

BIOMIMETIC INTERCONVERSIONS OF TWO NEW TYPES OF
METABOLITE FROM LAURENCIA PERFORATA¹

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The seaweed genus *Laurencia* is rich in many types of sesquiterpene skeletons, the more unusual of which come from the species *L Perforata*². We have reported^{3,4} the structure and stereochemistry of four sesquiterpenes, perforatone (I)⁵, perforenone-A (Va), perforenone-B (Ve) and perforene (VIII) from this alga. Other components, perforenone (IV)⁶ and perforenone-C (Vb)⁷ have now been characterized by means of chemical correlation with perforatone (I).

Our interest in the biogenesis⁸ and total synthesis of metabolites of types (I), (IV) and (V) led us to study the synthetic interconversions of the tricyclic (I) and bicyclic (IV, V) metabolites. We have observed a very high yield and possible biomimetic transformations in both directions: a) the 1,4-dehydrobromination/ring scission of (I) to (IV)(V) and b) the cation olefin cyclization(VIa) → (VII) → (II) (Scheme 1).

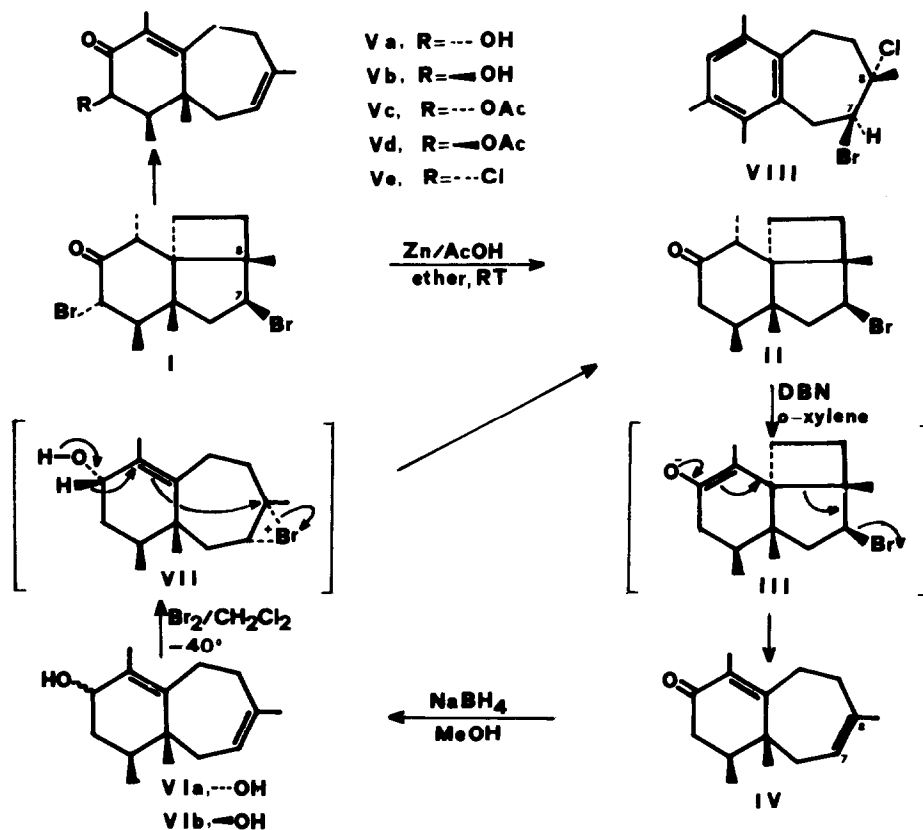
Reaction of (I) with zinc/acetic acid in ether (room temperature, 15 min) yielded debromo-perforatone (II) abundantly, as a crystalline solid³. Treatment of a hot (90°) xylene solution of (II) with slight excess of 1.5-diaza-bicyclo-4.3.0-non-5-ene (DBN) rapidly gave 97% perforenone (IV).

The α-β unsaturated ketone obtained in this fashion was identical to perforenone extracted directly from *L perforata*⁹.

(I), when treated with K₂CO₃ in THF/H₂O (reflux, 12 hr), produced a mixture of the isomeric naturally-occurring alcohols (Va) and (Vb) which may also be obtained by the action of sodium acetate/acetic acid (60°, 10 hr) on (I), followed by the chromatographic separation (silica gel/benzene) of the isomeric acetates (Vc) and (Vd) and saponification (methanolic potassium carbonate, 25°, 5 hr).

Reduction of perforenone (IV) with methanolic NaBH₄ (room temp, 2hr) afforded a plentiful mixture of the epimeric alcohols (VIa) and (VIb). Treatment of this mixture with bromine in methylene chloride (-40° to -60°) induced cyclization of the diene alcohol (VIa) to form the bromoketone (II)⁹.

The reactions and proposed mechanism for the interconversions described above are summarized in Scheme 1.

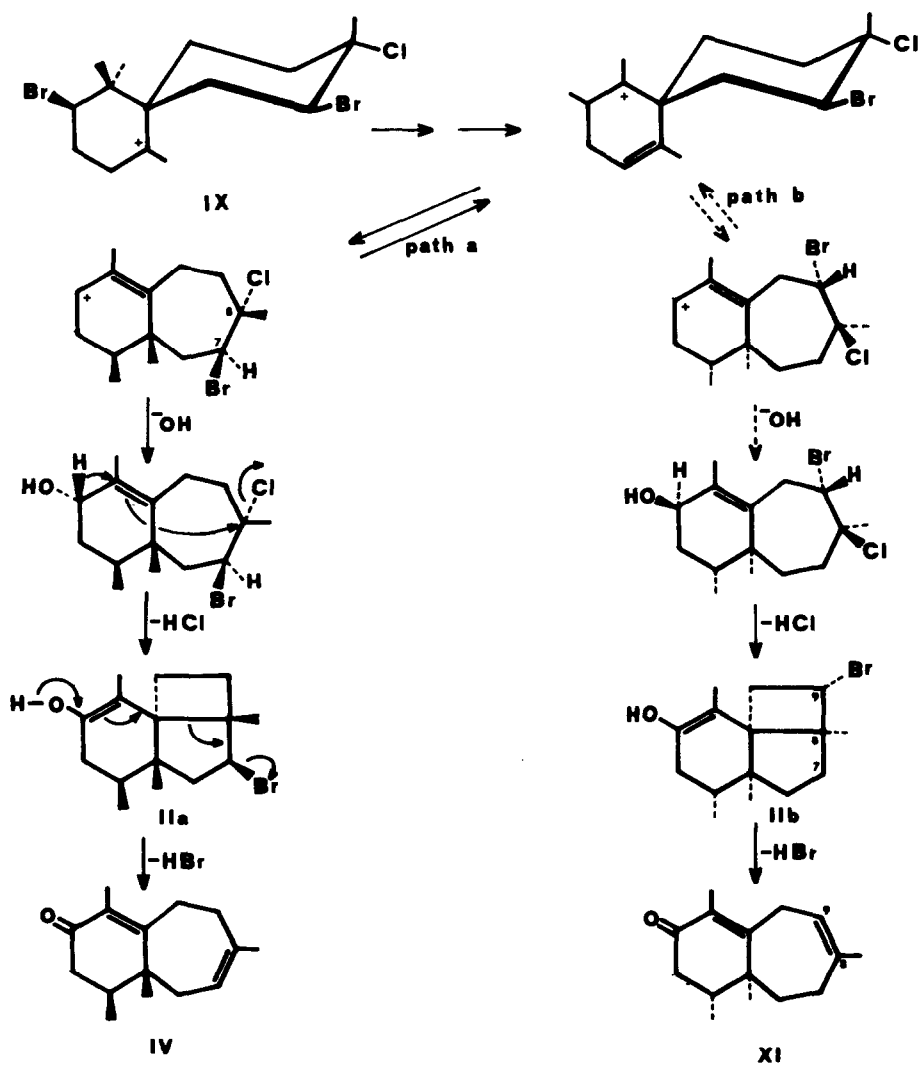


Scheme 1

The perforenones are interesting compounds from the biogenetic point of view. They are the last step in a series of biogenetic transformations involving stable and isolated intermediates such as perforatone (I). A biogenetic interpretation of the formation of the perforenone metabolites must take into account the influence of the covalent carbon-halogen bonds which may be formed by a brominated chamigrene precursor⁸ through the stages illustrated in Scheme 2 (path a).

Perforatone (I) has a bromine atom at C-7; perforene (VIII) has a bromine atom at C-7 and a chlorine atom at C-8; perforenone (IV) has a double bond between these carbons: these facts all tend to support path a as the biogenetic route for these metabolites. The alternative path b (dotted arrows, Scheme 2) via the halogenated chamigrene intermediate (IX) would lead to the perforatone skeleton (IIb) with a bromine atom at C-9 on the cyclobutane ring instead of at

C-7 on the cyclopentane ring as earlier suggested³. In view of the base-induced chemical transformation of 3-dehaloperforatone (II) to perforone (IV), (Scheme 1), we cannot discount the possibility of this sort of carbon-bond migration since the reaction mechanism involved is consistent with the bromine atom on the cyclobutane ring. Compound (XI) indistinguishable from (IV) is thus afforded. The position of the bromine atom at C-7 in the perforatone skeleton (IIa) and, also, the location of the cycloheptane double bond in perforone (IV) was definitively confirmed by the total synthesis of racemic perforone (IV)¹⁰ and the transformation in both directions of 3-dehaloperforatone (II) \leftrightarrow perforone (IV) (Scheme 1).



Scheme 2

- 1 Part 17 in the series "Marine Natural Products from the Atlantic Zone". For Part 16, see. A G González J M Arteaga J D Martín M L Rodriguez J Fayos and M Martínez-Ripolls, Phytochemistry, in press.
- 2 For a review: a) W Fenical, J Phycol 3 245-259 (1975); b) J D Martín and J Darias, in "Marine Natural Products: New Perspectives" (P J Scheuer, ed) Academic Press, New York, in press.
- 3 A G González J M Aguiar J D Martín and M Norte, Tetrahedron Letters 2499 (1975)
- 4 A G González J M Aguiar J D Martín and M L Rodriguez, Tetrahedron Letters 205 (1976)
- 5 The stereochemistry of the bromine atom at C-7 proposed as α -equatorial³ should be changed to β -equatorial in the light of the pmr spectrum at 220 MHz. The coupling constant between the geminal halogen proton and the vicinal methylene of the cyclobutane ring accords well with the new stereochemistry suggested.
- 6 Perforenone (III): oil, $[\alpha]_D -120^\circ$; was analyzed for $C_{15}H_{22}O$, M^+ at m/e 218; ir (CCl_4) 1670 cm^{-1} ; pmr δ 5.25 (1H, m, W1/2 18 Hz, $-\underline{CH}=C-$), 1.70 [3H, s, $-C=C(\underline{CH}_3)-C(=O)-$], 1.58 (3H, s, $\underline{CH}_3-C=C-$), 0.94 (3H, d, J 7Hz, \underline{CH}_3-CH-) and 0.92 (3H, s, \underline{CH}_3-C-). The remaining nine protons appeared as a complex pattern between 7.2 and 8.0.
- 7 Perforenone (IIb): mp $67-68^\circ\text{ C}$; $[\alpha]_D -29^\circ$; was analyzed for $C_{15}H_{22}O_2$, M^+ at m/e 234; ir (CCl_4) 3440 cm^{-1} (OH), 1640 cm^{-1} (C=O); pmr δ (1H, t, J 8Hz, $-\underline{CH}=C-$), 4.35 [1H, dd, J 3 and 5 Hz, $-C(=O)-\underline{CH}(\text{OH})-CH$], 3.38 [1H, d, J 3 Hz removed by shaking the sample with D_2O , $-C(=O)-\underline{CH}(\text{OH})-CH$], 1.80 (3H, s, $-C=C(\underline{CH}_3)-C(=O)-$], 1.75 (3H, bs, $\underline{CH}_3-C=C-$), 1.13 (3H, s, \underline{CH}_3-C-) and 0.85 (3H, d, J 7 Hz, \underline{CH}_3-CH-).
- 8 A G González J Darias A Díaz J D Fourneron J D Martín and C Pérez, Tetrahedron Letters 3051 (1976)
- 9 Homogeneous by tlc or pc, satisfactory ir and nmr spectra, exact ms.
- 10 Results being formulated for publication.