Structure of the Psammaplysins[1]

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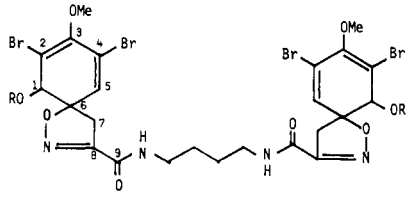
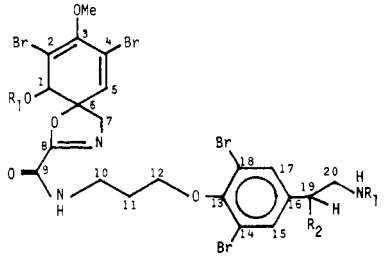
Abstract: Two antimicrobial constituents, psammaplysin-A (**7a**), $C_{21}H_{23}Br_4N_3O_6$, and -B (**8a**), $C_{21}H_{23}Br_4N_3O_7$, were isolated from a Palau sponge, *Psammaplysilla purpurea*. Identical compounds had previously been described, but their structures were based on formulas with one less oxygen atom. On the basis of ^{13}C–^{13}C connectivity and single-crystal X-ray diffraction studies on psammaplysin-A acetamide acetate (**7b**), $C_{25}H_{27}Br_4N_3O_8$, these compounds have a spiro[4.6]dioxazundecane and not a spiro[4.5]oxazadecane skeleton. Biogenetically, the psammaplysins (**7a**, **8a**) are derived from dibromotyrosine via benzene oxide–oxepin intermediates.

Marine sponges of the order Verongida possess distinct biological and chemical features, among them complex histology and nonterpenoid secondary metabolites derived from bromotyrosine.[2] Typical constituents vary from the simple aeroplysinin[3] to the relatively complex aerothionin (**1**)[4] or fistularin-3,[5] yet even in



1 R = H
2 R = Ac



3 $R_1 = R_2 = H$
4 $R_1 = H$, $R_2 = OH$
5 $R_1 = Ac$, $R_2 = H$

1 the spiroisoxazoline moiety is derived from an unrearranged tyrosine side chain. In a preliminary account in 1982,[6] which was followed by a detailed paper in 1983,[7] Kashman and co-workers describe the structures of psammaplysin-A (**3**) and -B (**4**) from the Red Sea verongid sponge *Psammaplysilla purpurea*. In common with other bromotyrosine-derived metabolites the psammaplysins have in vitro antibiotic activity, but their structures included an unprecedented spirooxazoline moiety which was based on a rearranged tyrosine side chain.

We were also engaged in the structural elucidation of two tetrabromo compounds from *P. purpurea* collected in Palau. Upon hearing of Kashman's work in 1982,[8] we made a direct comparison (HPLC, ^1H NMR, HRFDMS) of a sample of diacetylpsammaplysin-A, kindly provided by Professor Kashman, with our major metabolite. The compounds were identical, but we had serious reservations about the spirocyclohexadiene portion of Kashman's psammaplysin-A structure (**3**). Comparison (Table I) of ^{13}C NMR resonances for C-1 through C-9 of psammaplysin-A acetamide acetate (**5**)[7] with those of aerothionin diacetate (**2**)[7] shows excellent correspondence except for large downfield shifts of the C-5 (Δ 14.9) and C-6 (Δ 12.5) values. There is no a priori reason for these shifts, as these two carbons have nearly identical environments in both compounds. Another cause for concern was the anomalous UV maximum of psammaplysin-A (**3**)[7] with respect to the corresponding maxima of aerothionin[4] and fistularin-3[5] (Table II). Crucially however, the molecular formula of the crystalline *N,O*-diacetyl derivative of our compound (**7b**), mp 161–163 °C, as well as the comparison sample of Kashman's psammaplysin-A acetamide acetate (**5**), was $C_{25}H_{27}Br_4N_3O_8$ on the basis of HRFDMS. Kashman's structure corresponds to a molecular formula of $C_{25}H_{27}Br_4N_3O_7$, based on "a satisfactory elemental analysis".[7] The highest mass peak on EI occurs at m/z 481 and is assumed by Kashman to be M^+ –

Table I. Partial ^{13}C NMR Resonances (ppm) of Aerothionin Diacetate (**2**) and Psammaplysin-A Acetamide Acetate (**5**)

carbon	multiplicity	**2**	**5**
1	d	73.2	77.1
2	s	121.9	121.8
3	s	149.9	149.2
4	s	107.8	105.9
5	d	130.6	145.5
6	s	89.8	102.3
7	t	40.0	37.8
8	s	154.0	153.9
9	s	158.8	157.5

Table II. Comparison of Long-Wavelength UV Band of Aerothionin (**1**),[4] Fistularin-3,[5] and Psammaplysin-A (**3**)[6]

compd	λ_{max}, nm	ϵ
1	284	12660
Fistularin-3	283	10387
3	276	2500

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[§] Cornell University.

(1) In part from the Ph.D. Dissertation of D.M.R., University of Hawaii, 1984. C.W.J.C.'s permanent address: University of West Florida, Pensacola, FL 32514.
(2) Bergquist, P. R.; Wells, R. J. In "Marine Natural Products"; Scheuer, P. J., Ed.; Academic Press: New York, 1983; Vol. V, Chapter 1.
(3) Fattorusso, E.; Minale, L.; Sodano, G. *J. Chem. Soc., Chem. Commun.* **1970**, 751–752.
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(5) Gopichand, Y.; Schmitz, F. J. *Tetrahedron Lett.* **1979**, 3921–3924.
(6) Kashman, Y.; Groweiss, A.; Carmely, S.; Kinamoni, Z.; Czarkie, D.; Rotem, M. *Pure Appl. Chem.* **1982**, *54*, 1995–2010.
(7) Rotem, M.; Carmely, S.; Kashman, Y.; Loya, Y. *Tetrahedron* **1983**, *39*, 667–676.
(8) Fourth International Symposium on Marine Natural Products, Tenerife, Spain, July, 1982.

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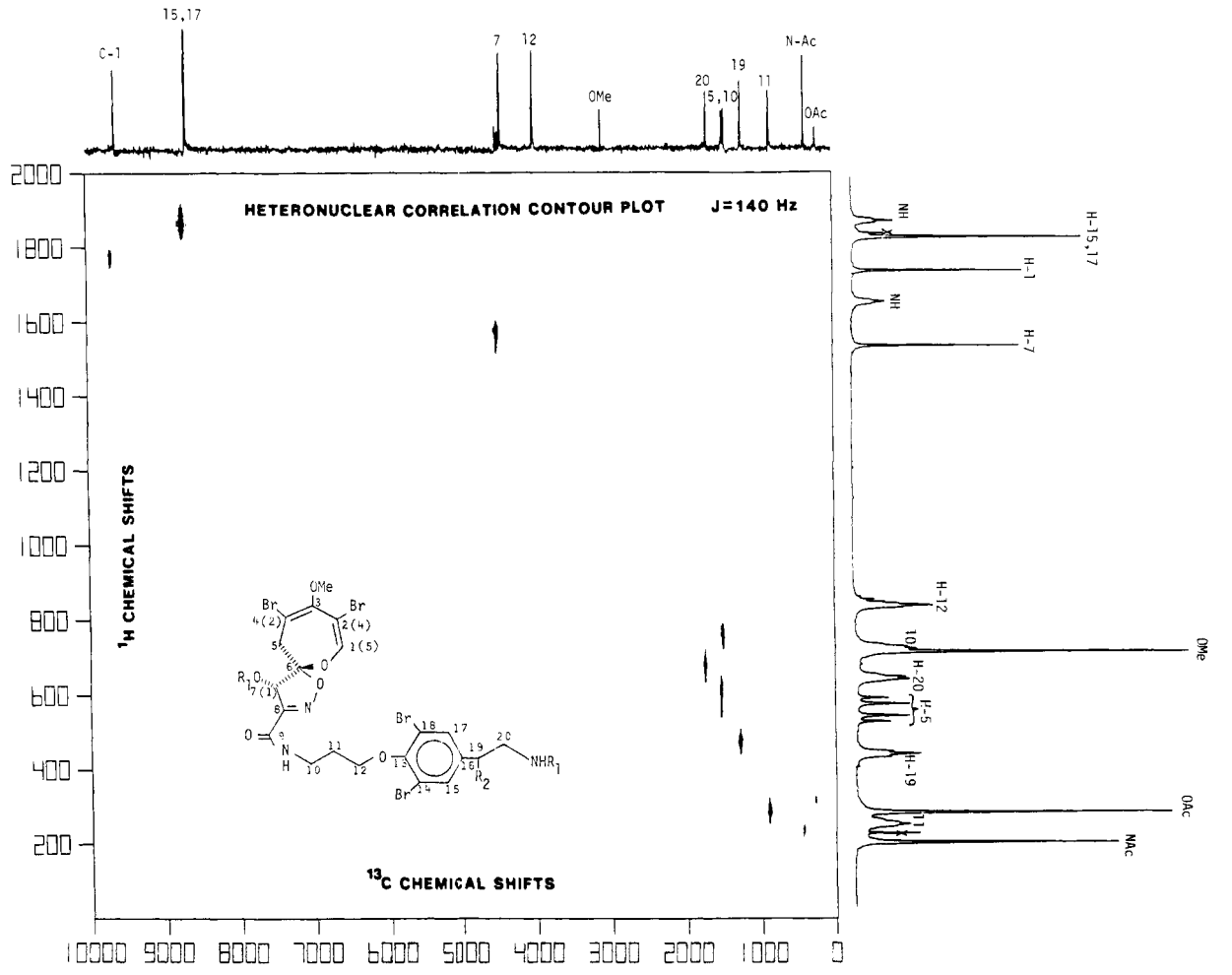


Figure 1. Heteronuclear correlation contour plot of **7b**.

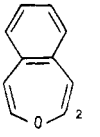
Table III. ^{13}C–^{1}H NMR Chemical Shift Assignment of Protonated Carbons of the Revised Structure of Psammaplysin-A Acetamide Acetate (**7b**)

δ ^{13}C	multiplicity	δ ^{1}H	assignment
145.1	d	7.07	C-1
132.5	d (2C)	7.38	C-15, 17
77.2	d	6.34	C-7
70.7	t	4.08	C-12
58.8	q	3.65	OMe
40.1	t	3.43, 3.39	C-19
37.2	t	3.20, 3.04	C-5
36.9	t	3.66	C-10
28.8	t	2.10	C-11
22.7	q	2.18	NAc
20.6	q	1.90	OAc

4Br. This peak in fact corresponds to $[C_{15}H_{17}Br_2N_2O_6]^+$, and appears in our EI spectra as a 1:3:1 triplet. Since all of our ^{1}H and ^{13}C NMR data, buttressed by extensive homo- and heteronuclear decoupling experiments, provided unequivocal evidence for the psammaplysin-A (**3**) part structure beginning with C-9, the additional oxygen atom must be part of the C-1 to C-8 atomic assembly. Hence Kashman's spiro[cyclohexadieneoxazoline] structure cannot be correct.

Kashman's chemical evidence for the psammaplysin structures (**3–5**) relies heavily on the results of a base degradation (3% KOH in aqeuous MeOH) which leads to two compounds. One of these, derived intact from C-9 to the amino terminus of the compound, needs no comment. The structure of the second product, 3-bromo-2,5-dihydroxy-4-methoxybenzaldehyde, a compound not previously described in the literature, rests on equivocal evidence. The formula, $C_8H_7BrO_4$, is based on "Satisfactory elemental analysis of all elements", an EIMS, incomplete IR data, and a base-induced bathochromic UV shift of 39 nm, while the expected shift for *p*-dihydroxybenzenes is hypsochromic.[9]

Our seach for an alternate structure for the psammaplysins first focused on the anomalous ^{13}C NMR data (Table I). The C-5 resonance of **5** (δ 145.1) is identical with the chemical shift of C-2 in 4,5-benzoxepin (**6**),[10] thereby suggesting that C-5 should



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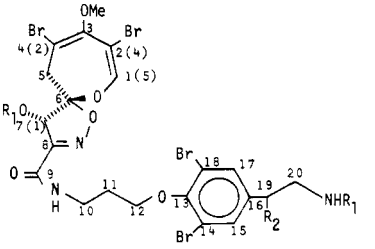

7 a $R_1 = H, R_2 = H$
b $R_1 = Ac, R_2 = H$

8 a $R_1 = H, R_2 = OH$
b $R_1 = Ac, R_2 = OAc$

(9) Scott, A. I. "Interpretation of the Ultraviolet Spectra of Natural Products"; Pergamon Press: Oxford, 1964; p 96.

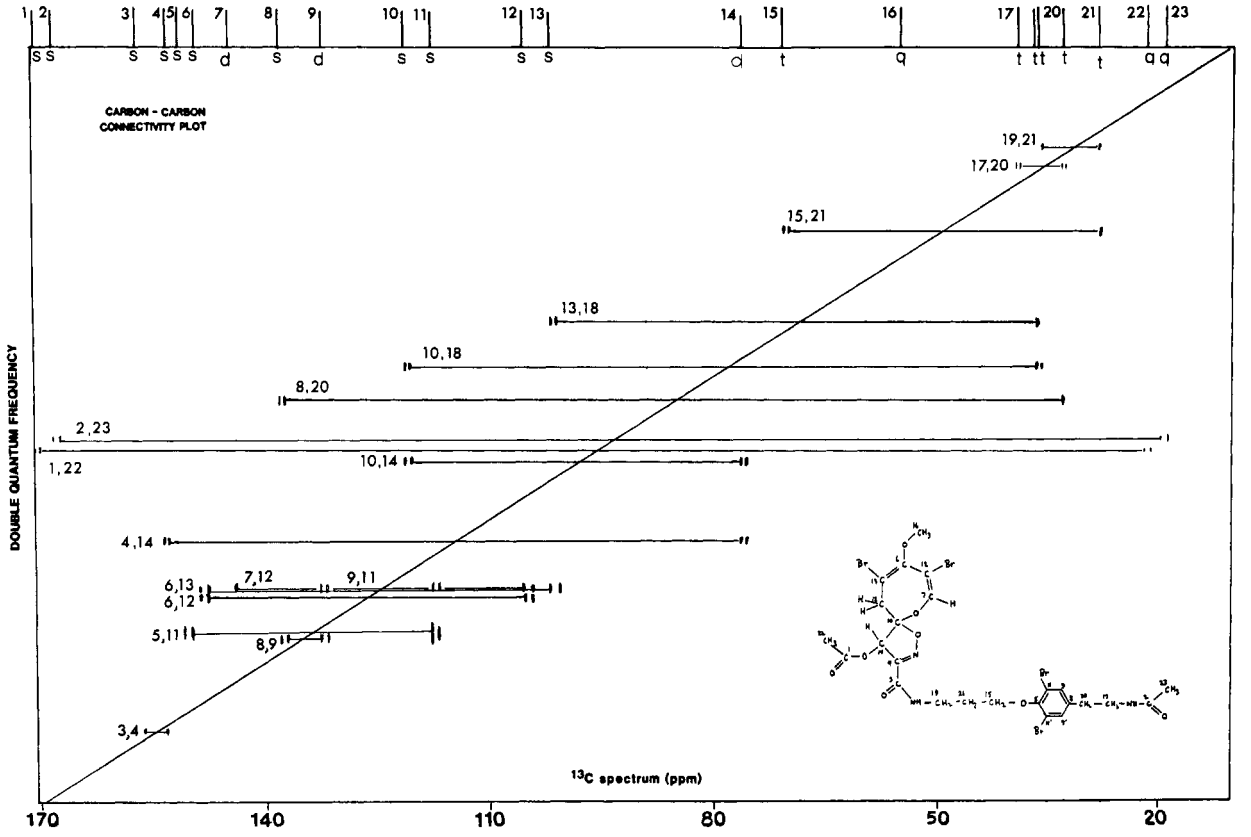

Figure 2. Carbon–carbon connectivity plot of **7b**.

be adjacent to oxygen. A two-dimensional ^{13}C–^{1}H NMR chemical shift correlation map (Figure 1) allowed complete assignment of all protonated carbons (Table III). Furthermore, a two-dimensional ^{13}C–^{13}C connectivity plot (Figure 2)[11] allowed construction of a complete and rational structure for the psammaplysins. For the part of the molecule that contains the additional oxygen atom (C-1 through C-9) the experiment provided unambiguous connectivities for the C-8–7–6–5–4–3–2 chain (**7**) as well as for the rest of the molecule. The C-9 to C-8 connection is less certain, but there is ample support from the C-9 coupling to NH and to the C-10 protons and from the C-8 coupling to the C-7 proton. Also less firm is the C-2 to C-1 connection, but C-3, C-2, and C-6 are coupled to H-5, though the coupling to C-6 is small. As a result of these NMR experiments it is clear that the additional oxygen atom has to be inserted between C-1 (δ 145.2, d) and C-6 (121.8, s), leading to a revised structure **7a** for psammaplysin-A, which is a spiroketal but shares with aerothionin (**1**) the isoxazoline portion of all known bromotyrosine-derived verongid metabolites. Ketal C-6 of the spiro[4.6]dioxazundecane system resonates at 121.8 ppm, which is considerably downfield from the chemical shift of the familiar spiro[5.5]dioxundecane. However, the ^{13}C–^{13}C evidence is unambiguous. Single-crystal X-ray diffraction of diacetylpsammaplysin-A (**7b**) fully confirmed the ^{13}C NMR data.

Biogenesis of the psammaplysins may proceed through an oximino epoxide as shown in Scheme I. In order to arrive at structure **3** a Beckmann type rearrangement concomitant with epoxide ring opening (path a) has been postulated.[7] If one assumes that the epoxide ring opening leads to ring enlargment, revised structure **7a** results (path b). The benzene oxide–oxepin pathway, first adumbrated on theoretical grounds by Vogel and Günther,[12] was experimentally demonstrated in the biosynthesis of aranotin by Neuss and co-workers.[13,14]

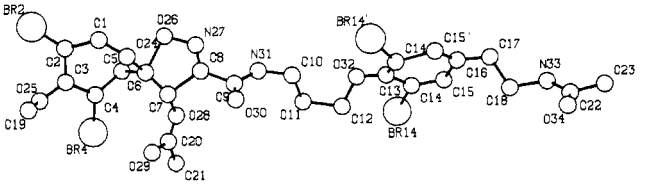

Figure 3. Computer-generated drawing of the X-ray model of psammaplysin-A acetamide acetate (**7b**).

Psammaplysin-A acetamide acetate (**7b**) was prepared from **7a** by treatment with Ac_2O/pyridine and crystallized from aqueous acetone, mp 161–163 °C. Figure 3 is a computer-generated drawing of the X-ray model of **7b**. The current X-ray model has defined only the relative stereochemistry, so the enantiomer shown is an arbitrary choice.

A second, more polar metabolite, psammaplysin-B (**8a**), was isolated as a colorless glass. Acetylation furnished an acetamide diacetate (**8b**), mp 84–87 °C. ^{1}H and ^{13}C NMR spectral analysis placed the additional hydroxyl at C-19.

Experimental Section

NMR spectra (chemical shifts in ppm) were recorded on Nicolet NT-300NB, NT-360NB, Varian XL-100, XL-300, and Bruker WM-500 spectrometers. IR spectra were measured on either a Perkin-Elmer 467 or Beckman IR-10 spectrometer. UV spectra were obtained from either a Beckman ACTA CIII or DU-7 instrument. Mass spectra were recorded on a Varian MAT 311 spectrometer (at 70 eV); high-resolution data are reported as m/z (fragment ion, formula, calculated mass, intensity). Elemental analyses were done by Chemical Analytical Serives, University of California, Berkeley. Optical rotations were measured on an AUTOPOL II (Rudolph) polarimeter. Melting points were taken on a Fisher-Johns block and are uncorrected.

Reagents were distilled from glass prior to use or were spectrophotometric grade. Column chromatographic adsorbents include Bio-Sil A (200–400 mesh) and Bio-Beads S-X8 and S-X12 (200–400 mesh)

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(Bio-Rad Laboratories) and Sephadex LH-20 (Pharmacia). Analytical TLC separations were performed using precoated Silica Gel 60 F-254 (Merck, Darmstadt) and KC18F reversed-phase plates (Whatman).

Antibiotic activity was tested against five test organisms (*Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*, and *Pseudomonas aeruginosa*) which were grown in sterile tryptic soy broth medium (Difco Laboratories) and incubated at 37 °C overnight to ensure sufficient growth. The organisms were then smeared on tryptic soy agar plates and incubated at 37 °C for 30–60 min.

Sterile bioassay disks were spotted with a solution of the compound to be tested and then air-dried. The disks were then placed on the inoculated agar and incubated at 37 °C for 12–24 h. A positive reaction was denoted by a clear ring of inhibition around the disk.

Isolation. *Psammaplysilla purpurea* (2 kg) was collected near Augulpelu Reef, Palau, Western Caroline Islands, in August 1977. The sponge had a red filamentous surface with an off-white interior. The frozen sponge had turned dark brown, and it had a strong ammonia odor. The sponge was either lyophilized or extracted frozen with 95% EtOH (1.5 L) at room temperature for 12 h. The extract was filtered, concentrated in vacuo, and partitioned first with $CHCl_3$, then with $CHCl_3$/MeOH, 4:1, to give fraction A. The sponge was then reextracted with 15% EtOH/$CHCl_3$ (2 × 1.5 L) at room temperature for 24 h (fraction B). Fractions A and B were combined to give 14.17 g of a brown semisolid. Repeated purification on Sephadex LH-20 (usually 3× with $CHCl_3$/MeOH, 4:1) or on silica gel (some loss of compound, $CHCl_3$/MeOH/NH_4OH, 90:10:1) columns would remove a persistant yellow impurity. The two major components, psammaplysin-A (**7a**) and -B (**8a**), were obtained as colorless glasses (0.40% and 0.13%, respectively) that yellowed upon exposure to light and air.

Psammaplysin-A (7A): Colorless glass, $[\alpha]^{22}_D$ −65.2° (*c* 0.52, MeOH).

IR ($CHCl_3$) 3420, 2950, 1675 s, 1660, 1625, 1600, 1540-1530, 1460, 1260, 1150, 1120, 910 cm^{-1}.

UV (MeOH) λ_{max} 229 (ε 12 700), 262 sh (7100), 276 sh (4650), 283 sh (3200) nm; no change in H^+ or OH^-.

^1H NMR (MeOH-d_4) δ 7.48 (2 H, s, H-15, 17), 7.13 (1 H, s, H-1), 5.48 (1 H, s, NH), 4.97 (1 H, s, H-7), 4.06 (2 H, t, *J* = 6.0, H-12), 3.64 (3 H, s, OMe), 3.61 (2 H, t, *J* = 7.0, H-10), 3.38, 3.05, (2 H, AB q, *J* = 16.1, H-5), 2.96 (2 H, dd, *J* = 7.5, 7.0, H-20), 2.76 (2 H, dd, *J* = 7.5, 7.0, H-19), 2.13 (2 H, overlapping t, *J* = 6.0, 7.0, H-11).

^1H NMR (CD_2Cl_2) δ 7.38 (2 H, s), 7.15 (1 H, br t, *J* = 6, amide NH), 7.04 (1 H, s), 5.4 (1 H, br s, NH), 5.05 (1 H, s), 4.08 (2 H, t, *J* = 6), 3.66 (3 H, s), 3.68 (2 H, t, *J* = 6), 3.37, 3.08 (2 H, AB q, *J* = 16), 2.90 (2 H, t, *J* = 7), 2.66 (2 H, t, *J* = 7), 2.1 (2 H, obscured by H_2O).

^{13}C NMR (MeOH-d_4) δ 160.2 (s), 158.2 (s), 153.0 (s), 149.4 (s), 146.3 (d), 136.9 (s), 134.1 (2 C, d), 120.4 (s), 119.1 (2 C, s), 104.3 (s), 103.9 (s), 80.2 (d), 71.9 (t), 59.3 (q), 41.5 (5), 38.2 (t), 37.9 (t), 32.9 (t), 29.9 (t).

EIMS *m/z* 406 (0.4%), 404 (0.4), 402 (0.4), 362 (1), 360 (2), 358 (2), 356 (1), 323 (1), 321 (2), 319 (2), 281 (2), 280 (7), 279 (6), 278 (17), 277 (4), 276 (4), 268 (1), 267 (4), 266 (2), 265 (6), 264 (1), 263 (7), 248 (5), 246 (3), 200 (6), 198 (4), 58 (100).

CIMS *m/z* + H 407, 405, 403, 361, 359, 281, 279, 277, 275, 249, 247, 233, 231, 221, 219, 193, 191, 166, 164, 125, 123, 121.

Psammaplysin-A Acetamide Acetate (7b). Thirteen milligrams of **7a** in 0.5 mL pyridine was cooled in dry ice/acetone. Ac_2O (0.5 mL) was added, and the solution was warmed to room temperature and stirred for 1.5 h. Toluene was added, and the resulting azeotrope was evaporated in vacuo to give one product by TLC (silica, R_f = 0.34, CH_2Cl_2/EtOAc, 1:1). The reaction mixture was then purified by HPLC on Lichrosorb Si-60 (CH_2Cl_2/EtOAc, 1:1) to give 9.4 mg (64.6%) of **7b** as a colorless glass. (A large-scale workup using the above procedure provided over 700 mg of **7b** for subsequent NMR ^{13}C–^{13}C coupling analysis.) Crystals from acetone/H_2O, mp 161–163 °C; $[\alpha]^{25}_D$ −84.6° (*c* 0.78, $CHCl_3$).

IR ($CHCl_3$) 3450, 3415, 2990, 2930, 2850, 1765, 1680–1675, 1590, 1530–1510, 1455, 1370, 1265, 1210, 1150, 1110, 1035, 900 cm^{-1}; UV (MeOH) δ_{max} 208 (ε 62 600), 219 sh (27 400), 254 (10 100), 263 sh (8900) nm.

UV (CH_3CN) λ_{max} (ε 53 200), 218 sh (23 200), 221 sh (21 800), 228 sh (17 600), 247 (8500), 255 (7800), 272 sh (5500), 282 sh (3300) nm.

^1H NMR (CD_2Cl_2) δ 7.38 (2 H, s, H-15, 17), 7.10 (1 H, br t, *J* = 6, NH), 7.07 (1 H, s, H-1), 6.34 (1 H, s, H-1), 5.53 (1 H, br t, *J* = 7, NH), 4.08 (2 H, t, *J* = 5.7, H-12), 3.66 (2 H, t, *J* = 6.3, H-10), 3.65 (3 H, s, OCH_3), 3.43, 3.39 (2 H, overlapping t, *J* = 7.0, H-20), 3.20, 3.04 (2 H, AB q, *J* = 16.0), H-5), 2.72 (2 H, t, *J* = 7.0, H-19), 2.18 (3 H, S, N-Ac), 2.10 (2 H, overlapping t, *J* = 5.7, 6.3, H-11), 1.90 (3 H, s, OAc).

^{13}C NMR (CD_2Cl_2) δ 170.3 (s, NH*C*OMe), 168.4 (s, O*C*OMe), 157.5 (s, C-9), 154.4 (s, C-8), 151.5 (s, C-13), 149.4 (s, C-3), 145.9 (d, C-1), 138.7 (s, C-16), 133.3 (2 C, d, C-15, 17), 121.8 (s, C-6), 118.3 (2 C, s, C-14, 18), 105.9 (s, C-2), 102.6 (s, C-4), 77.3 (d, C-7), 71.1 (t, C-12), 59.4 (q, OMe), 40.7 (t, C-20), 37.9 (t, C-5), 37.6 (t, C-10), 34.8 (t, C-19), 29.6 (t, C-11), 23.3 (q, C-NHCO*Me*), 21.2 (9, OCO*Me*).

EIMS *m/z* 483 (2%), 481 (4), 479 (1), 423 (22), 421 (48), 419 (21), 381 (4), 379 (10), 377 (6), 363 (41), 361 (68), 359 (49), 339 (5), 337 (10), 335 (5), 280 (68), 278 (74), 276 (69), 200 (52), 198 (60).

HRFDMS *m/z* 816.8618 (M^+, $C_{25}H_{27}{}^{79}Br_2{}^{81}Br_2N_3O_8$, calcd 816.849 08.

Anal. Calcd for $C_{25}H_{27}Br_4N_3O_8$: C, 36.91, H, 3.32; N, 5.17; Br, 39.37. Found: C, 36.86, H, 3.39; N, 4.84; Br, 40.86.

Single-Crystal X-ray Diffraction Analysis of Psammaplysin-A Acetamide (7b). Crystals of psammaplysin-A acetamide acetate (**7b**) could be grown from acetone–water, methanol–water, or 2-propanol–water. In all of these solvent systems the crystals were identical and grew as very thin, fragile plates which diffracted poorly. Preliminary X-ray photographis displayed monoclinic symmetry. Accurate cell constants of *a* = 16.340 (2) Å, *b* = 4.9619 (7) Å, *c* = 38.126 (9) Å, and β = 101.88 (3)° were obtained from a least-squares fit of 15 diffractometer-measured 2θ values. A rough measure of the experimental density indicated that this monoclinic unit cell contained four molecules of composition $C_{25}H_{27}Br_4N_3O_8$. The real space group is $P2_1$, but virtually all of the diffraction data followed a body-centering condition ($h + k + l = 2n$). For this reason, our initial attempts to define this structure were carried out in space group $I2_1$ (alternate setting of C2) and the results reported here refer to this unit cell.

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 (1.54 178 Å).[15] After correction for Lorentz, polarization, background, and "systematic" extinctions, 1327 (69%) of the body-centered data were judged observed ($|F_o| \geq 3\sigma(F_o)$). There were roughly 400 weak reflections that violated the body-centering condition ($|F_o| \geq 1.0\sigma(F_o)$). A phasing model, which consisted of the four independent bromines, was found by using a combination of Patterson and direct methods techniques.[15] Subsequent bromine-phased electron density syntheses revealed the entire non-hydrogen atom structure of psammaplysin-A acetamide acetate (**9b**). Block-diagonal least-squares refinements of this body-centered model have converged to a conventional crystallographic residual of 0.116 for the observed data. Attempts at refinement in space group $P2_1$ have been hampered by the strong correlations between the nearly body-centered atoms and the relatively few data. It appears that the body centering only breaks down in the regions of the *O*- and *N*-acetate fragments. Work on the refinement in space group $P2_1$ is continuing. Additional crystallographic details are described in the supplementary material.

Psammaplysin-B (8a). Colorless glass, $[\alpha]^{25}_D$ −60.2° (*c* 0.632, MeOH).

IR ($CHCl_3$) 3420, 2940, 1670 s, 1620, 1590, 1530 s, 1450, 1250, 1140, 1110, 900 cm^{-1}.

UV (MeOH) λ_{max} 218 (ε 28 600), 256 sh (7000), 262 sh (6400), 277 sh (4000), 282 (3000) nm.

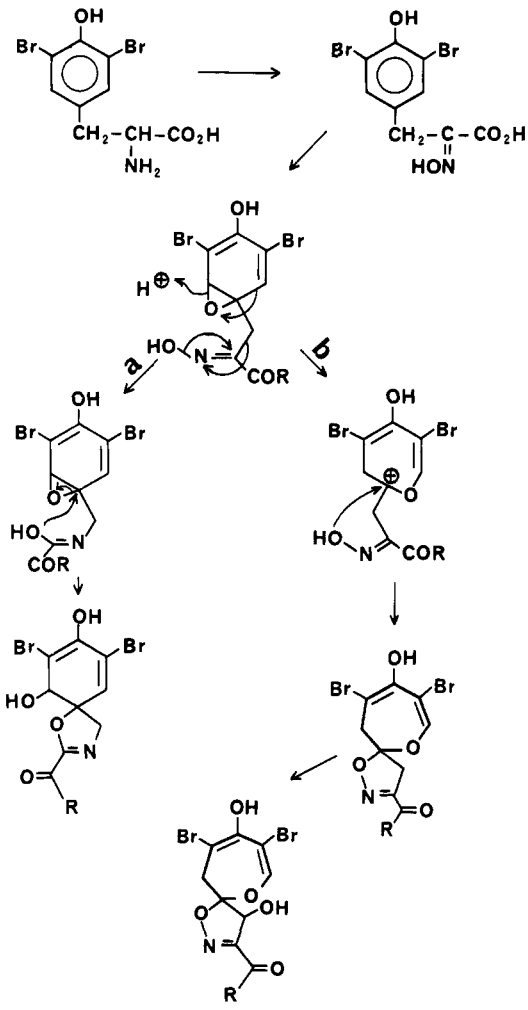
^1H NMR (MeOH-d_4) δ 7.90 (1 H, s), 7.62 (2 H, s), 7.13 (1 H, s), 7.51 (1 H, t), 4.97 (1 H, s), 4.70 (1 H, dd), 4.07 (2 H, t), 3.65 (3 H, s), 3.62 (2 H, t), 3.38, 3.07 (2 H, AB q), 2.97 (1 H, dd), 2.83 (1 H, dd), 2.1 (2 H, pentet).

^{13}C NMR (MeOH-d_4) δ 160.6 (s), 158.7 (s), 153.6 (s), 149.8 (s), 146.7 (d), 143.2 (s), 134.3 (d), 131.5 (d), 120.8 (s), 119.2 (2 C, s), 104.5 (s), 104.3 (s), 80.4 (d), 72.7 (d), 72.1 (t), 59.3 (q), 38.2 (t), 38.0 (t), 30.5 (t), 18.4 (t).

EIMS *m/z* 523 (9%), 521 (27), 519 (26), 517 (8) overlapping 2 Br clusters; 477 (3), 475 (4), 473 (2) 2 Br cluster; 441 (6), 439 (13), 437 (6), 2 Br cluster; 423 (5), 421 (11), 419 (4) 2 Br cluster; 407 (3), 405 (4), 403 (2), 2 Br cluster, 393 (11), 391 (39); 358 (2), 356 (6), 354 (2); 283 (8), 281 (16), 279 (12); 278 (9), 276 (20), 274 (18), 272 (8) 2 Br cluster; 249 (94), 247 (97) 1 Br cluster; 235 (16), 233 (14) 1 Br cluster; 221 (24), 219 (27) 1 Br cluster; 207 (11), 205 (24), 203 (16) 2 Br cluster;

(15) All crystallographic calculations were done on a PRIME 850 computer operated by the cornell Chemistry Computing Facility. Principal programs employed: 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 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, 1978 and 1980; DIRDIF written by P. T. Beurskens 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.

Scheme I



196 (9), 194 (100), 192 (17); 179 (9), 177 (18), 175 (8); 169 (4), 167 (19), 155 (45); 127 (38), 125 (43); 113 (9), 111 (12).

CIMS *m/z* 441, 439, 437 (2 Br), 407, 405, 403 (2 Br), 340, 338, 336 (2 Br), 249, 247 (1 Br), 233, 231 (1 Br), 221, 219 (1 Br).

HRFDMS *m/z* 749.8308 ($M^+ + H$, $C_{21}H_{24}{}^{79}Br_2{}^{81}Br_2N_3O_7$, calcd 749.83068).

Psammaplysin-B Acetamide Diacetate (8b). To 12.9 mg of **8a** in 0.5 mL pyridine cooled in acetone/dry ice Ac_2O (0.5 mL) was added, and the reaction mixture was warmed to room temperature. The solution was stirred for 1 h, when **8a** was completely converted to a less polar compound (based on TLC; silica, R_f = 0.19, CH_2Cl_2/EtOAc, 1:1). Toluene was added, and the resulting azeotrope was evaporated in vacuo. The crude product was purified on a silica gel column (CH_2Cl_2/EtOAc, 1:1) to give **10b** as a colorless oil; amorphous solid from acetone/H_2O, mp 84-87 °C; $[\alpha]^{22}_D$ -44.5° (*c* 1.93, MeOH).

IR ($CHCl_3$) 3400, 2950, 1760, 1680, 1550, 1460, 1380, 1200, 1100, 1000, 930 cm^{-1}.

UV (CH_3CN) λ_{max} 225 sh (ϵ 8000), 228 sh (12 500), 229 (18 700), 231 sh (17 500), 238 sh (12 300), 243 sh (9400), 253 sh (7400), 268 sh (5700), 276 sh (4100), 282 sh (2700).

^1H NMR ($CDCl_3$) δ 7.46 (2 H, s), 7.13 (1 H, t, J = 5.8), 7.02 (1 H, s), 6.37 (1 H, s), 5.81 (1 H, t, J = 5.8), 5.67 (1 H, dd, J = 4.2, 8.2), 4.05 (2 H, t, J = 5.7), 3.68 (2 H, dd, J = 5.8, 6.7), 3.63 (3 H, s), 3.59 (1 H, dd, J = 4.2, 5.8), 3.48 (1 H, dd, J = 5.8, 8.2), 3.17, 3.02 (2 H, AB q, J = 16.0), 2.19 (3 H, s), 2.10 3 H, s), 2.06 (2 H, overlapping t, J = 5.7, 6.7), 1.95 (3 H, s).

EIMS *m/z* 421 (8%), 419 (11), 417 (6) 2 Br cluster; 379 (6), 377 (9), 375 (6) 2 3r cluster; 366 (2), 364 (3), 362 (1) 2 Br cluster; 296 (2), 294 (4), 293 (7), 292 (1), 291 (4) overlapping 2 and 1 Br clusters; 273 (2), 271 (3), 269 (2) 2 Br cluster; 258 (5), 256 (8), 1 Br cluster; 214 (4), 212 (3); 194 (6), 192 (6).

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Registry No. 7a, 85819-66-5; **7b**, 95739-54-1; **8a**, 85819-67-6; **8b**, 95763-24-9.

Supplementary Material Available: Tables IV, listing of fractional coordinates and thermal parameters for psammaplysin-A acetamide acetate (**7b**) (1 page). Ordering material is given on any current masthead page.

anti-Tricyclo[5.1.0.$0^{3,5}$]octa-2,6-diyl Dications. Novel Bis(cyclopropylcarbinyl) Dications[1a]

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Abstract: A series of 2,6-*anti*-tricyclo[5.1.0.$0^{3,5}$]octa-2,6-diyl dications **4**-R have been prepared by the ionization of related diols **5**-R in superacid solutions and characterized by ^{13}C and ^1H NMR spectroscopy. All attempts to generate the parent secondary dication **4**-H and observe its potential degenerate circumambulatory rearrangement (cyclopropylcarbinyl type) were, however, unsuccessful. Only ring-opened homotropylium cation **8** was observed. However, a series of tertiary dications were successfully prepared and studied by ^{13}C and ^1H NMR spectroscopy, showing significant positive charge delocalization into the annulated cyclopropane rings.

The structure and facile interconversion of cyclopropylcarbinyl and cyclobutyl cations have been well documented.[2,3] Previously we reported[4] the dynamic behavior of 2-bicyclo[4.1.0]heptyl cations **1** under stable ion conditions. The 2-bicyclo[4.1.0]heptyl

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