Tetrahedron Letters No. 23, pp 2003 - 2006, 1974. Pergamon Press. Printed in Great Britain.

HALOGENATED SESQUITERPENOIDS FROM THE HAWAIIAN MARINE ALGA *LAURENCIA NIDIFICA*: NIDIFICENE AND NIDIFIDIENE

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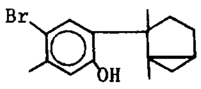
(Received in USA 3 April 1974; received in UK for publication 29 April 1974)

The algae of the marine genus *Laurencia* are currently enjoying phenomenal popularity due to their prolific elaboration of unusual halogenated sesquiterpenoid and C_{15} non-terpenoid structures.[1-9] During an antimicrobial screening study of Hawaiian marine algae, we noted marked activity was displayed against *Staphylococcus aureus* and *Mycobacterium smegmatis* by methanol-ether extracts of *Laurencia nidifica*. Accordingly, we initiated an investigation of the chemical composition of this species.

The alga was collected off Kahala Reef on the island of Oahu, Hawaii, during January and the summer of 1973. It was cleaned and homogenized to an aqueous paste. The filtered algal mass was extracted with methanol for several days, followed by ether. Concentration of the extracts gave a green-brown oil (0.4% fresh weight of alga).

The antimicrobial material was the major compenent of the extract (30%) and could be isolated by silica gel chromatography with benzene. Its identity was established as laurinterol (1) by comparison of its physical and spectral properties with those published.[10] The potent antimicrobial activity of laurinterol against *S. aureus* has previously been observed.[11] In addition to this known compound, we have also found substantially smaller amounts of aplysin (2)[12] and pacifenol (3)[5,13] in the *L. nidifica* extract.



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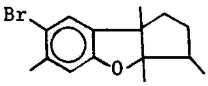

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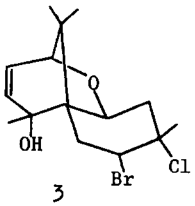

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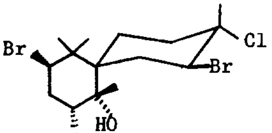
The 1:1 n-hexane-benzene eluant of the original extract (7%), on repeated tlc, gave two new compounds, nidificene (0.06% dry weight of alga) and nidifidiene (0.08% dry weight of alga) as colorless oils that slowly crystallized on standing. These two compounds are shown below to belong to the caespitol (4)[4] skeletal class.

Nidificene (5) analyzed for $C_{15}H_{23}Br_2Cl$ by mass spectroscopy: m/e M+ 402, 400, 398, 396;

high resolution m/e 397.98790 (calcd for $C_{15}H_{23}Br^{79}Br^{81}Cl^{35}$, 397.98346). The ir spectrum (CCl_4) displayed 3120, 3000, 2900, 1640, 1450, 1395, 1385, 1350, 1305, 1200, 1165, 1100, 1065, 915, and 870 cm^{-1}, indicating the presence of an exocyclic vinyl group. The pmr spectrum ($CDCl_3$) showed three methyl singlets at 1.06, 1.20, and 1.77 δ, the vinyl hydrogens as two broad singlets at 4.97 and 5.36 δ, and the bromomethine hydrogens as two overlapping multiplets centered at 4.67 δ. The remaining ten hydrogens appeared as a complex pattern between 1.83 and 2.50 δ. In CCl_4 the bromomethine signals were clearly visible as two overlapping doublets of doublets. The J values were the same for each set, 5 and 12 Hz, indicative of an axial-axial and an axial-equatorial coupling in each case consistent with the proposed structure (5).



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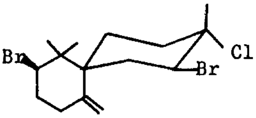

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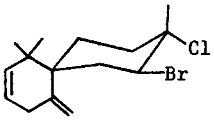
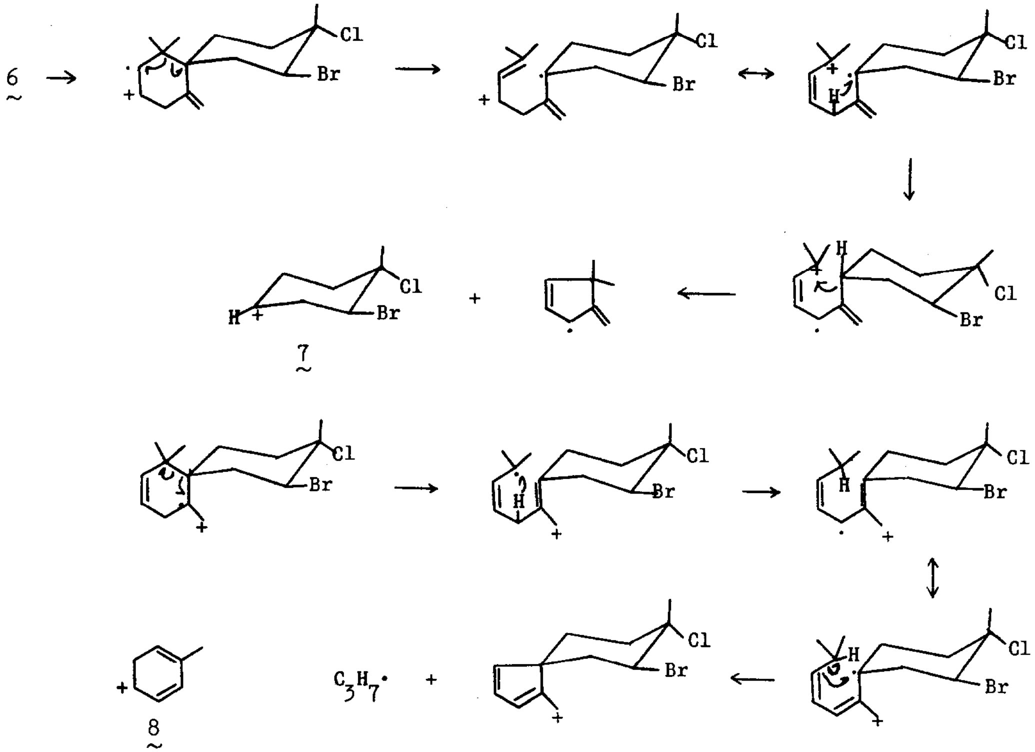


6

Nidifidiene (6) analyzed for $C_{15}H_{22}BrCl$ by mass spectroscopy: m/e M^+ 322, 320, 318, 316; high resolution m/e 316.06056 (calcd for $C_{15}H_{22}Br^{79}Cl^{35}$, 316.05933). Its ir spectrum (CCl_4) displayed 3120, 3045, 3000, 2900, 1640, 1655, 1455, 1440, 1395, 1385, 1370, 1350, 1305, 1260, 1210, 1150, 1100, 1065, 1010, 910, and 870 cm^{-1}, again indicative of an exocyclic vinyl group. The pmr spectrum ($CDCl_3$) showed three methyl groups: a 6-H singlet at 0.97 and a 3-H singlet at 1.75 δ. The olefinic region was complex with one of the exocyclic vinyl hydrogens appearing as a broad singlet at 4.95 δ and the remaining three vinyl hydrogens as overlapping multiplets centered at 5.42 δ. A 1-H multiplet at 4.67 δ was assigned to the bromomethine and a 2-H multiplet at 2.80 δ to the diallylic hydrogens of a methylene group. The remaining six hydrogens appeared as a complex pattern between 1.97 and 2.50 δ. Irradiation of the diallylic methylene protons at 2.80 δ greatly simplified the olefinic region of the spectrum. The exocyclic vinyl hydrogens appeared as singlets at 4.95 and 5.30 δ while the endocyclic double bond hydrogens appeared as two resolved doublets centered at 5.27 and 5.55 δ with J values of 10 Hz.

In the mass spectra, both nidificene (5) and nidifidiene (6) show loss of C_3H_7 as well as the expected loss of CH_3, Br, Cl, HBr, and HCl. The basic C_{15} hydrocarbon skeleton is seen at m/e 202 and 201 following complete halide loss. Nidifidiene, but not nidificene, shows a series of peaks at m/e 213, 211, and 209 corresponding to ion 7. One of several possible routes to this ion and to C_3H_7 loss is outlined below for nidifidiene. Both compounds show a C_7H_9 fragment (8) with its intensity being much greater for 6 than for 5.

In addition to the compounds described herein, there are further halogenated sesquiterpenoids present in the L. nidifica extract. These will be the subject of a future communication.



Acknowledgements

One of us (KLE) acknowledges with pleasure financial support from a National Institutes of Health Fellowship 1-F03-Gm-53,120-01, Division of General Medical Sciences. We would especially like to thank Dr. Paul J. Scheuer of the University of Hawaii in whose laboratory this work was initiated and who accommodated us on subsequent collecting trips. We are grateful to Dr. M. R. Brennan, S.L., University of Hawaii, for her untiring assistance in collecting the alga and for the initial mass spectral analyses, to Mr. B. Santelices, University of Hawaii, for the identification of the alga, to Mr. J. B. Keenaghan, Astra Pharmaceutical Products, Inc., Worcester, Mass., for the low resolution mass spectra, and to Dr. J. J. Sims, University of California, for spectral data on pacifenol and related compounds. The high resolution mass spectra required in this work were provided by the facility at the Massachusetts Institute of Technology supported by National Institutes of Health Grant RR00317 (Principal Investigator Professor K. Biemann) from the Biotechnology Resources Branch, Division of Research Resources.

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