

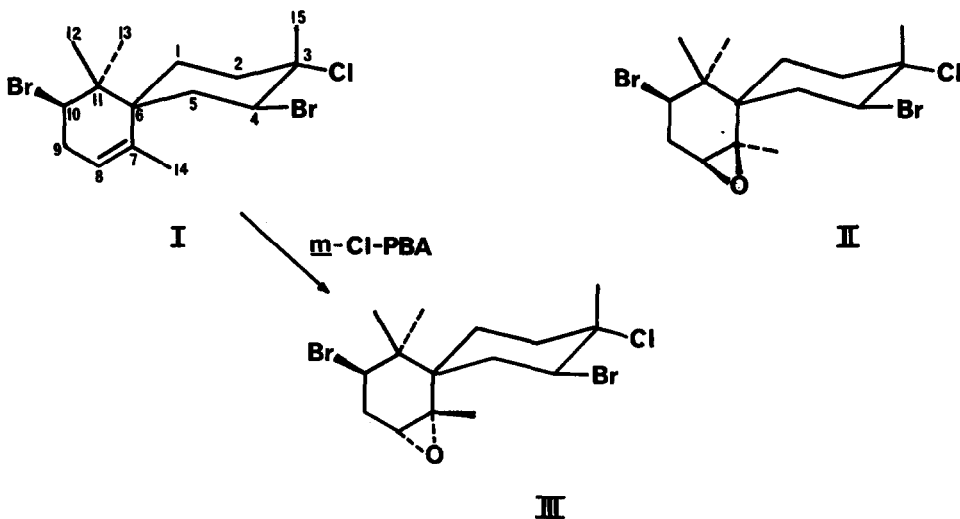
STRUCTURES AND CHEMISTRY OF TWO NEW HALOGEN-CONTAINING
CHAMIGRENE DERIVATIVES FROM LAURENCIA

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In the course of our continued chemical investigations of marine organisms from the Gulf of California, Mexico, we have recently described three new species of the halogen-metabolizing red seaweed Laurencia (Rhodomelaceae, Rhodophyta). These previously unrecognized species were readily separated and characterized chemotaxonomically by their individually unique synthesis of halogen-containing secondary metabolites. While two of these species contain the previously described molecules chondriol², rhodophytin³ and elatol^{4a}, the third alga contains a more complex mixture of undescribed compounds. We wish to report herein the structures and chemical transformations of two of the major metabolites of this alga, which are new additions to the known chamigrene derivatives from Laurencia species^{4a-h}, and which are structures interrelated by epoxide formation.

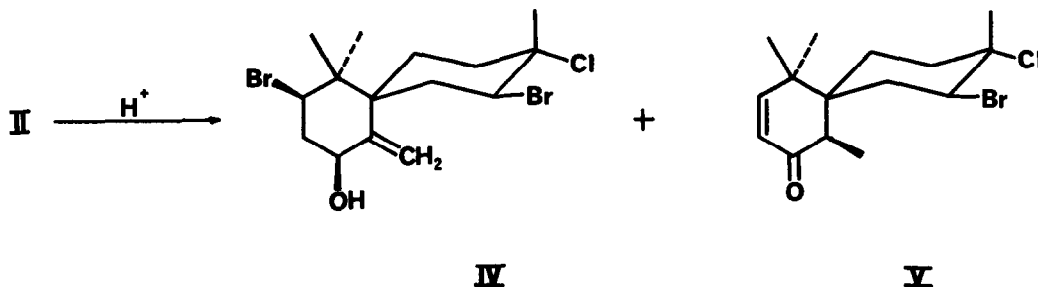
Silica gel column chromatography of the chloroform extract of the air-dried alga⁵ provided, on benzene elution, pure samples of the sesquiterpene I and the corresponding epoxide II (0.1 and 0.25% dry wt., respectively). The crystalline epoxide II, m.p. 142-4°, $[\alpha]_D^{25} + 28.2^\circ$ (c 2.3, CHCl₃), analyzed for C₁₅H₂₃OBr₂Cl by high resolution mass spectrometry (M⁺ obs. 411.9806, calc. 411.9805), and was readily assigned to structure II, based upon its spectral characteristics, particularly its 220 MHz proton nmr spectrum: δ 1.04, s (3H); 1.16, s (3H); 1.48, s (3H); 1.73, s (3H); 2.93, dd (1H) J = 3,3; 4.05, dd (1H)



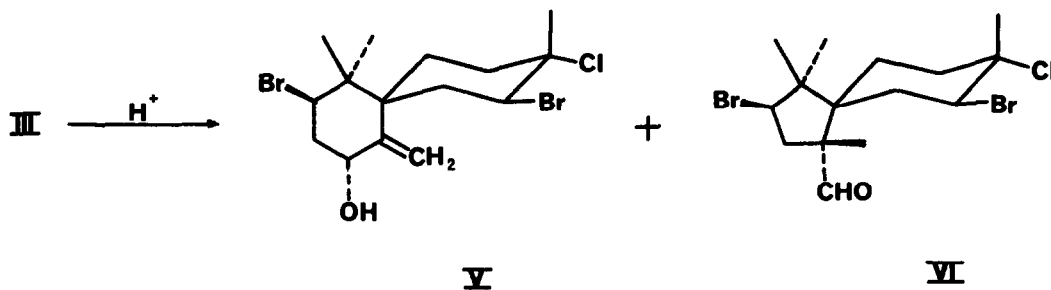
$J = 7,7$; 4.77, dd(1H) $J = 12,5$; 1.70-2.75, m(8H). The olefin I, related to nidificene^{4d} via a double bond migration, showed similar nmr bands: δ 0.89, s(3H); 1.16, s(3H); 1.61, s(3H); 1.95, s(3H); 4.39, dd(1H) $J = 12,6$; 4.75, dd(1H) $J = 8,8$; 5.16, bs(1H); 1.80-2.75, m(8H). The coupling constants for the lone protons on C-4 for both metabolites, $J = 12,5$ Hz for I and 12,6 Hz for II, were consistent with predictable equatorial bromine atoms and, hence, axial hydrogens in each metabolite⁶. The chemical shifts of these protons, as well as those noted for the C-15 methyl groups, indicated the assigned locations for bromine and chlorine, rather than the reversed situation observed in isocaespitol⁷.

Treatment of I with *m*-chloroperbenzoic acid in refluxing chloroform, in an attempt to generate II, resulted instead in a quantitative yield of the geometrically isomeric epoxide III. While the nmr spectra of these epoxides gave much structural information, the stereochemistry of the 7,8-epoxide function relative to the C-10 bromine substituent was not obvious, based upon the coupling constants of the protons at these respective centers. Fortunately, ring opening reactions of these epoxides gave epimeric allylic alcohols whose nmr spectra confirmed both the positions of these substituents and their relative stereochemistries.

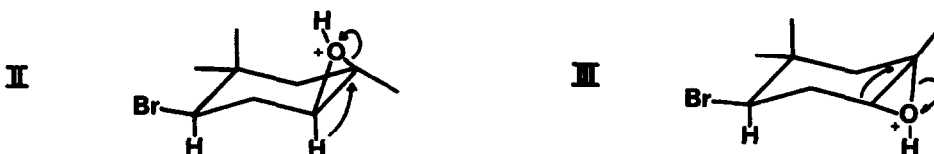
Treatment of II with p-toluenesulfonic acid in benzene provided the allylic alcohol IV and the cyclohexenone V in a 2/1 ratio. The structure of IV was readily determined by examination of the 220 MHz nmr of its corresponding



acetate ester. The nmr band of the α to hydroxyl proton at C-8, recognized via acetylation at δ 5.17 in the acetate, clearly gave coupling constants typical for an axial hydrogen, dd, $J = 12,5$ Hz. Since both substituents are equatorial in the ring open product IV, they are by necessity cis oriented in the natural epoxide II. Analogous ring opening of the synthetic epoxide III gave the epimeric alcohol VI and the ring contracted aldehyde VII in high yield. The α to hydroxyl proton in this epimer, recognized via acetylation at δ 5.36 in the nmr spectrum of the acetate, was confirmed equatorial by its coupling constants, dd, $J = 3,3$ Hz. Since the bromine substituent is equatorial and the alcohol function is axial, the relative stereochemistry in the synthetic epoxide must be trans.



The stereoselective formation of the cyclohexenone V and the aldehyde VII from the acid catalyzed opening of II and III strongly supports their assigned stereochemistries. Epoxide protonation yields a facile leaving group at C-7. In II, a proton is geometrically favored (anti-oriented) to migrate to the developing carbonium ion. In III, the anti-oriented group is carbon-9, and



migration yields the stereospecific aldehyde VII. An analogous situation is well known in the deamination reactions of the conformationally rigid epimers of 4-t-butyl-2-aminocyclohexanol⁸.

Acknowledgement

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References

1. W. Fenical and J. N. Norris, *J. Phycology* **11**, 106 (1975).
2. W. Fenical, K. B. Gifkins and J. Clardy, *Tetrahedron Lett.*, 1507 (1974).
3. W. Fenical, *J. Amer. Chem. Soc.* **96**, 5580 (1974).
4. (a) J. J. Sims, G. H. Y. Lin, and R. M. Wing, *Tetrahedron Lett.*, 3487 (1975). (b) J. J. Sims, W. Fenical, R. M. Wing and P. Radlick, *J. Amer. Chem. Soc.* **95**, 972 (1973). (c) M. Suzuki, E. Kurosawa and T. Irie, *Tetrahedron Lett.*, 4995 (1974). (d) S. M. Waraszkiewicz and K. L. Erickson, *Tetrahedron Lett.* 2003 (1974). (e) M. Suzuki, E. Kurosawa and T. Irie, *Tetrahedron Lett.*, 821 (1974). (f) D. J. Faulkner, M. O. Stallard and C. Ireland, *Tetrahedron Lett.*, 3571 (1974). (g) J. A. McMillan, I. E. Paul, R. H. White and L. P. Hager, *Tetrahedron Lett.*, 2039 (1974). (h) S. M. Waraszkiewicz and K. L. Erickson, *Tetrahedron Lett.*, 281 (1975).
5. Collected April 1974, Isla Angel de la Guarda, Golfo de California, Mexico.
6. D. J. Pasto and C. R. Johnson, "Organic Structure Determination," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1969.
7. A. G. González, J. Darias and J. D. Martín, *Tetrahedron Lett.*, 1249 (1974).
8. M. Chérest, H. Felkin, J. Sicher, F. Šipoš and M. Tichý, *J. Chem. Soc.*, **1965**, 2513.