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MARINE NATURAL PRODUCTS XIV. 1-*S*-BROMO-4-*R*-HYDROXYSELIN-7-ENE, A METABOLITE OF THE MARINE ALGA *LAURENCIA SP.*

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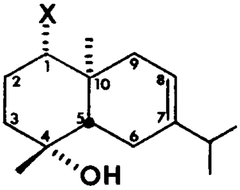
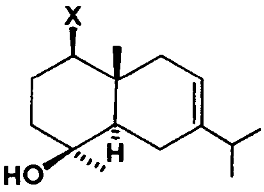
Investigations of marine red algae of the genus *Laurencia* have led to the isolation of a number of halogenated terpenes.[1] Continuation of our interest in *Laurencia sp.* from Australia has led to the isolation of a new brominated sesquiterpene (+)-1-*S*-bromo-4-*R*-hydroxyselin-7-ene, *1*.

Hexane extraction of the air dried alga, which was collected in Guerilla Bay, New South Wales, Australia, gave a dark green extract. Open column chromatography of the extract on silica gel gave, in addition to two previously unreported C_{15} eneyne compounds and elatol,[2] fraction A. High pressure liquid chromatography (Bio-Sil A, 8% ethyl acetate in hexanes, recycle mode) gave pure *1*, 42 mg (0.005%) as a viscous oil, $[\alpha]_D$ +54.4° (c 1.35, $CHCl_3$).



1 X = Br

2 X = H



3 X = OH

4 X = H

The mass spectrum of *l* displayed a molecular ion at m/e 300, 302, $C_{15}H_{25}OBr$, which in turn loses H_2O (m/e 282, 284), $H_2O + CH_3$ (m/e 267, 269) and H_2O + Br (m/e 203). The molecular formula of *l* requires three sites of unsaturation. The carbon-13 (cmr) spectrum (ppm in $CDCl_3$, TMS=0) reveals but one double bond (141.9, s, and 116.2, d) and no carbonyl absorption. Hence *l* is bicyclic. The pmr spectrum (δ in CCl_4, TMS=0) indicates the presence of two tertiary methyl groups (1.18, s, and 1.10, s), one of which is bonded to a carbon bearing oxygen, two methyl doublets (1.01, d, J=7Hz) and a one proton heptet (2.16, J=7Hz) characteristic of a vinyl isopropyl group, a doublet of doublets (3.98, J=12, 4Hz) indicative of an equatorial bromine and a vinyl proton (5.30, bd).

The lone oxygen atom is seen to be an alcohol by the ir band at 3500 cm^{-1} and cmr signal at 70.9. The tertiary nature of the alcohol is disclosed by the cmr off-resonance multiplicity (singlet) of this signal and by the failure of *l* to form an acetate with pyridine and acetic anhydride. Thus an ether linkage is excluded and the remaining ten carbons must be a carbobicyclic system. These ten carbons can be accommodated by a spiro [5.5], a bicyclo [5.3.0] or a bicyclo [4.4.0] system. An isoprenoid spiro [5.5] skeleton requires a cmr singlet near 54 ppm.[3] Since no such cmr signal is observed, the spiro system is eliminated. The bicyclo [5.3.0], exemplified by the carotane or pseudo-guiane skeleton, and the bicyclo [4.4.0], typified by the selinane or eremophilane skeleton, satisfy the pmr methyl group requirements. The carotane ring system is eliminated by a paramagnetic shift study (*vide infra*) which demonstrates the spatial proximity of the quatenary bridgehead methyl and the hydroxyl. The chemical shift of the bromomethine (δ 3.98) implies that it is not adjacent to an electronegative atom and hence, when considering the pseudo-guiane system, it must be placed on the 5-membered ring. However placement of the bromine on a 5-membered ring can not accommodate the observed coupling constants of 4 and 12 Hz. In 5-ring systems, vicinal coupling does not exceed 9 Hz.[4] The pseudo-guiane system is therefore eliminated.

Among the bicyclo [4.4.0] systems, the eremophilane skeleton can be eliminated by consideration of the bromomethine proton chemical shift (δ 3.98) and multiplicity (dd, J=4, 12Hz). It is not possible to place a tertiary hydroxyl and a bromine atom on this ring system and observe this chemical shift (*vide supra*) and multiplicity. The alternatives are now reduced to a *cis* fused (occidentalol skeleton) or *trans* fused (selinane skeleton) decalin. The cmr spectrum of *1* shows a high field methyl resonance (14.0 ppm). This signal is in agreement with the methyl chemical shift of *trans*-9-methyldecalin, 15.7 ppm, thereby excluding a *cis*-9-methyldecalin which has the angular methyl absorption at 28.2 ppm.[5a,b] The C-19 methyl resonance in steroids shows a similar shift to high field when the A/B ring juncture is *trans*.[6] Thus *1* can be assigned a selinane carbon skeleton.

The tertiary hydroxyl which is attached to a carbon bearing a methyl group requires it be attached at C-4. Support for this assignment was found in a contact shift study (*vide infra*). The allylic nature of the isopropyl methine places the olefinic bond at C-6,7 or C-7,8.

The relative sterochemistry of the C-4 hydroxyl and C-10 methyl groups is defined as follows. Treatment of *1* with excess lithium in ammonia gives a good yield of the debrominated alcohol, *2*, $[\alpha]_D$ +57.6° (c 4.325, dioxane). A paramagnetic contact shift study [Eu(fod)$_3$] of compound *2* clearly shows a rapid downfield shift of the C-4 methyl group and that the C-4 hydroxyl and the C-10 methyl are proximally located. This defines the relative sterochemistry of the C-4 and C-10 methyl groups as *trans*. Hence *1* has the same relative sterochemistry at C-4,5 and 10 as oplidiol (*3*). The isopropyl methyl absorbance was not strongly influenced by the addition of the shift reagent and excludes the rare gorgonene[7] ring system. The olefinic linkage of *2*, and hence of *1*, was located at C-7,8, rather than C-6,7, because the vinyl proton was not coupled to a proton which was paramagnetically shifted.

The absolute sterochemistry of *2* was determined by comparison of spectral data with an oplodiol degradation product. Oxidation of oplidiol *3* followed by Hauang-Minlon reduction of the resulting ketoalcohol gave an oily alcohol *4* [α] -62.1° (c 0.715, dioxane).[8] The nearly equal but opposite sign of rotation indicates that *2* is enantiomeric to the oplodiol degradation product.

The configuration of the bromine in *1* was assigned as equatorial by comparison with a similarly located bromine in oppositol[9] and Irieol A.[10] This assignment is supported by the appearance of the bromomethine proton as a doublet of doublets, δ 3.98, J=4, 12Hz. If the bromine were axial then molecular models suggest that the bromomethine signal should be a triplet because this proton bisects the angle of the adjacent methylene protons. Thus the absolute sterochemistry is as shown in *1*.[11]

Cmr chemical shift assignments are given in Table 1.

Table 1. CMR Chemical Shifts, ppm (TMS=0), CDCl$_3$

Cmpd	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C4Me	C10Me	C11Me
1	68.4	24.3	42.9	71.0	48.2	30.2	141.9	116.2	42.4	38.4	34.8	29.8	14.0	21.8,21.2
2	41.3	18.8	44.6	71.6	47.3	30.2	142.5	116.6	41.6	32.4	35.1	23.3	18.0	21.9,21.3

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