Phytochemistry, 1976, Vol. 15, pp. 511–512. Pergamon Press. Printed in England.

CHEMICAL VARIATION IN A NEW BROMOCHAMIGRENE DERIVATIVE FROM THE RED SEAWEED *LAURENCIA PACIFICA*

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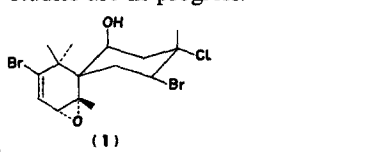
(*Received* 13 *August* 1975)

Key Word Index—*Laurencia pacifica*; Rhodophyta; red seaweed; bromochamigrene derivatives; geographical variation.

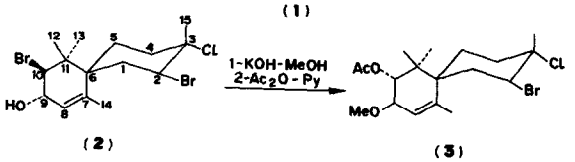
Abstract—The secondary metabolite chemistry of the red seaweed *Laurencia pacifica* Kylin varies geographically. The La Jolla, Calif. population (type locality) contains the sesquiterpene prepacifenol, while *L. pacifica* collected south of Ensenada, Mexico contains a new bromochamigrene derivative, the structure of which is described herein. Since chamigrene synthesis in *Laurencia* species has been demonstrated to be reasonably species-specific, *L. pacifica* may be a mixture of morphologically similar forms.

INTRODUCTION

The red seaweed *Laurencia pacifica* Kylin is distributed along the California coast from the Monterey Bay area in northern California, south to the Baja California peninsula. While *L. pacifica* was originally considered also to occur in the Gulf of California, we have recently shown that the gulf species is a mixture of three entities, none of which agree chemically with plants from the type locality [1]. Studies of the natural products chemistry of *Laurencia* species point out that this interesting genus is capable of the synthesis of halogenated sesquiterpenes, diterpenes and non-terpenoid acetylene-containing compounds [2]. The most interesting feature of this diverse biosynthesis is that it appears to be reasonably species-specific. While some synthetic consistencies exist between different species, most *Laurencia* species synthesize a characteristic metabolite not widely distributed within the genus. In a previous publication, we described the structure of prepacifenol, (**1**) a trihalochamigrene derivative characteristic of *L. pacifica* collected in La Jolla, California [3]. In my continuing study of the chemistry of this species, variable results have been obtained from collections in a number of locales. Reported herein are the details of a structure elucidation of a new metabolite from *L. pacifica* collected near Ensenada, Mexico. Since these chemical results question the purity of this species, detailed taxonomic studies are in progress.



(**1**)



(**2**) (**3**)

RESULTS AND DISCUSSION

Samples identified as *L. pacifica* Kylin [4] were collected during a low tide period in August 1974, air-dried and ultimately chloroform extracted. Chromatography of the crude extract gave samples of isolaurinterol [5], an unknown aromatic ether, and a new sesquiterpene alcohol, (**2**). The alcohol $[\alpha]_D^{25}$ 11·2° (*c* 2·35, $CHCl_3$) mp 120–1° (light petrol–C_6H_6) analyzed for $C_{15}H_{23}OBr_2Cl$ by high resolution mass spectrometry (Calc. M^+ 417·9736, measured 417·9740), showed only end absorption in the UV but showed characteristic IR absorptions at 3550, 3400 cm^{-1} (hydroxyl); and 1660 cm^{-1} (unsaturation). Interpretation of the 220 MHz NMR spectrum of this metabolite clearly showed the relationship of **2** to a number of chamigrene derivatives, in particular nidificene [6]. The spectrum consisted of a broad olefin band at δ 5·43 (1H), a one proton four line band at δ 4·89 (*J* 11·5 Hz), a sharp one proton doublet at δ 4·36 (*J* 8 Hz), a broadened one proton multiplet at δ 4·30 (*J* 8, ~1, ~1 Hz) and multiple ring protons from δ 1·70–2·5. Four methyl signals were easily recognized at δ 2·02 (doublet, *J* 1 Hz, olefin substituted), δ 1·69 (adjacent to chlorine), 1·20 and 0·96 δ (gem dimethyl). As is usually observed in these derivatives, a bromine in proximity to the gem dimethyl group results in a 0·25 ppm shift to lower field of the more eclipsed methyl.

A consideration of these spectral data with known *Laurencia* metabolites allowed partial structural features to be proposed. However, the relative positions of hydroxyl, bromine and olefin components were less secure. Jones' oxidation of **2** gave a high yield of an unsaturated ketone, ($\nu_{c=0}$ = 1680 cm^{-1}) which fixed the position of hydroxyl relative to other substituents. Hydrogenation of **2** with platinum in ether gave quantitatively the saturated halohydrin, the structure of which could be readily studied by high resolution NMR. Specifically, the relative stereochemistry of the vicinal halohydrin function could be obtained by an interpretation of the coupling constants of the deshielded protons on C-9and C-10. The proton α to bromine on C-10 appeared as an expected doublet, *J* 12 Hz, which can only result from axial-axial coupling with the lone proton on C-9. Since both protons are axial, both substituents are equitorial and therefore *trans* in cyclohexane systems. In an attempt to induce epoxide formation, **2** was treated with warm 10%

KOH in methanol. Under these conditions, the first formed epoxide quickly incorporated methanol to yield, after acetylation, the methoxy acetate **3**. A careful study of the free alcohol and its acetate by NMR allowed the stereochemistry of this derivative to be compared to the natural product **2**. The α to acetate proton on C-10 was observed as a doublet at δ 5·29. The coupling was identical (8 Hz) to the analogous situation in **2**; hence, both substituents are predicted to be equitorial. Considering the mechanism of nucleophilic epoxide displacement reactions, the stereochemistry of the substituents on C-9 and C-10 in **2** and **3** must be inverted.

Repetitive studies on the natural products of *L. pacifica* Kylin collected from the type locality in La Jolla, California have shown a consistent synthesis of large amounts of laurinterol and prepacifenol, accompanied by smaller quantities of johnstonol. Since these metabolites are rarely found in extracts of the alga under consideration here, and since a new bromochamigrene derivative, **2**, is the major lipid metabolite, the integrity of this species must be questioned. A detailed study of *L. pacifica* Kylin populations throughout its distributional range, considering morphological, anatomical and chemical features, is in progress.

EXPERIMENTAL

Isolation of **2**. 2·7 kg air dried *Laurencia pacifica* (collected near Ensenada, Mexico, 9-14-74) was powdered to 1 mm with a Wiley mill and Soxhlet extracted with $CHCl_3$. Removal of the solvent left 115 g of crude extract. A 30 g aliquot was chromatographed on a column (4 × 30 cm) of Davison grade 62 Si gel, eluting sequentially with various proportions of light petroleum, C_nH_n, Et_2O and MeOH. Pure benzene eluted mixtures of isolaurinterol [5] and an unknown aromatic ether, while 5% Et_2O in C_6H_6 gave **2** (3·5 g, 0·5% dry wt.); Crystallization from light petrol–C_6H_6 gave white needles, mp 120–1°. Compound **2** had the following spectral characteristics not reported in the text: IR $\nu_{max}^{CHCl_3}$ 3550, 3400, 1660, 1475, 1440, 1400, 1380, 1320, 1235, 1190, 1170, 1145, 1120, 1080, 1055, 1025, 1010, 990, 938, 920, 881, and 850 cm^{-1}; MS *m/e* (rel. intensity > 10% only) 41(54) 43(24) 53(39) 55(92) 59(16) 65(16) 67(17) 69(23) 71(11) 77(24) 79(24) 83(87) 84(34) 91(33) 93(28) 95(11) 105(32) 107(21) 109(14) 111(11) 119(100) 120(18) 121(19) 128(12) 129(18) 131(18) 133(18) 136(41) 143(11) 145(18) 149(18) 151(17) 157(16) 162(78) 164(76) 199(10) 217(19) 250(36) 252(47) 254(12) 333(20) 335(26) 399(<1) 401(<1) 403(<1) 412(<0·5) 414(<0·5) 416(<0·5) 418(<0·5).

Oxidation of **2**. In cold (0°) acetone by dropwise addition of Jones' reagent (CrO_3–H_2SO_4, acetone-water) afforded a light yellow oil (35 mg). The product ketone, M^+ 410/412/414/416 ($C_{15}H_{21}OBr_2Cl$) showed the following spectral characteristics IR $\nu_{max}^{CCl_4}$ 2960, 1680, 1620, 1460, 1395, 1380, 1325, 1310, 1280, 1255, 1215, 1170, 1115, 1080, 990 970 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 6·0 (*s*, 1H), 4·95 (*s*, 1H), 4·85 (*m*, 1H), 2·29 (*s*, 3H), 1·73 (*s*, 3H), 1·34 (*s*, 3H), 1·02 (*s*, 3H), 1·7–2·5 (multiple, 6H).

Hydrogenation of **2**. In Et_2O with Pt_2O–H_2 for 24 hr, gave a light colorless oil. The MS of this product indicated hydrogenation had occurred (M^+—414/416/418/420 for $C_{15}H_{25}OBr_2Cl$). The NMR spectrum (220 MHz, CCl_4) consisted of bands centered at δ 4·30 (4 lines, *J* 12, 4 Hz, 1H), 4·09 (*d*, *J* 12 Hz, 1H) 3·82 (*m*, *J* 12, 12, 5 Hz, 1H) 1·68 (*s*, 3H), 1·25 (*d*, 5 7 Hz, 1H), 1·16 (*s*, 3H), 1·09 (*s*, 3H), 1·6–2·5 (multiple bands, 10H).

Base treatment of **2**. With warm (40°) 10% KOH in anhydrous MeOH for 2 days. Gave the methoxy alcohol, (M^+ 364/366/368 for $C_{16}H_{26}O_2BrCl$) acetylation of which (Ac_2O–pyridine) gave the methoxy acetate (**3**) in quantitative yield. A comparison of the 220 NMR spectra of reactant and acetate product showed that acetylation resulted in a ~1 ppm low field shift of a clean doublet (*J* 7 Hz) located at δ 5·22 in the acetate. The remainder of the NMR spectrum of **3** consisted of the following: δ 5·50 (*s*, 1H), 5·14 (4 lines, *J* 13, 5 Hz, 1H), 3·71 (*bs*, 1H), 3·32 (*s*, 3H), 2·09 (*s*, 3H), 2·02 (*s*, 3H), 1·78 (*s*, 3H), 0·95 (*s*, 3H), 0·89 (*s*, 3H) 1·5–2·5 (multiple bands, 6H).

Acknowledgement—The author is grateful for the close guidance of Dr. J. N. Norris, Smithsonian Institution, in taxonomic studies of *Laurencia* species. Support of this research by the National Science Foundation under grant DES 75-03824 is gratefully acknowledged.

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