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PUKELEIMIDE C, A NOVEL PYRROLIC COMPOUND FROM THE MARINE CYANOPHYTE *LYNGBYA MAJUSCULA*

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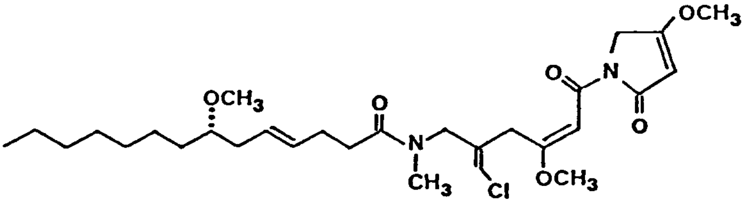
Summary. The crystal structure of pukeleimide C, a novel pyrrolic compound from a shallow-water variety of the marine blue-green alga *Lyngbya majuscula*, is reported.

The nitrogenous moiety of malyngamide A (1), an unusual chlorine-containing 7(*S*)-methoxytetradec-4(*E*)-enamide from a toxic, shallow-water variety of the blue-green alga *Lyngbya majuscula*,[1] consists of a 4-methoxy-Δ^3-pyrrolin-2-one attached via an imide linkage to a seven carbon amino acid having the same carbon skeleton as the sponge metabolite dysidin[2] and the fungal metabolite penicillic acid.[3] Minor amounts of several related compounds that lack the fatty acid unit are present in this strain of *L. majuscula*. We report here the structure of one of these novel compounds, pukeleimide C (2).[4]



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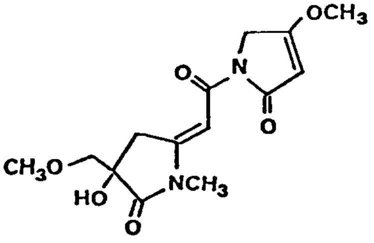

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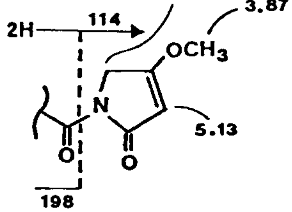


2a

The alga was collected at Kahala Beach, Oahu and extracted with methanol and chloroform. Chromatography of the extract on silica gel (elution with $CHCl_3$) followed by HPLC on μ-Porasil with $CHCl_3$ gave a 0.005% yield of pukeleimide C, mp 186° (partial sublimation) after recrystallizations from $CHCl_3$-hexane and acetone-hexane. High resolution mass spectrometry indicated that pukeleimide C had the elemental composition $C_{14}H_{18}N_2O_6$ and the presence of fourteen carbon atoms was confirmed by the ^{13}C-NMR spectrum.[5] The ^1H-NMR, IR,[5] and mass spectra showed that pukeleimide C had partial structure **2a**.

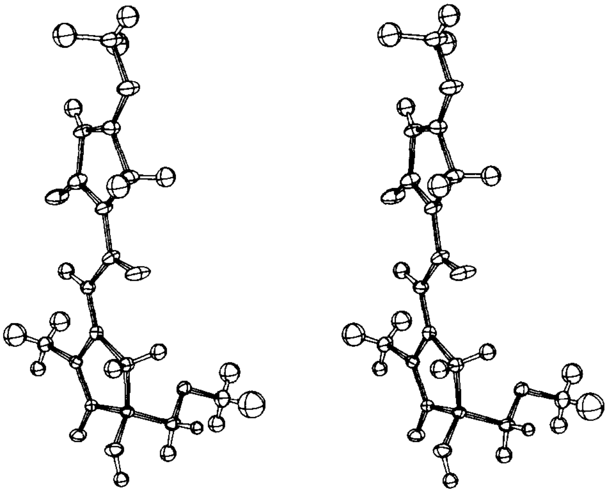
A single crystal of pukeleimide C, a parallelepiped with dimensions 0.24 × 0.13 × 0.07 mm, was mounted on a Syntex four-circle computer-controlled diffractometer. Monochromatized Mo $K\alpha$ radiation ($K\alpha_1$, λ 0.70930 Å; $K\alpha_2$, λ 0.71359 Å) was used for preliminary experiments and for the measurement of the diffraction intensities. The θ-2θ scanning mode was used with a constant scan rate in 2θ of 2° min^{-1}. Of the 1945 unique reflections measured ($2° < 2\theta < 45°$), 1064 had intensities such that $I > 2\theta(I)$. All intensities were corrected for Lorentz and polarization effects[6] (no absorption correction was made; $\mu = 1.0\ cm^{-1}$). Normalized structure factor amplitudes for the 240 reflections with $|E| \geq 1.51$ were used in the computer program MULTAN.[7] A three-dimensional E function, phased as indicated by the solution with the largest combined figure of merit, 2.36, revealed the positions of all nonhydrogen atoms. After several cycles of isotropic and anisotropic full-matrix least-squares refinement[8] of the 22 nonhydrogen atoms, all 18 hydrogen atoms were located on a Fourier difference synthesis. Finally, several cycles of least-squares refinement with anisotropic thermal parameters for the nonhydrogen atoms and isotropic thermal parameters for the hydrogen atoms led to the final error indices $R_1 = 0.057$ and $R_2 = 0.038$. The overdetermination ratio is 4.00.

Crystal Data: $C_{14}H_{18}N_2O_6$, triclinic, $P\bar{1}$, $a = 7.844(2)$ Å, $b = 14.953(3)$ Å, $c = 6.611(1)$ Å, $\alpha = 97.48(1)°$, $\beta = 103.24(2)$; $\gamma = 95.75(2)°$, $d_{calcd} = 1.390\ g\ cm^{-3}$, $Z = 2$, and $F(000) = 328$.

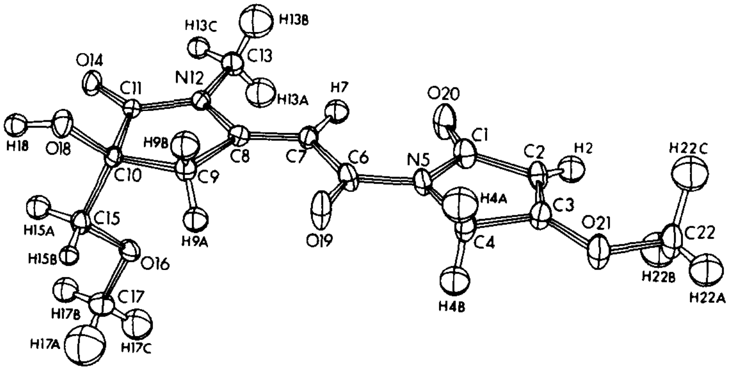
Except for the hydroxy and methyl-ether substituents at the chiral center, C(10), the molecule is quite planar. The maximum deviation from the least-squares plane determined by the 17 atoms C(1)-O(14) and O(19)-O(21), is 0.19 Å at C(10); the pyrrolidone methyl carbon, C(13), is only 0.17 Å out of the plane, while the pyrrolinone methoxide carbon, C(22), is nearly in the plane, only 0.02 Å from it. The pyrrolinone ring, C(1)-N(5), is planar with a maximum deviation of 0.007 Å; however, the pyrrolidone ring, C(8)-N(12), forms a poorer plane (maximum deviation = 0.06 Å).

The molecule geometry of the pyrrolinone ring in pukeleimide C is somewhat different from that in dysidin, as reported by Hofheinz and Oberhänsli.[2] (The pyrrolinone ring in dysidin has an isopropyl substituent located at the C(4) position.) The major differences in bond lengths between the corresponding bonds in pukeleimide C and in dysidin, respectively, are as follows: C(2)-C(3), 1.303(10) and 1.372(12) Å; C(3)-O(21), 1.356(7) and 1.308(10) Å; C(1)-C(2), 1.471(9) and 1.456(12) Å; O(21)-C(22), 1.440(6) and 1.480(10) Å; and C(4)-N(5), 1.454(8), and 1.488(10) Å.

Interestingly, pukeleimide C is racemic. The alkaloid does not have an optical rotation ($[\alpha]_D = 0°$) and its CD curve is flat.



Stereoview of pukeleimide C showing ellipsoids of 20% probability.[9]



Pukeleimide C is shown with ellipsoids of 20% probability.[9] Double bonds are present at C(2)-C(3) and C(7)-C(8), in addition to the three carbonyl bonds.

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2. W. Hofheinz and W. E. Oberhänsli, *Helv. Chim. Acta*, **60**, 660 (1977).
3. See references in C-L. Yeh, W. T. Colwell, and J. I. DeGraw, *Tetrahedron Lett.*, 3987 (1978)
4. From the Hawaiian word pukele which means to gather thickly in the water (such as an algal bloom).
5. Spectral data for pukeleimide C: UV (MeOH) λ_{max} 287 nm (ϵ 25200), 224 (11200); IR (KBr) 3380, 1705 (imide C = 0), 1660, 1595 cm^{-1}; ^{13}C NMR (CDCl$_3$) δ 177.1 (s), 175.7 (s), 170.0 (s), 164.1 (s), 158.2 (s), 94.7 (d, 2 carbons), 75.5 (t), 73.5 (s), 59.5 (q), 58.7 (q), 48.5 (t), 38.2 (t), 27.5 (q); ^{1}H NMR (CDCl$_3$) 7.00 (t, 1H, J = 1.5 Hz), 5.13 (s, 1H), 4.31 (s, 2H), 3.87 (s, 3H), 3.55 (d, 1H, J = -11 Hz), 3.46 (d, 1H, J = -11 Hz), 3.33 (s, 3H), 3.30 (obscured dd, 1H), 3.12 (s, 3H), 3.12 (obscured dd, 1H), 1.67 (br s, 1H); EI MS m/e (rel intensity) 310 (27, M$^+$), 265 (30, M-CH$_2$OCH$_3$), 198 (45), 152 (70, M-CH$_2$OCH$_3$-4-methoxy-Δ^3-pyrrolinone), 114 (100); high resolution MS m/e 310.1153 (calcd for $C_{14}H_{18}N_2O_6$, 310.1165), 265.0805 (calcd for $C_{12}H_{13}N_2O_5$, 265.0824), 152.0353 (calcd for $C_7H_6NO_3$, 152.0348), 114.0557 (calcd for $C_5H_8NO_2$, 114.0555).
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