NEW HALOGENATED CONSTITUENTS OF THE DIGESTIVE GLAND OF THE SEA HARE
APLYSIA DACTYLOMELA

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Summary: Two new unusually brominated labile sesquiterpenes were isolated from the mollusc Aplysia dactylolemela. The structures were solved by their spectral properties and X-ray diffraction analysis.

A group of 30 specimens of the herbivorous opisthobranch mollusc Aplysia dactylolemela were collected off Playa de Las Américas, Tenerife, Canary Islands, during August 1980, and the digestive glands were excised and homogenized in acetone. Chromatography of the ether-soluble material on silica gel led to the isolation of two undescribed halogenated terpenoids.

The fraction eluted with petrol ether-EtOAc (2%) gave a dibrominated alcohol, 1, m.p. 84-86
°C, [α]D -64 (c, 0.29, CHCl₃); C₁₅H₂₂Br₂O, M⁺ at m/z 380, 378, 376; UV λ<sub>max</sub> 246 nm (ε 39 000);
IR ν (KBr) 3560, 2926, 1460, 1368, 1300, 1195, 1170, 786 and 735 cm⁻¹; ¹H-NMR (CDCl₃): 0.83, 1.20
1.24 (s, 3H each); 4.56 (m, 1H); 5.80 (d, j = 11 Hz, 1H); 6.15 (s, 1H); 6.20 (d, j = 11 Hz, 1H).
Compound 1 is an exceptional bromochamigrene sesquiterpene possessing a bromine atom at C-9 instead of C-10 as is usual among the halogenated chamigrene-type metabolites obtained from marine sources<sup>2</sup>). In order to confirm the structure and establish the absolute configuration of 1, a single crystal of the compound was subjected to X-ray crystallographic analysis.

![Diagram](image)

The crystal data of 1 are as follows, C₁₅H₂₂Br₂O; monoclinic P₂₁ with two molecules in the cell a = 11.959(3), b = 8.488(1), c = 8.047(2) Å, β = 108.40(1)°, V = 1.620 g cm⁻³. The intensities of the 1238 observed independent Friedel pairs for 2 < θ < 65° were measured on a four-circle diffractometer, using graphite-monochromated CuKα radiation. During the three day experiment, the crystal decomposed decaying the diffracted intensity to 25% of the original value. No absorption correction was done. The crystal structure was solved by direct methods and anisotropically refined to R=0.060 and R<sub>W</sub>=0.081 by weighted least-squares. All H-atoms were previously located on a difference map<sup>3</sup>).
Anomalous dispersion, specially for Br atoms, revealed the absolute configuration shown in Figure 1. The 76 more relevant Bijvoet pairs with $\Delta F_C > 0.8$ gave an averaged Bijvoet difference of 0.65 for the right enantiomer, against 2.56 for the wrong one. Ring A is chair conformation with C-6 0.62 Å up and C-9 0.70 Å down the best plane through C-7,-8,-10,-11. Ring B is a half-chair with the best plane through C-6,-1,-2,-3 and a torsion angle 3-4-5-6 of +46°. The torsion 2-3-12-Br2 is 178°. The two double bonds $\Delta^1$ and $\Delta^1(12)$ are both of 1.32(1) Å. The bond lengths C-9-Br1 and C-12-Br2 are 1.99(1) and 1.89(1) Å respectively.

The fraction eluted with ether was further submitted to preparative thin layer chromatography on silica gel to give the E isomer $\text{E}^4$ as an oil, $\text{C}_{15}\text{H}_{22}\text{Br}_2\text{O}$, $\text{M}^+\text{ at m/z 380, 378, 376; IR (KBr) 3560, 2923, 1458, 1370, 1300, 1200, 1194, 1078, 780 and 735 cm}^{-1}; ^1\text{H-NMR (CDCl}_3): 0.83, 1.20, 1.24 (\text{3H each}); 4.50 (\text{m, 1H}); 5.90 (\text{s, 1H}); 6.00 and 6.60 (\text{d, J= 11 Hz, 1H each}).$ Halogenated compounds related with previously reported terpenoids from the red alga Laurencia caespitosa were also isolated\textsuperscript{5}.

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