Chinese Chemical Letters Vol. 16, No. 11, pp 1489-1491, 2005
http://www.imm.ac.cn/journal/ccl.html

A Novel Hydroperoxyl Substituted Cembranolide Diterpene from Marine Soft Coral *Lobophytum crassum*

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Abstract: A new cembranolide diterpene with a hydroperoxyl substitution was isolated from the marine soft coral *Lobophytum crassum*. The structure was elucidated on the basis of chemical and spectral methods.

Keywords: *Lobophytum crassum*, 2-hydroperoxysarcophine, cembranolide, diterpene.

Marine soft corals, especially in the genera *Sinularia*, *Sarcophyton*, and *Lobophytum*, are rich source of novel cembranoid diterpenes[1]. Screening cembranoids in therapeutically relevant assay systems has shown that some of them possess HIV-inhibitory[2], cytotoxic[3], and anticancer activity[4]. In this paper, we report the structural elucidation of a new cembranolide isolated from the alcohol extract of marine soft coral *Lobophytum crassum* collected from South China Sea.

Compound **1** was obtained as colorless crystal, $[\alpha]_{20}^{D}$ -153 (*c* 1.15, CH_3COCH_3). Its HRESI-MS provided a *quasi*-molecular ion peak $[M+NH_4]^+$ at *m/z* 366.2268 (calcd. 366.2280), suggesting the molecular formula $C_{20}H_{28}O_5$ and 7 degrees of unsaturation. The IR absorption peaks at 3353, 1767, 1669, and 1256 cm^{-1} indicated the presence of hydroxyl (or hydroperoxyl), γ-lactone, olefin, and epoxide functionalities in the molecule. The ^{13}C NMR spectrum (**Table 1**) exhibited all 20 signals divided by DEPT into seven quaternary carbons, three methines, six methylenes, and four methyl groups. The ^1H NMR spectrum (**Table 1**) showed the olefinic proton singlet resonating at δ ppm 5.47 (s, 1H, H-3), 4.99 (t, 1H, *J*=7.5 Hz, H-11), four methyl signals at δ 1.90 (s, 3H, H-17), 1.56 (s, 3H, H-18), 1.17 (s, 3H, H-19) and 1.54 (s, 3H, H-20). All these physical and spectral data suggested that **1** has a cembranoid-type carbon skeleton and structurally similar to the previously reported cembranoid diterpene, sarcophine[5,6]. The only difference was that proton at H-2 in sarcophine was replaced by a hydroperoxyl group in **1**. A positive reaction with the KI-HOAc-starch test showed it was also peroxide[7]. However, the structure of compound **1** be further confirmed by the following HMBC

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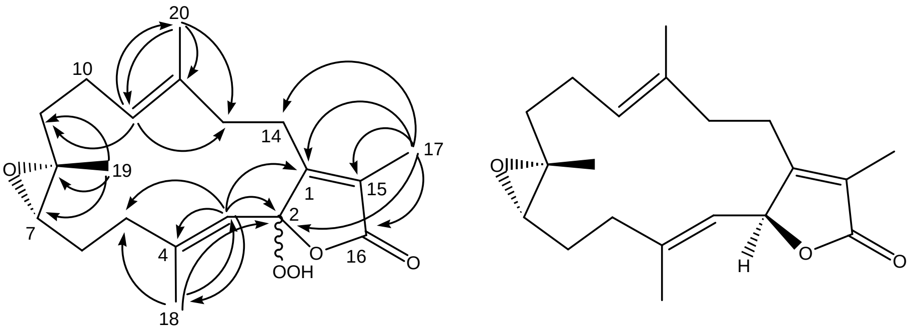
correlations: H-17/C-1, C-2, C-14, C-15, and C-16; H-18/C-2, C-3, and C-5; H-19/C-7, C-8, and C-9; H-20/C-11, C-12, and C-13; H-3/C-1, C-2, C-4, C-5, and C-18; and H-11/C-9, C-13, C-20 (**Figure 1**). Finally, the relative stereochemistry of **1** was established by the NOESY spectrum. The proton of H-7 (δ 2.42 ppm) showing a NOESY correlation with 19β-methyl group (δ 1.17 ppm) suggested the same orientation for both groups. However, the stereochemistry at C-2 remains unknown, since there is no cross peak could be detected between the hydroperoxyl proton and any other proton signals in our NOESY experiment. From the above evidence, compound **1** was identified as 2-hydroperoxy-sarcophine.

Figure 1 The structures of compound **1** and sarcophine and the key correlations in HMBC for **1**



1

Sarcophine

Table 1 ^{1}H- and ^{13}C-NMR data of compound **1** and sarcophine ($CDCl_3$, δ ppm, *J* Hz)

No.	δ_H for **1**$^{a)}$	δ_C for **1**$^{a)}$	δ_H for sarcophine$^{b)}$	δ_C for sarcophine$^{a)}$
1		151.1 s		162.2 s
2		85.0 s	5.55 (dq, 10, 1.5)	78.7 d
3	5.47 (s)	112.8 d	5.05 (dq, 10, 1.0)	120.5 d
4		147.9 s		143.9 s
5	1.08 (m), 1.86 (m)	37.2 t	NA	37.3 t
6	1.87 (m), 2.03 (m)	23.1 t	NA	25.1 t
7	2.42 (m)	63.0 d	2.68 (m)	61.3 d
8		60.2 s		59.8 s
9	2.20 (m), 2.35 (m)	37.8 t	NA	39.0 t
10	2.60 (m), 2.70 (m)	22.4 t	NA	23.2 t
11	4.99 (t, 7.5)	127.5 d	5.15 (br t, 5.0)	124.8 d
12		131.2 s		135.5 s
13	2.03 (m), 2.12 (m)	34.4 t	NA	36.3 t
14	1.34 (m), 2.15 (m)	23.2 t	NA	27.5 t
15		124.7 s		122.8 s
16		170.2 s		162.2 s
17	1.90 (s)	9.0 q	1.85 (s)	8.9 q
18	1.56 (s)	24.3 q	1.89 (s)	16.1 q
19	1.17 (s)	17.0 q	1.28 (s)	17.1 q
20	1.54 (s)	14.8 q	1.63 (s)	15.3 q
-OOH	8.78 (s)			

a) All spectra were recorded in $CDCl_3$ on a Bruker AM 400 NMR spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C). The assignments were based on DEPT and 2D NMR (^{1}H-^{1}H COSY, HMQC and HMBC) spectra. b) Data cited from reference 6. NA, not available.

Acknowledgments

This work was financed in part by the innovation program of the Institute of Oceanology, Chinese Academy of Sciences (IOCAS, L79032432) and the program of "Bairen Jihua" awarded from the Chinese Academy of Sciences (to B. G. Wang). Y. P. Shi wishes thank the Key Laboratory of Experimental Marine Biology at IOCAS for partial financial support.

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Received 18 March, 2005