

Bromoallenes from the Alga *Laurencia microcladia*

Derek J. Kennedy,^{a*} Ian A. Selby,^a Heather J. Cowe,^b Philip J. Cox,^b and Ronald H. Thomson^c

^a Merck, Sharp and Dohme, Hertford Road, Hoddesdon, Herts EN11 9BU, U.K.

^b School of Pharmacy, Robert Gordon's Institute of Technology, Schoolhill, Aberdeen AB9 1FR, U.K.

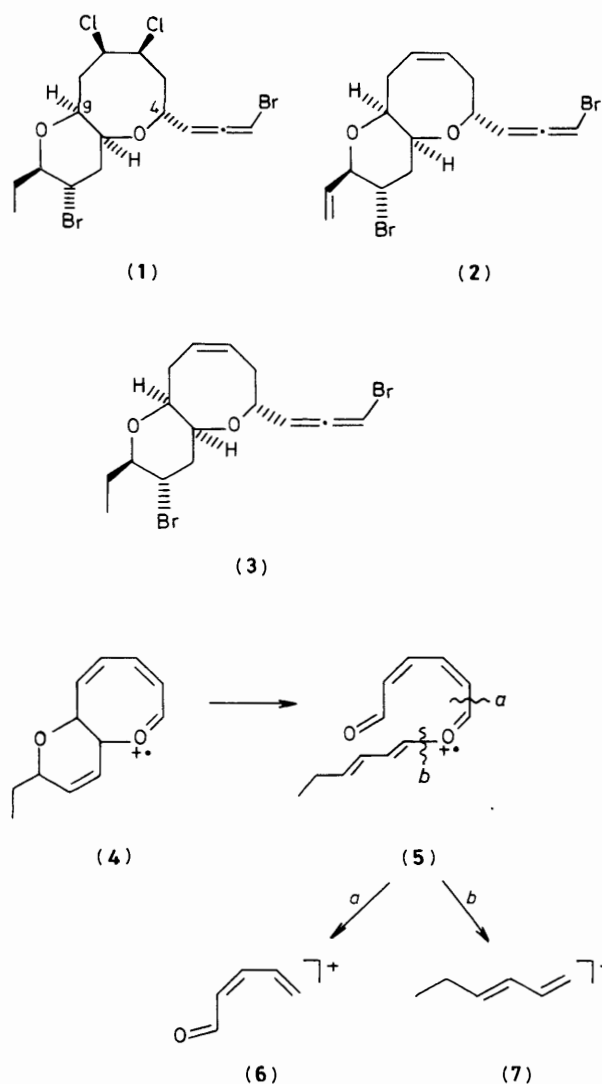
^c Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen AB9 2UE, U.K.

The structures of the microcladallenes A, B, and C have been established from spectroscopic data and X-ray crystallographic analysis of microcladallene B.

The red algal genus *Laurencia* elaborates a large number of metabolites¹ which include a C₁₅ family of halogenated cyclic ether enynes.² A second, closely related, C₁₅ family of allenes is now emerging,³ and we report here on the structures of three new bromoallenes isolated from *L. microcladia* (collected on the French coast at Cap Ferrat) by extraction with

methanol-toluene (3:1) followed by extensive chromatography.

Microcladallene C is an optically active, viscous oil, $[\alpha]_D^{20} + 116.7^\circ$ (c 0.5, Me₂CO). The molecular formula, C₁₅H₂₀Br₂Cl₂O₂, was derived from accurate mass measurement on the M⁺-Cl (found: *m/z* 424.9516; calc. 424.9517) and



$M^+ - \text{CH} = \text{C} = \text{CHBr}$ (found: m/z 342.9865; calc. 342.9866) ions. The ^1H and ^{13}C n.m.r. spectra† show the presence of a bromoallene side chain, an ethyl and three methylene groups, and seven $>\text{CHHal}$ and $>\text{CHO}$ methine protons, and to fit the molecular formula the compound must be bicyclic. Extensive decoupling of the 360 MHz ^1H n.m.r. spectrum‡ revealed both the gross structure and the relative stereochemistry (1) except at C-4. The gross structure (1) is consistent with the mass spectrum. In particular, a peak at m/z 191‡ ($\text{C}_{12}\text{H}_{13}\text{O}_2$) can be attributed to the backbone ion (4), derived from (1) by successive losses of the allenic side chain, HBr , and $2 \times \text{HCl}$, which, after retro-Diels–Alder conversion into (5), fragments at a and at b to give the two m/z 81 ions (6)

† ^1H δ (CDCl_3) (J in Hz) 0.98 (t, 7, 3H-15), 1.50 (ddq, 14,8,7, H-14), 1.78 (ddd, 14,2,2,2, H-8), 2.00 (ddd, 14,10,10, H-8), 2.04 (ddq, 14,2,2,7, H-14), 2.38 (ddd, 14,5,?, H-5), 2.40 (ddd, 14,12,4, H-11), 2.49 (ddd, 14,6,5,1,5, H-5), 2.73 (ddd, 14,4,3, H-11), 3.40 (ddd, 14,10,3, H-13), 3.88 (ddd, 10,2,1,8, H-9), 4.04 (ddd, 4,3,2, H-10), 4.06 (ddd, 12,10,4, H-12), 4.25 (dt, 10,2,2, H-7), 4.46 (m, H-6), 4.89 (m, H-4), 5.43 (t, 6,6, H-3), and 6.08 (dd, 6,2, H-1); ^{13}C δ (CDCl_3) 9.41 (C-15), 26.11 (C-14), 35.94 and 42.79 (each CH_2), 43.83 (C-11), 46.42 (C-12), 61.66 and 62.55 (C-6 and C-7), 74.14 (C-1), 73.54, 75.94 and 77.80 (each $-\text{CHO}-$), 83.63 (C-4), 101.24 (C-3), and 200.8 p.p.m. (C-2).

‡ All ions mentioned gave satisfactory accurate mass values.

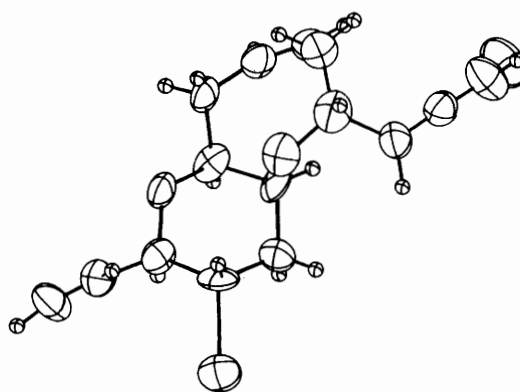
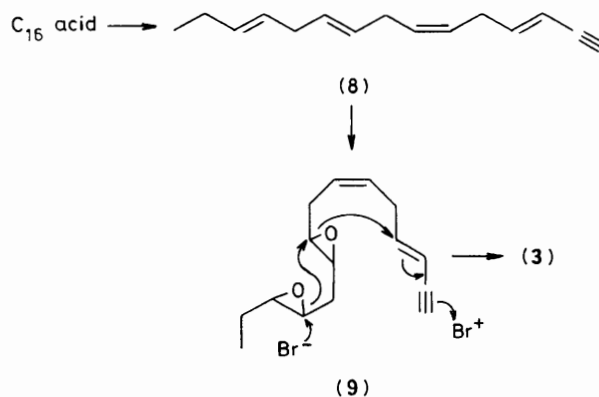


Figure 1. The atomic arrangement in microcladallene B (2).



($\text{C}_5\text{H}_5\text{O}$, calc. 81.0340) and (7) (C_6H_9 , calc. 81.0704), both of which were observed (81.0339 and 81.0701, respectively).

The structures of microcladallenes A { $\text{C}_{15}\text{H}_{20}\text{Br}_2\text{O}_2$, crystals, m.p. 90.5°C, $[\alpha]_D^{20} + 114.0^\circ$, (c 0.5, Me_2CO)} (3) and B { $\text{C}_{15}\text{H}_{18}\text{Br}_2\text{O}_2$, plates, m.p. 83°C, $[\alpha]_D^{20} + 96.0^\circ$ (c 0.5, Me_2CO)} (2) were deduced in the same way from spectral data. Decoupling of the ^1H n.m.r. spectra revealed the presence of the $\Delta^{6,7}$ double bond in both, and the vinyl group at C-13 in B. Final confirmation of structure (2) and the absolute configuration was obtained by X-ray crystallographic analysis of B which is crystalline. The similarity of the H-4 n.m.r. signal from A, B, and C suggests that all three have the same configuration at C-4.

Crystal data: $\text{C}_{15}\text{H}_{18}\text{Br}_2\text{O}_2$, $M = 389.2$, orthorhombic, space group $P2_12_12_1$, $a = 5.174(5)$, $b = 14.234(8)$, $c = 21.479(14)$ Å, $U = 1581.9$ Å³, $Z = 4$, $D_c = 1.634$ g cm⁻³, $\mu(\text{Mo-K}\alpha) = 50.0$ cm⁻¹. The 832 unique observed reflexions [$I > 3\sigma(I)$] with $2\theta < 50^\circ$ were measured on a Nicolet P3 automated diffractometer and corrected for crystal degradation. The structure was solved by direct methods⁴ and refined by full-matrix least-squares⁵ (Br, O, and C anisotropic, H calculated). The weighting scheme used was $w = 1.48/(\sigma^2 F_o)$ and convergence was reached at $R = 7.2\%$ (for the mirror image $R = 8.0\%$). § As considerable degradation of the crystal in the X-ray beam was observed, higher than usual e.s.d.'s are associated with geometrical parameters and the absolute configuration shown in Figure 1 may require future revision.

The biogenesis of these enyne and allenic systems is not known but the cyclisation of diepoxides, originally proposed

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

by Bu'Lock,⁶ remains highly attractive. Thus microcladallene A could arise by brominative cyclisation of (9) formed by selective epoxidation of (8), itself derived from the related C₁₆ non-conjugated polyene acid. While (8) has not been found the all-*cis* isomer, laurencenyne, has been isolated⁷ from *L. okamurai*.

We thank the Edinburgh University WH-360 NMR Service for n.m.r. spectra, the S.E.R.C. for a studentship (to H. J. C.), and particularly Dr. A. Meinesz, Laboratoire de Biologie et D'Ecologie Marines, 28 Av. de Valrose, 06034 Nice Cedex, France, for collection and identification of algal material.

Received, 3rd November 1983; Com. 1437

References

- 1 B. M. Howard and W. Fenical, in 'Progress in Phytochemistry,' eds. L. Reinhold, J. B. Harborne, and T. Swain, Pergamon Press, Oxford, 1981, Vol. 7, p. 263.
 - 2 R. E. Moore in 'Marine Natural Products,' ed. P. J. Scheuer, Academic Press, New York, 1978, Vol. 7, p. 43.
 - 3 A. Fukuzawa and E. Kurosawa, *Tetrahedron Lett.*, 1979, 2797; M. Suzuki and E. Kurosawa, *ibid.*, 1981, **22**, 3853; M. Suzuki and E. Kurosawa, *Chem. Lett.*, 1982, 289; K. Kurata, A. Furusaki, K. Suehiro, C. Katayama, and T. Suzuki, *ibid.*, 1982, 1031; P. J. Cox, S. Imre, S. Islimyeli, and R. H. Thomson, *Tetrahedron Lett.*, 1982, **23**, 579; M. Suzuki, K. Koizumi, H. Kikuchi, T. Suzuki, and E. Kurosawa, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 715.
 - 4 P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, MULTAN 78, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data,' University of York, 1978.
 - 5 G. M. Sheldrick, SHELX, 'A program for crystal structure determination,' University of Cambridge, 1976.
 - 6 J. D. Bu'Lock, in 'Comparative Phytochemistry,' ed. T. Swain, Academic Press, London, 1966, p. 79.
 - 7 H. Kigoshi, Y. Shizuri, H. Niwa, and K. Yamada, *Tetrahedron Lett.*, 1981, **22**, 4729; 1982, **23**, 1475.
-