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Two novel norsesquiterpene peroxides from basidiomycete *Steccherinum ochraceum*

Dong-Ze Liu [a,b], Ze-Jun Dong [a], Fang Wang [a], Ji-Kai Liu [a,*]

[a] State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, People's Republic of China
[b] South China Sea Institute of Oceanology, Chinese Academy of Sciences, Guangzhou 510301, People's Republic of China

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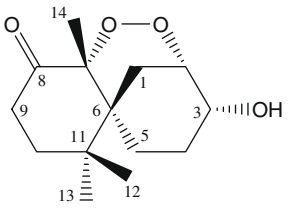
ABSTRACT

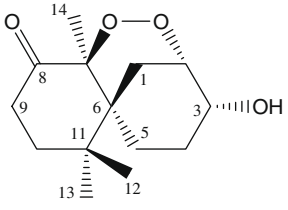
Two novel 3-nor-methyl-chamigrane sesquiterpene peroxides, named steperoxide A (**1**) and B (**2**), have been isolated from basidiomycete *Steccherinum ochraceum*. This is the first report on the isolation of chamigrane sesquiterpene from higher fungi. The structures of **1** and **2** were established on the basis of spectroscopic data and single-crystal X-ray analysis.

Mushrooms have proved to be a rich source of secondary metabolites with unusual structures as well as interesting biological activities. Despite their potential for drug development, few bioactive metabolites have been reported from mushrooms as compared with higher plants and microbes. Over the last 10 years, our main research focus has been secondary metabolites from the untapped resources of higher fungi found in China.[1–5] As a continuation of our studies on structurally interesting and biologically active natural products from higher fungi, chemical investigation on fermentation broth of *Steccherinum ochraceum* has resulted in the isolation of two rare and novel chamigrane norsesquiterpene peroxides, named steperoxides A (**1**) and B (**2**). So far, almost all chamigrane sesquiterpenoids were isolated from marine creatures, and most of them contained at least one halogen.[6–12] This is the first report on the isolation of chamigrane sesquiterpene from higher fungi. We present herein the structural elucidation of these two compounds by spectroscopic data in conjunction with single-crystal X-ray analysis.

Steperoxide A (**1**)[13] was obtained as colorless crystals (in MeOH) with a molecular formula of $C_{14}H_{22}O_4$ as established by HREIMS at *m/z* 254.1511 $[M]^+$ (calcd for 254.1513), requiring 4 degrees of unsaturation. The IR absorptions revealed the presence of hydroxyl (3502 cm^{-1}) and carbonyl (1707 cm^{-1}) functionalities. The ^1H NMR spectrum (Table 1) showed the presence of three methyls (δ_H 1.86, 1.20, and 0.93) attached to quaternary carbons, and two oxymethine groups (δ_H 4.12 and 3.71). The ^{13}C NMR and HSQC spectra (Table 1) resolved 14 carbon resonances comprising one carbonyl group at δ_C 208.1, two oxygenated methine carbons at δ_C 80.2 and 70.1, one oxygenated quaternary carbon at δ_C 89.6, as well as three methyls (δ_C 27.2, 25.0, and 23.9), five methylenes (δ_C 36.6, 35.2, 32.6, 28.0, 25.9), and two quaternary carbons (δ_C 42.7 and 35.7). Accordingly, a three-ring structure was required for **1** to fulfill the unsaturation requirement.



1



2

Extensive analyses of 1D and 2D NMR data prompted us to consider that **1** was a 3-nor-methyl-chamigrane sesquiterpene peroxide. The HMBC cross-peaks displayed the following correlations: H-1, H-2, H-4, H-5, H-10, H-12, H-13, and H-14 to C-6, H-1, H-5, H-9, and H-14 to C-7, H-12 and H-13 to C-10, H-1, H-2, and H-4 to C-3, H-1 and H-4 to C-2. The aforementioned data, along with three proton spin systems deduced from the COSY spectrum, H-1/H-2, H-9/H-10, H-3/H-4, and H-4/H-5, led to the determination of partial structure of **1** (Fig. 1). Considering the molecular weight and tricyclic feature, this required connecting two of three unassigned oxygen atoms to make a peroxide ring. In general, the chemical shifts of carbon atoms bearing peroxide bridge are between 80 and 90 ppm, which suggested that a peroxide bridge should be located between C-2 and C-7 to tentatively establish the gross structure of **1**. A single-crystal X-ray diffraction analysis (Fig. 2) was successfully conducted to confirm the planar structure of **1** and allowed the determination of its relative configuration.

Steperoxide B (**2**)[14] was obtained as colorless crystals (in MeOH), and had the molecular formula of $C_{14}H_{22}O_4$ with 4 degrees

* Corresponding author. Tel.: +86 871 5216327; fax: +86 871 5150227.
E-mail address: jkliu@mail.kib.ac.cn (J.-K. Liu).

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Table 1
NMR spectroscopic data for steperoxides A and B (**1**–**2**) in $CDCl_3$

No.	**1**		**2**	
	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C
1a	2.45 (m)	25.9 (t)	2.02 (m)	30.5 (t)
1b	1.29 (dd, 17.5, 1.0)		1.54 (overlapped)	
2	4.12 (t, 3.5)	80.2 (d)	4.10 (m)	79.0 (d)
3	3.71 (m)	70.1 (d)	3.75 (m)	69.3 (d)
4a	2.28 (m)	32.6 (t)	2.14 (2H, m)	32.0 (t)
4b	2.09 (m)			
5a	1.79 (m)	28.0 (t)	2.07 (m)	25.5 (t)
5b	1.66 (overlapped)		1.56 (overlapped)	
6		42.7 (s)		41.2 (s)
7		89.6 (s)		90.1 (s)
8		208.1 (s)		208.0 (s)
9a	2.76 (m)	35.2 (t)	2.66 (m)	35.5 (t)
9b	2.28 (m)		2.40 (dm, 14.5)	
10a	1.96 (overlapped)	36.6 (t)	1.98 (overlapped)	35.7 (t)
10b	1.59 (overlapped)		1.55 (overlapped)	
11		35.7 (s)		37.2 (s)
12	0.93 (3H, s)[a]	27.2 (q) [b]	0.97 (3H, s) [c]	26.2 (q) [d]
13	1.20 (3H, s) [a]	25.0 (q) [b]	1.27 (3H, s) [c]	24.6 (q) [d]
14	1.86 (3H, s)	23.9 (q)	1.38 (3H, s)	21.4 (q)

[a,b,c,d] Interchangeable.

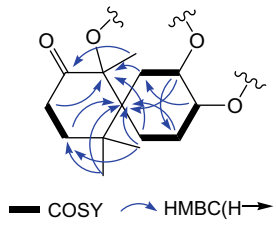

Figure 1. Partial structure, key 1H–1H COSY, and HMBC correlations of **1**.

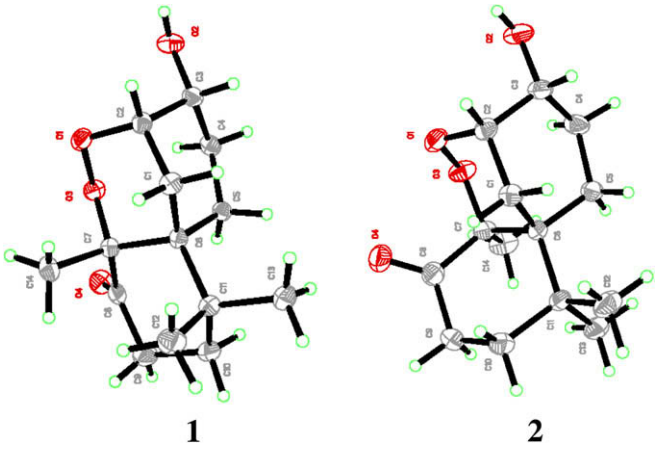

Figure 2. Single-crystal X-ray structures of **1** and **2**.

of unsaturation as determined by HREIMS at *m/z* 254.1514 $[M]^+$ (calcd for 254.1513). In comparison with compound **1**, the ^1H and ^{13}C NMR data revealed that both compounds shared the same planar structure, which was further confirmed by detailed 2D NMR (HSQC, 1H–1H COSY, and HMBC spectra) analysis of **2**. A single-crystal X-ray diffraction (Fig. 2) study of **2** indicated that **1** and **2** have the same stereochemistry except for C-7 contrary to that of **1**.

The culture broth (20 L) was filtered to remove the mycelium. The filtrate was then successively extracted twice with ethyl acetate, and the crude extract (3.5 g) was chromatographed on a silica gel column using a $CHCl_3$/MeOH gradient. Several fractions of increasing polarity were collected. Fraction II (850 mg) eluted with $CHCl_3$/MeOH (100:1, v/v) was subjected to column chromatography over silica gel and Sephadex LH-20, using a petroleum ether/ethyl acetate (8:1, v/v) and $CHCl_3$/MeOH (1:1, v/v), respectively, and further purified by repeated recrystallization from MeOH to yield **1** (360 mg) and **2** (150 mg).

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.048.

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13. Steperoxide A (**1**): Colorless crystals, mp 169–170 (MeOH), $[\alpha]_D^{25}$ +278.1 (*c* 0.27, MeOH); IR (KBr) ν_{max} 3502, 2976, 2927, 1707, 1461, 1398, 1275, 1122, 1082, 1020, 950, 854, 756 cm^{-1}; ^1H and ^{13}C NMR data: see Table 1; HREIMS *m/z* 254.1511 (calcd for $C_{14}H_{22}O_4$, 254.1513).
14. Steperoxide B (**2**): Colorless crystals, mp 210–212 (MeOH), $[\alpha]_D^{27}$ +193.9 (*c* 0.16, MeOH); IR (KBr) ν_{max} 3514, 2970, 2929, 1719, 1454, 1368, 1076, 1015, 638 cm^{-1}; ^1H and ^{13}C NMR data: see Table 1; HREIMS *m/z* 254.1514 (calcd for $C_{14}H_{22}O_4$, 254.1513).