Tetrahedron Letters No. 26, pp 2175 - 2178, 1975. Pergamon Press. Printed in Great Britain.

(1R,2S,4S,5R)-1-BROMO-*TRANS*-2-CHLOROVINYL-4-5-DICHLORO-1,5-DIMETHYL-CYCLOHEXANE, A NEW MONOTERPENE SKELETAL TYPE FROM THE RED ALGA, *PLOCAMIUM VIOLACEUM*

Jon S. Mynderse and D. John Faulkner

Scripps Institution of Oceanography, La Jolla, California 92037

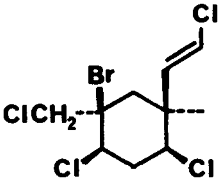
and

Janet Finer and Jon Clardy[1]

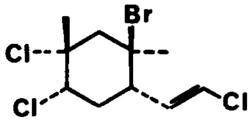
Ames Laboratory-USAEC and Department of Chemistry, Iowa State University
Ames, Iowa 50010

(Received in USA 11 April 1975; received in UK for publication 13 May 1975)

We have recently reported the occurrence of violacene (**1**) as the major constituent of the non-polar oil of *Plocamium violaceum*[2]. From the same source we have isolated a second major constituent **2**, having a new monoterpene skeleton.



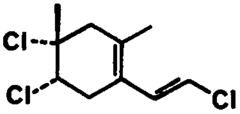
1

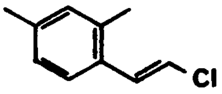


2

Repeated chromatography of the hexane extract of air-dried *P. violaceum*[3] resulted in the isolation of crystalline **2**, mp 43.5-44.5° (0.07% yield). The molecular formula, $C_{10}H_{14}BrCl_3$, was established by high resolution mass spectrometry[4]. The nmr spectrum contained two methyl singlets at δ 1.64 and 1.91 ppm and an AB quartet at 2.63 and 2.91 ppm (J = 15.0 Hz) due to the isolated methylene group. In contrast to all other halogenated monoterpenes which we have encountered[5], the olefinic proton at 6.00 ppm was coupled both to a second olefinic proton at 6.10 ppm (J = 14.0 Hz) and to an allylic proton at 2.83 ppm (J = 7.0 Hz). The proton at 1.70 was further coupled to two methylene protons at 1.99 and 2.19 ppm which were in turn coupled to each other and to a chloromethine proton at 3.81 ppm. Analysis of the coupling constants in this system indicated that the <u>trans</u> vinyl group and the chlorine were 1,3-diequatorial substituents on a cyclohexane ring.

Ozonolysis of 2, using a dimethyl sulfide workup procedure followed by alumina chromatography, gave 2,4-dimethylbenzaldehyde[6], establishing the gross carbon skeleton. The location of the halogen substituents was determined when it was shown that treatment of 2 with hydrogen chloride in carbon tetrachloride caused loss of hydrogen bromide to obtain a conjugated diene 3 (uv 245 mm). More rigorous dehydrohalogenation using lithium carbonate and lithium bromide in dimethylformamide[7] gave an aromatic vinyl chloride 4. In order to determine the stereochemistry of 2, a single crystal X-ray diffraction analysis was performed.


3


4

Crystals of 2 belong to the hexagonal crystal class with a = 18.200(5) and c = 7.395(2) Å. Systematic extinctions required space group $P6_5$ (or the enantiomorphic space group $P6_1$) and a calculated (Z = 6) and measured density of 1.50 g/cc indicated that one molecule of $C_{10}H_{14}BrCl_3$ comprised the asymmetric unit. A total of 1230 unique reflections with $\theta \leq 57^\circ$ were measured on a fully automated four circle diffractometer using an ω-scan technique and monochromated CuK_α radiation (1.5418 Å). The crystal decomposed during data collection; periodically measured standards indicated a 15% decrease. After correction for the effects of decomposition, Lorentz-polarization and background, 927 (75%) reflections were judged observed ($F_o \geq 3\sigma(F_o)$).

The structure was solved by routine application of direct methods[8], and the first three-dimensional synthesis revealed the bromine and three chlorine atoms. The remaining non-hydrogen atoms were located on subsequent electron density maps. Full-matrix least-squares refinement[9] of this model, with anisotropic temperature factors for all atoms and corrections for anomalous scattering corrections for the bromine and chlorine atoms, reduced the discrepancy index to .089. Hydrogens were added to the model to give a final discrepancy index of .083. The discrepancy index of the refined enantiomer was .084, a small but significant difference indicating the correct mirror image had been chosen at the outset[10]. A careful remeasurement of enantiomorph sensitive reflections supported this conclusion. Bond distances and angles generally agree well with accepted values, although the standard deviations are rather high, no doubt due to the effects of decomposition and a few very heavy atoms. There were no abnormally short intermolecular contacts. Figure 1 is a drawing of the final X-ray model.

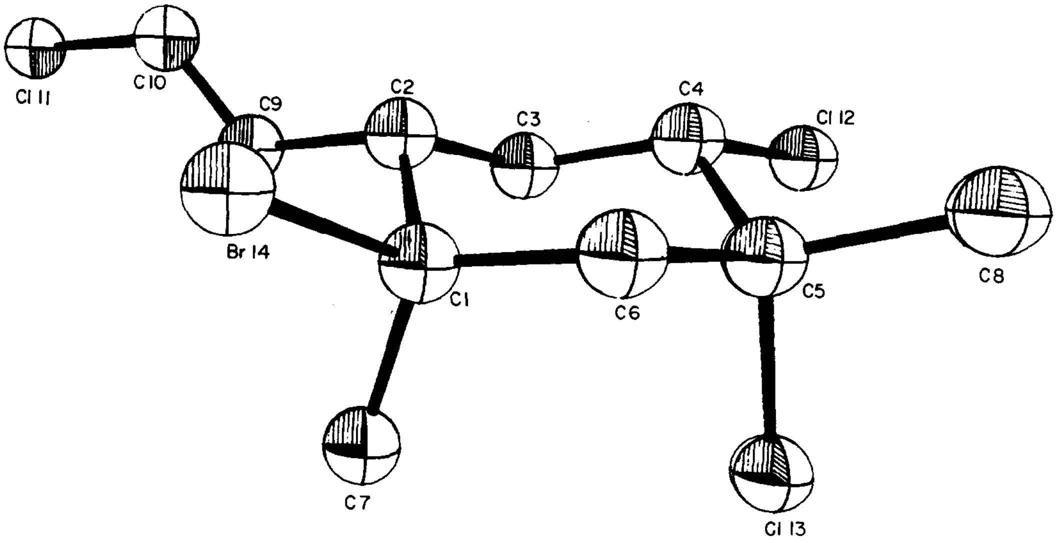


Fig. 1. A computer-generated perspective view of **2**

The unusual carbon skeleton of **2**, which deviates from the isoprene rule, can be derived biosynthetically from the carbon skeleton of violacene (**1**) through a 1,2 shift of the chlorovinyl group. However, the different patterns of halogenation seem to preclude a common biosynthetic precursor. The two species of *Plocamium* in the La Jolla area can be clearly differentiated by their chemical constituents; *P. cartilagineum* contains only linear monoterpenes, while the monocyclic monoterpenes are obtained from *P. violaceum*.

Acknowledgement

This research was supported by a grant (04-3-158-22) from the NOAA Office of Sea Grant, Department of Commerce.

References

1. Camille and Henry Dreyfus Teacher-Scholar Grant Awardee, 1972-1977, and Fellow of the Alfred P. Sloan Foundation, 1973-1975.

2. J. S. Mynderse and D. J. Faulkner, *J. Amer. Chem. Soc.*, *96*, 6771 (1974).

3. *Plocamium violaceum* was collected intertidally at Bird Rock, La Jolla, in March, 1974.

4. All new compounds reported in this paper have been fully characterized by nmr and mass spectrometry. Satisfactory high resolution mass measurements were obtained for all these substances.

5. (a) D. J. Faulkner, M. O. Stallard, J. Fayos, and J. Clardy, *J. Amer. Chem. Soc.*, *95*, 3413 (1973); (b) D. J. Faulkner and M. O. Stallard, *Tetrahedron Lett.*, 1171 (1973); (c) J. S. Mynderse and D. J. Faulkner, *Tetrahedron*, in press; (d) reference 2, above.

6. Identical in all respects with authentic material.

7. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis, Vol. 1," John Wiley and Sons, Inc., New York (1967), p. 606.

8. G. Germain, P. Main and M. M. Woolfson, *Acta Cryst.*, *B24*, 274 (1970).

9. The following library of crystallographic programs was used: C. R. Hubbard, C. O. Quicksall, and R. A. Jacobson, "The Fast Fourier Algorithm and the Programs ALFF, ALFFDP, ALFFT and FRIEDEL," USAEC Report IS-2625, Iowa State University-Institute for Atomic Research, Ames, Iowa, 1971; W. R. Busing, K. O. Martin, and H. A. Levy, "A Fortran Crystallographic Least Squares Program," USAEC Report ORNL-TM-305, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965; C. Johnson, "ORTEP, A Fortran Thermal-Ellipsoid Plot Program," U. S. Atomic Energy Commission Report ORNL-3794, Oak Ridge, Tenn., 1965.

10. W. Hamilton, *Acta Cryst.*, *18*, 502 (1965).