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THREE NEW SESQUITERPENOIDS FROM THE MARINE ALGA *LAURENCIA PERFORATA*¶.

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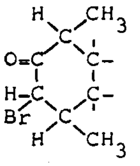
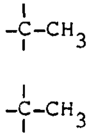
During our continuing search for constituents from marine algae, ether extracts of sun-dried *Laurencia perforata* (Rhodomelaceae), collected off Corralejos, Fuerteventura, Canary Islands, were subjected to repeated silica gel column chromatography, yielding a variety of compounds. We wish to report here on the structure elucidation of three new sesquiterpenes having new carbon skeletons, designated as perforatone (I), perforenone A (VIIa) and perforenone B (VIIb), on the basis of their spectroscopic analysis, chemical transformations and biogenetic considerations.

Perforatone (I), mp. 106-108º, $[\alpha]_D$ +186 (c, 1.58); was analyzed for $C_{15}H_{22}OBr_2$; *m/e* M^+ 380, 378, 376; M^+-Br *m/e* 299, 297; high resolution M^+-Br-HBr *m/e* 217.1593 (calcd for $C_{15}H_{21}O$, 217.1592). The ir spectrum (KBr) 1730 cm^{-1} (C=O). The nmr spectrum (100 MHz, $CDCl_3$,τ-scale) 5.92 (1H, dd, J 12 and 6Hz, $-CH_2-C\underline{H}Br-$), 6.11 (1H, d, J 12Hz, $-C\underline{H}Br-\overset{|}{C}H-$), 6.83 [1H, q, J 7Hz, $-C\underline{H}(CH_3)-$], 7.54 [1H, dd, J 13 and 6Hz, $-C\underline{H}(H)-CHBr-$]. The spectrum showed furthermore, a broad envolope from 7.7 to 8.5 arising from five protons in methylene groups and one methine proton, two secondary methyl doublets at 8.77 and 8.84 (J 7Hz, 3H each) and two tertiary methyl signals at 8.77 and 9.24 (s, 3H each).

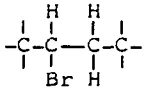
Treatment of perforatone (I) with Zn/AcOH yielded the monobromoketone II, mp. 78-80º, M^+ 300, 298, $C_{15}H_{23}OBr$; ir (CCl_4) 1722 cm^{-1} (C=O); nmr 5.87 (1H, dd, J 10 and 7Hz, $-CH_2-C\underline{H}Br-$), 7.39 [1H, q, J 7Hz, $-C(=O)-C\underline{H}(CH_3)-$], $C\underline{H}_3-\overset{|}{C}H-$ 8.92, 9.07 (d, J 7Hz, 3H each) and $CH_3-\underset{|}{\overset{|}{C}}-$ 8.93, 9.15 (s, 3H each).

Dehydrobromination of I with Li_2CO_3/LiBr/DMF afforded a conjugated ketone III, mp. 80-81º; M^+ 298, 296, $C_{15}H_{21}OBr$; uv λ_{max} 237 nm (ϵ, 11550); ir (CCl_4) 1680 cm^{-1}; nmr 4.15 [1H, s, $-C(=O)-C\underline{H}=\overset{|}{C}-$], 6.32 (1H, dd, J 12 and 6Hz, $-CH_2-C\underline{H}Br-$), 7.30 [1H, q, J 7Hz, $-C(=O)-C\underline{H}(CH_3)-$], 8.03 [3H, s, $-C(C\underline{H}_3)=CH-$], $C\underline{H}_3-\overset{|}{\underset{|}{C}}-$ 8.77, 9.00 (s, 3H each) and $C\underline{H}_3-\overset{|}{C}H-$ 8.90 (3H, d, J 7Hz). Reduction of perforatone with excess of LAH in refluxing ether yielded a complex mixture from which partially debrominated alcohols (IV,V) and the dibromo-alcohol (VI) were isolated. All these results indicate the presence of the following structural units in perforatone:

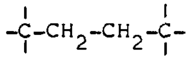




$$-\overset{|}{\underset{|}{C}}-CH_3 \qquad -\overset{|}{\underset{|}{C}}-CH_3$$



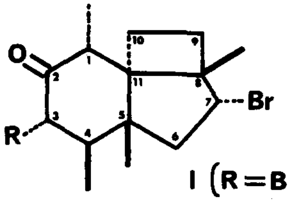
$$-\overset{|}{\underset{|}{C}}-\overset{H}{\underset{Br}{C}}-\overset{H}{\underset{H}{C}}-\overset{|}{\underset{|}{C}}-$$



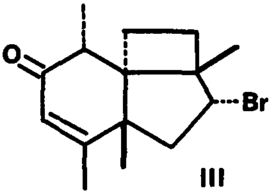
$$-\overset{|}{\underset{|}{C}}-CH_2-CH_2-\overset{|}{\underset{|}{C}}-$$

In view of the molecular formula, from where a tricyclic system is easily deduced, the afore-mentioned structural units can be conected giving the formula I as the most favorable for perforatone. The mass spectra of the isomeric alcohols IV and V showed intense peaks at m/e 274, 272 (M^+-28) and 193 (M^+-Br-28) which were probably formed by cleavage of cyclobutane ring with loss of C_2H_4. Evidence for the relative stereochemistry showed in I, could be obtained by examining the nmr spectrum of the dibromo-alcohol VI on gradual addition of $Eu(fod)_3$ shift reagent. At a concentration of 24.2 mg of $Eu(fod)_3$ for 16 mg of VI in $CDCl_3$, the nmr spectrum, H_b 3.52 (dd, J_{ba} 3Hz, J_{bc} 2Hz), H_c 4.21 (dd, J_{cd} 11Hz, J_{cb} 2Hz), H_f 5.35 (dd, $J_{fe'}$ 12Hz, J_{fe} 6Hz), H_a 6.02 (dq, J_{ab} 3Hz, J 7Hz), H_d 6.81 (dq, J_{dc} 11Hz, J 7Hz), H_e 7.45 (dd, $J_{ee'}$ 13Hz, J_{ef} 6Hz), $C_{10}(H_2)$ 7.54 (2H, m), $H_{e'}$ and $C_9(H_2)$ 7.7-7.9 (3H, m), $C_{5,8}(CH_3)$ 8.20, 8.76 (s, 3H each), and $C_{1,4}(CH_3)$ 8.07, 8.46 (d, J 7Hz, 3H each) was completely resolved so that the interrelationship of nearly all hydrogens could be established by decoupling experiments.

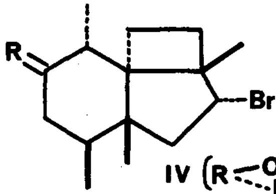
The two other compounds described here are the bicyclic conjugated ketones VIIa and VIIb. Perforenone A, VIIa, mp. 120-121º, $[\alpha]_D$ -116 (c, 1.29), was analyzed for $C_{15}H_{22}O_2$, M^+ at m/e 234; uv λ_{max} 247 nm (ϵ, 10140); ir (KBr) 3480 cm^{-1} (OH), 1665 cm^{-1} (C=O); nmr 4.75 (1H, m, $W_{1/2}$ 18Hz, $-C\underline{H}=\overset{|}{C}-$), 6.01 [1H, bd,



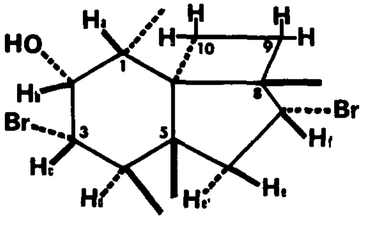
I (R=Br)
II (R=H)



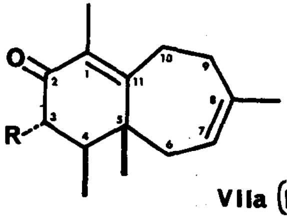
III



IV $(R\lessdot^{OH}_{H})$
V $(R\lessdot^{H}_{OH})$



VI

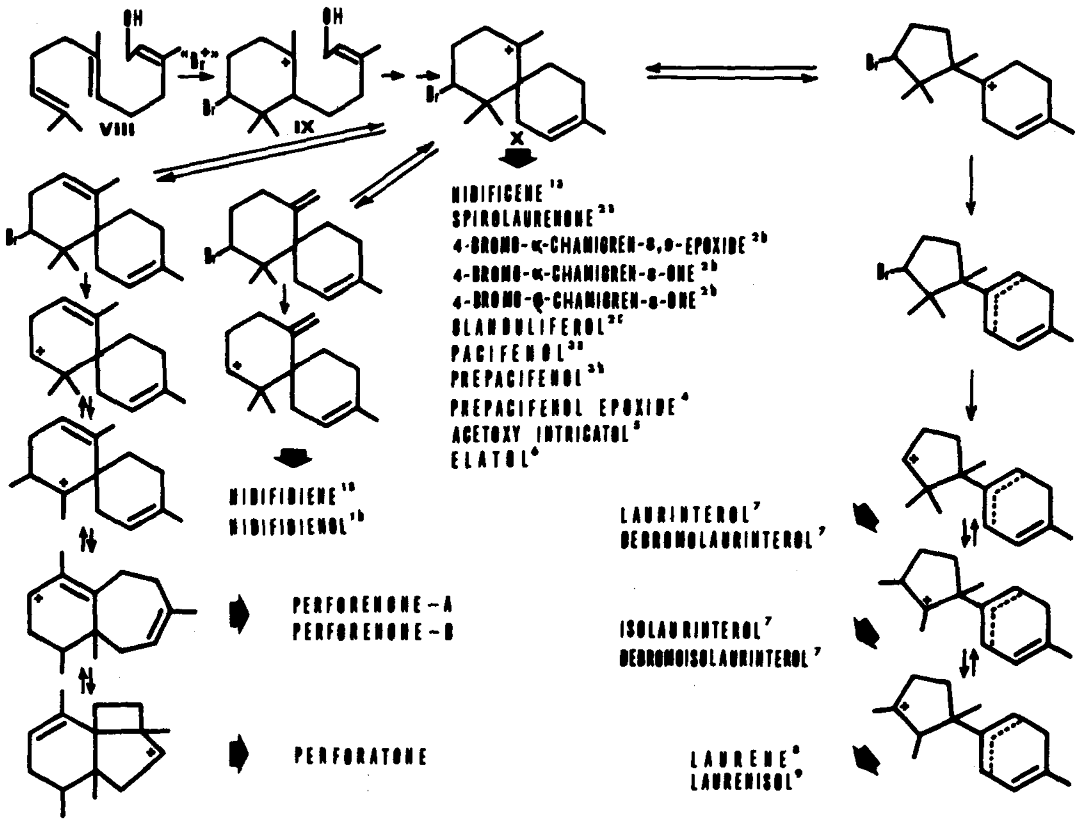


VIIa (R=OH)
VIIb (R=Cl)

J 12Hz, $-C(=O)-C\underline{H}(OH)-\overset{|}{C}H-]$, 6.30 [1H, bs, removed by shaking the sample with D_2O, the doublet at 6.01 being simultaneously sharpened, $-C(=O)-CH(O\underline{H})-\overset{|}{C}H-]$, 8.15 [3H, s, $-\overset{|}{C}=C(C\underline{H}_3)-C(=O)-]$, 8.43 (3H, bs, $C\underline{H}_3-\overset{|}{C}=\overset{|}{C}-$), 8.85 (3H, d, J 7Hz, $C\underline{H}_3-\overset{|}{C}H-$) and 8.95 (3H, s, $C\underline{H}_3-\underset{|}{\overset{|}{C}}-$). The remaining seven hydrogens appeared as a complex pattern between 7.2 and 8.0. Analysis of the $Eu(fod)_3$ induced shifts simplified the signal of the proton at C_4 which appeared as a doublet of quartets [J 12 and 7Hz, $-CH(OH)-C\underline{H}(CH_3)-]$.

Perforenone B, VIIb, mp. 190º, $[\alpha]_D$ -117 (c, 1.07), was analyzed for $C_{15}H_{21}OCl$, M^+ at m/e 254, 252, M^+-Cl 217 (base peak); uv λ_{max} 252 nm (ϵ,15700); ir (KBr) 1678 cm^{-1} (C=O); nmr 4.70 (1H, m, W½ 18Hz, $-CH=\overset{|}{C}-$), 5.60 (1H, d, J 12Hz, $-C\underline{H}Cl-\overset{|}{C}H-$), 8.14 [3H, s, $-\overset{|}{C}=C(C\underline{H}_3)-C(=O)-]$, 8.40 (3H, bs, $C\underline{H}_3-\overset{|}{C}=\overset{|}{C}-$), 8.80 (3H, d, J 7Hz, $C\underline{H}_3-\overset{|}{C}H-$), and 9.00 (3H, s, $C\underline{H}_3-\underset{|}{\overset{|}{C}}-$).

The carbon skeletons of perforatone (I) and perforenone (VII) have not been found previously among naturally occurring sesquiterpenes. Chemical interrelationship between these two novel skeletons will be discussed elsewhere together with the structure elucidation of other members of the seaweed. The biosynthesis of these interesting compounds can be rationalized as resulting from the ion X, a cyclization product of the bromo carbenium ion IX, a process which we propose in the following scheme to explain the generation of the wide variety of sesquiterpenes isolated from marine algae genus Laurencia.



Possible sequence in biosynthesis of sesquiterpenes from marine algae genus Laurencia.

R E F E R E N C E S

*Part XIII in the series "Marine Natural Products from the Atlantic Zone". For part XII see: A.G. González, J. Darias, J.D. Martín, C. Pérez, J.J. Sims, G.H.Y. Lin, and R.M. Wing, Tetrahedron, in the press.

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