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PERFORENOL, A NEW POLYHALOGENATED SESQUITERPENE FROM *LAURENCIA PERFORATA* [1]

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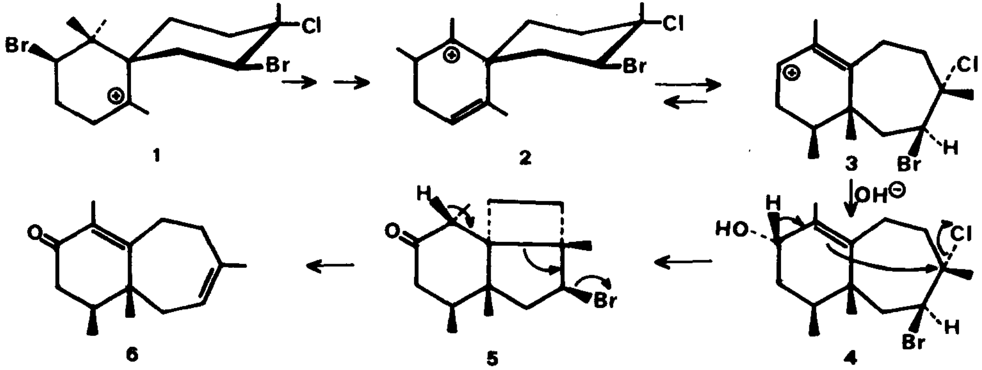
It is generally accepted that most of the varied polyhalogenated sesquiterpenes isolated from marine algae of the genus *Laurencia* are related via one common chamigrene precursor [2,3]. The biomimetically interconvertible *L perforata* metabolites perforatone (5) and perforenone (6) may possess skeletons biogenetically related to the bromochamigrene ion 1, as is shown in Scheme 1 [4]. In this sequence, the compound 4 is mooted as the possible biogenetic intermediate in both new skeletons.

To find the expected biosynthetic intermediates, frequently present as minor or less stable constituents, it is at times worthwhile to re-examine previously studied extracts. Repeated silica gel chromatography of the ether-soluble material from freshly collected *Laurencia perforata* yielded perforenol (7), mp 105-107°, $[\alpha]_D$ -107° (0.00025% of dry-weight alga). The mass spectrum of 7 has a molecular ion at m/e 412, 414, 416, 418, $C_{15}H_{23}OBr_2Cl$; ir (KBr): 3520, 3445 cm^{-1} (OH). The pmr spectrum (δ in CCl_4) shows two tertiary methyl groups (1.14 s; 1.78 s) one of which is bonded to a carbon-bearing halogen, one methyl



SCHEME 1

doublet (1.18 d J=7Hz), one methyl vinyl group (1.87 s) and signals for three protons at 4.20 (1H dd J=10,4Hz), 4.22 (1H d J=10Hz) and 4.26 (1H d J=4Hz) corresponding to hydrogens bonded to carbons bearing hydroxy and halogen atoms. Two vinyl carbons were present as shown by the signals at 139.8 and 127.9 ppm in the cmr spectrum of 7 (Table 1).

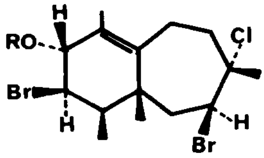
TABLE 1

CMR Chemical Shift of 7 and 8 ppm (TMS=0) $CDCl_3$

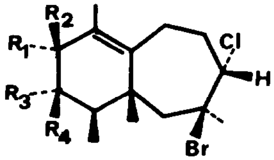
7	8	Multiplicity	Assignment	7	8	Multiplicity	Assignment
127.9	124.4	s	C-1	44.4	44.5	t	C-9
74.5	75.7	d	C-2	24.4	24.6	t	C-10
60.1	55.1	d	C-3	139.8	142.4	s	C-11
35.5	36.2	d	C-4	25.8	25.7	q	C-12
42.3	42.2	s	C-5	17.7	17.2	q	C-13
46.6	46.8	t	C-6	15.3	15.2	q	C-14
59.4	59.7	d	C-7	22.1	22.0	q	C-15
74.7	74.2	s	C-8				

7, when treated with Ac_2O/Py, gave the acetate 8 [5], which, by mild hydrolysis with K_2CO_3 in THF/H_2O produces the compounds 9 [6], 10 [7] and 11 [8], a formation easy to understand once the epoxide 12 is assumed to be a common intermediate. Treatment of 7 with 2 equiv of pyridinium chlorochromate [9] in dry methylene chloride gave 13 [10]. Reduction of 13 with Zn/AcOH in ether yielded a mixture of the partially debrominated ketone 14 [11] and perforenone (6) [12].

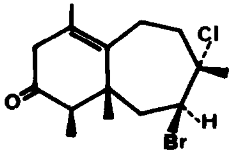
In order to establish the absolute configuration and the relative location of the halogen atoms, the colourless needles of perforenol obtained by re-crystallization from *n*-hexane were subjected to X-ray crystallographic analysis. The compound crystallizes in the monoclinic system, space group $P2_1$, 4 molecules in a cell with *a*=15.446(2), *b*=11.509(1), *c*=9.849(1)Å, *β*=99.14(1)°, D_c=1.59 g cm^{-3} and



7 R=H
8 R=Ac



9 R_1=R_4=OH R_2=R_3=H
10 R_2=R_3=OH R_1=R_4=H



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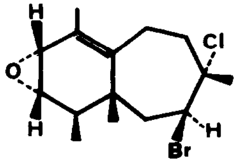

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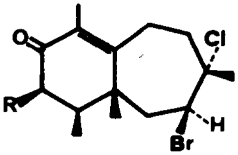

13 R=Br
14 R=H

μ(CuKα)=79.52 cm^{-1}. Two crystals were used to collect the intensity of 2696 independent Friedel pairs up to θ=60°. An automatic four-circle diffractometer with monochromated CuKα radiation was used. Both crystals showed an intensity decay of 44% in ~ 35 h experiment. The intensities of the 1100 Friedel pairs (1075 observed) from the first well-developed crystal were corrected for absorption. Only these data were used for last refinement and enantiomer discrimination. The crystal structure was solved by the heavy atom method. A mixed model, anisotropic for Br´s and Cl´s and isotropic for the rest (including fixed H atoms) was least squares refined[13] to an R_{obs} of 0.046 (0.052 for the enantiomorph). The absolute configuration shown in Figure 1 was confirmed by comparing the 30 more relevant Bijvoet pairs, which gave an averaged Bijvoet difference of 0.91 (7.903 for the enantiomorph) and an averaged Bijvoet ratio of 0.04 (0.37). The two crystallographically independent molecules show no significant differences. The seven-membered ring is α-substituted to the six-membered ring, both best planes displaying a 60° dihedral angle. The six-ring conformational model[14] provides τ_m=25.8, q=23.9°, ε_o=7° as parameters and while essentially it is chair-like it is very near to being a half-chair with δ=0. The E_1,E_2 estimators are within the margin for experimental error. The only double bond present is C_1-C_{11}=1.31(2)Å.

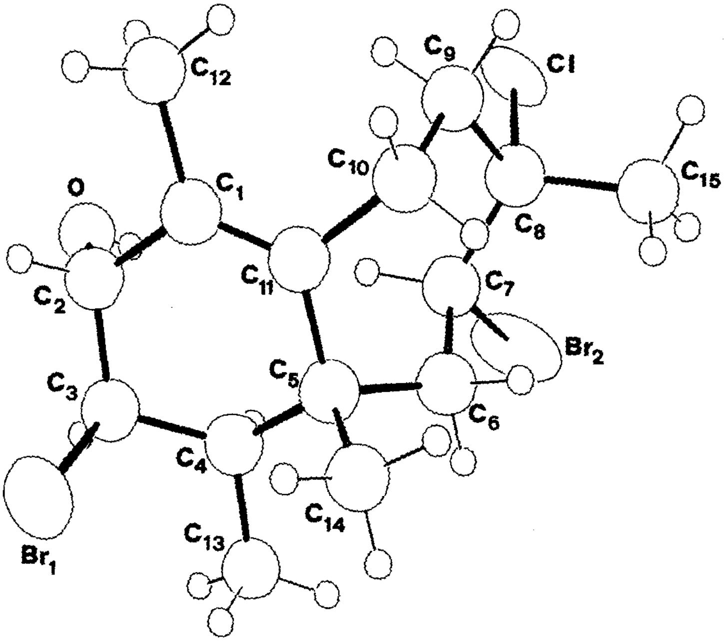

FIGURE 1

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5 Monoacetate (8): mp 75-77°, $C_{17}H_{25}O_2Br_2Cl$, M^+ at m/e 454, 456, 458, 460; ir (KBr) 1735 cm^{-1}; pmr (δ $CDCl_3$) 1.13 (3H d J=7Hz), 1.14, 1.72, 1.80, 2.13 (3H each s), 4.22 (1H dd J=10,4Hz), 4.25 (1H dd J=10,1Hz) and 5.45 (1H d J=4Hz).

6 Diol (9): mp 165-167°, $C_{15}H_{24}O_2BrCl$, M^+ at m/e 350, 352, 354; ir (KBr) 3525, 3390 cm^{-1}; pmr (δ Py-d_5) 0.80 (3H s), 1.23 (3H d J=7Hz), 1.83, 1.89 (3H each s), 3.73 (1H dd J=11,4Hz), 4.10 (1H d J=4Hz) and 4.54 (1H d J=10Hz). Diacetate of 9: mp 113-115°; pmr (δ $CDCl_3$), 0.87 (3H s), 0.93 (3H d J=7Hz), 1.64, 1.81, 2.01, 2.15 (3H each s), 4.27 (1H d J=10Hz), 4.99 (1H dd J=11,4Hz) and 5.42 (1H d J=4Hz).

7 Diol (10): mp 155-157°, $C_{15}H_{24}O_2BrCl$, M^+ at m/e 350, 352, 354; ir ($CHCl_3$) 3300 cm^{-1}; pmr (δ Py-d_5) 0.80 (3H s), 1.28 (3H d J=7Hz), 1.87, 1.91 (3H each s), 3.90 (1H dd J=12,8Hz), 4.28 (1H d J=8Hz) and 4.60 (1H d J=10Hz). Diacetate of 10: mp 182-184°; pmr 0.94 (3H s), 0.95 (3H d J=7Hz), 1.58, 1.81 (3H each s), 2.07 (6H s), 4.21 (1H d J=10Hz), 5.16 (1H dd J=12,8Hz).

8 Ketone (11): mp 143-145°, $C_{15}H_{22}OBrCl$, M^+ at m/e 332, 334, 336; ir (KBr) 1715 cm^{-1}; pmr (δ $CDCl_3$) 0.72 (3H s), 1.11 (3H d J=7Hz), 1.71, 1.86 (3H each s) and 4.39 (1H dd J=10,1Hz).

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10 (13): mp 102-103°, $C_{15}H_{21}OBr_2Cl$, M^+ at m/e 410, 412, 414, 416; uv λ_{max} 250 nm (ε 15900); ir (KBr) 1680 cm^{-1}; pmr (δ $CDCl_3$) 1.22 (3H d J=7Hz), 1.28, 1.83, 1.92 (3H each s), 4.14 (1H d J=10Hz) and 4.53 (1H d J=4Hz).

11 (14): mp 119-120°, $C_{15}H_{22}OBrCl$, M^+ at m/e 332, 334, 336; ir (CCl_4) 1670 cm^{-1}; pmr (δ $CDCl_3$) 0.98 (3H s), 1.05 (3H d J=7Hz), 1.82, 1.89 (3H each s) and 4.32 (1H d J=10Hz).

12 Compound 6 was identical with the natural sample (see ref 4).

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