

BROMINATED BENZENEACETONITRILES, THE DIBROMOTYROSINE METABOLITES FROM THE SPONGE *PSAMMAPLYSILLA PURPUREA*¹

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ABSTRACT.—Three compounds, 3,5-dibromo-4-methoxyphenylacetonitrile [1], 3-bromo-4-methoxyphenylacetonitrile [2], and 3,5-dibromo-4-methoxybenzoic acid [3], have been isolated from the sponge *Psammaphysilla purpurea* and characterized by spectral methods.

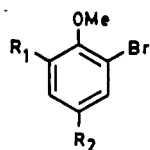
In a continuation of our search for biologically active secondary metabolites from marine organisms, we have investigated the sponge *Psammaphysilla purpurea* (Carter) (Verongidae), collected off the coast of the Tuticorin, Tamilnadu, India, at a depth of 40 feet during April 1993. A literature survey revealed that the genus *Psammaphysilla* has provided a series of antibiotics, namely, the psammaphysins, containing a spirocyclohexadienyl oxazoline moiety (1), the purpuramines (2), and the macrocyclic bastadins comprised of several bromotyrosine units (3).

The CH₂Cl₂-MeOH (1:1) extract of the sponge *Psammaphysilla purpurea* was subjected to Si gel cc resulting in the isolation of three non-optically active compounds, 3,5-dibromo-4-methoxyphenylacetonitrile [1], 3-bromo-4-methoxyphenylacetonitrile [2], and 3,5-dibromo-4-methoxybenzoic acid [3].

Compound 1, which was obtained as a semi-solid, analyzed for C₉H₇Br₂NO, by eims [*m/z* (M⁺) 303, (M⁺+2) 305, (M⁺+4) 307 in a 1:2:1 ratio] and combustion analysis. From the molecular for-

mula, the ¹H-nmr spectral signals at δ 7.45 (2H, s), 3.85 (3H, s), and 3.65 (2H, s), and the ir bands at 2270, 1610, and 1580 cm⁻¹, compound 1 was identified as 3,5-dibromo-4-methoxyphenylacetonitrile. The demethylated derivative of 1 was isolated earlier by Rinehart *et al.* in a radiolabeled phenylalanine (Phe) and tyrosine (Tyr) feeding experiment on the sponge *Aplysina fistularis*, in order to demonstrate that Phe and Tyr were biosynthetic precursors for brominated phenols and quinones (4). Later, compound 1 was isolated from another sponge, *Verongia aurea* (5), and also synthesized by Okamoto *et al.* (6).

Compound 2 was obtained as a crystalline solid, mp 50–52°, and analyzed for C₉H₈BrNO, by eims [*m/z* (M⁺) 225, (M⁺+2) 227, in a 1:1 ratio] and combustion analysis. The uv and ir spectra indicated the aromatic nature of compound 2 and the presence of a nitrile group, as was found in compound 1. The ¹H-nmr spectrum of 2 revealed the presence of a trisubstituted benzene by an ABX pattern of signals at δ 7.51 (1H, d, *J*=1.5 Hz), δ 7.25 (1H, dd, *J*=7 and 1.5 Hz), and δ 6.85 (1H, d, *J*=7 Hz). Furthermore, the ¹H-nmr spectrum showed the presence of a methoxyl signal at δ 3.85 (3H, s) and a benzylic methylene signal at δ 3.65 (2H, s). From the foregoing spectral data, compound 2 was identified as 3-bromo-4-methoxyphenylacetonitrile. Previously, compound 2 and its demethylated derivative were reported from the sponge *Verongia aurea* (5) and from an unidentified sponge (7).



- 1 R₁=Br, R₂=CH₂CN
- 2 R₁=H, R₂=CH₂CN
- 3 R₁=Br, R₂=COOH

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Compound **3** was obtained as a crystalline solid, mp 220–222° (lit. mp 219–220°), and analyzed for $C_8H_6Br_2O_3$ by eims [m/z 308 (M^+), 310 ($M^+ + 2$), 312 ($M^+ + 4$) in a 1:2:1 ratio]. Compound **3** was identified as 3,5-dibromo-4-methoxybenzoic acid by comparison of physical and spectral data with those of the reported synthetic compound (8).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The 1H - (200 MHz) and ^{13}C -nmr (50 MHz) spectra were recorded on a Varian Gemini 200 MHz spectrometer, using TMS as internal standard. Chemical shifts are reported in δ (ppm) values and coupling constants (J) in Hz. Uv and ir spectra were recorded on a Shimadzu spectrometer. Mass spectra were recorded on a Finnigan MAT 1020.

ANIMAL MATERIAL.—The sponge *Pisammaphysilla purpurea* was collected using scuba at a depth of 40 feet from the Tuticorin coast, Tamilnadu, India, during April 1993. A voucher specimen (IIC-119) is on deposit at the NIO Museum, Goa, India.

EXTRACTION AND ISOLATION.—The freshly collected specimen (300 g dry wt after extraction) was extracted with CH_2Cl_2 -MeOH (1:1, 3×1.5 liters) at room temperature. The combined extract was filtered and the solvent was removed under reduced pressure. The crude extract (4 g) was subjected to cc on Si gel using hexane/EtOAc gradients and yielded 3,5-dibromo-4-methoxyphenylacetonitrile [**1**, 60 mg], 3-bromo-4-methoxyphenylacetonitrile [**2**, 45 mg], and 3,5-dibromo-4-methoxybenzoic acid [**3**, 10 mg]. Compound **1** was obtained as a semi-solid, *anal.*, found C, 35.53%, H, 2.22%, N, 4.51%; required for C_9H_7BrNO , C, 35.44%, H, 2.31%, N, 4.59%; uv (MeOH) λ max (ϵ) 242 (23,000), 275 (10,000), 285 (10,000); ir (KBr) ν max 2270, 1610, 1580 cm^{-1} ; 1H nmr ($CDCl_3$, 200 MHz) δ 7.45 (2H, s), 3.85 (3H, s), 3.65 (2H, s); eims (70 eV) m/z 307 ($M^+ + 4$, 45), 305 ($M^+ + 2$, 90), 303 (M^+ , 45), 289

(60), 226 (25), 224 (25), 183 (90), 102 (90), 75 (100).

3-Bromo-4-methoxyphenylacetonitrile [**2**].—Obtained as a crystalline solid, mp 50–52°, *anal.*, found C, 47.74%, H, 3.62%, N, 6.24%; required for C_9H_8BrNO , C, 47.81%, H, 3.56%, N, 6.19%; uv (MeOH) λ max (ϵ) 242 (16,800), 275 (25,500); 285 (24,000) nm; ir (KBr) ν max 2270, 1610, 1580 cm^{-1} ; 1H nmr ($CDCl_3$, 200 MHz) δ 7.51 (1H, d, $J=1.5$ Hz), 7.25 (1H, dd, $J=7$ and 1.5 Hz), 6.85 (1H, d, $J=7$ Hz), 3.85 (3H, s), 3.65 (2H, s); ^{13}C nmr (50 MHz, $CDCl_3$) δ 155.86 s, 132.89 d, 127.82 d, 123.30 s, 116.83 s, 112.61 s, 112.12 d, 56.09 q, 22.42 t; eims (70 eV) m/z 227 ($M^+ + 2$, 30), 225 (M^+ , 30), 146 (100), 103 (58).

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