible.


2a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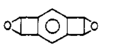
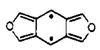

2c


2d

(8) Benzo[1,2-c:3,4-*c*′]difuran, for which one can draw such a structure, has been reported: Stringer, M. B.; Wege, D. *Tetrahedron Lett.* **1980**, *21*, 3831.

(9) A highly substituted sulfur analogue, hexaphenylbenzo[1,2-*c*:4,5-*c*′]dithiophene, has been reported: Potts, K. T.; McKeough, D. *J. Am. Chem. Soc.* **1974**, *96*, 4268.

(10) A more conventional bisisobenzofuran has recently been described and used for linear acene construction; see: Chiba, T.; Kenny, P. W.; Miller, L. L. *J. Org. Chem.* **1987**, *52*, 4327 and references cited therein.

(11) Fieser, L. F.; Haddadin, M. J. *J. Am. Chem. Soc.* **1964**, *86*, 2081. Fieser, L. F.; Haddadin, M. J. *Can. J. Chem.* **1965**, *43*, 1599.

(12) In each case, addition was exo with respect to the 1,4-endoxide; stereochemistry of the carbonyl bridge was not determined. In subsequent experiments, the adduct of *anti-***1** was mainly used, but the syn adduct or adduct derived from a syn/anti mixture of **1** can be used just as effectively.

(13) All new compounds were identified by their spectra and elemental analyses, and in many cases by further chemical conversions. Details will appear in a full account.