

MARGINATAFURAN, A FURANODITERPENE WITH A NEW CARBON SKELETON  
FROM THE DORID NUJIBRANCH CADLINA LUTEOMARGINATA

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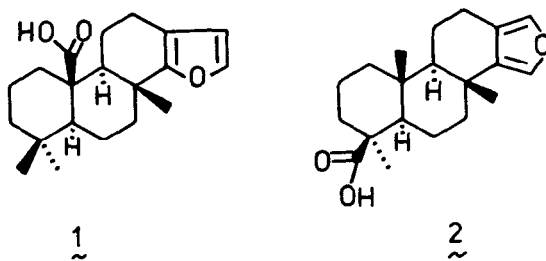
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Summary: The structure of marginatafuran (1), a furanoditerpene isolated from specimens of Cadlina luteomarginata collected in the Queen Charlotte Islands, was solved via X-ray diffraction analysis.

Cadlina luteomarginata is found along the Pacific coast of North America from Auke Bay, Alaska to Point Eugenia, Mexico.<sup>1</sup> The secondary metabolites found in the skin extracts of C. luteomarginata have been shown to differ from one collecting site to another. Faulkner and co-workers<sup>2</sup> have isolated furanosesquiterpenes, a furanosesterterpene, a sesquiterpene isonitrile and a sesquiterpene isothiocyanate from La Jolla collections of C. luteomarginata. We have isolated furanosesquiterpenes<sup>3</sup>, a degraded sesterterpene<sup>4</sup>, and a drimane sesquiterpene acetate<sup>3</sup> from Straight of Georgia and Barkley Sound collections. The observed variation in metabolite content with location results from variations in the chemistry of the dietary sponges from which the nudibranch sequesters many of its interesting metabolites. In this paper we report the structure of a new furanoditerpene isolated from specimens of C. luteomarginata collected in the Queen Charlotte Islands.

Freshly collected whole nudibranchs (twelve individuals) were immediately immersed in methanol and stored at -5°C. After twelve months the methanol was decanted and evaporated in vacuo to give a residue which was suspended in water and extracted with chloroform. Silica

gel HPLC purification of the chloroform extract gave pure marginatafuran (1, 4 mg): colorless needles mp 208° (hexane);  $[\alpha]_D = -102^\circ$  (C 0.22, CHCl<sub>3</sub>); MS M<sup>+</sup>, m/z (rel. intensity) 316.2041 (25) req'd for C<sub>20</sub>H<sub>28</sub>O<sub>3</sub> 316.2039, 301(20), 255(25), 109(25), 44(100); IR (CCl<sub>4</sub>) 3300–2300, 1705, 1465, 1255 cm<sup>-1</sup>; <sup>1</sup>H NMR (CCl<sub>4</sub>, 270 MHz) δ 0.92(s,6H), 1.08(s,3H), 6.00(d, J=1Hz,1H), 7.10(d, J=1Hz, 1H).



The observed spectral data indicated that marginatafuran (1) was closely related to the furanoditerpene 2 isolated from the bath sponge *Spongia officinalis*.<sup>5</sup> <sup>1</sup>H NMR resonances at δ 6.00 and 7.10 suggested, however, that the furan ring was αβ disubstituted, and the biogenetic isoprene rule demanded that it be fused as shown in 1. A disparity in the <sup>1</sup>H NMR chemical shifts of the tertiary methyl groups in 1 (0.92, 6H; 1.08 3H) and 2 (0.82, 1.21, 1.25 all 3H) indicated that the carboxylic acid functionality could not be attached at the 4β position in 1 as it is in 2. In order to verify the nature of the carbon skeleton and to unambiguously establish the position of attachment of the carboxylic acid functionality, marginatafuran (1) was subjected to single crystal x-ray diffraction analysis.

Marginatafuran (1) crystallized in the triclinic system, and accurate lattice parameters of a=7.6551(18), b=10.3979(22), c=11.9196(23) Å, α=81.043(16), β=81.215(18), and γ=102.759(18)° were determined from a least squares fit of fifteen moderate 2θ-values. The crystal density and presence of chirality were accommodated by space group P1 with one molecule of composition C<sub>20</sub>H<sub>28</sub>O<sub>3</sub> forming the asymmetric unit. All unique diffraction maxima with 2θ < 114° were collected on a computer controlled four-circle diffractometer using variable speed, 1° ω-scans and graphite monochromated Cu Kα radiation (1.54178 Å). Of the 2428 reflections collected in this manner, 2002 (82%) were judged observed ( $|F_o| > 3\sigma(F_o)$ ). A phasing model was found using direct methods techniques, and hydrogens were located on a difference electron density synthesis following partial refinement<sup>6</sup>. Block diagonal least squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens have converged to a conventional crystallographic residual of 0.0524 for the observed reflections<sup>7</sup>.

Figure 1 is a computer generated perspective drawing of the final x-ray model. The x-ray experiment did not define the absolute configuration so the enantiomer shown is an arbitrary choice. The A- and B-rings are in the chair conformation and the C-ring is in the half-chair conformation. The furan ring is planar. Bond distances and angles agree well with generally accepted values.

Marginatafuran (**1**) has a new diterpene carbon skeleton for which we propose the trivial name marginatane.

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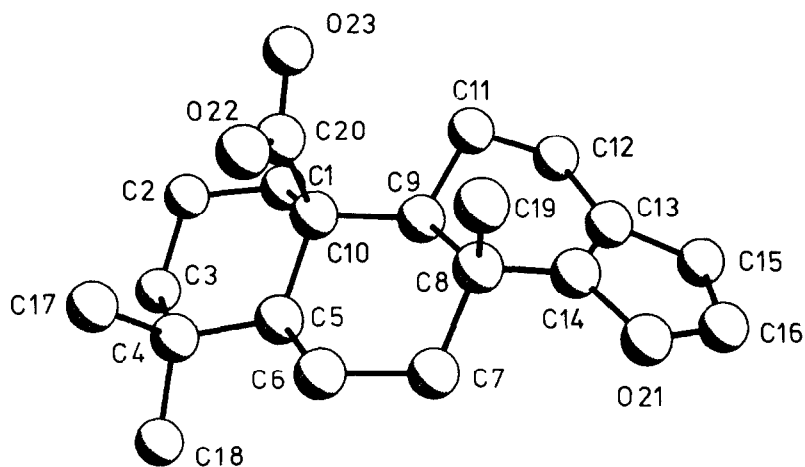


Figure 1

References:

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- 6) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M.E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from x-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S.E. Hull, L. Lessinger, G. Germain, J.P. De-clercq and M.M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P.T. Beurskens et al., University of Nijmegen, Netherlands, 1981; MITHRIL, an automatic solution package written by C.J. Gilmore, University of Glasgow, Scotland, 1983; an anisotropic block diagonal least squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W.D.S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.
- 7) Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, ENGLAND CB2 1EW and are available from them.

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