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MARINE NATURAL PRODUCTS: DACTYLOXENE-B, A SESQUITERPENE ETHER FROM THE SEA HARE, APLYSIA DACTYLOMELA

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A variety of interesting and novel natural products have been isolated from sea hares (genus Aplysia) and the algae upon which they feed.[1] We wish to report the isolation of three new sesquiterpene ethers from the sea hare Aplysia dactylomela and to propose a structure for one of these, named dactyloxene-B, 1.

Whole sea hares were first extracted by soaking with isopropyl alcohol/water (60/40) and then the air-dried animal residue was extracted continuously with hexane. Vacuum distillation of the hexane extract of the whole, dried animals gave a low boiling fraction (78-82° @ 0.75 mm and 120-140° bath temp.) which upon repeated chromatography over silica gel yielded three pure oils shown by comparison of their analyses and spectral properties to be isomeric sesquiterpene ethers. The three ethers have been named dactyloxene-A, -B, and -C according to their order of increasing gas chromatographic retention time on a non-polar methyl silicone column.

Dactyloxene-B, 1, a colorless oil (0.3% of dry wt.), $C_{15}H_{24}O^2$, n_D 1.4925, α_D + 106° (c 0.74, $CHCl_3$), lacked hydroxyl and carbonyl absorptions in its ir spectrum (neat), but exhibited bands at 3080, 1640, 910 (vinyl group), and 810 (trisubstituted double bond), in addition to a strong band at 990 cm^{-1} indicative of an ether link. Only end absorption was noted in the uv spectrum of dactyloxene-B.

Carbon-13 resonance data, see table 1, reveals that there are four sp^2 carbon atoms and hence only two double bonds in dactyloxene-B. Therefore the remaining two degrees of unsaturation implied by the formula of 1 must be due to rings. The carbon 13 data further shows unequivocally that the only oxygen atom in dactyloxene-B is present in the form of an ether, and that the carbons directly attached to the oxygen are fully substituted.

Table 1

^{13}C Chemical Shift Data[3] and Assignments[4]

Ppm	Type Carbon	Ppm	Type Carbon	Ppm	Type Carbon	Ppm	Type Carbon
15.016	$-CH_3$	32.141	$\geq$C-H	83.212	$\geq$C-O	110.740	$=CH_2$
19.972	$-CH_3$	32.638	$-CH_2-$	86.139	$\geq$C-O	124.238	=CH-
20.863	$-CH_3$	34.969	$-CH_2-$			136.874	=C$<$
27.830	$-CH_3$	38.003	$-CH_2-$			145.602	=CH-
		45.555	$\geq$C-H				

The proton magnetic resonance spectrum (100 MHz, $CDCl_3$) of 1 along with the results of decoupling experiments are shown in Figure 1. Four methyl group signals are evident: δ0.97 (d) and 1.06 (d), secondary methyls, 1.34 (s), CH_3-C$\leq$O, and 1.70 ppm, vinyl methyl. The secondary methyl signals at δ0.97 and 1.06 ppm are collapsed to singlets by irradiation at δ1.77 and 1.52 ppm, respectively, thus demonstrating that these signals are due to two methyl groups bonded to separate carbons. The multiplets centered at δ5.04 and 6.07 ppm constitute an AMX pattern which indicates the presence in 1 of a vinyl group attached to a fully substituted carbon, hence to one of the ether carbons. The olefinic proton signal at δ5.44 collapses to a triplet upon irradiation at δ1.70 (vinyl methyl position) indicating that the partial structure $-CH_2-CH=C(CH_3)-$C$\leq$

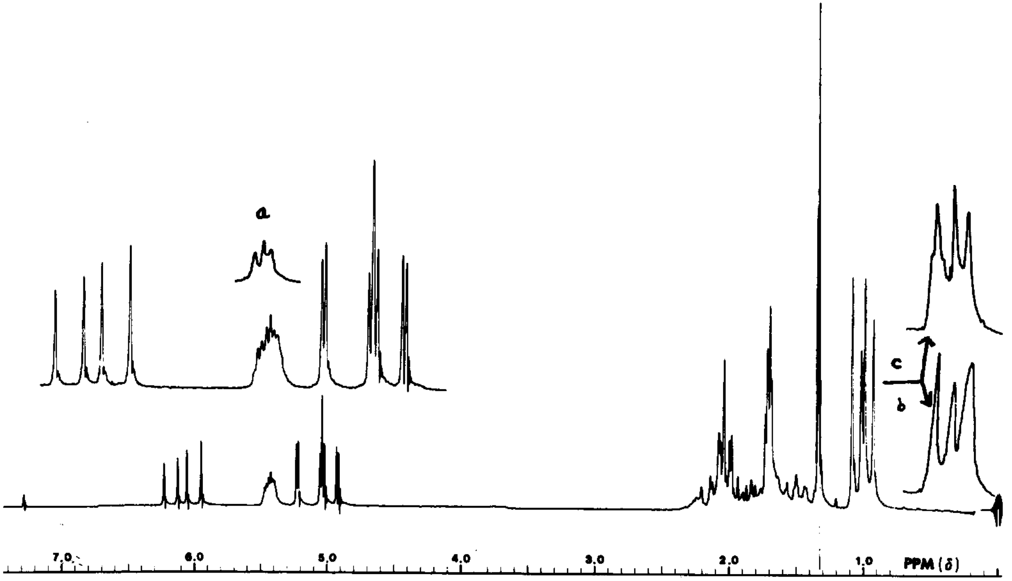
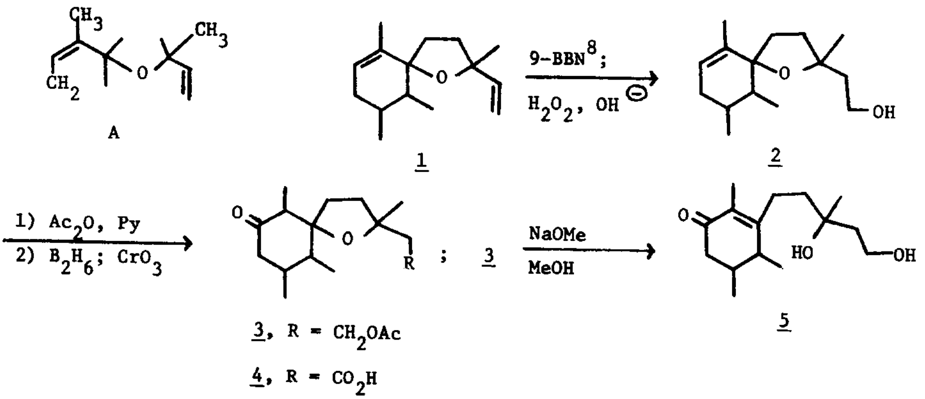


Figure 1. Pmr spectrum (100 MHz, $CDCl_3$) of Dactyloxene-B. Decouplings (expanded sweep width): (a) irr. at δ1.70; (b) irr. at δ1.52; (c) irr. at δ1.72.

is present in dactyloxene-B.

The structural features elucidated by the above ^{13}C and ^{1}H nmr data can be synthesized most conveniently by focusing on the two fully substituted carbons first. These are each attached to the oxygen atom and also to the following structural units: a vinyl group, a methyl group and, most likely, the more substituted sp^2 carbon in the $-CH_2-CH=C(CH_3)-$ fragment. This combination results in the partial formula A. The remaining units identified by ^{13}C and ^{1}H nmr data, two $-CH(CH_3)-$ and two $-CH_2-$, can be added to A so as to form a bicyclic structure in several ways. However, incorporation of these units so as to give the gross structure 1 for dactyloxene-B is proposed on the basis of mass spectral evidence, i.e., an intense M-56 ion (base peak) at m/e 164 (calcd for $C_{11}H_{16}O$: 164.12011; found: 164.11990) corresponding to a facile loss of C_4H_8 in a retro Diels-Alder fragmentation of a cyclohexene ring.

Some confirmatory evidence for the proposed structure 1 has been obtained by the conversion of dactyloxene-B via the reactions outlined below to the alcohol 2[6] and then to the keto diol 5.[7] The facile conversion of the keto acetate 3 under basic conditions to an α,β-unsaturated ketone, 5, demonstrates that one end of the ether link is β- to the carbonyl group in 3 and hence allylic to the ring double bond as proposed for 1.



The carbon skeleton in the proposed structure 1 for dactyloxene-B can be envisioned as arising biogenetically via a single methyl migration in the skeleton of known sesquiterpenes such as trans-γ-monocyclicfarnesol[9a] and farnesiferol-B and -C[9b]. Experiments designed to elucidate the stereochemistry of dactyloxene-B are in progress.

Acknowledgements

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2. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98; M^+, 220.18271. Found: C, 81.94; H, 11.04; M^+, 220.18140.

3. 25.2 MHz, $CDCl_3$, values in ppm from internal TMS.

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6. Clear oil: ir (neat) 3450 cm^{-1}; nmr (100 MHz, $CDCl_3$): δ 0.99, 1.03 [6 H, overlapping doublets, J = 6 Hz, 2 $-CH(C\underline{H}_3)-$], 1.30 (3 s, $C\underline{H}_3$ -C-O), 1.74 (3, m, vinyl methyl), 3.44-3.96 (2, m, $HO-C\underline{H}_2-CH_2-$), and 5.14 (1, m, olefinic H).

7. Clear oil: ir (neat): 3400, 1660, 1650 cm^{-1}; λ_{max}^{EtOH} 249 nm (ϵ 16,100); nmr (100 MHz, $CDCl_3$): δ 1.06, 1.25 (3 ea, d, 2 $C\underline{H}_3-CH\lessdot$), 1.32 (3, s, $C\underline{H}_3-C\lessgtr OH$), 1.78 [(3, s, $-CO-C(C\underline{H}_3)=C\lessdot$], 3.94, (2, t, $HO-C\underline{H}_2-CH_2-$).

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