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EMBLIDE, A NEW POLYFUNCTIONAL CEMBRANOLIDE FROM THE SOFT CORAL *SARCOPHYTON GLAUCUM*[1a]

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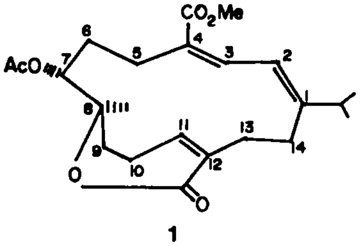
Abstract—From a Pacific marine coelenterate we have isolated emblide, a cembrane diterpenoid which bears acetoxy, dienoic ester, and α,β-unsaturated ϵ-lactone functions. Its structure (1) was deduced from spectral and X-ray crystallographic data.

Cembrane diterpenoids, while first isolated from terrestrial plants, are the predominant non-steroidal metabolites of certain marine coelenterates. Recent reviews[2] and continued activity, particularly by Tursch[3] and by Coll[4] and their collaborators, attest to the versatility of these frequently oxygenated isoprenoids featuring a 14-membered carbocycle.

From *Sarcophyton glaucum* (Quoy and Gaimard, 1882) (Family Alcyoniidae, Order Alcyonacea, subclass Alcyonaria, class Anthozoa, phylum Coelenterata),[5] collected at Enewetak atoll, Marshall islands, we have isolated a new cembrane derivative, which possesses structure 1 and which we have named emblide.[6]



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Ethanol extraction of the wet animals followed by silica gel chromatography and recrystallization from methanol yielded emblide as a colorless crystalline solid, $C_{23}H_{32}O_6$, m.p. 119–120°. Spectral features of emblide (1), of its C-7 alcohol (2), and of hexahydroemblide (3) secured the nature of all functional groups. Ready loss of methanol (*m/e* 372), and of acetic acid (*m/e* 344) from the molecular ion (*m/e* 404) showed the presence of methyl ester and acetoxy groups; these functions were confirmed by appropriate three-proton singlets at δ 3.7 and 2.0. A UV maximum at 284 nm (ϵ 15,600) suggested a dienoic ester (supported by IR ν_{max} 1695 cm^{-1}), in agreement with absorption expected of a trialkylated methyl sorbate.[7] Two one-proton doublets at δ 7.11 and 6.15 (J = 12 Hz) may thus be assigned to *beta* and *gamma* protons of the dienoate system. A third C=C double bond is indicated by a total of six olefinic ^{13}C NMR signals (155.0–120.8 ppm), three singlets and three doublets. One unassigned olefinic carbon doublet bears the remaining olefinic proton, a broadened triplet at δ 6.02, which appears to be the *beta* proton of a monoenoate. A signal at δ 5.26 (1 H dd, J = 6, 2 Hz) in the ^{1}H NMR spectrum of emblide (1), assigned to an ester methine, cannot be associated with this α,β-unsaturated ester. It must be the methine proton of the acetate since in the free alcohol (2) this resonance is seen at δ 4.12 (dd, J = 8, 2 Hz). Conversely, a Me singlet at δ 1.42 in 1 remains unchanged in 2 and in 3, thereby placing it at the carbon (C-8) bearing the oxygen of the monoenoate. These interpretations are further supported by a corresponding ^{13}C NMR doublet at 68.2 ppm (C-7) and a singlet at 82.3 (C-8). Three ester CO signals at 169.3, 168 and 166.1 ppm, matched by a single IR frequency at 1735 cm^{-1}, require that the remaining function be an α,β-unsaturated lactone of six or more members.

Biogenetic considerations favor a 14-membered isoprenoid system, but available data do not permit unambiguous placement of the functional groups or correct determination of the lactone ring size. A crystal of emblide (1) was therefore subjected to X-ray diffraction studies.

Preliminary X-ray photographs of emblide showed orthorhombic symmetry. Accurate lattice constants, determined by a least-squares fitting of fifteen moderate 2θ-values, were a = 10.138(2), b = 11.098(2) and c = 19.505(2) Å. Systematic extinctions, the known chirality and a crystal density of 1.22 g/cc were uniquely consistent with space group $P2_12_12_1$ with one molecule of $C_{23}H_{32}O_6$ per asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were recorded on a fully automated four-circle diffractometer using graphite monochromated CuKα radiation (1.54178 Å) and 1° ω-scans. A total of 1720 reflections were recorded in this way and after correction for Lorentz, polarization and background effects, 1557 (91%) were judged observed ($F_o^2 \geq 3\sigma(F_o^2)$).

A phasing model was derived using a weighted multiple solution tangent formula approach. A chemically plausible 22 atom fragment was located in the resulting E-synthesis and a tangent formula recycling procedure revealed all 29 nonhydrogen atoms. H atoms were located on a difference electron density synthesis after partial refinement. Full matrix least-squares refinements with anisotropic non-H atoms and isotropic hydrogens have converged to the current crystallographic residual of 0.044 for the observed data, see Tables I and II. There were no unusual intermolecular contacts or large peaks in a final difference synthesis. The X-ray diffraction experiment defined only the relative stereochemistry of emblide.

A computer generated perspective drawing of the final X-ray model is shown in Fig. 1. Emblide has the 14-membered carbocyclic ring of the cembrane diterpenes. The double bond at C(1) has the *E* configuration while those at C(3) and (C11) have the *Z* configuration. The relative configurations are C7(S*) and C8(R*). The molecular geometry agrees well with generally expected values.

EXPERIMENTAL

UV spectra (95% EtOH) were recorded on a Carey-14 Recording Spectrophotometer; IR spectra on a Perkin-Elmer 467 or a Beckman IR-10 Spectrophotometer. ^{1}H NMR spectra were determined on a Varian HA-100 or a Varian XL-100 instrument, using TMS as internal standard $\delta = 0$. ^{13}C NMR spectra were obtained on a Varian XL-100 spectrometer in the Fourier transform mode. Optical rotations were determined on a Bendix–Ericsson Automatic Polarimeter type 143A. Mass spectra were measured on a Varian MAT-311 instrument. Melting points determined on a Fisher–Johns apparatus and uncorrected.

Isolation. A wet sample (650 g) of *Sarcophyton glaucum*, collected February, 1974 from the coral pinnacle near Bogen Island, Enewetak atoll, and identified by J. Verseveldt, was extracted with several portions of EtOH. This extract was partitioned between water and ether. The ether phase yielded 17 g of oily residue, which was subjected to preparative tlc in 250 mg portions (10% ether/90% CH_2Cl_2; silica gel HF). Recrystallization from MeOH yielded 270 mg emblide, m.p. 119–120°; $[\alpha]_D^{25°} = +92°$ (*c* 1.3, CCl_4); MS: *m/e* 404 (4), 372 (6), 344 (2 rel%). IR: 1735, 1695, 1660, 1475, 1380, 1370, 1240 cm^{-1}; UV (EtOH) 284 (ϵ 15,600), 220 nm (8800); ^{1}H NMR ($CDCl_3$) δ 7.11 (1 H d, J = 12 Hz), 6.15 (1 H d, J = 12 Hz), 6.02 (1 H br t, J = 4 Hz), 5.25 (1 H dd), 3.70 (3 H s), 3.10 (1 H br m), 2.35 (8 H, br m), 2.0 ppm (5 H br s), 1.8 (1 H br s), 1.77 (1 H br m), 1.43 (3 H s), 1.15 (6 H dd); ^{13}C NMR ($CDCl_3$), 169.3 (s), 168.0 (s), 166.1 (s), 155.0 (s), 142.0 (d), 135.4 (d), 131.9 (s), 124.4 (s), 120.8 (d), 82.3 (s), 68.2 (d), 51.2 (q), 37.1 (s), 35.9 (q), 34.3 (s), 27.1 (2), 26.3, 25.3, 23.7, 22.7, 21.9, 20.9. (Found: M$^+$ 404.21689. Calcd for $C_{23}H_{32}O_6$: M$^+$ 404.21957).

Deacetylemblide (2). Emblide (40.0 mg) was dissolved in 15 ml MeOH and 1 mg Na was added. The soln was gently refluxed 1 hr and then stirred 4 hr at room temp. Extraction with $CHCl_3$ and evaporation gave 28 mg of 2, $C_{21}H_{30}O_5$, M$^+$ 362; IR ($CHCl_3$) 3450, 1720, 1680, 1450, 1380, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.94 (1 H d, J = 12 Hz), 6.25 (1 H d, J = 12 Hz), 6.08 (1 H t, J = 4 Hz), 4.12 (1 H dd, J = 8, 2 Hz), 3.80 (3 H s), 1.43 (3 H s), 1.28 (14 H, br), and 1.10 (6 H dd).

Hexahydroemblide (3). A soln of 1 (51.5 mg) in 20 ml Me_2CHOH was hydrogenated over 10% Pd/C for 20 hr. The hydrogenated product was isolated as an oil; IR ($CHCl_3$) 1735, 1450, 1380, 1370, 1240 cm^{-1}; UV (EtOH) 275 nm (ϵ 1150); ^{1}H NMR ($CDCl_3$) appeared to show a mixture of isomers.

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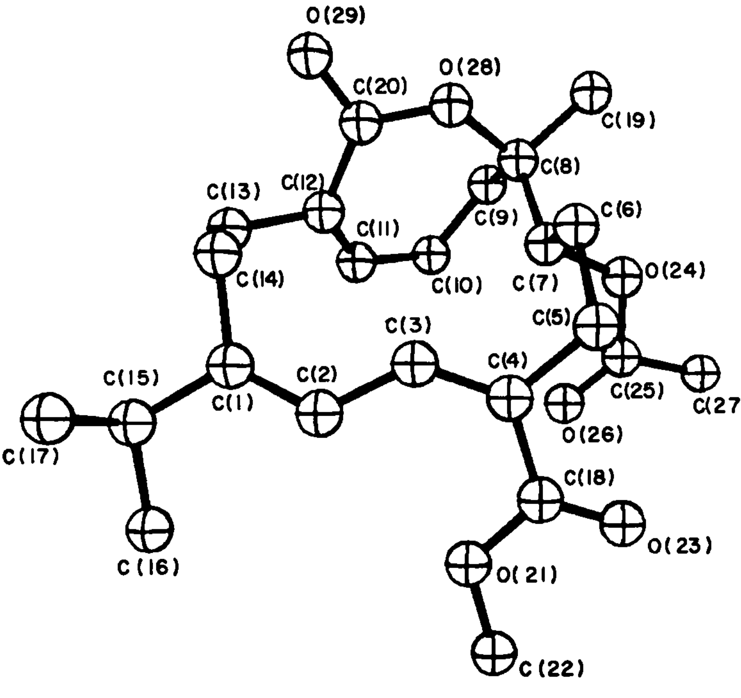

Fig. 1. Computer-generated X-ray model of emblide (1).

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