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Marine Natural Products. Dactylone, an Acetylenic Dibromochloro Ether from the Sea Hare *Aplysia dactylomela*

Summary: Dactylone, a new acetylenic dibromochloro ether isolated from the sea hare, *Aplysia dactylomela*, has been determined by single-crystal X-ray diffraction analysis to be a substituted tetrahydropyran having the structure and absolute configuration shown in 1.

Sir: Marine organisms, in particular algae, are proving to be a rich source of halogenated natural products,¹ among which are a small group of halogenated ethers characterized by a straight-chain C-15 carbon skeleton and a terminal enyne function.² In our continuing investigation³ of the chemistry of a sea hare, *Aplysia dactylomela*, we have now isolated a new compound in this class and herein report its structure.⁴

Dactylone, $C_{15}H_{19}OBr_2Cl$,⁵ mp 62.2–63.3°, $[\alpha]^{25}_D -36^\circ$ (c 15.2, $CHCl_3$), was obtained from the hexane extracts³ of the sea hare by chromatography first over Florisil and then repeated chromatography of selected fractions over silicic acid. The presence in dactylone of a conjugated terminal enyne group similar to that present in laureatin and related compounds² was indicated by ir ($CHCl_3$) [3305, 2100 (very weak) cm^{-1}], uv [λ_{max} (isooctane), 222.5 nm (ϵ 12,000)] and nmr data (see Table I, signals at 3.18, 5.6 and 6.12 ppm). Nmr data also indicated the presence of a $CH_3CH_2CX=CHCH_2$ group (δ 1.14, 2.48, and 5.8 ppm signals) in dactylone.

The complete structure and absolute stereochemistry of dactylone were determined by single-crystal X-ray diffraction. A suitable single crystal was obtained by recrystallization from a hexane–ether mixture. The space group is $P2_12_12_1$ with unit cell dimensions $a = 8.788$ (2), $b = 12.1383$ (8), $c = 15.752$ (4). The intensities of all reflections with $\theta < 65^\circ$ were measured with Cu $K\alpha$ radiation [λ (Cu $K\alpha$) = 1.5418 Å], on a CAD-4 automatic diffractometer using θ – 2θ scans. Only the intensities for which $I > 1.4\sigma(I)$ were used in the structure determination. The structure was solved by the heavy-atom method. The present R value, on F , for the 1263 observed reflections is 0.109. The absolute configuration was determined using the method of

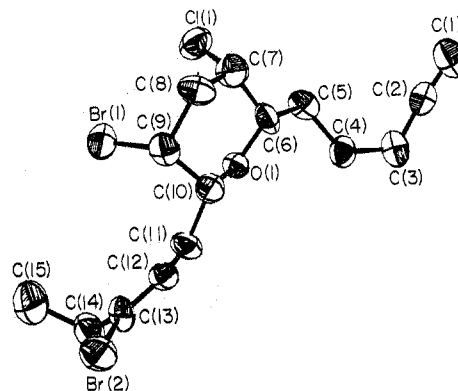
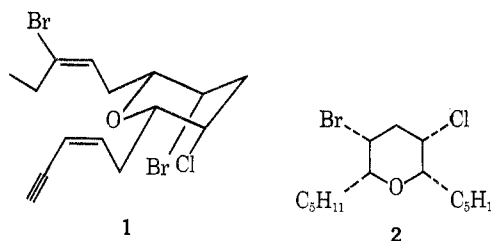


Figure 1. Computer perspective drawing of dactylone.

Bijvoet, Peerdeman, and van Bommel.⁶ A view of the molecule showing the stereochemistry and absolute configuration is given in Figure 1. The distances of 1.35 (2) Å and 1.34 (3) Å for C(3)–C(4) and C(12)–C(13) establish them as double bonds, while a distance of 1.21 (3) Å for C(1)–C(2) establishes it as a triple bond.

Catalytic reduction (platinum/ethyl acetate) of dactylone gave octahydromonobromodactylone (2, $C_{15}H_{28}OBrCl$).⁷ Retention of both halogens on the ring was indicated by the similarity of the proton absorptions ($CDCl_3$) due to deshielding by the halogens and oxygen in 2 [δ 4.14, (2, m, $CHBr$, $CHCl$), 3.54 and 3.31 ppm (1 each, m, 2 CHO)] compared with the corresponding absorptions of 1 (see Table I) and also to the presence at δ 2.76 ppm of a distinct pair of doubled triplets whose intense inner members overlap, corresponding to the ring methylene protons flanked by halogen-substituted carbon atoms.⁸ Irradiation of the δ 4.14 ppm signal collapsed the 2.76 multiplet to a broad singlet and altered each of the multiplets at 3.31 and 3.54 ppm. In the nmr spectrum of 2 taken in benzene- d_6 the ring methylene proton signals appear as a well-resolved pair of doubled triplets centered at 1.78 ($J = 16, 4$) and 2.45 ppm ($J = 16, 2$).⁹



Dactylone differs from all of the other reported members of the algal derived halogenated ethers having a straight-chain C-15 skeleton in that it has a six-membered ether ring rather than a four-, five-, eight-, or nine-membered ether ring as found in other members of this group. Dactylone is similar to chondriol^{2e} and rhodophytin^{2f} in that it is chlorinated at C-7 rather than oxygenated as it is in all of the other members of this family, but the absolute configurations at C-6 and C-7 in 1 are opposite to those in chondriol.^{2e} Dactylone is assumed to be of algal origin since it has been demonstrated in other cases^{1b,10} that halogenated compounds isolated from sea hares are present in the algae on which the animals feed.

Table I
Nmr Spectral Data^a for Dactylone

δ	No. of H's	Assignment	Multiplicity, J
1.14	3	H-15	t, 7
3.0–2.20	8	H-5,8,11,14	m ^b
3.18	1	H-1	dd, 2, 1
3.37	1	H-10 (or 6)	dt, 7, 2
3.71	1	H-6 (or 10)	d of dd, 8, 7, 2 ^c
4.12	2	H-7,9	m
5.60	1	H-3	d (11) with further fine splitting 2,1
5.8	1	H-12	t, 7
6.12	1	H-4	Complex m

^a $CDCl_3$ solvent. ^b δ 2.3–2.65 appears as a quintet superimposed on other absorption; at 220 MHz an unambiguous quartet centered at 2.48 ppm is evident. ^c Central members overlapped.

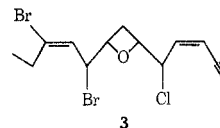
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References and Notes

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- (3) F. J. Schmitz and F. J. McDonald, *Tetrahedron Lett.*, 2541 (1974).
- (4) In a preliminary report [F. J. Schmitz, D. C. Campbell, and F. J. McDonald, *Int. Symp. Chem. Nat. Prod., Abstr.*, 95th, 12e (1974)] the structure **3**, see footnote 8 below, was proposed for dactylone.
- (5) *Anal.* Calcd for $C_{15}H_{19}OBr_2Cl$: C, 43.85; H, 4.66; Br, 38.93; Cl, 8.63. Found: C, 44.20; H, 4.73; Br, 37.61; Cl, 8.59; M^+ , 412 (2%), 410 (3%), 408 (1.5%) (high resolution ms: obsvd, 407.94890; calcd, 407.94911).
- (6) J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, **168**, 271 (1951).
- (7) Mp 52–53°, $[\alpha]^{25}_D$ -0.90° (c 5.4, $CHCl_3$). Calcd for $C_{15}H_{28}BrClO$: C,

53.10; H, 8.26; Br, 23.55; Cl, 10.44; Found: C, 53.47; H, 8.24, Br, 23.11; Cl, 10.09; M^+ , 340 (6%), 338 (5%).

- (8) It is interesting to note that the protons on the carbons bearing different halogens absorb at the same chemical shift position while the protons on the two ether carbons, which might be expected to absorb at the same position, in fact resonate at different positions. If the assignments of the protons on carbons bearing oxygen (C-6, C-10), see Table I and above, and those of carbons bearing halogen (C-7, C-9) are reversed, the nmr data alone (including decoupling) would suggest the structure **3**



for dactylone as was proposed in a preliminary report.⁴ This indicates that extreme caution must be exercised in making chemical shift assignments in this group of compounds.

- (9) The marked difference in chemical shift of these two methylene protons in benzene- d_6 can be rationalized by assuming that the aromatic solvent is much more closely associated with the unhindered face of **2** and hence the axial methylene proton is shifted upfield more than its equatorial counterpart. The observed coupling constants of 4 and 2 Hz are also in accord with expectations for an axial-equatorial coupling and a diequatorial coupling, respectively [R. U. Lemieux and J. W. Lown, *Can. J. Chem.*, **42**, 893 (1964)].
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