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MARINE NATURAL PRODUCTS XVII. THE STRUCTURE OF (1*S*, 4*R*, 7*R*)-1-BROMO-4-HYDROXY-7-CHLOROSELINANE, A METABOLITE OF THE MARINE ALGA *LAURENCIA SP.*

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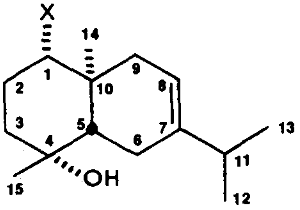
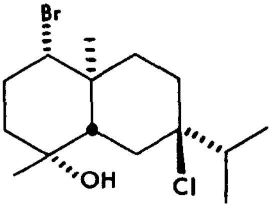
In recent years an increasingly large number of ring systems have been discovered in red algae of the genus Laurencia.[1,2] The latest addition to this manifold of sesquiterpenes is (1*S*, 4*R*)-1-bromo-4-hydroxyselin-7-ene, *1*, recently reported from *Laurencia* species collected in the Gulf of California[3] and Australia.[4] We have isolated a second selinane *2*, (1*S*, 4*R*, 7*R*)-*1*-bromo-*4*-hydroxy-*7*-chloroselinane, and determined its structure including absolute configuration by X-ray diffraction.



1 X = Br

3 X = H



2

Hexane extraction of the air dried alga, which was collected in Guerilla Bay (north), New South Wales, Australia, gave the usual dark green extract. Open column chromatography of the extract on silica gel eluting with hexanes followed by step-gradient elution with increasing proportions of diethyl ether in hexanes gave a fraction which contained predominantly *1* and *2*. High pressure liquid chromatography (Bio-SilA, 10% ethyl acetate in hexanes) gave *1*, 174mg (0.035%), and *2*, 98mg (0.02%).

Recrystallization of *2* from hexane gave orthorhombic crystals, m.p. 128-131° dec, $[\alpha]_D$ +32.7 (c 1.07, $CHCl_3$). The low resolution mass spectrum of *2* did not display a molecular ion but did contain ion clusters at m/e 325, 323, 321 ($C_{14}H_{23}OBrCl$, $M^+ - CH_3$), m/e 287, 285 ($C_{14}H_{22}OBr$, $M^+ - CH_3 - HCl$), m/e 284, 282 ($C_{15}H_{23}Br$, $M^+ - H_2O - HCl$) and m/e 241, 239 ($C_{15}H_{24}Cl$, $M^+ - H_2O - Br$). The infrared spectrum ($CHCl_3$) exhibited hydroxyl stretching at 3600 and 3500 cm^{-1} with additional absorptions at 1460, 1380, 1365, 1175, 955 and 890cm^{-1}.

The 220 MHz pmr spectrum (δ in $CDCl_3$, TMS=0) indicates the presence of an isopropyl group (1.06, d, J=6.6Hz; 1.08, d, J=6.6Hz) whose methyl groups are nonequivalent due to the chiral center at C-7, a methyl group on a carbon bearing oxygen (1.16, s), a bridgehead methyl (1.12, s), a one proton doublet of doublets (4.03, J=12.5, 4.2Hz) indicative of an equatorial bromine adjacent to a methylene, a one proton multiplet centered at 2.43 and a complex series of multiplets, 12H, 2.10-1.45.

The carbon chemical shifts for *1* and *3* are given in the table.[4] The cmr chemical shift assignments for ring A of *2* follow by comparison to *1*. The three methylene carbons of ring B could not be unambiguously assigned. The lowest field signal, 37.3 ppm, was assigned to C-6 which is *alpha* to the quaternary halogen bearing carbon (C-7) and the bridgehead (C-5). The chemical shift of C-7, 81.0 ppm, is at unexpectedly low field. In halogenated monoterpenes which possess 1-chloro-1-methylcyclohexane systems, the quaternary chloride carbon resonates near 70 ppm.[5]

The structure of *2* was confirmed and the conformation and absolute configuration established by a single crystal X-ray diffraction study. Slow evaporation of a hexane

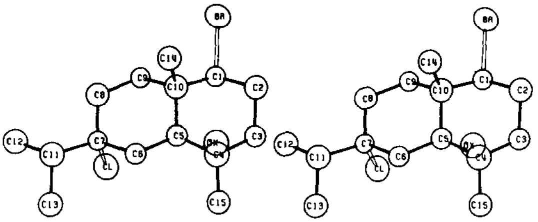


Figure. Stereoscopic pair drawing of *2*.

solution gave orthorhombic needles (0.18 X 0.22 X 1.1mm) with well developed 110 and $1\bar{1}0$ faces. The space group is $P2_12_12_1$ with cell constants $\underset{\sim}{a}$=20.60(6), $\underset{\sim}{b}$=12.34(3), and $\underset{\sim}{c}$=6.07(1). Reflection intensities were collected on a computer controlled diffractomer out to sin θ/λ=0.48 using $MoK\bar{\alpha}$ radiation. Of the possible 891 reflections, 797 were retained after rejection of those smaller than their own standard deviation.

The solution to the structure[6] was readily derived from the Patterson map and refinement to a final R factor of 8.3% based on F was obtained for a model[7] in which only the Br and Cl atoms were refined anisotropically. The real and imaginary part of the anomalous dispersion for Br and Cl was made and the H atoms, clearly observed (ρ_{ave}=0.55e/A^3) in the final difference fourier, were ignored. Since the enantiomeric structure could only be refined to a R factor of 9.8%, the absolute configuration is established[8] to be that shown in the figure. The final weighted R was 9.1% and chi square was 4.84.

Table. CMR Chemical Shifts, ppm (TMS=0), $CDCl_3$

Cmpd	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12 or C13	C14	C15
1	68.4	24.3	42.4*	71.0	48.2	30.2	141.9	116.2	42.9*	38.4	34.8	21.8, 21.2	14.0	29.8
2	67.5	30.3	42.7	71.4	47.4	37.3	81.0	33.8*	33.0*	39.4	40.9	17.7, 17.6	14.3	29.8
3	41.3	18.8	41.6*	71.6	47.3	30.2	142.5	116.6	44.6*	32.4	35.1	21.9, 21.3	18.0	23.3

* Assignments may be reversed

All bond angles and lengths are within normal limits.[9,10] The A-ring chair is flattened significantly ($|\tau|_{ave}=50°$ vs a value of 56° for cyclohexane) as a result of the axial chlorine.

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6. Calculations were done on the time shared HP-3000 computer in the U. C. Riverside Instrumentation Network using Zalkin's FORDAP for fouriers and Spark and Gantzel's BDLSQ for refinement. Several cycles of full matrix refinement were done on our IBM360-50 using Busing, Martin and Levy's ORFLS.
7. Scattering powers for valence C and neutral O, H, Br and Cl were taken from the International Tables for X-ray Crystallography (1962) Vol. III pp202-206, Birmingham-Kynoch Press. Anomalous dispersion corrections were taken from Table 3.3.2.C on p215 of the same publication.
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10. A list of structure factors and atom coordinates for this structure can be obtained from R. M. W.