C_{15}-HALOGENATED COMPOUNDS FROM THE HAWAIIAN MARINE ALGA
LAURENCIA NIDIFICA.   V.   THE MANEONENES

S. M. Waraszkiewicz, H. H. Sun, and K. L. Erickson[*]
Jeppson Laboratory, Clark University
Worcester, Massachusetts 01610

The several varieties of <u>Laurencia nidifica</u> collected off the south coast of Oahu, Hawaii, have been a rich source of interesting C_{15} compounds.[1] From the green variety of this alga, we have isolated two nonhalogenated sesquiterpenoid alcohols[2] and six new C_{15}-halogenated nonterpenoid ethers. The characterization of three of these new ethers is reported here.

Extraction of the air-dried alga followed by column and thin layer chromatography afforded <u>cis</u>-maneonene A (1), <u>cis</u>-maneonene B (2), and <u>trans</u>-maneonene B (3).[3] The spectral data of these three compounds clearly showed their very close structural relationship and strongly suggested that they belonged to the nonterpenoid straight chain cyclic ether class of <u>Laurencia</u> compounds.[4,5]

<u>cis</u>-Maneonene A (1) analyzed for $C_{15}H_{18}BrClO_2$ by high resolution mass spectrometry. Its uv $(\lambda_{max}^{EtOH}$ 222 nm) and ir $(CCl_4,$ 3310, 2985 cm$^{-1})$ indicated the presence of a conjugated <u>cis</u>-enyne group, which was corroborated by pmr and cmr (Table I, C_1, C_3, C_4). The nature of C_1-C_4 (Fig. I) is thereby delineated.

The ir also showed a vinyl ether group (1685 cm^{-1}). Strong C-O bands (1100, 1040 cm^{-1}) with no hydroxyl or carbonyl absorption suggested that both oxygens were involved in ether links. This was verified by cmr which showed three O-bearing carbons, and pmr which showed three downfield methines (Table I, C_7, C_9, C_{10}). Only one other downfield absorption was observed in the pmr (H_5) which was not already assigned, and this can be ascribed to a halogen-bearing carbon. The second halogen must therefore be attached at a quaternary center.

A vinyl ethyl group on a tetrasubstituted double bond was established by pmr and cmr (Table I, C_{14}, C_{15}). That this tetrasubstituted double bond also bears the vinyl ether function and one of the halogen atoms is established as follows: A total of twelve peaks are observed in the cmr, only two of which are in the olefinic region (C_3, C_4). The three carbons which are not observed must be quaternary centers.[6] One of these centers is already accounted for by the acetylenic C_2. The other two centers must be those involved in the second and only other double bond (C_{12}, C_{13}), and these centers must bear the ethyl, the vinyl ether, and the quaternary halide functions.

The cmr value (58.3) for the carbon bearing both a hydrogen and a halogen suggested that this halogen was chlorine, and, therefore, the vinylic halogen would have to be bromine. This was verified when the chlorine atom was removed from 1 by reaction with $Cr(en)_2SO_4$.[7] Bromine was retained in the product, and the enyne grouping was converted into an allene (4) (Scheme I).[8] This is readily explained if the chlorine is made allylic to the enyne function.[9] In addition, decoupling experiments had shown that the halogen methine hydrogen was adjacent to the vinylic hydrogen at C_4.

With the chlorine placed at C_5, the bromine atom must be at C_{12} or C_{13} of the tetrasubstituted double bond. Hydrogenation studies (Scheme I) provided the evidence to place it at C_{13} with the

Table I. $^{13}C^{\underline{a}}$ and $^{1}H^{\underline{b}}$ NMR Data for cis-Maneonene A ($\underline{1}$)

Carbon No.	^{13}C δ	^{1}H δ	Multiplicity, J (Hz)
1	84.8	2.67	d, $J_{1,3} = 2.3$
3	111.9	5.36	dd, $J_{1,3} = 2.3$, $J_{3,4} = 10.5$
4	142.0	6.05	t, $J_{3,4} = J_{4,5} = 10.5$
5	58.3	5.08	t, $J_{4,5} = J_{5,6} = 10.5$
6	58.3	1.89	dd, $J_{5,6} = 10.5$, $J_{6,11} = 1.5$
7	78.3	4.62	d, $J_{7,8_{exo}} = 5$
8	38.6	1.34 (exo)	td, $J_{8_{exo},8_{endo}} = 14$, $J_{7,8_{exo}} = 5$, $J_{8_{exo},9} = 8$
		0.96 (endo)	d, $J_{8_{exo},8_{endo}} = 14$
9	80.4	4.06	dd, $J_{8_{exo},9} = 8$, $J_{9,10} = 5$
10	82.2	4.34	t, $J_{9,10} = J_{10,11} = 5$
11	46.1	2.75	dd, $J_{10,11} = 5$, $J_{6,11} = 1.5$
14	26.7	2.47	sextet, $J_{14,14} = 14$, $J_{14,15} = 7$
		2.51	sextet, $J_{14,14} = 14$, $J_{14,15} = 7$
15	13.0	1.06	t, $J_{14,15} = 7$

$\underline{a}$Proton decoupled values (ppm downfield from TMS) in C_6D_6 solvent. $\underline{b}$ 270 MHz values (ppm downfield from TMS) in C_6D_6 solvent.

ethyl group. In the saturated product ($\underline{5}$),[8] where all multiple bonds and both halogens have been removed, but where both ether functions are intact, the mass spectrum shows strong peaks for the loss of a propyl group. If the bromine had been at C_{12} (interchanged with either the oxygen or the carbon substituent at C_{12} in Fig. I) then reduction would give rise to an ethyl, not a propyl, side chain. The hydrogenated material ($\underline{5}$) also shows a loss of C_5H_{11} which indicates that the C_1-C_5 group is at a branch point. When the reduction was carried out with Na/NH$_3$ followed by careful hydrogenation, a compound ($\underline{7}$) was produced which retained the bromine but not the chlorine and in which all multiple bonds had been hydrogenated.[8] The new bromo methine hydrogen appeared as a complex multiplet at 3.52 δ (60 MHz pmr). Dehydrobromination of this material regenerated a vinyl ether ($\underline{8}$) which now displayed a vinyl hydrogen adjacent to the C_{14} hydrogens and clearly coupled with them (J = 7 Hz; the vinyl hydrogen and both C_{14} hydrogens were well defined in the 270 MHz pmr).[8] Hence, the position of the bromine atom at C_{13} is firmly established.
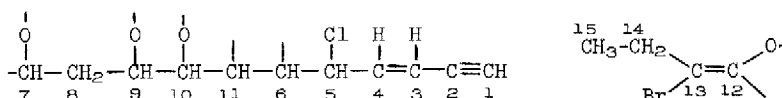
Figure I[10]

The nature of twelve of the fifteen carbons of $\underline{1}$ has now been defined (C_1-C_5,C_7,C_9,C_{10},C_{12}-C_{15} in Fig. I), and that of the three remaining carbons is established by the 270 MHz pmr spectrum (Table I). Four proton signals are yet to be assigned. Since there are no more quaternary centers or methyl groups, two of the three remaining carbons must carry one hydrogen each, and the third must be a CH_2 group (C_6,C_{11},C_8 in Fig. I). Verification of the latter comes from the doublet signal at 0.96 δ with a J value of 14 Hz, ascribable to a geminal coupling.
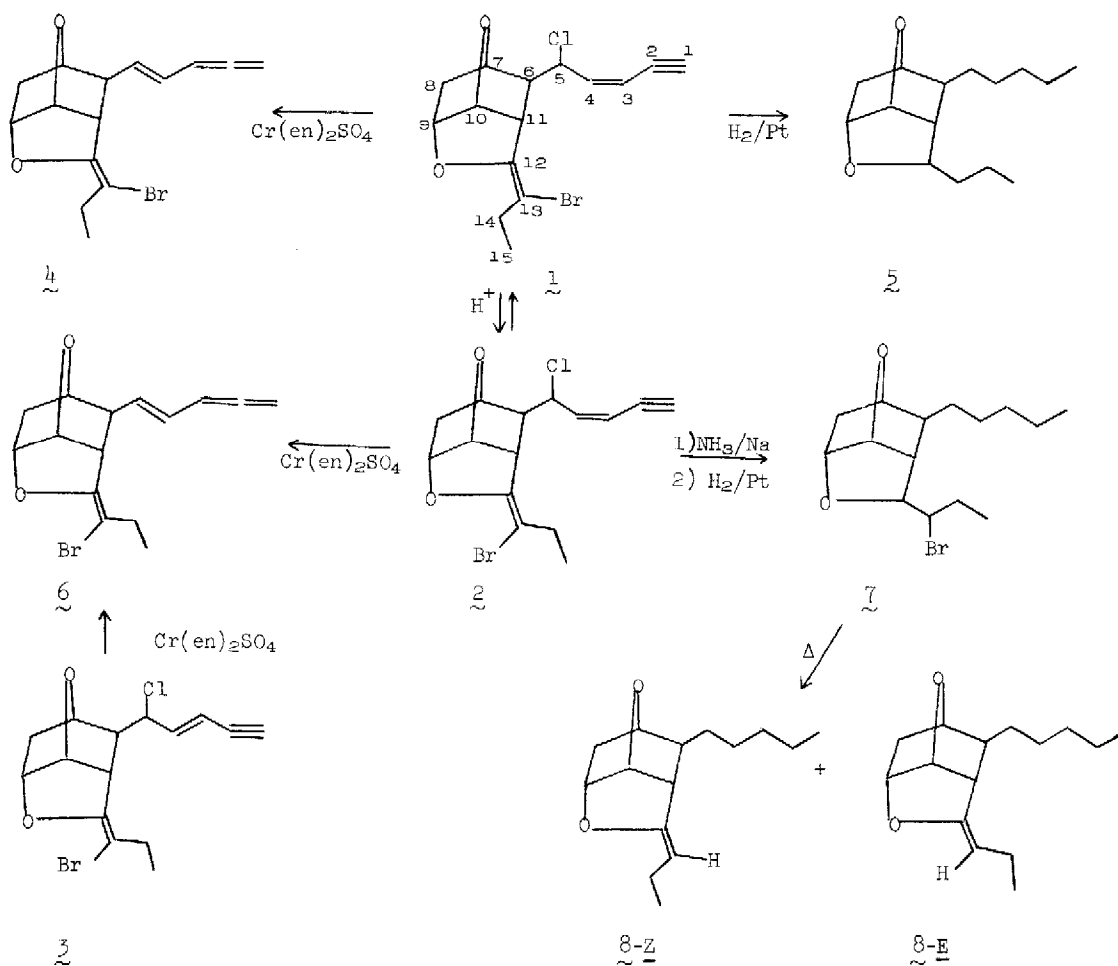
Scheme I

Since the spectral and hydrogenation data had established the presence of one triple and two double bonds, cis-maneonene A ($\underset{\sim}{1}$) must be tricyclic. An analysis of the H-H coupling constants (Table I) together with decoupling data[8] established the proton sequence in the carbon chain as shown in Figure I. Furthermore, specific ^{1}H-^{13}C decoupling firmly established the ^{13}C assignments and therefore the heteroatom sequence.

The point of attachment of C_{12} to the main chain may be at C_7, C_{11}, or C_6. C_7 can be ruled out as this would necessitate additional bonding between C_6 and C_{11} yielding a third double bond which obviously is not present in the molecule. Attachment of C_{12} at C_6 or C_{11}, followed by ether closures, affords six possible skeletal structures for $\underset{\sim}{1}$. Two of these are epoxides and can be ruled out on that basis. An examination of the models of all possible stereoisomers of the remaining four structures shows that only one is viable in terms of the pmr spectrum, namely that of $\underset{\sim}{1}$. This structure gives a most satisfactory fit to all the data when the substituent at C_6 is placed in an exo configuration and the C_9 and C_{11} substituents are placed endo (geometrically required). Thus, in the pmr, $J_{6_{endo},7} = J_{7,8_{endo}} = J_{8_{endo},9_{exo}} = 0$ as required by the data and in excellent

agreement with the literature, as are all of the other H-H couplings (Table I) of the carbocyclic ring.[11,12]

That the C_{12}-C_{13} double bond is of the E-configuration in 1 is shown by comparison with its isomer, cis-maneonene B (2). These materials are interconvertible by treatment with HOTs/ϕH. Their spectral characteristics are essentially identical except in the region influenced by the C_{12}-C_{13} double bond. Thus, in the pmr, H_4 in 1 (6.05 δ) is 0.3 ppm further downfield than H_4 in 2 (5.75 δ) showing the deshielding effect of the bromine on this proton in 1. Similarly, in 1 the C_{14} protons (2.47 and 2.51 δ) are 0.2 ppm further downfield than those in 2 (2.32 δ), a consequence of the nearby oxygen atom in 1. Finally, 2 is more polar than 1 as would be expected from the dipole alignment shown.

The structure of trans-maneonene B is established as 3 by a comparison of the C_3-C_4 double bond region with 1 and 2. In 3 this is shown to be trans by the 15.5 Hz coupling constant of the vinyl protons. Moreover, 3, on treatment with $Cr(en)_2SO_4$, is converted to the same allene as that derived from 2 (6).

The structures of these three compounds differ from those of other members of this class[4,5] in that the straight C_{15} carbon chain has cyclized back on itself (C_6-C_{11} bond) to form a carbocyclic ring. Such carbocyclic ring formation appears to be the pattern followed in these systems for this variety of Laurencia.[13]

References and Notes

1. S. M. Waraszkiewicz and K. L. Erickson, Tetrahedron Letters, 1443 (1976) and references cited therein.

2. H. H. Sun, S. M. Waraszkiewicz, and K. L. Erickson, ibid., 585 (1976).

3. Limu mane'one'o (ticklish seaweed) is the Hawaiian name for Laurencia.

4. For a review and leading references, see W. Fenical, J. Phycol., 11, 245 (1975).

5. F. J. McDonald, D. C. Campbell, D. J. Vanderah, F. J. Schmitz, D. M. Washecheck, J. E. Burks, and D. van der Helm, J. Org. Chem., 40, 665 (1975).

6. The long T_1 values for quaternary carbons render their signals too weak to be seen under the operating conditions employed for this spectrum. All 15 carbons are detected when the pulse rate is appropiately adjusted.

7. J. K. Kochi and P. E. Mocadlo, J. Am. Chem. Soc., 88, 4094 (1966).

8. Experimental and spectral details will be subsequently published in a full paper.

9. J. K. Crandell, D. J. Keyton, and J. Kohne, J. Org. Chem., 33, 3655 (1968); T. L. Jacobs and R. D. Wilcox, J. Am. Chem. Soc., 86, 2240 (1964); J. P. Dulcere, M. Santelli, and M. Bertrand, C.R.H. Acad. Sci., 271, 585 (1970).

10. The numbering system shown is in keeping with that used for other members of this class of compounds.

11. F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N.Y., 1969.

12. D. Gagnaire and E. Payo-Subiza, Bull. Chim. Soc. Fr., 2627 (1963).

13. Unpublished observations.