

LOBOLIDE: A NEW EPOXY CEMBRANOLIDE FROM MARINE ORIGIN

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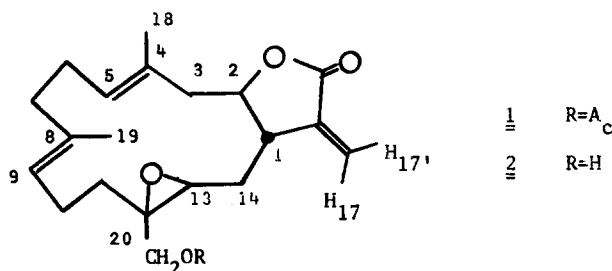
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The occurrence of cembrane diterpenes in the gorgonians and alcyonarians (soft corals) have been reported recently in an increasing number of examples.¹ We wish to report herein on the isolation and structure elucidation of a new cembranolide which we have named lobolide. Lobolide was isolated from the Petrol-ether extract of a freeze-dried lobophytum sp. collected in the Gulf of Eilat (Red Sea).

As in the case of sarcophine, which was isolated by us from another soft coral (*Sarcophytum Glaucum*)², lobolide was found to be toxic to fish, and thus may play a role in the protective mechanism of the coral against predators.

Structure 1 was deduced for lobolide according to the following spectral data; 1, m.p. 114°-115°, $[\alpha]_D^{25} -58^\circ$ (c, 2.7, CHCl₃), λ_{max}^{MeOH} 209 nm ($\epsilon=7600$), $\nu_{max}^{CCl_4}$ 1770, 1740, 1660 cm⁻¹, showed only a weak molecular peak at m/e 374 standing for C₂₂H₃₀O₅. This peak was accompanied by a stronger fragment at m/e 332 (M-CH₂=C=O) which can indicate on an acetate group (1740 cm⁻¹). The two other strong absorptions in the IR spectrum can suggest the presence of an unsaturated γ -lactone.



Most significant for the structure elucidation were the ¹³C nmr and the high resolution ¹H-nmr spectra. ¹H nmr (270MHz, CDCl₃): 1.52dd(H₁₄), J=14.9, 6.9Hz; 1.61brs and 1.72brs (Me₁₈ and Me₁₉); 1.88dt(H₁₄), J=14.9, 3.8Hz; 2.12s(OCOCH₃); 2.85m(H₁); 2.94dd(H₁₃), J=6.9, 3.8Hz; 3.93 and 4.34 AB-quartet (CH₂OAc), J=12.0Hz; 4.17ddd(H₂), J=9.7, 6.7, 2.9Hz; 5.04brt and 5.18brq (H₅ and H₉); 5.93d(H₁₇) J=2.8Hz; and 6.28d(H₁₇), J=3.1Hz. ¹³C nmr (22.63 MHz, CDCl₃, ppm relative to TMS) 170.4s; 169.4s; 139.7s; 135.0s; 130.2d; 129.5s; 124.5d; 122.7t; 79.6d; 64.3t; 61.9d; 60.4s; 45.3t; 45.0d; 38.7t; 32.4t; 31.8t; 24.8t; 23.2t; 20.5q; 17.0q; 15.6q. From the nmr data all the functional moieties of 1 could be accounted for, namely the existence of an α -methylene γ -lactone, one epoxide, two trans-three substituted double bonds and one acetate. Moreover, the primary acetate group which in the ¹H nmr spectrum, exhibits an AB-quartet has to be located near the epoxide ring. This latter vicinity was further established by the neighbouring group participation of the acetate during the opening of the epoxide under acidic conditions. The various

functional groups count for seven out of the eight degrees of unsaturation of lobolide which should thus possess only one carbocyclic ring. There are several examples in the literature for $\alpha\beta$ -unsaturated cembranolides from marine origin^{1a}, moreover a cembranolide possessing the α -methylene γ -lactone, named lobophytolide, was isolated from Lobophytum cristagalli.^{1b} This diterpene contains all the functional groups as in lobolide except for the acetoxy one. Based on the above knowledge we suggested for lobolide a cembrane structure. We first considered a similar structure and location of functional groups in lobolide as in lobophytolide, i.e. an epoxide at C₄-C₅.

The first indication which disagreed with this suggestion came from the LIS nmr spectrum of 2⁴, obtained by mild hydrolysis of 1. According to this measurement, the primary alcohol has to be relatively close to the exocyclic double bond as the following order of $\Delta\delta$'s H₂₀, H_{20'} > H₁₃ > H₁ > H₁₇ > H₂ > H_{17'} > H₅, H₉ was obtained. Position 8(9) for the epoxide being of low probability on grounds of the shift reagent nmr measurement, was finally excluded by a micro-ozonolysis³ which gave levulinialdehyde. The formation of the latter aldehyde, together with the existence of two allylic protons coupled with H₂, confirms the C₄-C₉ segment in 1. Unequivocal proof for the location of the oxirane ring at C₁₂-C₁₃, and hence of the acetate at C₂₀, was obtained from a double resonance experiment summarized in the following table:

Irradiated proton (δ , ppm)	Observed protons and changes (J in Hz)
H ₁₃ (2.94)	H ₁₄ (1.88dt) + dd, J=14.9, 3.8; H _{14'} (1.52dd) + brd, J=14.9.
H ₁₄ (1.88)	H ₁₃ (2.94dd) + d, J=6.9; H ₁ (2.85m) + change in the multiplicity.
H ₁ (2.85)	H ₂ (4.17ddd) + dd, J=6.7, 2.9; H ₁₇ (5.93d) + s; H _{17'} (6.28d) + s; H ₁₄ (1.88dt) + brd, J=14.9; H _{14'} (1.52dd) unchanged.

The structure of other related cembranolides and other diterpenes from other lobophytum sp. will be reported in the completed paper.

References

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4. The lanthanide induced shifts (LIS) were obtained by the addition of Eu(fod)₃ to the carbontetrachloride solution of 2.