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SHORT REPORTS

2-CHLORO-1,6(*S**),8-TRIBROMO-3-(8)(*Z*)-OCHTODENE: A METABOLITE OF THE TROPICAL RED SEAWEED *OCHTODES SECUNDIRAMEA*

WILLIAM H. GERWICK

Department of Chemistry, University of Puerto Rico, Rio Piedras, Puerto Rico 00931

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Key Word Index—*Ochtodes secundiramea*, Rhizophyllidaceae; ochtodanes; halogenated natural products; seaweed chemistry.

Abstract—A major new metabolite was isolated from the tropical red seaweed *Ochtodes secundiramea* and its structure determined on the basis of spectral features as 2-chloro-1,6(*S**),8-tribromo-3-(8)(*Z*)-ochtodene.

The isolation of an abundance of halogenated secondary metabolites is a notable feature of red algal biochemistry, in particular in the Rhodomelaceae, Plocamiaceae and Bonnemaisoniaceae [1]. *Ochtodes secundiramea* (Montagne) Howe (Cryptonemiales, Rhizophyllidaceae) is a common seaweed of shallow and exposed coasts in the Caribbean, and terpenes are easily detected in the fresh plants by their sickly sweet smell. Examination of this alga from Bacolet Reef, Tobago, has revealed a major new metabolite (**1**) with a novel arrangement of halogen atoms, the structure of which is reported herein.

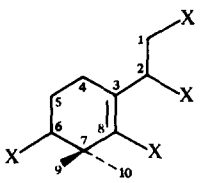
Silica gel chromatography of the chloroform–methanol extract gave non-polar fractions rich in terpene odour. The major component of several of these fractions, **1** was purified to a colorless oil by repeated HPLC. This distinctively acid-charring metabolite on TLC (yellow to blue to red) showed $[\alpha]_D + 55°$ (*c* 0.74, $CHCl_3$) and analysed for $C_{10}H_{14}{}^{79}Br_3{}^{35}Cl_1$ by HRMS. The two degrees of unsaturation inherent in this molecular formula were accounted for by one tetrasubstituted olefin [^{13}C NMR (125 MHz, d-6-bz) 134.5 *s*, 131.5 *s*] and one ring.

High field ^{1}H NMR (500 MHz, d-6-bz) indicated that four of the ten carbon atoms were exocyclic to the ring, two as singlet methyl groups (δ 1.06 and 1.26) and two as a 1,2-dihaloethylene substituent (δ 5.34, 1H, *dd*, *J* = 7.0, 10.0 coupled exclusively to a second order ABX pattern centered at δ 3.05, 2H, *m*; ^{13}C NMR δ 62.2 *d*, 31.8 *t*; carbon assignments on basis of *J* values in Table 1). The two methyl groups were present as a *gem*-dimethyl constellation (^{13}C NMR 28.3 *q*, 27.3 *q*, 44.2 *s*; IR 1382 cm^{-1}). The remaining carbons were most logically grouped into a cyclohexene ring bearing these substituents and two additional halides.

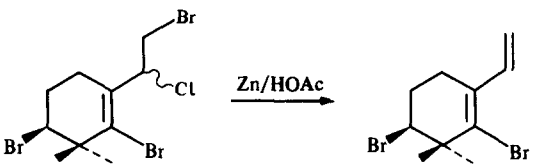
Three of the ring carbons contained five protons (δ 61.1 *d*, 28.5 *t*, 23.9 *t*) which were positioned on adjacent carbon atoms by spin decoupling (δ 3.74, 1H, *dd*, *J* = 6.5, 5.0 Hz; 1.75, 2H, *m*; 1.92, 2H, *dd*, *J* = 5.5, 5.5 Hz). The constraint that three sequential carbon atoms possess hydrogens, and therefore, that three do not, is best accommodated for by the ochtodane ring system [2] with the substitution pattern shown below in partial structure **a**.

Location of a bromine atom at C-1 was made via spectroscopic arguments (^{13}C NMR: δ 31.8, gated decouple *td*, *J* = 156.2, 4.2 Hz) [3] and location of a pseudoequitorial bromine at C-6 secured by comparison of carbon chemical shifts (δ 61.1, gated decouple *dd*, *J* = 154.0, 4.0 Hz) with known compounds [2,4] and coupling constant analysis of the corresponding proton peak multiplicity [*dd*, *J* = 6.5, 5.0 Hz; in $CDCl_3$ (90 MHz) **1** shows the C-6 methine proton at δ 4.36, *dd*, *J* = 7.3, 3.9 Hz].

Resolution of the remaining halogen pattern at C-2 and C-8 was accomplished via treatment of **1** with Zn–HOAc to yield the diene **2**. LRMS gave a molecular formula for **2** of $C_{10}H_{14}Br_2$ identifying the vinyl halide (C-8) as bromine and the allylic halide (C-2) as chlorine, as shown for **1**. The stereochemistry at C-2 has not been determined.



a



1 **2**

Table 1. Analysis of carbon multiplicities for correlation of carbon and proton bands in **1***

Assignment	^{1}H NMR chemical shift (δ)	^{13}C NMR chemical shift (δ)†	Off resonance multiplicity§	J_{CH}‖	J_R§	$\frac{J_{CH}-J_R}{J_{CH}} \times 10^2$¶	J_{CCH}‖
C-1	3.05	31.8	*t*	156.2	132.6	15.1	4.2
C-2	5.34	62.2	*d*	158.1	124.2	21.4	
C-3		131.5	*s*				
C-4	1.92	23.9	*t*	129.1	112.7	12.7	
C-5	1.75	28.5	*t*	130.6	114.6	12 3	
C-6	3 74	61.1	*d*	154.0	128.2	16.7	4.0
C-7		44.2	*s*				
C-8		134 5	*s*				
C-9	1.06	28.3‡	*q*	130.3	114.5	12.1	
C-10	1.26	27.3‡	*q*	129.1	112.8	12.6	

*Performed on a Bruker HX 500 NMR spectrometer (d-6-bz).
†Irradiation at center line of proton spectrum (8000 Hz).
‡Assignments may be reversed.
§Obtained by partial proton decoupling centered at 12 000 Hz.
‖Obtained under normal gated decouple conditions, proton irradiation at 8000 Hz.
¶Percent values are proportionate to distance of proton frequency and center line of off resonance irradiation frequency; for a similar analysis see ref. [5].

Metabolite **1** was inactive in the KB 9 antitumor assay and did not inhibit the growth of *Pseudomonas aeruginosa* cultures at standard test levels (100 μg/disc). This is the first report of a metabolite within the ochtodane series to possess a vinyl halide within the cyclic portion of the molecule.

EXPERIMENTAL

All NMR chemical shifts are reported relative to TMS (= 0), and coupling constants are in Hertz. Low-resolution mass spectra (LRMS) were obtained on a Hewlett–Packard 5995A mass spectrometer, and high-resolution mass spectra (HRMS) were obtained through the Department of Chemistry, University of California, Berkeley. All solvents were distilled from glass prior to use.

Collection, extraction and chromatography *Ochtodes secundiramea* was collected in 1 to 2 m of water at Bacolet Reef, Tobago in December 1982, and immediately stored in IPA Homogenization in $CHCl_3$–MeOH (2.1) with heating (55°) yielded after filtration and solvent removal *in vacuo* 6.6 g of extractable oil from 198.4 g dry wt of seaweed

Conventional silica gel column chromatography with hexane gave several fractions rich in **1** These were combined and purified from the mixture by repeated HPLC over 25 cm of μ-Porasil (3.9 mm) using 100% hexane (380 mg, 5.7% of extract) In addition to the data reported in the text, **1** showed the following IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2980, 2930, 2860, 1440, 1382, 1350, 1120, 1075, 930, 840, 635; ^{1}H NMR (90 MHz, $CDCl_3$). δ 5.50 (1H, *dd*, *J* = 9 0, 6 9), 4 36 (1H, *dd*, *J* = 7 3, 3 9), 3 64 (2H, *m*), 2.37 (4H, *m*), 1.41 (6H, *s*); HRMS, *m/z* (rel. int.) 411.8244 (M^+, $C_{10}H_{14}{}^{79}Br_1{}^{81}Br_2{}^{37}Cl$, 1.9 mmu dev, 13 2), 409.8278 (M^+, $C_{10}H_{14}{}^{79}Br_1{}^{81}Br_2{}^{35}Cl$, 1.5 mmu dev, 25 6), 407.8313 (M^+, $C_{10}H_{14}{}^{79}Br_2{}^{81}Br_1{}^{35}Cl_1$, 2 6 mmu dev, 5 8), 327.9057 ($C_{10}H_{13}{}^{79}Br_1{}^{35}Cl_1$, 48 2), 248 9869 ($C_{10}H_{13}{}^{81}Br_1{}^{35}Cl_1$, 67 7), 213 0125 ($C_{10}H_{12}{}^{82}Br_1$, 51 9), 167.0622 ($C_{10}H_{12}{}^{35}Cl_1$, 39.2), 133 018 ($C_{10}H_{13}$, 67.9), 117 0703 ($C_9H_9$, 53 6) 91.0544 ($C_7H_7$, 98 9), 65.0391 ($C_5H_5$, 100); LRMS (70 eV) 412 (3 2), 410 (6.6), 408 (4.4), 293 (19), 249 (13), 213 (21), 167 (14), 133 (100), 118 (67), 91 (79)

Dehalogenation of **1** *to form diene* **2**. To 43 mg of **1** (0.106 mmol) in 2.0 ml dry HOAc (3 drops Ac_2O) at room temp (30°) was added 47 mg Zn dust (0.72 mmol) and allowed to react under a positive pressure of N_2 After 1 hr, the reaction was diluted with 10 ml Et_2O, filtered and the reaction mixture washed with satd $NaHCO_3$ (3 × 50 ml) and H_2O (3 × 50 ml). The Et_2O was dried ($MgSO_4$) and reduced *in vacuo* to give pure **2** (as judged by TLC, GC and ^{1}H NMR; 23 mg, 81%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400, 2975, 2930, 1635, 1520, 1365, 1160, 1120, 990, 910, 890, 700; UV (MeOH) λ_{max} 243 nm, ε = 6600; ^{1}H NMR (90 MHz, $CDCl_3$). δ 6 92 (1H, *dd*, *J* = 17.6, 11.0), 5.28 (1H, *dd*, *J* = 17.6, 0 9), 5.17 (1H, *dd*, *J* = 11.0, 0.9), 4.29 (1H, *dd*, *J* = 8 1, 4.9), 2 30 (4H, *m*), 1.38 (3H, *s*), 1.36 (3H, *s*); ^{13}C NMR ($CDCl_3$, 22.5 MHz): δ 137.7, 133 2, 131.1, 116.3, 61.8, 44.2, 29.2 (2C), 27 2, 25.6; LRMS (70 eV) *m/z* (rel int.): 296 (3.4), 294 (7.4), 292 (3.6), 279 (3.9), 213 (9 5), 197 (10 1), 133 (100), 118 (59), 91 (53)

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