# Psammaplysin C: A New Cytotoxic Dibromotyrosine-Derived Metabolite from the Marine Sponge Druinella (=Psammaplysilla) purpurea

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# PSAMMAPLYSIN C: A NEW CYTOTOXIC DIBROMOTYROSINE-DERIVED METABOLITE FROM THE MARINE SPONGE *DRUINELLA (=PSAMMAPLYSILLA) PURPUREA*

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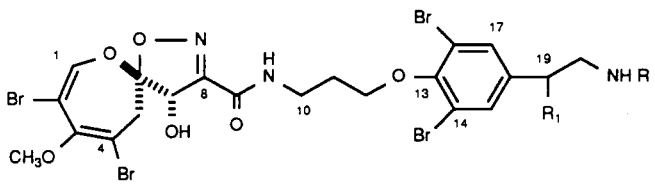
ABSTRACT.—The new, cytotoxic dibromotyrosine-derived metabolite psammaplysin C [**3**], in addition to the two known psammaplysins A [**1**] and B [**2**], was isolated from the marine sponge *Druinella purpurea*. All three compounds were found to possess moderate in vitro cytotoxicity towards the human colon tumor cell-line HCT116.

Sponges of the order Verongida have been a prolific source of bromotyrosine-derived metabolites, many of which have been reported to exhibit in vitro and in vivo biological activities (1). Among these compounds are the in vitro antimicrobial metabolites psammaplysins A [**1**] and B [**2**], the structures of which were established by a combination of $^{13}C$-$^{13}C$ nmr and X-ray crystallographic studies (2).

As part of our continuing search for biologically active secondary metabolites from marine sources, we now report the isolation of a third psammaplysin, C [**3**], from an extract of the sponge *Druinella (=Psammaplysilla) purpurea* Carter [order Verongida, family Druinellae (=Aplysinellidae)]. Bioactivity-directed fractionation of the extract, using Sephadex LH-20 cc and silica hplc, afforded the three principal active components. Psammaplysins A [**1**] and B [**2**] were identified by comparison of the observed spectral data with those previously published (2).

The structure of the new metabolite, psammaplysin C [**3**], was determined by comparison with the data observed for **2**. The structure of psammaplysin C was concluded to be the *N*-methyl derivative




**1** $R_1=R_2=H$
**2** $R_1=OH$, $R_2=H$
**3** $R_1=OH$, $R_2=Me$

of psammaplysin B, because of fabms indicating the presence of an additional 14 mass units ($CH_2$), and nmr indicating the presence of an *N*-methyl signal [$\delta_H$ 2.73 (3H, s), $\delta_C$ 33.92]. Complete nmr structural assignment of **3** was achieved by comparison with the data reported for both psammaplysins A [**1**] and B [**2**] (2). The relative stereochemistry at C-6 and C-7 in psammaplysin A was assigned in the original paper by X-ray analysis (2). This same stereochemistry was assumed in psammaplysin B because the two

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compounds had very similar optical rotations. The stereochemistry at C-6 and C-7 in psammaplysin C is assigned as shown for the same reason (the rotation is the same sign ± a couple of degrees). The stereochemistry at C-19 has not been assigned for any member of this family.

Psammaplysins A, B, and C were found to exhibit in vitro cytotoxicity towards the human colon tumor cell-line HCT116 with $IC_{50}$'s of 6, 6, and 3 μg/ml, respectively.

## EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. Uv spectra were recorded on a Beckman DU-8 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 polarimeter using a 10-cm microcell. $^1$H- and $^{13}$C-nmr spectra were obtained at 500 and 125 MHz, respectively, on a Varian Unity 500 spectrometer. Mass spectra were obtained on a Varian MAT-731 spectrometer.

COLLECTION, EXTRACTION, AND ISOLATION PROCEDURES.—The sponge was collected by SCUBA from shallow reef waters off Makaluva Island of the Fiji Island Group in the South Pacific in 1988 and 1990. A voucher specimen (P1132) has been deposited in the Scripps Institute of Oceanography Benthic Invertebrate Collection. Sponge specimens (100 g) were extracted repeatedly with MeOH/$CHCl_3$ solvent mixtures. The crude extract was partitioned by cc on Sephadex LH-20 using MeOH solvent to give a fraction which consisted of a mixture of psammaplysins A, B, and C. These compounds were separated by $SiO_2$ hplc (80% $CHCl_3$/20% MeOH/0.1% $NH_4OH$) to give psammaplysin A [**1**] (14 mg), psammaplysin B [**2**] (11 mg), and psammaplysin C [**3**] (10 mg).

*Psammaplysin C* [**3**].—Glass: hrfabms $[MH]^+$ 763.8499 ($C_{22}H_{26}{}^{79}Br_2{}^{81}Br_3N_3O_7$ requires 763.8466) (Δ 3.3 mmu); $[\alpha]^{23}D$ −57.1° (*c* = 0.014, MeOH); ir ν max (KBr smear) 3362, 2925, 2851, 1668, 1652, 1558, 1540, 1456, 1258, 1197, 1146, 1118, 1044, 1024 $cm^{-1}$; uv λ max (MeOH) 218 nm (ε 17600), 255 (6700 sh), 279 (3000 sh); $^1$H nmr ($CD_3OD$) δ 7.67 (2H, s, H-15 and 17), 7.13 (1H, s, H-1), 4.98 (1H, s, H-7), 4.92 (1H, dd, *J* = 3.0, 10.0 Hz, H-19), 4.08 (2H, t, *J* = 6.0 Hz, H-12), 3.64 (3H, s, OMe), 3.61 (2H, t, *J* = 6.0 Hz, H-10), 3.38, 3.06 (2H, AB q, *J* = 16.0 Hz, H-5), 3.21 (1H, dd, *J* = 3.0, 13.0 Hz, H-20), 3.09 (1H, dd, *J* = 10.0, 13.0 Hz, H-20), 2.73 (3H, s, NMe), 2.14 (2H, overlapping triplets, *J* = 6.0, 6.5 Hz, H-11); $^{13}$C nmr ($CD_3OD$) δ 160.68 (s, C-9), 158.73 (s, C-8), 154.18 (s, C-13), 149.87 (s, C-3), 146.69 (d, C-1), 141.48 (s, C-16), 131.57 (d, C-15 and 17), 120.90 (s, C-6), 119.44 (s, C-14 and 18)], 104.54* (s, C-2), 104.37* (s, C-4), 80.41 (d, C-7), 72.23 (t, C-12), 68.59 (d, C-19), 59.33 (q, OMe), 56.39 (t, C-20), 38.27 (t, C-5), 37.96 (t, C-10), 33.92 (q, NMe), 30.53 (t, C-11). Asterisks indicate assignments may be interchanged.

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## LITERATURE CITED

1. M.H.G. Munro, R.T. Luibrand, and J.W. Blunt, in: "Bioorganic and Marine Chemistry." Ed. by P.J. Scheuer, Springer-Verlag, Berlin, 1987, Vol. 1, p. 93.
2. D.M. Roll, C.W.J. Chang, P.J. Scheuer, G.A. Gray, J.N. Shoolery, G.K. Matsumoto, G.D. Van Duyne, and J. Clardy, *J. Am. Chem. Soc.*, **107**, 2916 (1985).

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