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PLOCAMENONE, A UNIQUE HALOGENATED MONOTERPENE FROM THE RED ALGA, PLOCAMIUM

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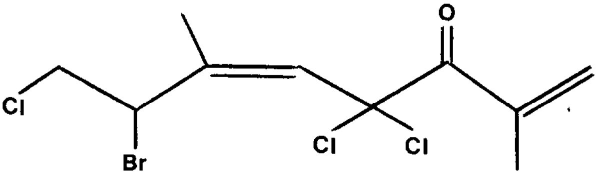
Abstract

The unique halogenated monoterpene, 7-bromo-2,6-dimethyl-4,4,8-trichloro-1,5(z)-octadiene-3-one, was isolated from the marine red alga Plocamium.

Polyhalogenated monoterpenes have been reported from several species of the genus Plocamium[1,2]. Our examination of a Plocamium species, collected off the coast of New South Wales, Australia, has revealed a new polyhalogenated monoterpene ketone, 1. Ketone 1 was isolated as the major constituent from the alga by extraction with hexane followed by silica gel chromatography.

Ketone 1 $[\alpha]_d$ = -17.3 ($CHCl_3$), (1.6% dry weight) was shown to have the formula $C_{10}H_{12}BrCl_3O$ by high resolution mass spectrometry. The presence of an unsaturated ketone was shown by the carbonyl band at 5.95μ in the IR spectrum and the absorption, $\lambda^{MeOH}_{(max.)}$ at 232 nm (log ε = 3.80), in the UV spectrum. The pmr spectrum (220 MHz, CCl_4) contained a sharp olefinic singlet at 6.18δ and a broadened, two-proton olefinic multiplet, at 6.06δ that was coupled to an olefinic methyl at 1.95δ. This indicated the partial structures



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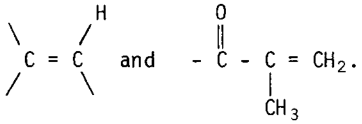
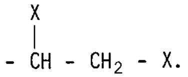


$$\begin{array}{c}\diagdown\quad\ \diagup^{H}\\ C=C\\ \diagup\quad\ \diagdown\end{array}\quad\text{and}\quad -\overset{\overset{O}{\|}}{C}-\underset{\underset{CH_3}{|}}{C}=CH_2.$$

The pmr spectrum also contained three mutually coupled doublet of doublets at 3.70 (J = 12.5, 9.4 Hz), 4.21 (J = 12.5, 3.1 Hz) and 4.35δ (J = 9.4, 3.1 Hz) indicative of the partial structure



$$-\overset{\displaystyle X}{\overset{|}{CH}} - CH_2 - X.$$

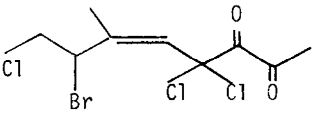
In addition, the pmr spectrum contained a methyl singlet at 1.74δ.

The cmr spectrum of ketone 1 showed four olefinic carbon atoms (141.6, s; 133.0, s; 130.9, t; 129.8 ppm, d) a quaternary carbon (68.8, s) and four additional carbons at 61.9 (d), 46.1 (t), 26.7 (q) and 16.2 (q). The ketone carbon appeared at 191.2 ppm (s) which was shifted about 10 ppm upfield from a simple unsaturated ketone. The presence of two chlorine atoms alpha to the carbonyl can explain this high field shift[3].

The placement of the single bromine atom in 1 was accomplished by consideration of the mass spectral fragmentation pattern and calculation of cmr chemical shifts. The isotopic cluster pattern at 191, 193, 195 in the low resolution EI spectrum displayed a Cl_2 pattern and indicated the loss of a C_2H_3ClBr fragment. Assuming the position of the bromine at C_7 or C_8 and using a modified Lindeman and Adams approach[4] to calculate carbon chemical shifts, the best fit was obtained by placing the bromine at C_7.

The stereochemistry of the internal double bond was deduced by consideration of the cmr chemical shifts of the methyl carbons. The upfield methyl carbon (16.2 ppm) was assigned to the enone methyl by comparison to the vinyl methyl in 3-methyl-3-butene-2-one (17.0 ppm)[5]. The downfield shift of the other methyl (26.7 ppm) indicates the Z stereochemistry for the double bond[6].

Treatment of 1 with O_3 in methanol at -78°C followed by reduction of the ozonide by catalytic hydrogenation gave selective cleavage of the disubstituted double bond to yield diketone 2. When diketone 2 was treated with o-phenylenediamine at 100°C it gave the quinoxaline 3[7].



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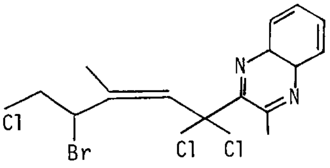

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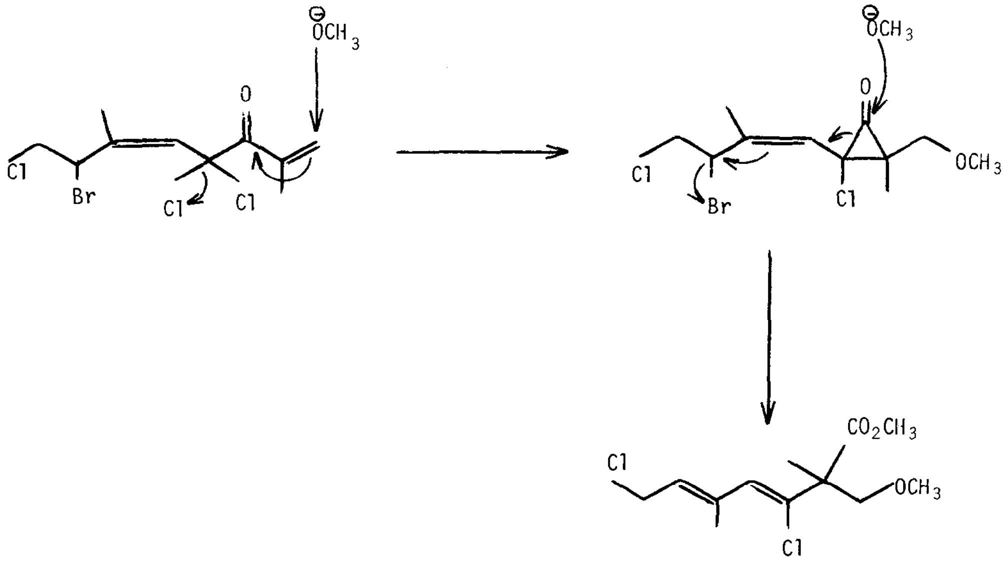
When 1 was treated with sodium methoxide in methanol for two hours an interesting rearrangement occurred. The product had a molecular formula of $C_{12}H_{18}Cl_2O_3$ and showed losses of Cl and $C_2H_3O_2$ in the EI mass spectrum. The IR (5.75μ), pmr[8] and cmr[9] spectra indicated the presence of a methyl ester, three carbons attached to oxygen and a conjugated diene (UV, $\lambda^{MeOH}_{(max.)}$ 248 nm). The structure of this rearranged product was assigned that of 4. The ketone 1 is believed to have undergone a modified Favorskii rearrangement as in the Figure.



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Plocamenone is unique in several respects to halogenated monoterpenes isolated from other Plocamium species. It contains a dichloromethylene group and a ketone, both of which are unique to plocamenone. The proximity of these two groups gives this molecule some of its interesting chemical reactivity. This may be why plocamenone has been shown to be a potent mutagen in the Ames reversion assay, much more potent than other Plocamium metabolites[10].

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References

1. W. Fenical, J. Phycol, 11, 245 (1975).
2. D. B. Stierle, R. M. Wing, and J. J. Sims, Tetrahedron Letters, 445 (1976).
3. J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, NY, page 288, 1972.
4. D. B. Stierle, Ph.D. Dissertation, University of California, Riverside, CA, page 23, 1972.
5. D. H. Marr and J. B. Stothers, Can. J. of Chem., 43, 596 (1965).
6. P. A. Couperus, A. D. H. Clague and J. P. C. M. van Dongen, Org. Mag. Res. 8, 426 (1976).
7. Pmr Spectrum (CCl_4, δ) 1.61 (s, 3H), 2.82 (s, 3H), 3.65 (dd, J = 9.0, 12.0 Hz, 1 H), 4.38 (dd, J = 2.0, 12.0 Hz, 1H), 4.77 (dd, J = 2.0, 9.0 Hz, 1H), 6.56 (s, 1H), 7.67-8.20 (m, 4H).
8. Pmr spectrum (CCl_4, δ) 1.40 (s, 3H), 1.96 (bs, 3H), 3.31 (s, 3H), 3.57 (s, 2H), 3.64 (s, 3H), 4.09 (d, J = 8 Hz, 2H), 5.57 (bt, J = 8 Hz, 1H), 6.00 (bs, 1H).
9. Cmr spectrum ($CDCl_3$, δ) 16.3, 20.5, 40.3, 52.5, 56.0, 59.6, 75.9, 128.2, 128.4, 134.2, 136.5, 173.0.

10. J. V. Leary, R. Kfir, J. J. Sims and D. W. Fullbright, Mutation Research, 68, 301 (1979). In this article plocamenone is referred to as the cross-conjugated ketone, whose structure is wrong. This paper gives the revised structure.

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