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PERFORENE, A NEW HALOGENATED SESQUITERPENE FROM THE RED ALGA LAURENCIA PERFORATA [1]

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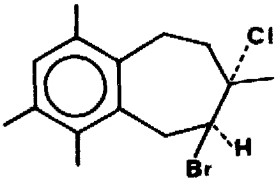
While perforatone[1] was the most plentiful of the halogenated sesquiterpenes newly isolated in our recent studies of the marine alga, Laurencia perforata, repeated silica gel column fractionation of the petroleum ether extract yielded 0.005% (based on dried seaweed weight) of a new polyhalogenated sesquiterpene, perforene, as an oil $[\alpha]_D = -3º$.

The molecular formula of perforene (1), $C_{15}H_{20}BrCl$, was established by elemental analysis and by high resolution mass spectrometry. IR spectrum ν_{max} 1470, 1450, 1380, 1120, 1075, 870 and 580 cm^{-1}. The pmr spectrum (CCl_4) indicates the presence of one aromatic proton at δ 6.80 (1H,s) and three aromatic methyl groups at δ 2.25 (6H,s) and 2.21 ppm (3H,s); perforene (1) was therefore bicyclic. The remaining pmr signals reveal a methyl at δ 1.79 (3H,s,Me-CCl-), two methylene groups at δ 2.01 (2H,m) and 2.95 ppm (2H,m,ϕ-CH_2-) and a three-signal pattern at δ 3.46 (dd,J=7,15 Hz), 3.73 (dd,J=2,15 Hz) and 4.50 ppm (dd,J=2,7 Hz), indicative of the partial structure ϕ-CH_2-$\overset{|}{C}HBr$ contained within a seven-membered ring.

Treatment of perforene (1) with Zn/AcOH gave a single hydrocarbon 9 in 95% yield. The pmr spectrum of 9 shows one olefinic methyl at δ 1.55, three aromatic methyl groups at δ 2.19, 2.22 and 2.25 ppm, four benzyl protons at δ 3.03 (2H,m) and 3.40 ppm (2H,d,J=8 Hz), one olefinic proton at 5.57 (1H,t,J=8 Hz) and one aromatic proton at 6.89 ppm (1H,s).

The structure of 9 was confirmed by synthesis. By treatment with ceric ammonium nitrate in 50% aqueous AcOH at room temperature[2], 1,2,4,5-tetramethylbenzene (2) was converted, in 75% yield, into the aldehyde 3. Lithium aluminium hydride reduction of 3 gave quantitatively the benzylic alcohol 4. The conversion to the bromide 5 was accomplished using a slight equivalent excess of PBr_3 in hexane at 0º; the bromide 5 was then used to alkylate ethyl acetoacetate, after generation of its anion with MeONa in MeOH. The crude ketoester was hydrolyzed and decarboxylated by treatment with potassium carbonate, followed by acidification, to give 6. With Wadsworth and Emmons' variant on the Wittig reaction[3], compound 6 was converted to 40:60 trans,cis α,β-unsaturated ester 7 mixture. After LAH reduction, the cis-alcohol 8 was purified by chromatographic means [pmr: δ 1.78 (3H,s), 2.13 (6H,s), 2.20 (3H,s), 3.74 (2H,d,J=7 Hz), 5.35 (1H,t, J=7 Hz), 6.75 (1H,s) and 6.80 ppm (1H,s)].

Treatment of 8 with 0.1 molar equiv of boron trifluride in dry dioxane for 15 min at room temp yielded 70% of compound 9, which was identical in all respects to the sample obtained from perforene (1).



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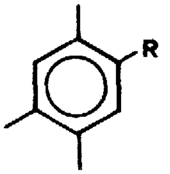
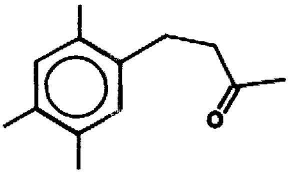


2 $R=CH_3$

3 $R=CHO$

4 $R=CH_2OH$

5 $R=CH_2Br$



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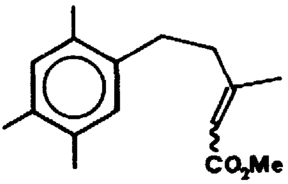

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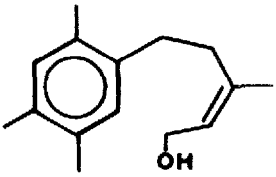

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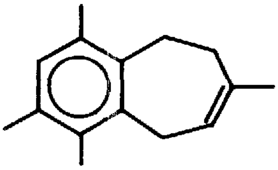
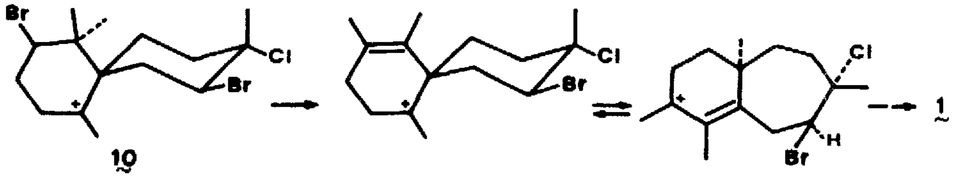


9

The carbon skeleton of perforene has not been found previously among natural sesquiterpenes. The biosynthesis of this interesting compound may be rationalized as resulting from the bromo carbenium ion 10[1] through a stereospecific pathway shown in the following scheme.



R E F E R E N C E S

1 Part XIV in the series: "Marine Natural Products from the Atlantic Zone" For Part XIII, see: A.G. González, J.M. Aguiar, J.D. Martín, and M. Norte, Tetrahedron Letters, 2499 (1975).

2 L. Syper, Tetrahedron Letters, 4493 (1966).

3 W.S. Wadsworth and W.D. Emmons, J. Amer. Chem. Soc., 83, 1733 (1961).