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A Cembranoid, Trocheliophorol, from the Cultured Soft Coral *Sarcophyton trocheliophorum*

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A new cembranoid, trocheliophorol (**1**), and a known cembranoid sarcophine have been isolated from the cultured soft coral *Sarcophyton trocheliophorum*. The structure of **1** was determined on the basis of extensive spectroscopic analysis. Compound **1** is the first α,β-unsaturated-γ-lactone cembrane that was found to possess a tetrahydrofuran moiety with an 8,11-ether linkage in a 14-membered ring.

Our search of marine natural products has revealed that soft corals are important sources of novel secondary metabolites such as steroids,[1,2] sesquiterpenoids,[3,4] and diterpenoids.[5,6] We have previously isolated a series of natural products, including cembranes and eunicellin-base diterpenoid from the cultured soft corals *Sinularia flexibilis*[7] and *Klyxum simplex*.[8] Recently, our chemical examination of the cultured soft coral *Sarcophyton trocheliophorum* (Alcyoniidae) has resulted in the isolation of two metabolites including one new cembranoid, trocheliophorol (**1**) (Chart 1), along with a known cembranoid sarcophine.[9] The structure of **1** was elucidated on the basis of extensive spectroscopic analysis.

Specimens of the octocoral *S. trocheliophorum* were collected off the coast of Pingtung, southern Taiwan, and transplanted to a 4-ton cultivating tank equipped with a flow-through sea water system in December 2003. The cultured soft coral was harvested in December 2007. The sliced bodies of *S. trocheliophorum* (0.8 kg, wet wt) were minced and extracted exhaustively with EtOH (1 L × 4). The EtOH extract was filtered and concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 and H_2O. The solvent-free CH_2Cl_2 extract was concentrated and the residue (10.6 g) was chromatographed on Si gel by CC and eluted with EtOAc in *n*-hexane (0–100%, gradient) to yield 20 fractions. Fraction 9, eluted with *n*-hexane–EtOAc (3:1), was further purified by normal phase HPLC using *n*-hexane–EtOAc (4:1) to yield sarcophine (2.1 mg).[9] Fraction 11, eluted with *n*-hexane–EtOAc (1:1), was further purified by normal phase HPLC using *n*-hexane–EtOAc (2:1) to yield **1** (1.5 mg).

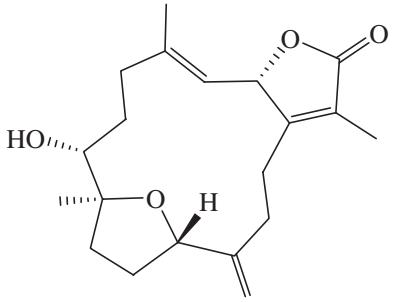

Chart 1.

Trocheliophorol (**1**) was obtained as a white powder. The HR-ESI-MS spectrum of **1** exhibited a sodiated molecule peak at m/z 355.1885 $[M + Na]^+$, with a molecular formula $C_{20}H_{28}O_4$ (calcd for $C_{20}H_{28}O_4 + Na$, 355.1882) and implying seven degrees of unsaturation. The IR spectrum revealed the presence of carbonyl (ν_{max} 1749 cm^{-1}) and hydroxy (ν_{max} 3446 cm^{-1}) groups. The ^{13}C NMR spectrum of **1** measured in $CDCl_3$ (Table 1), showed the presence of twenty carbon signals, which were assigned by the assistance of DEPT spectrum to three methyls, six sp^3 methylenes, one sp^2 methylene, one sp^2 methine, three sp^3 oxymethines, one sp^3 quaternary carbon, and five sp^2 quaternary carbons (including one ester carbonyl). The NMR signals appearing at δ_C 174.9 (C), 162.0 (C), 124.1 (C), 79.2 (CH), and 9.2 (CH_3) and δ_H 5.43 (1H, d, $J = 9.0$ Hz) and 1.89 (3H, s), and the IR absorption at 1749 cm^{-1} were assigned to an α,β-unsaturated-γ-lactone functionality by comparison with those of similar metabolites,[9,10] such as the corresponding data of sarcophine.[9] Furthermore, one 1,1-disubstituted carbon–carbon double bond (δ_C 145.8, C and 111.7, CH_2) and a

Table 1. ^1H and ^{13}C NMR data of **1**

C/H	$^1H^a/\delta$	$^{13}C^b/\delta$	
1		162.0	(C)[d]
2	5.43 d (9.0)[c]	79.8	(CH)
3	5.20 d (9.0)	117.9	(CH)
4		146.6	(C)
5	2.48 m, 2.15 m	34.1	(CH_2)
6	2.10 m, 1.60 m	31.8	(CH_2)
7	3.39 dd (7.5, 3.0)	74.6	(CH)
8		82.9	(C)
9	2.07 m, 1.82 m	36.9	(CH_2)
10	1.97 m, 1.74 m	31.6	(CH_2)
11	4.17 dd (11.0, 3.5)	76.8	(CH)
12		145.8	(C)
13	2.44 m	32.9	(CH_2)
14	2.52 dd (12.0, 8.5), 2.22 m	25.1	(CH_2)
15		124.1	(C)
16		174.9	(C)
17	1.89 s	9.2	(CH_3)
18	1.92 s	19.3	(CH_3)
19	1.16 s	20.0	(CH_3)
20	5.00 s, 4.93 s	111.7	(CH_2)

Spectra recorded at [a]500 and [b]125 MHz in $CDCl_3$, respectively. [c]J values (in Hz) in parentheses. [d]Deduced from DEPT.

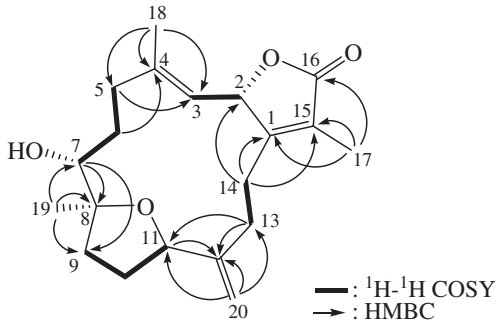

Figure 1. Key COSY and HMBC correlations for **1**.

trisubstituted olefinic bond (δ_C 146.6, C and 117.9, CH) were observed. The gross structure of **1** was further determined by the assistance of 2D NMR experiments (^{1}H–^{1}H COSY and HMBC). From the ^{1}H–^{1}H COSY spectrum of **1** (Figure 1), it was possible to establish four partial structures of consecutive proton systems extending from H-2 to H-3; H_2-5 to H-7; H_2-9 to H-11; and H_2-13 to H_2-14. These findings together with the HMBC correlations (Figure 1) observed from H_2-5 to C-3; H_2-6 to C-4; H-7 to C-8 and C-9; H-11 to C-12; H_2-13 to C-11 and C-12; and H_2-14 to C-1, C-2, and C-12 established the 14-membered ring structure of **1**. The exocyclic methylene group was found to be attached to C-12, based on the HMBC correlations observed from H_3-20 to C-11, C-12, and C-13. The methyl groups attached at C-4 and C-8 were confirmed by HMBC correlations between H_3-18 to C-3, C-4, and C-5 and H_3-19 to C-7, C-8, and C-9, respectively. The molecular framework of **1** was further established by other HMBC correlations between H_2-14 to C-15 and H_3-17 to C-1, C-15, C-16. In considering the degrees of unsaturation and molecular formula, an oxa-bridged ether linkage was placed between C-8 and C-11. By comparison of ^{13}C NMR data of the tetrahydrofuran moiety of **1** with those of a known metabolite, uprolide E acetate, which was isolated from the gorgonian *Eunicea mammosa*,[11] the carbon shifts of **1** at positions from C-7 to C-12 were found to be in good agreement with those of uprolide E acetate at positions from C-3 to C-8.[11] On the basis of the above findings, the planar stucture of **1** could be established unambiguously.

The relative configurations of the four chiral centers at C-2, C-7, C-8, and C-11 in **1** were elucidated by detailed NOE analysis, as shown in Figure 2. It was found that H_3-18 showed NOE interactions with H-2 and H-7. Thus, assuming the β-orientation of H-2, H-7 should be positioned on the β face. The NOE correlation observed between H-7 and H-11 also reflected the β-orientation of H-11. One of the methylene protons at C-9 (δ 2.07) exhibited NOE correlations with H-7, H-11 and was assigned as H-9β while the other (δ 1.82) was denoted as H-9α. The NOE correlation observed between H-9α and H_3-19 reflected the α-orientation of methyl substituent at C-8. Furthermore, NOESY spectrum showed NOE interaction of H_3-18 with H-2, but not with H-3, revealing the *E* geometry of the C-3/C-4 double bond. From the above evidence and the other NOE correlations (Figure 2) the structure of **1** was established unambiguously.

It was noted that **1** is the first example of an α,β-unsaturated-γ-lactone cembrane posessing a tetrahydrofuran moiety with a rare 8,11-ether linkage.

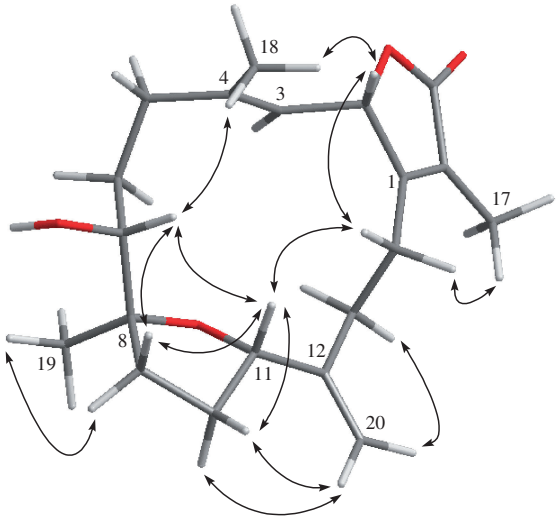

Figure 2. Selective NOESY correlations of **1**.

Trocheliophorol A (**1**): white powder; mp 175–177 °C; $[\alpha]_D^{25}$ +32.3 (*c* 0.3, $CHCl_3$); IR (KBr) ν_{max} 3446, 2935, 1749, 1455, 1376, and 1220 cm^{-1}; UV (MeOH) λ_{max} 216 nm ($\log \varepsilon = 3.8$); ^{1}H and ^{13}C NMR data, see Table 1; ESIMS *m*/*z* 457 $[M + Na]^+$; HRESIMS *m*/*z* 355.1885 $[M + Na]^+$ (calcd for $C_{20}H_{28}O_4$ + Na, 355.1882).

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