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THE STRUCTURES AND ABSOLUTE STEREOCHEMISTRY OF TWO HALOGENATED CHAMIGRENES FROM THE RED ALGA LAURENCIA MAJUSCULA HARVEY[1]

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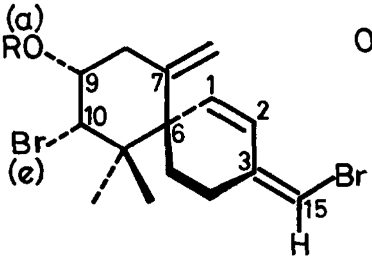
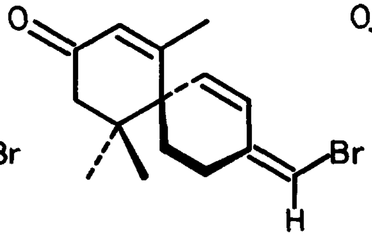
We recently reported the structures of two halogenated sesquiterpenes (1) and (2), which were isolated from the red alga Laurencia majuscula Harvey, on the basis of chemical and spectroscopic evidence.[2]

Compound 1 is a bromochamigrene derivative, having an unusual conjugated diene system among the halogenated chamigrene-type metabolites from the genus Laurencia.[3-10] As shown in structural formula 1, the configurations of the bromine at C-10, the hydroxyl group at C-9 and the double bond between C-3 and C-15 could be assigned as equatorial, axial and Z configurations, respectively. But the stereochemistry of the spiro carbon atom at C-6 remained unresolved.



1: R=H
3: R=Ac



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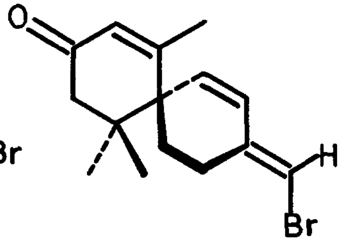

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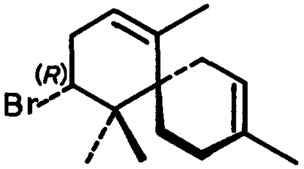

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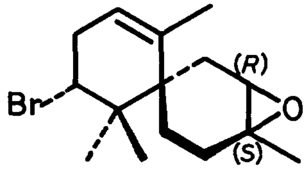

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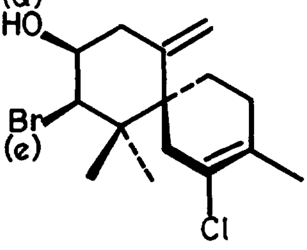

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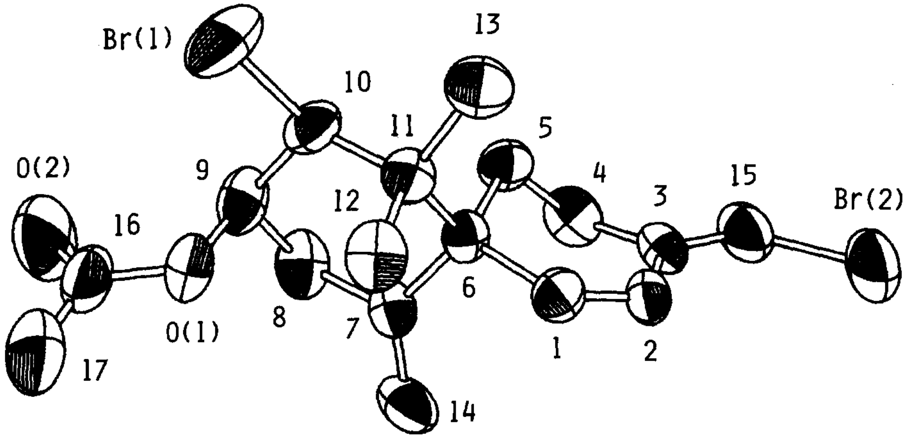

Fig. 1. A perspective view of the acetate (3) molecule.

In order to confirm the structure and establish the absolute configuration of 1, a single crystal of the acetate (3) was subjected to X-ray crystallographic analysis. Treatment of 1 with acetic anhydride in pyridine at room temperature yielded the corresponding acetate (3), mp 113-114° (recrystallized from MeOH), and the spectral data[2] of which indicate that the skeletal change did not occur during the acetylation of 1.

The crystal data of 3 are as follows: $C_{17}H_{22}O_2Br_2$; orthorhombic; space group $P2_12_12_1$; a = 10.469(3), b = 23.258(5), c = 7.367(3) Å; Z = 4, D_c = 1.548 gcm^{-3}. Intensity data with 2θ-values up to 140° were collected on a Rigaku four-circle diffractometer using CuKα radiation monochromatized with an LiF crystal. 1758 independent structure factor amplitudes greater than their estimated standard deviations were selected for the structural study. The structure was solved by the Monte Carlo direct method[11] on the basis of 504 E-values above 1.20. The 13th random phase set for the 20 strongest reflections led to the correct solution; that is, an E-map calculated with 474 phases revealed all 21 non-hydrogen atoms. After 15 of the 22 hydrogen atoms had been located in a difference Fourier map, block-diagonal-matrix least-squares refinement was repeated including these hydrogen atoms. The final R-value is 7.2%.[12]

The absolute configuration was determined by using the anomalous dispersion effects of bromine atoms for CuKα radiation. The intensity measurement was made on 60 pairs of hkl and $\bar{h}kl$ reflections having the greatest values of $||F_c(hkl)|-|F_c(\bar{h}kl)||/(|F_c(hkl)|+|F_c(\bar{h}kl)|)$. The observed and calculated Bijvoet inequalities were in good agreement with each other, thus establishing the full structure of 3 including the absolute configuration as shown in Fig. 1.

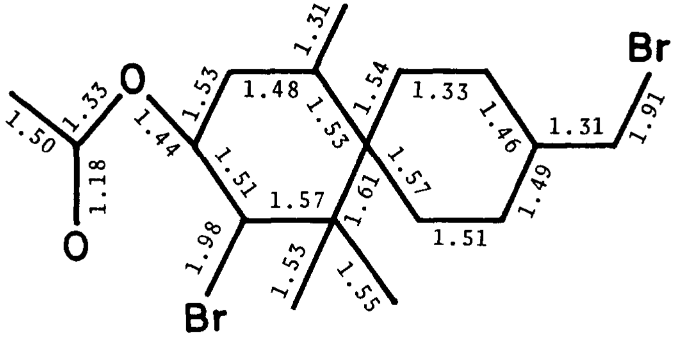

Fig. 2. Bond distances (Å). The e.s.d.'s are 0.01-0.02 Å.

The bond distances are given in Fig. 2. If their estimated standard deviations are taken into consideration, all these values are normal. The cyclohexene ring takes a nearly symmetrical half-chair form in which the C(4) and C(5) atoms deviate from the C(6)-C(1)=C(2)-C(3) plane onto the same side as the C(7) and C(11) atoms respectively. As a result of such a conformation, the C(1)=C(2) and C(3)=C(15) double bonds are not coplanar, their azimuthal angle around the C(2)-C(3) bond being 167(1)°. On the other hand, the cyclohexane ring has a somewhat flattened chair form; the C(5), C(12), and O(1) atoms are axial, while the C(1), C(13), and Br(1) atoms equatorial. This conformation makes the C(12) and O(1) atoms approach each other, their distance being 2.89(1) Å.

The acetate (3) when treated with 5% methanolic potassium hydroxide (5 min reflux) afforded the mixture of 2 and its E-isomer (4).[2] Thus the structure of natural ketone (2) is represented by formula 2, including the absolute configuration. The absolute configurations at C-6 and C-10 in 1 were consistent with those of (-)-(10R)-10-bromo-α-chamigrene (5),[8c] 10-bromo-3,4-epoxy-α-chamigrene (6)[13] and the related halo-chamigrenes from L. glandulifera Kützing.[10] In addition, the majority of the halogenated chamigrenes from the genus Laurencia have also the same absolute configuration as (-)-(10R)-10-bromo-α-chamigrene (5), which would be considered as a possible precursor of these halogenated chamigrenes.[14] However, it is interesting that a few examples with the enantiomeric absolute configuration, such as elatol (7) from L. elata[6] and L. obtusa[9a] and several halo-chamigrenes from L. obtusa[9a,9b] have been reported.

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