

GELIDENE, A NEW POLYHALOGENATED MONOCYCLIC MONOTERPENE FROM THE RED MARINE ALGA *GELIDIUM SESQUIPEDALE*

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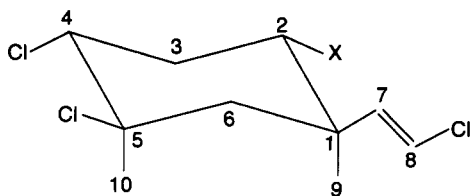
ABSTRACT.—The red marine alga *Gelidium sesquipedale* was found to contain a new polyhalogenated monocyclic monoterpene that was identified as 1-(2-chlorovinyl)-2,4,5-trichloro-1,5-dimethylcyclohexane [**1**] by ^1H -, ^{13}C -, and 2D-homonuclear ^1H - ^1H chemical shift correlation nmr experiments.

Previous studies of natural products from marine organisms have revealed a fascinating array of halogenated monoterpenes (1). As part of our program on the phytochemical and physicochemical studies of *Gelidium sesquipedale* (Clemente) Thuret (Gelidiaceae), a red marine alga used in Morocco for its nutritional value, we have isolated from the unsaponifiable hexane extract a new cyclic tetrachlorinated monoterpene. We have named it gelidene and established its structure as 1-(2-chlorovinyl)-2,4,5-trichloro-1,5-dimethylcyclohexane [**1**].

The molecular formula for gelidene [**1**] (mp 82° , $[\alpha]^{20}_{\text{D}} - 55^\circ$) was established by hrms to be $\text{C}_{10}\text{H}_{14}\text{Cl}_4$ [m/z 274, 276, 278, 280, 127 (base peak)]. A single trans olefinic bond was indicated by an AB quartet at δ 5.87 and 6.08 ppm ($J = 13.6$ Hz) in the ^1H -nmr spectrum and by CH signals at 119.12 and 140.18 ppm in the ^{13}C -nmr spectrum. Close inspection of the remaining ^1H -

nmr signals confirmed the presence of the following subgroups: (a) two quaternary methyl groups (singlets at 1.23 and 1.77 ppm); (b) an isolated methylene group [an AB quartet, ($J = 14.5$ Hz) at 2.20 and 2.37 ppm]; and (c) a partial structure $-\text{CHCl}-\text{CH}_2-\text{CHCl}-$ contained within a six-membered ring [a four-signal pattern at 4.17 (dd, $J = 4.3, 12.5$ Hz), 3.84 (dd, $J = 4.3, 12.5$ Hz), 2.53 (dt, $J = 4.3, 4.3, 14$ Hz), and 2.25 ppm (dt, $J = 12.5, 12.5, 14$ Hz)]. A full assignment of the ^{13}C chemical shifts of gelidene was made based upon a DEPT spectrum (2), selective decoupling experiments (3), and reference to chemical shift data for several model compounds (4). The ^{13}C -nmr spectrum of **1** showed the presence of two additional tetrasubstituted carbon atoms with signals at 43.68 and 70.45 ppm. Consequently, the combined spectral data for gelidene were most consistent with the structure **1**.

The stereochemistry of gelidene was



established by a careful analysis of the nmr data. The coupling constants of the two protons on the ring carbon atoms bearing chlorines indicated that the chlorine atoms were equatorial on a cyclohexane ring in the chair conformation. Moreover, the distinct broadening observable for the methylene proton at 2.37 ppm must arise from long-range couplings. The analysis of the COSY-90 diagram (5-7) also showed correlations of this proton with the two methyl groups, indicative of a trans diaxial disposition of those two methyl groups (8). Carbon chemical shifts, especially in cyclohexane ring systems, are extremely sensitive to stereochemical factors (9). The comparison between ^{13}C methyl shifts of gelidene [1] and model compounds (4) suggested axial methyls at each site.

Finally, the ^1H - and ^{13}C -nmr results (Table 1) of gelidene [1] were remarkably similar to those observed for mertensene [2] from *Plocanium mertensii* (10), whose structure and stereochemistry are unambiguously known from X-ray analysis (11).

$[\alpha]^{20}_{\text{D}}$ was recorded on a Perkin-Elmer model 241 Polarimeter. Mass spectra were determined on an MS-50 AEI spectrometer (Kratos). All nmr spectra were recorded on a Bruker AM-200 multinuclear spectrometer. Samples for ^{13}C measurements were prepared in a 10-mm o.d. tube by mixing 15 mg of gelidene with 2 ml of CDCl_3 , and ^1H measurements were carried out using a 5-mm o.d. tube containing 5 mg of 1 in 0.5 ml of CDCl_3 ; TMS was used as an internal standard in both measurements. ^1H coupling constants were extracted from the resolution-enhanced ^1H spectrum using the Gaussian multiplication technique (12).

Resonance multiplicities for ^{13}C were established via the acquisition of DEPT spectra obtained for proton pulses $P_0 = 90^\circ$ (CH only) and $P_0 = 135^\circ$ (CH and CH_3 , differentiated from CH_2). For the DEPT sequence the width of a ^1H 90° pulse was 29 μsec , the width of a ^{13}C 90° pulse was 13 μsec , and the $(2J)^{-1}$ delay was set equal to 3.7 msec.

The homonuclear (^1H - ^1H) shift-correlated 2D diagram was obtained using the COSY-90 pulse sequence. The spectral widths were $F_2 = 1436$ and $F_1 = \pm 718$ Hz, allowing a digital resolution of 2.8 Hz. The spectrum was collected as 2048×1024 blocks of data and was processed using sinusoidal multiplication of the final data matrix. Other parameters were as follows: number of increments in t_1 , 512; scans, 16; phase cycling, 16; and relaxation delay, 1 sec.

FRACTIONATION AND ISOLATION.—*G. ses-*

TABLE 1. ^1H - and ^{13}C -nmr Chemical Shift^a Assignments of Gelidene [1] in CDCl_3 .

Atom	^1H	^{13}C
1	—	43.68
2	3.84 (dd, $J = 4.3, 12.5$)	62.85
3	2.25 (ax, dt, $J = 12.5, 12.5, 14$) 2.53 (eq, dt, $J = 4.3, 4.3, 14$)	39.89
4	4.17 (dd, $J = 4.3, 12.5$)	66.60
5	—	70.45
6	2.20 (eq, d, $J = 14.5$) 2.37 (ax, d, $J = 14.5$)	52.85
7	6.08 (d, $J = 13.6$)	140.18
8	5.87 (d, $J = 13.6$)	119.12
9	1.23 (s)	18.79
10	1.77 (s)	26.06

^aIn ppm from TMS; multiplicity and J values are in parentheses.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—

Melting points were determined on a Buchi 510 apparatus and are uncorrected. Optical rotation

quipedale, collected in October 1986 from the shore at Sidi Bouzid along the Atlantic coast of Morocco, was identified, carefully sorted, and washed before extraction (voucher specimen is deposited in the laboratoire de Chimie des Sub-

stances Naturelles, Université de Marrakech). The algae was dried (40°), ground to a fine powder, and Soxhlet extracted for 10 h with CHCl₃-MeOH (2:1). The evaporation of the solvents in vacuo gave a dark green oil which was saponified with refluxing two h with 2 M KOH in EtOH. The unsaponifiable crude fraction was extracted with Et₂O in the usual manner. After evaporation of Et₂O, the crude extract was applied to a column of Si gel (Merck 60, 70–230 mesh ASTM). The column was eluted with a solvent gradient system from hexane to Et₂O; fractions of 20 ml were collected and those exhibiting similar tlc profiles were combined. Fractions 7–13 eluted with pure hexane were taken to dryness to afford 221 mg which was analyzed by gc-ms (Ribermag R 10-10); two components were identified; the minor was heptadecane and the major showed molecular ion [M]⁺ at *m/z* 274. Further purification by repeated cc of these combined fractions gave the pure major component, which was identified by ¹H- and ¹³C-nmr spectra (Table 1).

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