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C_{15}-HALOGENATED COMPOUNDS FROM THE HAWAIIAN MARINE ALGA *LAURENCIA NIDIFICA*. VI. THE ISOMANEONENES

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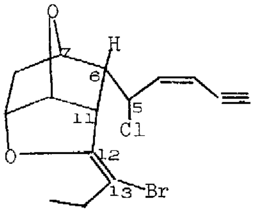
We recently reported the structures of the maneonenes, three nonterpenoid C_{15}-halogenated ethers from the green variety of *Laurencia nidifica*.[1] Two other components of this extract, isomaneonene-A (**1**) and isomaneonene-B (**2**), have now been characterized in addition to a fourth maneonene, *cis*-maneonene-C (**3**).

cis-Maneonene-C (**3**) is the C_6-endo isomer of *cis*-maneonene-A (**4**).[1] This structural assignment was made by application of the same spectral and chemical methods described for the other maneonenes.[1,2] The difference in stereochemistry at C_6 is clearly evident from the pmr where $J_{6,7} = 4.5$ and $J_{6,11} = 9.5$ Hz in **3** while $J_{6,7} = 0$ and $J_{6,11} = 1.5$ Hz in **4**.[3]



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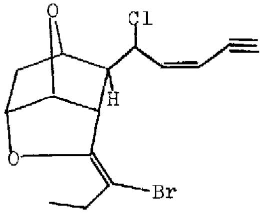

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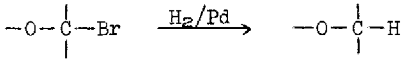
Isomaneonene-A (**1**) and isomaneonene-B (**2**) both analyzed for $C_{15}H_{16}Br_2O_2$ by high resolution and field desorption mass spectroscopy, and their spectral data indicated a close relationship with *cis*-maneonene-C (**3**). The *cis*-enyne function was established by uv (λ_{max}^{EtOH} 229 nm, ϵ = 14,500 for **1** and 228 nm, ϵ = 13,500 for **2**), ir (CCl_4, 3300 and 2970 cm^{-1}), pmr and cmr (Tables I and II, C_1-C_4). The infrared showed no hydroxyl or carbonyl absorption, but strong bands in the 1000-1100 cm^{-1} region indicated that the oxygen moieties were present as ethers. Unlike the maneonenes, neither **1** nor **2** showed vinyl ether absorption. That the *cis*-enyne group is the only multiply-bonded system in the molecule is established by pmr and cmr (Tables I and II), and therefore isomaneonene-A (**1**) and isomaneonene-B (**2**) must be tetracyclic.

Decoupling experiments in the pmr established a proton sequence for C_1-C_{11} and specific hydrogen decoupling in the cmr verified that C_7, C_9, and C_{10} were oxygen-bearing carbons (Figure I). The four remaining carbons are two deshielded quaternary centers with an ethyl group attached (Tables I and II, C_{12}-C_{15}) (Figure I). The chemical shift values of the quaternary carbons C_{12} and C_{13} indicate that the two bromine atoms and the fourth oxygen bond are attached to these carbons. Furthermore, one of these quaternary centers bears both a bromine and an oxygen for when both bromines are reductively removed, the fully saturated diether obtained (**5**, Scheme I)[2] displays four, rather than three, oxygen methines in the pmr indicative of the following transformation:



$$-O-\overset{|}{\underset{|}{C}}-Br \xrightarrow{H_2/Pd} -O-\overset{|}{\underset{|}{C}}-H$$

This same ether bond is cleaved when 1 or 2 is treated with Na/NH_3. Hydrogenation of the resulting olefin gives rise to a secondary alcohol (6, Scheme I). The other ether bonds are unaffected.

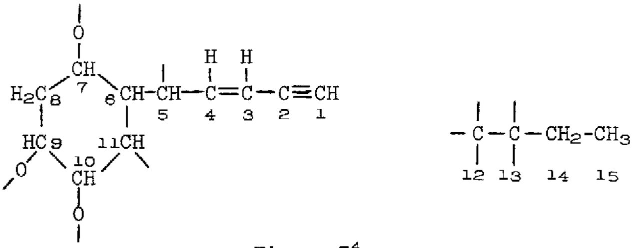
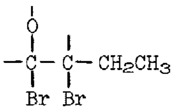


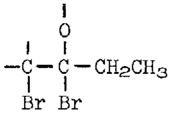
Figure I[4]

With both an oxygen and a bromine on one quaternary center, the second bromine must then be attached to the adjacent quaternary carbon. The C_{12}-C_{15} moiety shown in Figure I may then be represented by either of two structures:



$$-\overset{\overset{|}{O}}{\underset{Br}{C}}-\overset{|}{\underset{Br}{C}}-CH_2CH_3$$

a



$$-\overset{|}{\underset{Br}{C}}-\overset{\overset{|}{O}}{\underset{Br}{C}}-CH_2CH_3$$

b

That a is the correct structure is shown by the mass spectra of secondary alcohol 6 and its corresponding ketone 7 where both bromines and the ether link to the bromine-bearing carbon have been replaced by hydrogens. These materials lose butyl and ethyl fragments on electron impact. Had b been the correct structure, reduction would have given rise to a propyl, not an ethyl, side chain.

Attaching a to the main chain in Figure I at C_5 and C_{11} and closing the ether functions so as to exclude an epoxide link (for which there is no evidence), results in two possible skeletal structures for isomaneonene-A and isomaneonene-B. An examination of the molecular models of these two structures shows that only one skeleton will fit the data, that represented by 1 and 2 (Scheme I). It can be seen that these structures, differing only in stereochemistry at C_{13}, are identical to the maneonene system with an extra carbocyclic ring formed between C_5 and C_{13} and the second halogen attached at C_{12} rather than C_5.

The distinction between isomaneonene-A (1) and isomaneonene-B (2) is readily made on the basis of their pmr spectra. In 1 the bromine atom on C_{13} is cis to H_5 and trans to the enyne function and H_4, while the opposite situation obtains in 2. The deshielding effect of this bromine is shown where H_5 occurs 0.80 ppm further downfield in 1 than in 2 while H_4 is 0.68 ppm further downfield in 2 than in 1. H_6 and H_{11} also occur substantially further downfield when the C_{13}-bromine is cis to them (Tables I and II).

The cis relationship of H_5 and H_6 in 1 and 2 is established by their large coupling constants (10 and 9 Hz respectively), comparable to $J_{6,11}$ (10 Hz). From the models the dihedral angles of H_5,H_6 and $H_{6,11}$ are identical. The stereochemistry at all other centers is fixed by virtue of the fused ring systems.

It should be noted that the green variety of *L. nidifica* from which this varied group of secondary metabolites has been isolated[1,5] may itself consist of several different varieties.

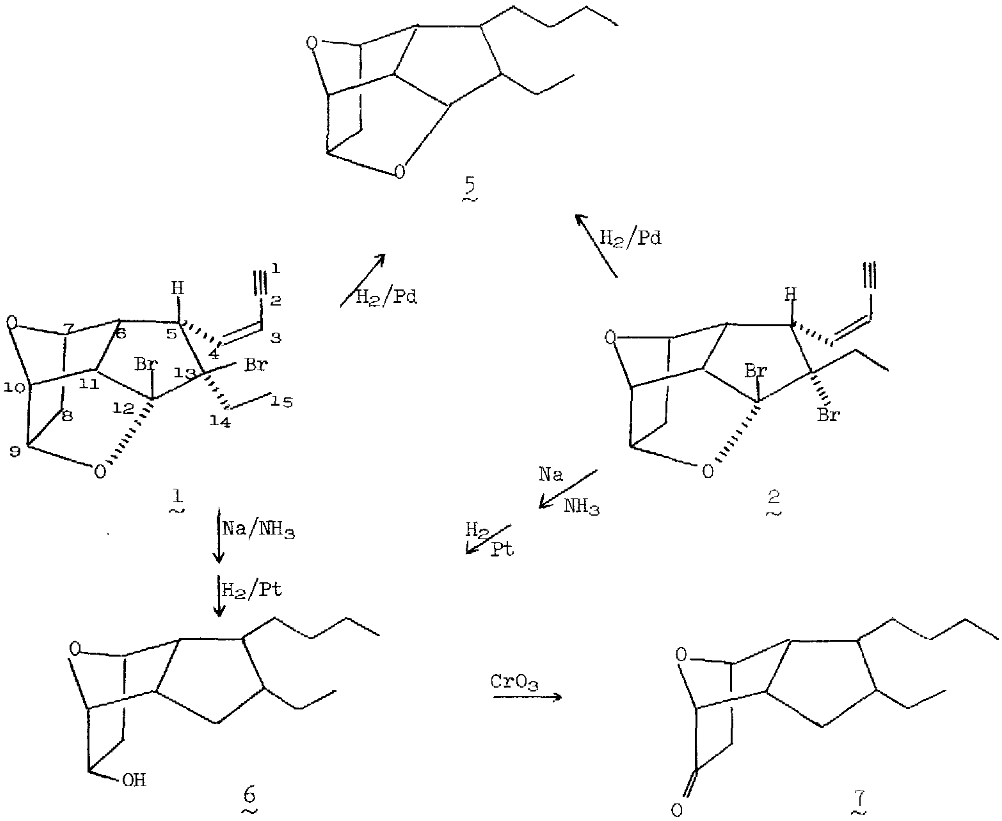
Table I. ^{13}C[a] and ^{1}H[b] NMR Data for Isomaneonene-A (1)

arbon No.	^{13}C δ	^{1}H δ	Multiplicity, J (Hz)
1	84.7	2.72	d, $J_{1,3} = 2$
2	79.5[c,d]	-	-
3	109.2	4.98	dd, $J_{1,3} = 2$, $J_{3,4} = 10.5$
4	144.5	5.66	dd, $J_{3,4} = 10.5$, $J_{4,5} = 8$
5	49.7	4.33	dd, $J_{4,5} = 8$, $J_{5,6} = 10$
6	50.5	3.38	sextet, $J_{5,6} = J_{6,11} = 10$, $J_{6,7} = 5$
7	77.6	4.19	t, $J_{6,7} = J_{7,8_{exo}} = 5$
8	41.4	1.15 (exo) 1.59 (endo)	dt, $J_{7,8_{exo}} = J_{8_{exo},9} = 5$, $J_{8_{exo},8_{endo}} = 13$ d, $J_{8_{exo},8_{endo}} = 13$
9	83.3	4.31	t, $J_{8_{exo},9} = J_{9,10} = 5$
10	82.9	5.02	t, $J_{9,10} = J_{10,11} = 5$
11	63.1	3.88	dd, $J_{10,11} = 5$, $J_{6,11} = 10$
12	110.6[c]	-	-
13	89.7[c]	-	-
14	26.8	2.08 2.33	sextet, $J_{14,14} = 14$, $J_{14,15} = 7$ sextet, $J_{14,14} = 14$, $J_{14,15} = 7$
15	10.0	1.06	t, $J_{14,15} = 7$

Table II. ^{13}C[a] and ^{1}H[b] NMR Data for Isomaneonene-B (2)

rbon No.	^{13}C δ	^{1}H δ	Multiplicity, J (Hz)
1	83.5	2.72	d, $J_{1,3} = 2$
2	79.9[c,d]	-	-
3	108.7	5.08	dd, $J_{1,3} = 2$, $J_{3,4} = 10.5$
4	146.9	6.34	dd, $J_{3,4} = 10.5$, $J_{4,5} = 9$
5	43.2	3.53	t, $J_{4,5} = J_{5,6} = 9$
6	50.0	2.75	sextet, $J_{5,6} = 9$, $J_{6,7} = 5$, $J_{6,11} = 10$
7	77.6	4.08	t, $J_{6,7} = J_{7,8_{exo}} = 5$
8	41.1	1.15 (exo) 1.67 (endo)	dt, $J_{7,8_{exo}} = J_{8_{exo},9} = 5$, $J_{8_{exo},8_{endo}} = 13$ d, $J_{8_{exo},8_{endo}} = 13$
9	81.4	4.25	t, $J_{8_{exo},9} = J_{9,10} = 5$
.0	84.6	5.03	t, $J_{9,10} = J_{10,11} = 5$
.1	58.7	2.96	dd, $J_{10,11} = 5$, $J_{6,11} = 10$
.2	109.5[c]	-	-
3	85.2[c]	-	-
4	38.0	1.30 2.36	sextet, $J_{14,14} = 14$, $J_{14,15} = 7$ sextet, $J_{14,14} = 14$, $J_{14,15} = 7$
5	10.6	0.95	t, $J_{14,15} = 7$

Proton decoupled values (ppm downfield from TMS) in $CDCl_3$ solvent. [b] 270 MHz values (ppm downfield from TMS) in C_6D_6 solvent. [c] Quaternary carbon. [d] Reference 6.



Scheme I

Acknowledgements

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References and Notes

1. S. M. Waraszkiewicz, H. H. Sun, and K. L. Erickson, Tetrahedron Letters, 3021 (1976).
2. Complete experimental details will be published in a full paper.
3. D. Gagnaire and E. Payo-Subiza, Bull. Soc. Chim. France, 2627 (1963).
4. The numbering system shown is in keeping with that used for other members of this class of compounds.
5. H. H. Sun, S. M. Waraszkiewicz, and K. L. Erickson, Tetrahedron Letters, 585 (1976).
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