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KETOEMBLIDE AND SARCOPHYTOLIDE, TWO NEW CEMBRANOLIDES WITH ε-LACTONE FUNCTION FROM THE SOFT CORAL *SARCOPHYTA ELEGANS*

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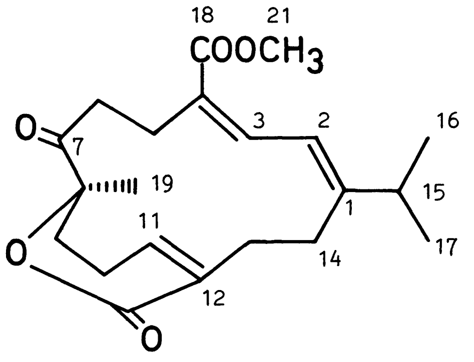
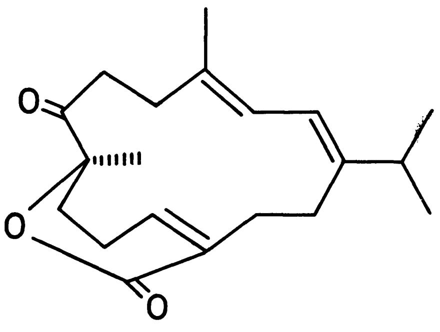
Two new cembranolides, ketoemblide and sarcophytolide, with ε-lactone function have been isolated from the soft coral *Sarcophyta elegans*. The structures were elucidated on the basis of chemical correlation with emblide and spectral data.

During our continuing search[1)] for biological active compounds from soft corals, we have isolated two new cembrane derivatives 1 and 2, which closely related to the recently described cembranolide emblide (3),[2)] from *Sarcophyta elegans* collected at the coral reef near Kagoshima. We wish to report herein on the structure elucidation of these new cembranolides which we have named ketoemblide (1) and sarcophytolide (2).

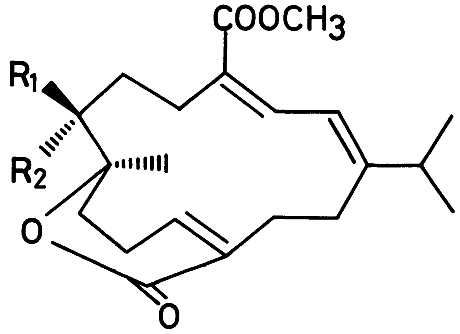


1

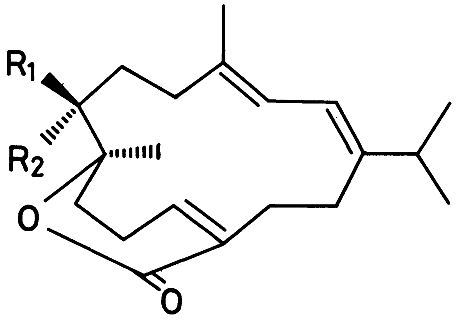


2

Conventional silica gel column chromatography and preparative TLC of the $CHCl_3$/MeOH extract of the wet *S. elegans* yielded ketoemblide (1) and sarcophytolide (2) as the oils. Ketoemblide (1), $[\alpha]_D$ +51.5° (c 1.70, $CHCl_3$), analyzed for $C_{21}H_{28}O_5$ by high mass measurement ($M^{+\cdot}$ 360.1920, calcd. 360.1934). The spectral features of this highly oxygenated diterpenoid were very similar to those of reported cembranolide emblide (3),[2)] with exception that 1 possessed a ketone. Thus the same major structural characteristics of 3 were observed for the IR ($CHCl_3$), UV (EtOH), ^1H and ^{13}C NMR[3)] ($CDCl_3$) spectra of 1: an isopropyl group (δ 1.07 and 1.12, each 3H, d, J=6.5 Hz; δ 21.7q and 22.8q), a methyl (δ 1.54, 3H, s; δ 29.0q) on a carbon carrying oxygen, a methoxycarbonyl group (ν 1700 cm^{-1}; δ 3.78, 3H, s; δ 51.4q and 168.0s) conjugated with a diene system



3: R_1=H, R_2=OAc
4: R_1=H, R_2=OH
5: R_1=OH, R_2=H



6: R_1 =H , R_2=OH
7: R_1 =OH , R_2=H
8: R_1 = H, R_2=OAc

(δ 6.27 and 6.97, AB q, J=11.5 Hz), which was supported by a UV maximum at 284 nm (ε 12000) for the dienoic ester, an α,β-unsaturated lactone (ν 1685 cm^{-1}; δ 166.5s) with the β-olefinic proton (δ 5.97, 1H, br t, J=4.5 Hz), and a ketone (ν 1720 cm^{-1}; δ 208.3s). From the above data and a consideration of the eight degrees of unsaturation required by the molecular formula, structure **1** was deduced for ketoemblide and this was confirmed by a correlation of ketoemblide and emblide (**3**) which was isolated from a Pacific soft coral *Sarcophyton glaucum*.2)

Reduction of the ketone function of **1** with $NaBH_4$ in tetrahydrofuran afforded two isomeric alcohols **4** and **5**.4) **4**: $C_{21}H_{30}O_5$ ($M^{+\cdot}$ 362), mp 159.0-160.0 °C, $[\alpha]_D$ +140.2° (c 1.50, $CHCl_3$); IR ($CHCl_3$) 3475, 1700 (sh), 1680 and 1630 cm^{-1}; ^1H NMR (Table 2). **5**: $C_{21}H_{30}O_5$ ($M^{+\cdot}$ 362), an oil; IR ($CHCl_3$) 3500, 1705 (sh), 1690 and 1630 cm^{-1}; ^1H NMR (Table 2). Acetylation of **4** with Ac_2O/Py yielded a monoacetate **3**, $C_{23}H_{32}O_6$ ($M^{+\cdot}$ 404), mp 133.5-134.5 °C, $[\alpha]_D$ +177.6° (c 0.76, $CHCl_3$)[+125.0° (c 0.76, CCl_4)] ; whose spectra (UV, IR, ^1H and ^{13}C NMR) listed below were identical with those of authentic emblide.5) UV (EtOH) λ_{max} 284 nm (ε 13500); IR ($CHCl_3$) 1735, 1690, 1680, 1628, 1380, 1370 and 1240 cm^{-1}; ^1H NMR (Table 1); ^{13}C NMR δ 20.9q, 21.9q, 22.7q, 23.8q, 25.3t, 26.4t, 27.2t, 27.2t, 34.5t, 35.9d, 37.1t, 51.3q, 68.3d, 82.4s, 121.0d, 124.5s, 132.1s, 135.5d, 142.2d, 155.3s, 166.4s, 168.4s and 169.6s. Thus the structure of ketoemblide was determined as shown in **1**.

Sarcophytolide (**2**), $[\alpha]_D$ +201.4° (c 1.43, $CHCl_3$), had the molecular formula $C_{20}H_{28}O_3$ ($M^{+\cdot}$ 316.1994, calcd. 316.2037), indicating seven degrees of unsaturation. The IR bands at 1720 and 1682 cm^{-1} suggested the presence of a ketone and an α,β-unsaturated lactone by comparison with the spectrum of **1**. Twenty signals from the ^{13}C NMR spectrum ($CDCl_3$) showed a marked structural resemblance to ketoemblide (**1**), the major difference being the presence of a methyl signal at δ 18.8q in place of the methoxycarbonyl group (δ 51.4q and 168.0s) of **1**. The ^1H NMR spectrum also indicated that the methoxycarbonyl group in **1** at δ 3.78 (3H, s) had become a methyl group in **2** at δ 1.76 (3H, br s) because the AB pattern at δ 6.97 (1H, d, J=11.5 Hz) and 6.27 (1H, d, J=11.5 Hz) due to the β and γ protons in the dienoic ester group of **1** shifted to the upper field at δ 5.50 (1H, br d, J=11.0 Hz) and 6.07 (1H, d, J=11.0 Hz) due to the protons on the diene system of **2**, while the isopropyl group, the methyl on a carbon carrying oxygen, and the β proton on the α,β-unsaturated lactone group in **2** appeared at δ 1.03 and 1.06 (each 3H, d, J=6.5 Hz), 1.53 (3H, s),

Table 1. ^{1}H NMR Data (90 MHz, $CDCl_3$, δ) for **1**, **2**, **3** and **8**

	1	**2**	**1** (C_6D_6)	**2** (C_6D_6)	**3**	**8**
H-2	6.27 (d, 11.5)	5.50 (br d, 11.0)	6.29 (d, 11.0)	5.61 (br d, 11.0)	6.28 (d, 12.0)	5.59 (br d, 11.0)
H-3	6.97 (d, 11.5)	6.07 (d, 11.0)	7.29 (d, 11.0)	6.15 (d, 11.0)	7.17 (d, 12.0)	6.20 (d, 11.0)
H-7	-	-	-	-	5.42 (dd, 9.0, 2.5)	5.59 (overlaps with H-2)
H-11	5.97 (br t, 4.5)	6.04 (br t, 4.0)	5.59 (br t, 4.0)	5.79 (br t, 4.0)	6.12 (br t, 4.0)	6.10 (br t, 4.0)
H-16	1.07 (d, 6.5)	1.03 (d, 6.5)	0.94 (d, 7.0)	1.00 (d, 7.0)	1.08 (d, 7.0)	1.05 (d, 6.5)
H-17	1.12 (d, 6.5)	1.06 (d, 6.5)	1.05 (d, 7.0)	1.03 (d, 7.0)	1.13 (d, 7.0)	1.09 (d, 6.5)
H-18	-	1.76 (br s)	-	1.69 (br s)	-	1.71 (br s)
H-19	1.54 (s)	1.53 (s)	1.09 (s)	1.18 (s)	1.47 (s)	1.46 (s)
H-21	3.78 (s)	-	3.43 (s)	-	3.75 (s)	-
OAc	-	-	-	-	2.03 (s)	2.04 (s)

Coupling constants in parentheses are given in Hz.

Table 2. ^{1}H NMR Data (90 MHz, $CDCl_3$, δ) for **4**-**7**

	4	**6**	**5**	**7**
H-2	6.26 (d, 12.0)	6.16 (d, 11.5)	6.48 (d, 12.0)	6.08 (d, 11.0)
H-3	6.96 (d, 12.0)	5.57 (br d, 11.5)	7.03 (d, 12.0)	5.80 (br d, 11.0)
H-7	4.13 (br d, 9.5)	4.30 (br d, 10.0)	4.26 (dd, 11.0, 2.5)	4.15 (dd, 11.0, 2.5)
H-11	6.09 (br t, 4.0)	6.12 (br t, 4.0)	5.93 (m)	5.92 (m)
H-16	1.09 (d, 7.0)	1.07 (d, 7.0)	1.09 (d, 7.0)	1.06 (d, 7.0)
H-17	1.12 (d, 7.0)	1.09 (d, 7.0)	1.12 (d, 7.0)	1.09 (d, 7.0)
H-18	-	1.77 (br s)	-	1.68 (br s)
H-19	1.41 (s)	1.38 (s)	1.13 (s)	1.16 (s)
H-21	3.79 (s)	-	3.77 (s)	-

and 6.04 (1H, br t, J=4.0 Hz), respectively, with very slight different chemical shifts from those of 1 in both $CDCl_3$ and C_6D_6 (Table 1). Furthermore, UV absorption maximum of 2 at 238 nm (ε 20700, EtOH), which showed blue shift from that of 1, accounted for the replacement of the methoxycarbonyl group of 1 by a methyl group. We therefore proposed the structure 2 for sarcophytolide.

Assignment of this structure was reinforced by preparation of the alcohol derivatives 6 and 7, which were obtained by $NaBH_4$ reduction of 2 as in the case for 1. 6: $C_{20}H_{30}O_3$ ($M^{+\cdot}$ 318), mp 81.0-82.0 °C, $[\alpha]_D$ +160.0° (c 1.10, $CHCl_3$); IR ($CHCl_3$) 3475, 1680 and 1645 cm^{-1}. 7: $C_{20}H_{30}O_3$ ($M^{+\cdot}$ 318), an oil, $[\alpha]_D$ +70.9° (c 1.27, $CHCl_3$); IR ($CHCl_3$) 3430, 1685 and 1635 cm^{-1}. Comparison of the ^1H NMR spectra of the above alcohols with those of 4 and 5, shown in Table 2, exhibited mutually the strong similarities between 4 and 6, and 5 and 7, except for the signals (H-2, 3, 18 and 21) which were derived from the methyl dienoate and the methyl-bearing diene system. This was also recognized when the ^1H NMR spectrum of the acetate 8, $C_{22}H_{32}O_4$ ($M^{+\cdot}$ 360), an oil, $[\alpha]_D$ +170.0° (c 0.40, $CHCl_3$); IR ($CHCl_3$) 1730, 1680, 1375, 1365 and 1240 cm^{-1}, which was acetylation (Ac_2O/Py) product of 6, was compared with that of emblide (3), as seen in Table 1. On the basis of the above spectral and chemical evidence the structure of sarcophytolide was elucidated as 2.

Ketoemblide and sarcophytolide may be derived in nature by oxidation of cembrene C(6) precursor.

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3) ^{13}C NMR data: 1: δ 21.7q, 22.8q, 24.4t, 27.0t, 27.9t, 29.0q, 33.2t, 34.0t, 35.1d, 35.1t, 51.4q, 86.8s, 120.7d, 125.1s, 130.7s, 136.2d, 143.8d, 155.5s, 166.9s, 168.0s, 208.3s. 2: δ 18.8q, 22.0q, 22.9q, 27.2t, 27.2t, 29.6q, 29.8t, 31.9t, 33.8t, 35.3d, 36.8t, 86.8s, 119.0d, 119.7d, 131.1s, 133.9s, 143.1d, 145.5s, 166.5s, 209.3s.

4) Compounds 4 and 5 were obtained in a ratio of about 10 : 1 and the optical rotation of 5 of minute quantities was not able to be determined.

5) Mp 119-120 °C and $[\alpha]_D$ +92° (c 1.3, CCl_4) are reported for emblide in Ref. 2.

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