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TWO POLYHALOGENATED MONOTERPENES FROM THE RED ALGA PLOCAMIUM COSTATUM

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Several recent reports have described the isolation of a number of polyhalogenated monoterpenes from two species of the algal genus *Plocamium*[1-5]. *P.cartilagineum* yielded a series of acyclic polyhalogenated monoterpene hydrocarbons (eg. (1)) together with alcohols of which (2) is an example[1,2], while the trichloromonoterpene aldehyde (3) was derived from a different collection of the same genus[3]. The novel cyclic monoterpene (4) has been reported from *P.violaceum*[4] whereas the rearranged compound (5) has been found to co-occur with (4) in some collections of this species[5].

We now report the isolation of two new acyclic representatives from *P.costatum* collected near Port MacDonnell — South Australia. Exhaustive extraction of the freeze-dried alga with methanol, followed by concentration *in vacuo* and partition between ether and water gave ether soluble material which was separated into two major crystalline halogenated monoterpenes by chromatography on silica gel.

The less polar compound (6), for which we propose the name costatol, separated from hexane as orthorhombic prisms mp. 88-89°, $[\alpha]_D$-103° (c=1.0, $CHCl_3$) which analysed for $C_{10}H_{14}O\ Br\ Cl_3$. The ^1H n.m.r. spectrum in $CDCl_3$ showed two ABX patterns at δ5.54 (1H, d of d, J=4,9 Hz), 3.24 (1H, d of d, J=9, 15 Hz), 2.70 (1H, d of d, J=4, 15 Hz, peaks broad) and at δ4.74 (1H, d of d, J=4, 9 Hz), 3.66 (2H, m) together with a narrow multiplet at δ5.94 (1H), and a six proton broad singlet at δ1.90. The ^{13}C n.m.r. spectrum established the presence of tetra- and trisubstituted double bonds (136.0(s), 134.0(s), 129.9(s) and 115.6(d)ppm) together with two doublets at 71.3 and 56.4 ppm, two triplets at 41.4 and 37.0 ppm and two quartets at 16.2 and 14.4 ppm.

The presence of a secondary alcohol in (6) was established by Jones oxidation to give a ketone ($C_{10}H_{12}O\ Br\ Cl_3$). The ^1H n.m.r. of this compound showed one ABX system at δ5.48 (1H, d of d, J=4.5, 8 Hz), 3.30 (1H, d of d, J=15, 8 Hz) and 2.90 (1H, d of d, J=15, 4.5 Hz), a singlet at 3.98 (2H), a broad singlet at 5.89 (1H), and two three proton singlets at δ2.16 and 1.86.

The structure and absolute configuration of (6) was solved by a single crystal X-ray structure. Suitable crystals separated from hexane; crystal system:- orthorhombic, lattice type:- primitive, space group:- P 2-1 2-1 2-1 with cell constants (Angstrom and degrees) A 8.106 ($\pm$0.003), B 10.931 ($\pm$0.003), C 15.755 ($\pm$0.004); α90.00, β90.00, γ90.00. The unit cell contained four molecules and had a total volume of 1396.00 $\mathring{A}^3$. Molybdenum K- α radiation was employed with an omega -2 theta scan (0.28^o) and 1158 of the 1940 measured reflections were taken to be observed. The phase problem was solved with a multisolution method and a tangent formula refinement. The parameters of the heavier atoms were refined anisotropically, the parameters of the hydrogen atoms carried along as constants during the last cycles of refinement and atomic co-ordinates refined by block-diagonal least squares. After 14 L.S. cycles an R-value of 6.70% was found. The absolute configuration was established using the anomalous scattering by bromine and chlorine. This refinement converged at a reliability value of 6.7% being much better than that for the mirror image (8.15%).

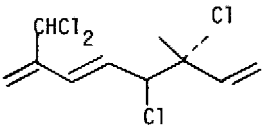
A stereodrawing of (6) is shown in Fig. 1[6] and the absolute stereochemistry (C_3: $\underline{R}$, C_7: $\underline{S}$) demanded by this drawing has been incorporated into (6).

The second more polar major metabolite (7) of *P.costatum* separated from hexane as prisms mp 70^o, $[\alpha]_D$-52.4^o (c=1, $CHCl_3$). Elemental analysis established the formula $C_{10}H_{12}O_2Br_2Cl_2$ and the 12 ev mass spectrum showed no M^+ but the base peak occurred at m/e 221, 223, 225 ($C_9H_{11}O_2Cl_2$) corresponding to the loss M^+ $-CHBr_2$. ^{1}H n.m.r. in $CHCl_3$ demonstrated the presence of an ABX system δ5.22 (1H, d of d, J=4, 10 Hz); 2.50 (2H,m), a sharp singlet at δ5.84 ($Br_2CH-\overset{O}{C}-O$), a fine quartet at δ5.94 (J=1.5 Hz), a 6 proton singlet at δ1.88 and an -OH proton at δ3.2 which was exchanged by D_2O. A ^{13}C n.m.r. spectrum of (7) established the presence of two double bonds, one trisubstituted and the other tetrasubstituted (137.1(s), 132.0(s), 125.6(s), 113.4(d) ppm). In addition two quartets (16.0, 13.8 ppm), one triplet (35.1 ppm), two doublets (67.5, 51.6 ppm) and a singlet (97.1 ppm) appeared. Therefore (7) was a monocyclic di-unsaturated monoterpene and ^{13}C n.m.r. evidence strongly supported a partial structure $-C-CH-O-\underset{C}{\overset{C}{C}}-O-$. Comparison with structure (6) and the ready loss of $-CHBr_2$ in the mass spectrum of (7) supported the proposed structure. Further evidence for this structure was obtained from the products of spontaneous decomposition of a crystalline sample of (7) when allowed to stand at room temperature in diffuse light.

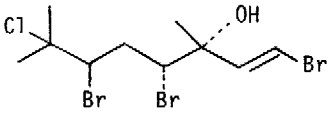
A colourless sample of (7) was found to convert to a mixture of the conjugated-enones (8) and (9) with a half life of ca. 7 days. These products were formed almost quantitatively when (7) was heated to 155^o *in vacuo* for two minutes. The mixture of (8) and (9) was separated by HPLC on silica gel. The ^{1}H n.m.r. spectral data for the major component showed signals at δ1.92, (3H,s, C_2-$\underline{Me}$); 2.30 (3H,s, C_6-$\underline{Me}$); 6.16 (1H,bs, C_1-$\underline{H}$); 6.32 (1H,s, C_8-$\underline{H}$); 6.81 (1H,d, J=14 Hz, C_4-$\underline{H}$) and 7.41 (1H,d, J=14 Hz, C_3-$\underline{H}$)), the ^{13}C n.m.r. which showed resonances (in ppm from TMS) at 188.4(s), 142.4(s), 133.5(s), 132.8(d), 130.2(s), 125.2(d), 120.6(d), 41.6(d), 18.7(q) and 17.9(q) and the u.v. spectrum (λ max 272, 327; log ϵ 4.15, 4.10).

The ^{1}H n.m.r. of the minor component showed resonances at δ1.98 (3H,s C_2-Me); 2.30 (3H,s, C_6-Me); 6.23 (1H, C_8-H); 6.35 (1H,bs, C_1-H); 6.80 (2H,s, C_3-H + C_4-H); ^{13}C n.m.r.:- 188.4(s), 142.4(s), 137.7(d), 136.7(s), 129.2(s), 125.0(d), 122.9(d), 41.6(d), 18.7(q), 13.0(q) ppm; u.v. spectrum (λ max 263, 336; log ε 4.26, 4.18). The mass spectra of (8) and (9) were almost identical and showed molecular ion clusters at m/e 374, 376, 378, 380 and the base peak cluster appeared at m/e 203, 205, 207 (M^+-$CHBr_2$). This spectral data however, does not unambiguously differentiate between structures (8) and (9) for the major component.

The stereochemistry and absolute configuration shown in (7) have been found from an independent X-ray study of this compound[7]. It is interesting to note that the absolute configuration at C_3 in (6) is R whereas in (7) it is S which suggests that (7) is formed by an S_N2 substitution of a chloro-group from a precursor similar to (6).



(1)



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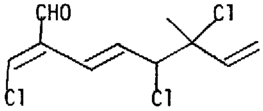

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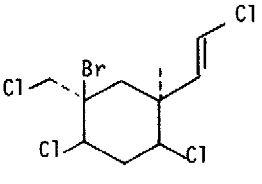

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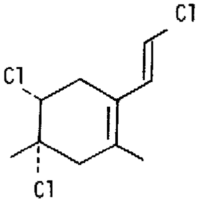
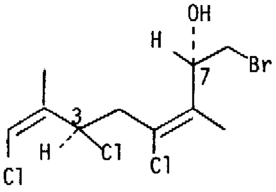
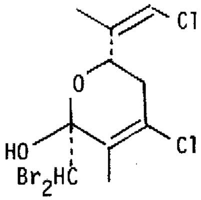


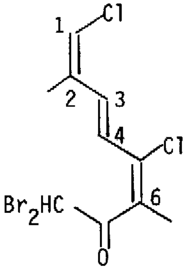
(5)



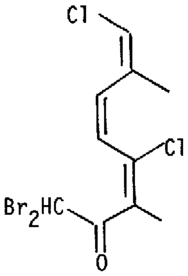
(6)



(7)

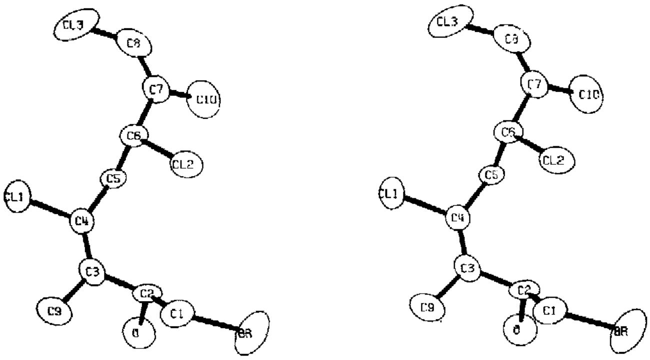


(8)



(9)

FIG 1



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