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NEW HALOGENATED CONSTITUENTS OF THE DIGESTIVE GLAND OF THE SEA HARE APLYSIA DACTYLOMELA[1)]

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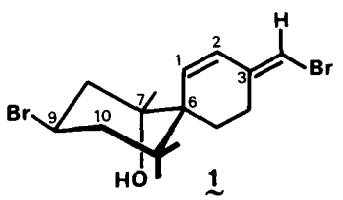
Summary: Two new unusually brominated labile sesquiterpenes were isolated from the mollusc Aplysia dactylomela. The structures were solved by their spectral properties and X-ray diffraction analysis.

A group of 30 specimens of the herbivorous opisthobranch mollusc *Aplysia dactylomela* 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, $[\alpha]_D$ -64 (c, 0.29, $CHCl_3$); $C_{15}H_{22}Br_2O$, M^+ at m/z 380, 378, 376; UV λ_{max}^{EtOH} 246 nm (ε 39.000); IR ν (KBr) 3560, 2926, 1460, 1368, 1300, 1195, 1170, 786 and 735 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 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[2)]. 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.



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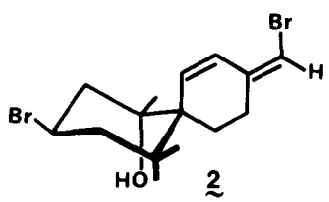

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The crystal data of 1 are as follows, $C_{15}H_{22}Br_2O$; monoclinic $P2_1$ with two molecules in the cell a = 11.959(3), b = 8.488(1), c = 8.047(2) Å, β = 108.40(1)°, ρ_x = 1.620 g cm^{-3}. The intensities of the 1238 observed independent Friedel pairs for $2 < \theta < 65°$ were measured on a four-circle diffractometer, using graphite-monochromated CuK_α 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 strcture was solved by direct methods and anisotropically refined to R=.060 and R_w=.081 by weighted least-squares. All H-atoms were previously located on a difference map[3)].

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

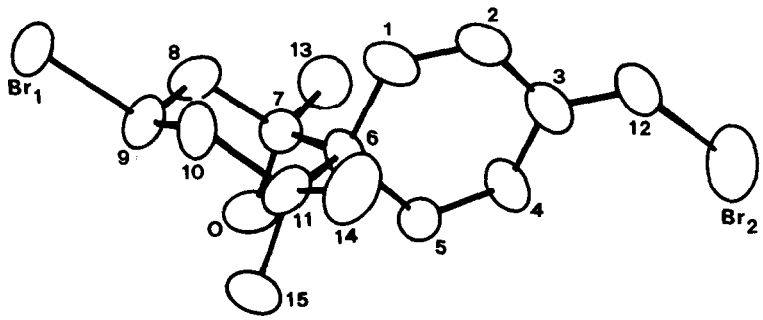

FIGURE 1: A perspective view of the absolute X-ray molecular model of compound 1

of 0.65 for the right enantiomer, against 2.56 for the wrong one. Ring A is chair conformated, 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 Δ^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 2[4] as an oil, $C_{15}H_{22}Br_2O$, M^+ at m/z 380, 378, 376; IR (KBr) 3560, 2923, 1458, 1370, 1300, 1200, 1194, 1078, 780 and 735 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 0.83, 1.20, 1.24 (*s*, 3H each); 4.50 (*m*, 1H); 5.90 (*s*, 1H); 6.00 and 6.60 (*d*, *J*= 11 Hz, 1H each). Halogenated compounds related with previously reported terpenoids from the red alga *Laurencia caespitosa* were also isolated[5].

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