

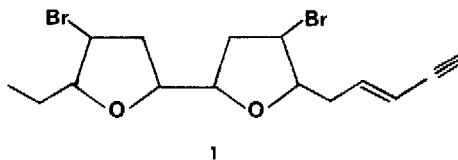
LAUROXOLANES FROM THE MARINE ALGA LAURENCIA MAJUSCULA

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Summary: Enyne 1 was isolated from the marine red alga Laurencia majuscula, and its structure was elucidated by spectroscopic means. 1 is the first 2,2'-bis-tetrahydrofuran lauroxane to be found as a Laurencia metabolite.

The lauroxanes are a group of C₁₅-halogenated ethers elaborated by marine algae of the genus Laurencia.¹ Oxane ring sizes in this group of metabolites vary from three to twelve atoms with the oxolane ring system occurring rather infrequently.² From a collection of Laurencia majuscula off the North Shore of Oahu, Hawaii, we have characterized a new oxolane C₁₅-metabolite possessing a 2,2'-bis-tetrahydrofuran moiety, a structural class not yet encountered in Laurencia.

Methylene chloride extraction of the dried alga afforded 325 mg of extract from which 27 mg of enyne 1 was obtained by preparative TLC (CH₂Cl₂). A molecular formula of C₁₅H₂₀O₂Br₂ for 1 was established by high resolution mass spectroscopy (obsd 391.9837; calcd for C₁₅H₂₀O₂⁷⁹Br⁸¹Br 391.9810). Enyne 1 displayed an acetylenic C-H stretch at 3325 cm⁻¹ in the IR spectrum. ¹H- and ¹³C-NMR spectra established the presence of the trans-enyne system (Table I, H₁, H₃, H₄, and C₁-C₄). In addition to the vinyl hydrogens, six downfield protons appeared in two complex patterns centered at 3.5 and 3.8 δ. Extensive overlapping in the ¹H-NMR spectrum was not altered significantly by solvent changes or shift reagents although the latter did induce decomposition of the sample.

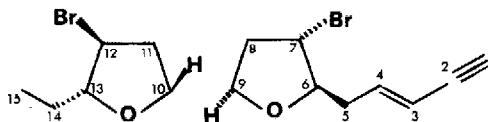


The structure of 1 was deduced from ¹H-¹H and ¹H-¹³C shift correlated 2D spectra at 250 and 400 MHz. The results of these experiments are summarized in Table I. Thus, a ¹J_{CH} experiment established connectivities between directly bonded carbons and hydrogens while the ¹H-¹H COSY experiment permitted a proton sequence to be written. Proton J-resolved spectra revealed the coupling patterns and J-values for the individual protons.

TABLE I: ^{13}C - AND ^1H -NMR SPECTRA OF **1** (400 MHz, C_6D_6)¹²

Carbon No.	δ , C	δ H, J (Hz)
1	77.31	2.54 $J_{1,3} = 2.3$, $J_{1,4} = 0.9$, $J_{1,5a} = 0.8$, $J_{1,5b} = 0.8$
2	82.13	
3	112.18	5.35 $J_{3,4} = 16.0$, $J_{1,3} = 2.3$, $J_{3,5a} = 1.5$, $J_{3,5b} = 1.5$
4	140.82	6.11 $J_{3,4} = 16.0$, $J_{4,5a} = 7.2$, $J_{4,5b} = 7.0$, $J_{1,4} = 0.9$
5a	36.56	1.99 $J_{5a,5b} = 14.9$, $J_{4,5a} = 7.2$, $J_{5a,6} = 4.7$, $J_{3,5a} = 1.5$, $J_{1,5a} = 0.8$
5b		1.83 $J_{5a,5b} = 14.9$, $J_{4,5b} = 7.0$, $J_{5b,6} = 7.3$, $J_{3,5b} = 1.5$, $J_{1,5b} = 0.8$
6	85.91	3.86 $J_{5b,6} = 7.3$, $J_{6,7} = 5.8$, $J_{5a,6} = 4.7$, $J_{6,8b} = 0.6$
7	48.34	3.44 $J_{7,8b} = 7.5$, $J_{6,7} = 5.8$, $J_{7,8a} = 5.4$, $J_{7,9} = 0.6$
8a		1.94 $J_{8a,8b} = 13.8$, $J_{8a,9} = 6.9$, $J_{7,8a} = 5.4$
8b	38.76	1.84 $J_{8a,8b} = 13.8$, $J_{7,8b} = 7.5$, $J_{8b,9} = 6.8$, $J_{6,8b} = 0.6$
9	79.88	3.75 $J_{8a,9} = 6.9$, $J_{8b,9} = 6.8$, $J_{9,10} = 7.0$, $J_{7,9} = 0.6$
10	79.36	3.79 $J_{10,11a} = 7.1$, $J_{10,11b} = 6.8$, $J_{9,10} = 7.0$, $J_{10,12} = 0.6$
11a		1.80 $J_{11a,11b} = 13.8$, $J_{11a,12} = 7.6$, $J_{10,11a} = 7.1$, $J_{11a,13} = 0.7$
11b	39.22	1.98 $J_{11a,11b} = 13.8$, $J_{10,11b} = 6.8$, $J_{11b,12} = 5.0$
12	49.09	3.48 $J_{11a,12} = 7.6$, $J_{12,13} = 5.9$, $J_{11b,12} = 5.0$, $J_{10,12} = 0.6$
13	88.60	3.88 $J_{13,14b} = 7.6$, $J_{12,13} = 5.9$, $J_{13,14a} = 4.6$, $J_{11a,13} = 0.7$
14a		1.37 $J_{14a,14b} = 13.8$, $J_{14a,15} = 7.5$, $J_{13,14a} = 4.6$
14b	26.76	1.21 $J_{14a,14b} = 13.8$, $J_{13,14b} = 7.6$, $J_{14b,15} = 7.4$
15	10.10	0.8 $J_{14a,15} = 7.5$, $J_{14b,15} = 7.4$

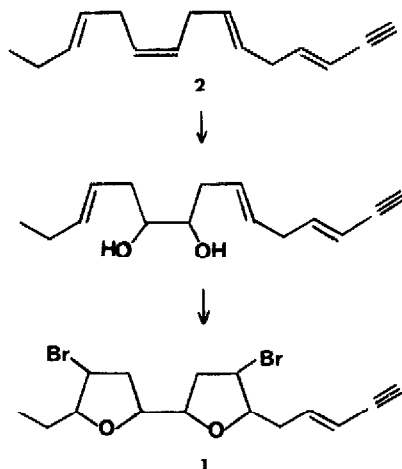
While it is not possible to firmly assign the complete stereochemistry of **1** with the data available, an analysis of the proton couplings suggests the relative stereochemistry around each tetrahydrofuran ring as depicted below:



Small couplings ($J = 0.6$ Hz) observed for the bromomethine protons are ascribed to long range trans-interactions with H_9 and H_{10} .³ The latter protons also display a 0.6 Hz coupling, albeit the patterns for these protons are not as clear as those of the bromomethines. H_{8b} and H_{11a} each show a long range trans-coupling (0.6-0.7 Hz) to H_6 and H_{13} respectively, analogous to the H_7 - H_9 and H_{10} - H_{12} couplings. No coupling is observed between H_6 and H_9 or between H_{10} and H_{13} . As H_6 and H_{13} display only one long range coupling each, a cis-relationship of H_6 and H_9 and of H_{10} and H_{13} is indicated, which places the side chains trans to their adjacent bromo substituents. The observed J -values of 5.8 and 5.9 Hz for H_6 - H_7 and for H_{12} - H_{13} respectively, confirms this stereochemical assignment.⁴

The relative stereochemistry between the two tetrahydrofuran rings remains undefined. If one assumes a gauche relationship of the ring oxygens,⁵ the coupling constant $J_{9,10} = 7$ Hz indicates an anti arrangement of these two hydrogens⁶ and, therefore, a threo relationship for the two rings. However, the erythro form with the ring oxygens in an anti conformation could also provide the trans-coupling of 7 Hz.

Laurencia majuscula collections from the coast of Japan,⁷ Australia,⁸ and the Mediterranean⁹ were found to elaborate sesquiterpenes of the chamigrane type. A recent Japanese collection also provided a norchamigrane derivative,¹⁰ but no lauroxolanes have been reported from this species. Biogenetically, enyne **1** may be viewed as arising from an acetylenic polyene precursor such as **2**, which undergoes hydroxylation and bromine-induced oxide ring closures:



The 3Z,6Z,9Z,12Z- and 3E,6Z,9Z,12Z-isomers of 2 have recently been reported as constituents of Laurencia okamurai.¹¹

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References and Notes

1. K. L. Erickson, in "Marine Natural Products," Vol. 5, Ed. P. J. Scheuer, Academic Press, New York, 1983, p. 131.
2. D. J. Faulkner, Nat. Prod. Reports, 1, 251 (1984).
3. R. Lozach, B. Lemarie, and B. Braillon, J. Chim. Phys., 72, 873 (1975); D. Gagnaire and P. Vottero, Bull. Soc. Chim. Fr., 873 (1972); H. Kessler, W. Bermel, A. Friedrich, G. Krack, and W. E. Hull, J. Am. Chem. Soc., 104, 6297 (1982).
4. L. Crombie and R. D. Wyvill, J. Chem. Soc. Perkin I, 1971 (1985).
5. T. M. Connor and K. A. McLauchlan, J. Phys. Chem., 69, 1888 (1965); N. A. Porter, A. N. Roe, and A. T. McPhail, J. Am. Chem. Soc., 102, 7574 (1980); A. San Martin, J. Rovirosa, O. Munoz, M. H. M. Chen, R. D. Guneratne, and J. Clardy, Tetrahedron Lett., 24, 4063 (1983).
6. M. Karplus, J. Am. Chem. Soc., 85, 2870 (1963); J. B. Lambert, *ibid.*, 89, 1836 (1967); H. R. Buys, Rec. Trav. Chim., 88, 1003 (1969).
7. M. Suzuki and E. Kurosawa, Tetrahedron Lett., 4805 (1978); M. Suzuki, A. Furusaki, N. Hashiba, and E. Kurosawa, *ibid.*, 879 (1979).
8. R. J. Capon, E. L. Ghisalberti, T. A. Mori, and P. R. Jefferies, J. Nat. Prod., 51, 1302 (1988).
9. S. Caccamese, A. Compagnini, R. M. Toscano, F. Nicolo, and G. Chapuis, Tetrahedron, 43, 5393 (1987).
10. M. Suzuki, E. Kurosawa, and K. Kurata, Bull. Chem. Soc. Jpn., 60, 3795 (1987).
11. H. Kigoshi, Y. Shizuri, H. Niwa, and K. Yamada, Tetrahedron, 42, 3781 (1986).
12. Serious overlapping of the bromomethine protons with the oxygen methine protons was alleviated when C₆D₆ replaced CDCl₃ as solvent. The bromomethines underwent a greater upfield shift in C₆D₆ than the oxygen methines.

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