

Note

A new polyhalogenated epoxymonoterpene from *Plocamium cartilagineum*

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A new alicyclic monoterpene has been isolated from the red alga *Plocamium cartilagineum* (L.) Dixon and its structure determined on the basis of spectral features as 4-bromo-5-chloro-2-(*E*)chlorovinyl-1,5-dimethyl-1,2-epoxycyclohexane **1**.

Although marine red algae (Rhodophyta) have been the subject of wide investigation for their halogen terpenoid content, the recent discovery of new cytotoxic polyhalogenated monoterpenes^{1,2} has renewed the interest on these metabolites. In continuation of our studies on the red alga *Plocamium cartilagineum* (L.) Dixon (Plocamiaceae), collected along the Portuguese coast^{3,4}, we wish to report in this communication the isolation of a new alicyclic monoterpene, 4-bromo-5-chloro-2-(*E*)chlorovinyl-1,5-dimethyl-1,2-epoxy-cyclohexane **1**.

The chloroform extract of *P. cartilagineum* was fractionated by silica gel flash chromatography to yield compound **1**, whose high resolution mass spectrum corresponded to a molecular formula of C₁₀H₁₃OBrCl₂. Subsequent investigation by HRMS showed several oxygen-containing ion clusters which illustrated the halogen content: C₁₀H₁₃OBrCl (m/z 263, 265, 267), C₁₀H₁₃OCl₂ (m/z 219, 221, 223), C₁₀H₁₂OCl (m/z 183, 185) and C₁₀H₁₁O (m/z 147). The ¹³C-INEPT spectrum revealed the presence of two methyl groups (δ 20.7 and 32.5), two sp² olefinic carbons assigned to a chlorovinyl group (δ 122.9 and 130.2)⁵, two methylene groups (δ 38.8 and 48.2), one halomethine group (δ 54.2) and three quaternary carbons bearing an electronegative atom (δ 62.4, 64.9 and 69.6). ¹H NMR and ¹H-¹H COSY

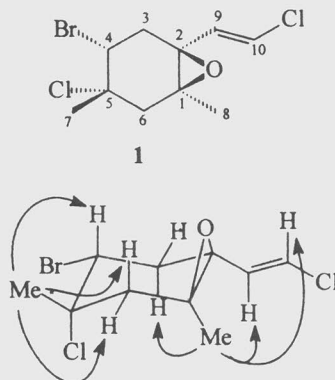


Figure 1—NOE selected interactions in **1**

spectra displayed an axial proton at δ 4.02 (dd, *J*=8.8, 4.0 Hz) coupled to two methylene protons at δ 2.59 (dd, *J*=11.6, 4.0 Hz) and 2.71 (*J*=11.6, 8.8 Hz), an isolated -CH₂- *AB* quartet centred at δ_A 2.29 and δ_B 2.55 (*J*=12.8 Hz), two *trans* olefinic protons that resonated as an *AB* quartet centred at δ_A 6.00 and δ_B 6.23 (*J*=13.4 Hz), and two methyl singlets at δ 1.29 and 1.67. According to the HMBC spectrum, these two methyl groups are respectively bonded to the quaternary carbons at δ 62.4 (C-1) and 69.6 (C-5), whereas NOE interactions (Figure 1) indicated an equatorial conformation of 7-Me and a *pseudo*-axial conformation of 8-Me. The absence of hydroxyl adsorption in the IR spectrum suggests that the oxygen atom is involved in an ether linkage. The presence of a bridged cyclic ether was excluded on the basis of the quaternary carbon resonances, considering that in the series of chamigrene and maneone halogenated cyclic ethers isolated from *Laurencia* species⁶, the oxygen bearing carbons resonate in the range of δ 74-114 ppm. The remaining structural possibility is a tetrasubstituted epoxide, in which the chemical shifts of the two epoxy ring carbons (δ 62.4 and 64.9) (cf. Table I) are in good agreement with those encountered in epoxychamigrene derivatives^{6,7} and in a linear polyhalogenated epoxy-monoterpene previously isolated from a New Zealand specimen of *P. cartilagineum*⁸.

Table I— ^1H and ^{13}C NMR spectral data of **1**

	δ_{C}	δ_{H}
1	62.4	
2	64.9	
3	38.8	2.59 (1H, dd, $J=11.6, 4.0$ Hz, $\text{H}_{3\text{eq}}$), 2.71 (1H, dd, $J=11.6, 8.8$ Hz, $\text{H}_{3\text{ax}}$)
4	54.0	4.02 (1H, dd, $J=8.8, 4.0$ Hz)
5	69.6	
6	48.2	2.29 (1H, d, $J=12.8$ Hz, $\text{H}_{6\text{eq}}$), 2.55 (1H, d, $J=12.8$ Hz, $\text{H}_{6\text{ax}}$)
7	32.5	1.67 (3H, s)
8	20.7	1.29 (3H, s)
9	130.2	6.00 (d, $J=13.4$ Hz)
10	122.9	6.23 (d, $J=13.4$ Hz)

Spectra in CDCl_3 , δ in ppm and coupling constants (J) in Hz.

The halogen regiochemistry in **1** was assigned by comparison of its ^{13}C NMR data with those of model compounds^{5,9,10} which support a 1-ethyl-2,4-dimethylcyclohexane framework bearing a bromide and chlorine at C-4 and C-5 respectively. To our knowledge this is the first report of a naturally occurring alicyclic polyhalogenated epoxy monoterpene.

Experimental Section

General. Experimental procedures have been described earlier³ by us.

Plant material. The algal material was collected in Sesimbra in July 1990, and air dried. A voucher specimen is deposited at the herbarium of IPIMAR, Lisbon.

Extraction and isolation. Air-dried alga (4 kg) was successively extracted with hexane and CHCl_3 . Successive silica gel flash chromatography of CHCl_3 extract (37 g), using hexane with

increasing proportions of EtOAc as eluents afforded compound **1** (7 mg), m.p. 49–50°C; $[\alpha]_{\text{D}}^{25}$ 48° (CHCl_3 ; c 0.4); IR (KBr): 2917, 2849, 1463, 759, 719 cm^{-1} ; HREIMS [70 ev, m/z (rel. int)]: 297.96140 [M^+ Calcd for $\text{C}_{10}\text{H}_{13}\text{O}^{79}\text{Br}^{35}\text{Cl}_2$: 297.95268] (6), 280.95112 [$\text{M}^+ - \text{OH}$] (2), 262.98199 [$\text{M}^+ - \text{Cl}$] (9), 219.03900 [$\text{M}^+ - \text{Br}$] (10), 183.06280 [$\text{M}^+ - \text{HBr} - \text{Cl}$] (47), 147.08318 [$\text{M}^+ - \text{HBr} - \text{HCl} - \text{Cl}$] (62); for ^1H and ^{13}C NMR data, see Table I.

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References

- Fuller R W, Cardellina J H II, Kato Y, Brinen L S, Clardy J, Snader K M & Boyd M R, *J Med Chem*, 35, **1992**, 3007.
- Ortega M J, Zubia E & Salvá J, *J Nat Prod*, 60, **1997**, 482.
- Arbreu P M & Galindro J M, *J Nat Prod*, 59, **1996**, 1159.
- Arbreu P M, Galindro J M, Relva A M & Ramos A M, *Phytochemistry*, 45, **1997**, 1601.
- Naylor S, Hanke F J, Manes L V & Crews P, *Progress in chemistry and organic natural products*, Vol. 44, edited by W Herz, H Grisebach & G W Kirby (Springer-Verlag, Wien New York), **1983**, pp. 189–241.
- Sims J J, Rose A F & Izax R R, *Marine natural products*, Vol. II, **1978**, 297.
- Suzuki M, Furusaki A & Kurosawa E, *Tetrahedron*, 35, **1979**, 823.
- Blunt J W, Bowman N J, Munro M H G, Parsons M J, Wright G J & Kon Y K, *Austral J Chem*, 38, **1985**, 519.
- Higgs M D, Vanderah D J & Faulkner D J, *Tetrahedron*, 33, **1977**, 2775.
- Crews P, Naylor S, Hanke F J, Hogue E R, Kho E & Braslau R, *J Org Chem*, 40, **1984**, 1371.