



Vibralactone Biogenesis-Associated Analogues from Submerged Cultures of the Fungus *Boreostereum vibrans*

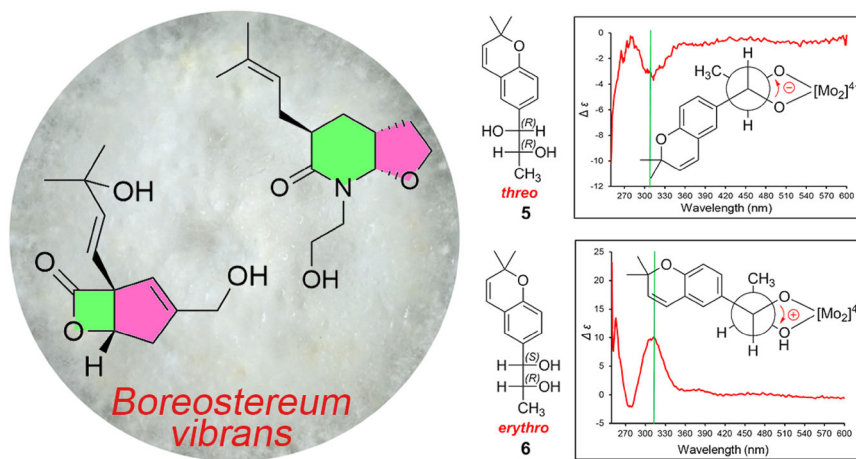
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Abstract

A scale-up fermentation of the fungus *Boreostereum vibrans* facilitated the isolation of six new vibralactone biogenesis-associated analogues, namely vibralactamide A (1), vibralactone T (2), 13-*O*-lactyl vibralactone (3), 10-*O*-acetyl vibralactone G (4), (11*R*,12*R*)- and (11*S*,12*R*)-vibradiol (5, 6). Their structures were established via extensive spectroscopic analyses, specific optical rotation comparison, and Sneath's method. The biosynthetic pathway for vibralactamide A was postulated. The absolute configuration of vibralactone B was revised by single crystal X-ray diffraction analysis. This work puts the divergent vibralactone biosynthesis pathway one step further and expands the structural diversity of vibralactone-associated compounds.

Graphical Abstract



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Keywords Basidiomycete · *Boreostereum vibrans* · Vibralactone · Structure revision · Snatzke's method

1 Introduction

Natural products from higher fungi origin are irreplaceable sources of architecturally distinct scaffolds for drug discovery [1, 2]. The fungus *Boreostereum vibrans* is featured by producing a lipase inhibitor named vibralactone which harboring an unusual β -lactone group. In recent years, endeavors to explore the potential of producing diverse metabolites of *B. vibrans* by scale-up fermentation and/or changing culture medium compositions led to the isolation of plenty of bioactive vibralactone congeners and vibralactone biosynthetic-associated compounds [3–11], including vibralactoximes A–P which represented the first class of natural oxime esters [3]. The biosynthesis of vibralactone and divergent biosynthetic pathway for skeletally distinct vibralactone-associated compounds were illuminated [12, 13]. It was proved that all these compounds shared the biosynthetic precursor 3-prenyl-4-hydroxybenzylalcohol. An FAD-binding monooxygenase (VibMO1) from *B. vibrans* that converted prenyl 4-hydroxybenzoate into prenylhydroquinone was also characterized for the first time.

This study, as part of our ongoing interest in bioactive metabolites from higher fungi, focused on the trace compounds of scale-up submerged cultures of *B. vibrans*. As a result, six previously undescribed vibralactone biogenesis-associated analogues were identified. Herein, we report the isolation, structure elucidation, and absolute configuration determination via comparison of specific optical rotations and application of Snatzke's method of these new compounds (Fig. 1). We also make a revision of the absolute configuration of vibralactone B.

2 Results and Discussion

Compound **1** was obtained as colorless oil. It had a molecular formula $C_{14}H_{23}O_3N$ as deduced from the HREIMS molecular ion peak at m/z 253.1672 $[M]^+$ (calcd for 253.1678, $C_{14}H_{23}O_3N$), indicating four degrees of hydrogen deficiency. The IR spectrum absorption bands at 3447 and 1637 cm^{-1} indicated the presence of hydroxy and carbonyl groups, respectively. The 1D NMR spectroscopic data (Tables 1 and 2) displayed fourteen carbon signals ascribable to two methyl singlets, six methylenes (two oxygenated), four methines (one olefinic, one oxygenated), and two quaternary carbons. The presence of a carbonyl (δ_C 173.8, C-7) and a double bond (δ_C 123.2, C-9; 133.5, C-10) accounting for two degrees of unsaturation suggesting two cycles in **1**. Further elucidating the 2D

NMR spectra allowed the completion of planar structure of **1**. The HMBC correlations (Fig. 2) from the two methyl singlets (δ_H 1.60, 1.68) to C-9 and C-10, along with the 1H – 1H COSY correlations between H-8 (δ_H 2.50, 2.13) and H-9 (δ_H 5.14) suggested the existence of an isopentenyl group. Analysis of the 1H – 1H COSY spectrum allowed the following sequential connectivity from C-8 to C-5, from C-3 to C-13 (Fig. 2). The HMBC correlations from H-8 to C-1 (δ_C 38.3), C-2 (δ_C 28.9), and C-7 revealed that the carbonyl group connected to C-1. The key HMBC correlations from H-13 (δ_H 5.17) to the typical oxygenated methylene C-5 (δ_C 65.7) and carbonyl C-7 as well as the chemical shift of C-13 (δ_C 91.6) [14] led to the assignments of an ether bond between C-5/C-13, and a nitrogen atom between C-7/C-13, which constructed a hexahydrofuro[2,3-*b*]pyridin-6(2*H*)-one scaffold. The remaining two carbons (C-1', δ_C 49.7; C-2', 61.5) was assigned to a 2'-hydroxyethyl substituted at the nitrogen atom as supported by the 1H – 1H COSY correlations between H-1' (δ_H 3.61, 3.38) and H-2' (δ_H 3.61), and HMBC correlations from H-1' to C-7 and C-13. When changing NMR solvents from acetone- d_6 to DMSO- d_6 , the resultant 2'-OH proton signal at δ_H 4.66 (t, $J = 5.6$ Hz) and less overlapped signals reinforced the above assignments.

The relative configuration of compound **1** was established by interpretation of the ROESY spectrum. Evident ROESY signals between H-3 (δ_H 2.71)/H-13, H-1 (δ_H 2.34)/H-4 α (δ_H 1.82), H-8 α (δ_H 2.13)/H-2 β (δ_H 1.81) indicated that the two rings were *cis*-fused and the isopentenyl group was β -oriented (Fig. 3). Therefore, compound **1** was established as shown in Fig. 1 and was trivially named as vibralactamide A.

The biosynthetic pathway of vibralactamide A (**1**) was proposed as shown in Scheme 1. It was supposed that 3-prenyl-4-hydroxybenzylalcohol (**A**) underwent a C–C cleavage reaction to give 1,5-*seco*-vibralactone (**B**). The intermediate **B** was then subjected to cascade reduction and oxidation reactions to give **C**. The key intermediate **D** which formed by nucleophilic addition of **C** with 2-aminoethanol was subjected to hydroxylation/nucleophilic addition/dihydroxylation processes to afford compound **1**.

Compound **2** was obtained as colorless oil. The molecular formula was established as $C_{12}H_{16}O_4$ by the sodium adduct ion peak at m/z 247.0937 $[M + Na]^+$ (calcd for 247.0941, $C_{12}H_{16}O_4Na$) in HRESIMS analysis. The 1D NMR spectra of compound **2** displayed signals of two overlapped methyl singlets, two methylenes, four methines (three olefinic, one was oxygenated), and four quaternary carbons (one carbonyl, one olefinic) (Tables 1 and 2). All

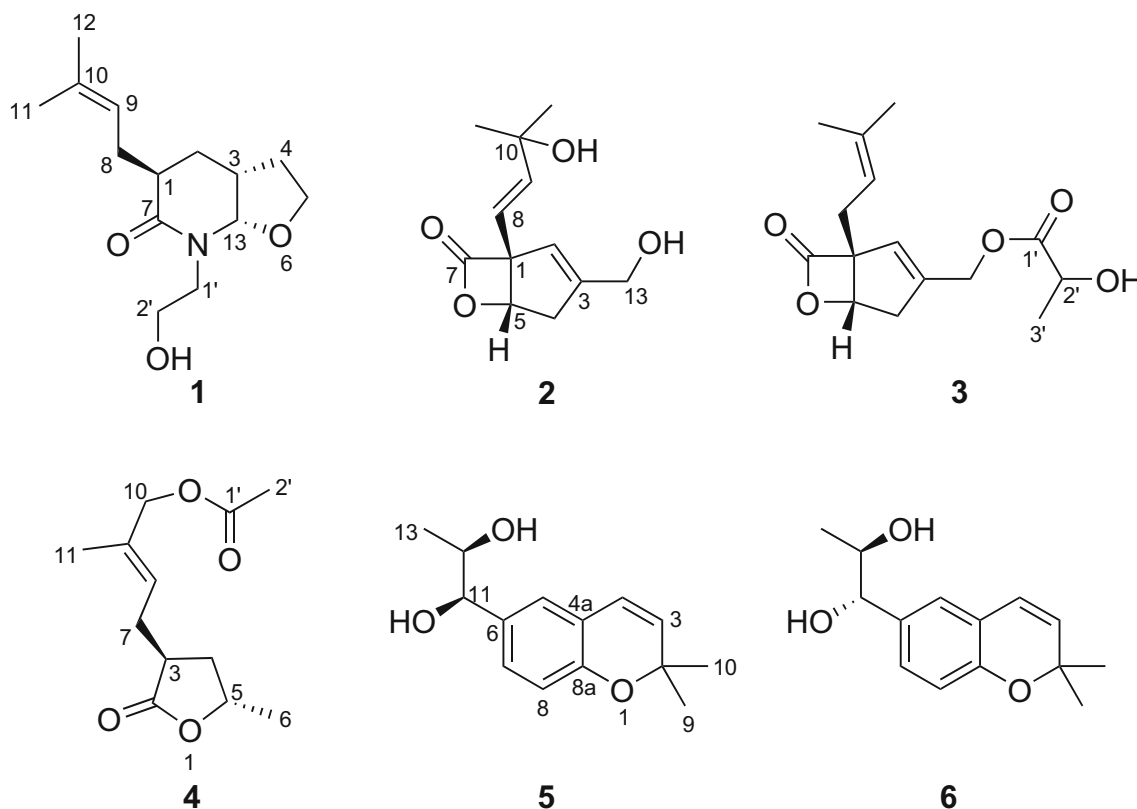


Fig. 1 Chemical structures of compounds 1–6

these data exhibit similarities to those of vibralactone [8]. However, the presence of two *trans*-double bond protons (δ_{H} 5.88, $J = 16.0$ Hz, H-8; δ_{H} 5.99, $J = 16.0$ Hz, H-9), and the HMBC correlations from H-9 to Me-11/Me-12 (δ_{C} 30.1), C-10 (δ_{C} 76.4), and from H-8 to C-1 (δ_{C} 70.2), C-7 (δ_{C} 172.5), and C-2 (δ_{C} 121.2) suggested that the C9-C10 double bond in vibralactone shifted to the position C8–C9, while C-10 was substituted by a hydroxy in **2** (Fig. 2). This assignment was consistent with the HRESIMS result. The relative configuration of compound **2** was determined as *1R*,5S** via ROESY correlations between H-5 (δ_{H} 4.99) and H-8 (δ_{H} 5.88) (Fig. 3), and the absolute configuration was assigned as *1R,5S* by comparison of the specific optical rotation value with those of vibralactone ($[\alpha]_{\text{D}}^{25} -61.3$ for **2**, $[\alpha]_{\text{D}}^{26} -135.1$ for vibralactone). Thus, compound **2** was elucidated as shown in Fig. 1, and was given the trivial name vibralactone T.

The ^{13}C NMR and DEPT spectra (Tables 1 and 2) of the colorless oil compound **3** exhibited signals ascribable to three methyls, three methylenes, four methines, and five quaternary carbons (two carbonyls). These data show high resemblance to those of vibralactone [8]. Compared to vibralactone, the additional three carbons at δ_{C} 176.0 (C-1'), 68.0 (C-2'), 20.8 (C-3') and corresponding protons at δ_{H} 1.39 (d, $J = 6.9$ Hz, H-3'), 4.31 (q, $J = 6.9$ Hz, H-2')

as well as the HMBC correlations from H-3' to C-2' and C-3' indicated the presence of a lacyl moiety in **3**. The lacyl moiety attached at the oxygen atom at C-13 by the key HMBC correlation from H-13 (δ_{H} 4.74, 4.79) to C-1'. This assignment agreed with the HRESIMS result which gave a sodium adduct ion peak at m/z 303.1206 $[\text{M} + \text{Na}]^+$ (calcd for 303.1203, $\text{C}_{15}\text{H}_{20}\text{O}_5\text{Na}$). The absolute configuration of the vibralactone part was determined as *1R,5S* via biogenetic consideration and evident ROESY correlations between H-5/H-8. However, attempt to settle the absolute configuration of chiral center C-2' of the lacyl moiety by Mosher's method failed. With (*R*)-MTPA derivative of **3** in hand, while the counterpart (*S*)-MTPA derivative was missing because of the insufficient quantity of compound **3**. Therefore, compound **3** was identified as 13-*O*-lacyl-vibralactone (Fig. 1).

Compound **4** was isolated as colorless oil. The 1D NMR data (Tables 1 and 2) displayed high similarities to those of vibralactone G [9], a γ -lactone derivative obtained from the same fungus but from different batches of cultures. Analysis of the 2D NMR spectra suggested that the 10-OH of vibralactone G was acetylated to give compound **4**, which supported by the HMBC correlation from H-10 (δ_{H} 4.43) and H-2' (δ_{H} 2.01) to the carbonyl C-1' (δ_{C} 170.8). The relative configuration of compound **4** was proved to be

Table 1 ^1H NMR spectroscopic data for compounds **1–6** (600 MHz)

No.	1 ^a	1 ^b	2 ^a	3 ^c	4 ^a	5 ^c	6 ^a
1	2.34, m	2.30, m					
2	1.65, ddd (13.6, 11.0, 5.4) 1.81, ddd (13.6, 4.6, 4.3)	1.56, ddd (13.6, 10.7, 5.3) 1.70, overlapped	5.64, s	5.68, s			
3	2.71, m	2.61, m			2.79, ddd (16.8, 7.7, 5.0)	5.68, d (9.8)	5.70, d (9.8)
4	2.14, m 1.82, m	2.08, m 1.73, m	2.66, d (18.7) 2.87, dd (18.7, 5.7)	2.72, d (19.0) 2.83, dd (19.0, 6.0)	2.12, ddd (12.8, 7.7, 7.7) 2.04, overlapped	6.36, d (9.8)	6.38, d (9.8)
5	3.84, dd (13.8, 13.8, 5.8) 3.69, br. dd (13.8, 7.8)	3.74, ddd (8.2, 8.1, 6.1) 3.64, ddd (8.2, 8.1, 6.5)	4.99, d (5.7)	4.89, d (6.0)	4.65, m	6.99, d (2.1)	7.04, d (2.0)
6					1.32, d (6.4), 3H		
7					2.46, m 2.31, m	7.07, dd (8.3, 2.1)	7.10, dd (8.2, 2.0)
8	2.50, br. ddd (14.3, 5.3, 5.3) 2.13, overlapped	2.41, m 2.05, overlapped	5.88, d (16.0)	2.43, dd (15.0, 7.5) 2.61, dd (15.0, 7.5)	5.50, t (7.5)	6.68, d (8.3)	6.66, d (8.2)
9	5.14, br. t (7.3)	5.10, t (7.3)	5.99, d (16.0)	5.17, t (7.5)		1.39, s, 3H	1.38, s, 3H
10					4.43, s, 2H	1.39, s, 3H	1.38, s, 3H
11	1.60, s, 3H	1.59, s, 3H	1.26, s, 3H	1.66, s, 3H	1.68, s, 3H	4.24, d (7.2)	4.44, d (4.0)
12	1.68, s, 3H	1.68, s, 3H	1.26, s, 3H	1.73, s, 3H		3.77, m	3.82, m
13	5.17, d (7.0)	5.15, d (7.0)	4.17, dd (15.6, 6.8) 4.20, dd (15.6, 6.8)	4.74, d (13.0) 4.79, d (13.0)		0.96, d (6.4), 3H	1.04, d (6.3), 3H
1'	3.61, overlapped 3.38, m	3.31, dd (13.8, 6.6, 6.6) 3.41, overlapped					
2'	3.61, overlapped, 2H	3.46, overlapped, 2H		4.31, q (6.9)	2.01, s, 3H		
3'				1.39, d (6.9), 3H			
2'-OH	3.84, overlapped	4.66, t (5.6)					
11-OH							4.12, br. s
12-OH							3.54, br. s
13-OH			4.22, t (6.8)				

^aRecorded in acetone- d_6 ^bRecorded in DMSO- d_6 ^cRecorded in CD₃OD

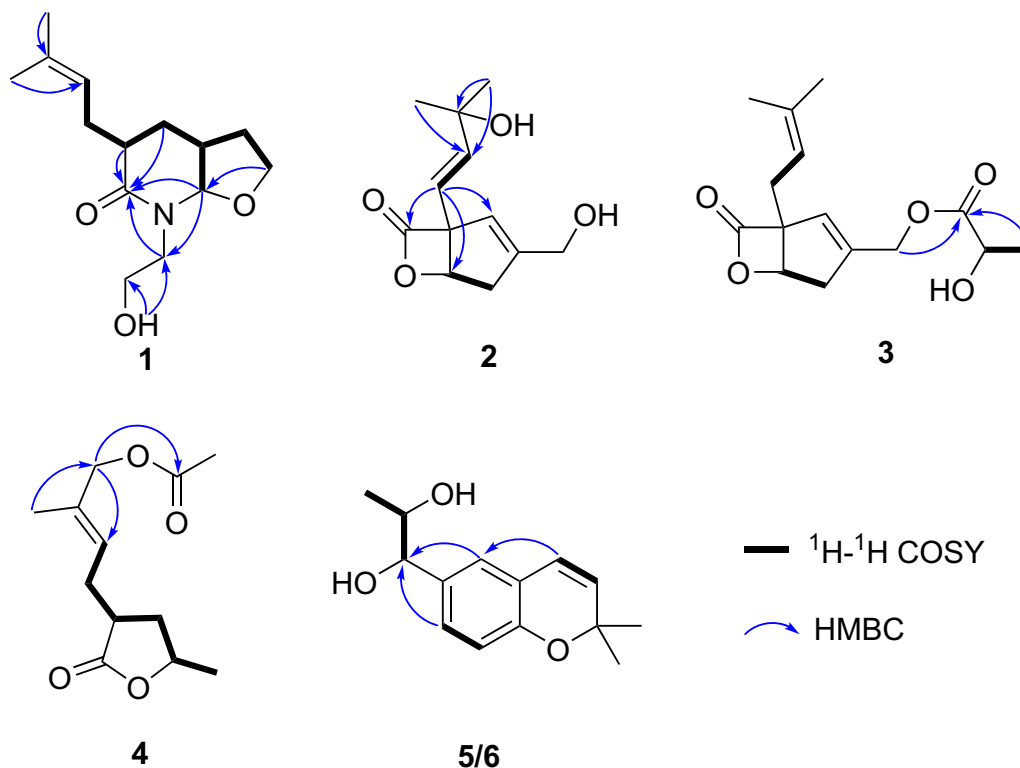
same with that of vibrallactone G according to the ROESY correlations between H-3 (δ_{H} 2.79) and Me-6 (δ_{H} 1.32). Thus, compound **4** was identified as 10-*O*-acetyl vibrallactone G (Fig. 1).

Compounds **5** and **6** were purified as white powder. HREIMS analyses suggested that these two compounds

had the same molecular formula of C₁₄H₁₈O₃. The close NMR data (Tables 1 and 2) of these two compounds which showed resemblance to those of vibranether revealed that compounds **5** and **6** possessed same planar structure and were analogues of vibranether [10]. The absence of the methoxy signal in ^1H NMR spectra of compounds **5** and **6**

Table 2 ^{13}C NMR Spectroscopic Data for Compounds **1–6** (150 MHz)

No.	1 ^a	1 ^b	2 ^a	3 ^c	4 ^a	5 ^c	6 ^a
1	38.3, CH	36.9	70.2, C	76.8, C			
2	28.9, CH ₂	27.7	121.2, CH	126.4, CH	178.7, C	77.3, C	76.6, C
3	35.0, CH	33.7	149.5, C	143.3, C	39.7, CH	132.1, CH	131.5, CH
4	30.8, CH ₂	29.6	37.8, CH ₂	38.7, CH ₂	34.8, CH ₂	123.4, CH	123.2, CH
4a						122.4, C	122.4, C
5	65.7, CH ₂	64.7	81.2, CH	80.0, CH	75.4, CH	126.2, CH	125.7, CH
6					21.3, CH ₃	135.6, C	135.9, C
7	173.8, C	172.2	172.5, C	174.6, C	29.0, CH ₂	128.9, CH	128.3, CH
8	29.8, CH ₂	28.9	119.4, CH	28.5, CH ₂	125.6, CH	116.9, CH	116.1, CH
8a						153.8, C	152.8, C
9	123.2, CH	122.2	143.2, CH	118.8, CH	133.9, C	28.1, CH ₃	28.1, CH ₃
10	133.5, C	132.5	76.4, C	137.2, C	69.8, CH ₂	28.2, CH ₃	28.1, CH ₃
11	17.9, CH ₃	17.8	30.2, CH ₃	18.2, CH ₃	14.1, CH ₃	79.9, CH	77.9, CH
12	26.0, CH ₃	25.7	30.2, CH ₃	26.1, CH ₃		72.8, CH	71.9, CH
13	91.6, CH	90.0	61.1, CH ₂	63.5, CH ₂		19.2, CH ₃	18.2, CH ₃
1'	49.7, CH ₂	47.3		176.0, C	170.8, C		
2'	61.5, CH ₂	58.7		68.0, CH	20.8, CH ₃		
3'				20.8, CH ₃			

^aRecorded in acetone-*d*₆^bRecorded in DMSO-*d*₆^cRecorded in CD₃OD**Fig. 2** Selected $^1\text{H}-^1\text{H}$ COSY and HMBC correlations of compounds **1–6**

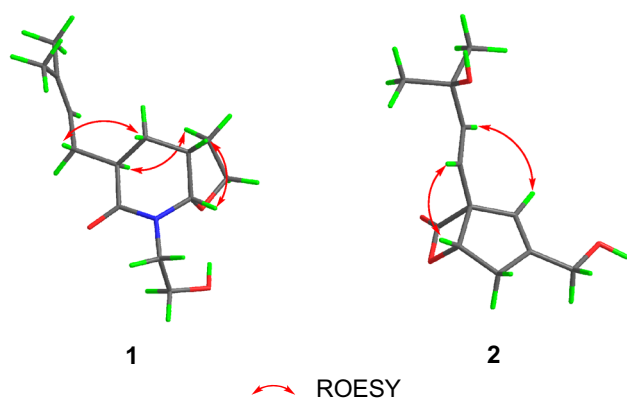


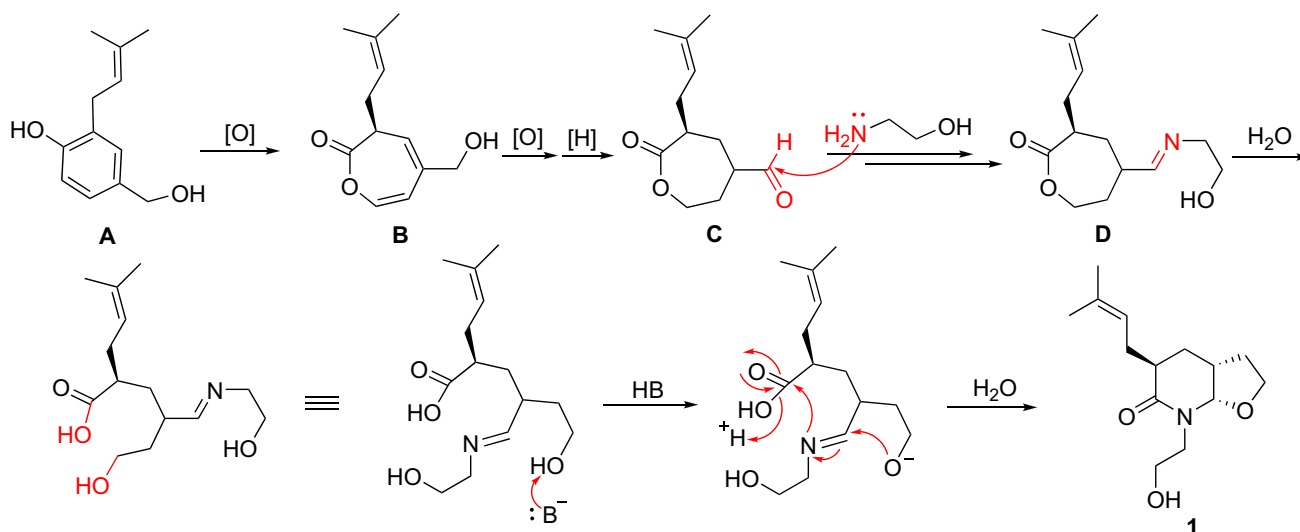
Fig. 3 Selected ROESY correlations of compounds **1** and **2**

compared to that of vibranether enabled the establishment of planar structure of these two compounds as chromene vicinal diol derivatives (Fig. 1). The remarkable differences of chemical shifts at the position C-11, C-12, and C-13 though recorded in different NMR solvents suggested that these two compounds were C-11/C-12 diastereomers. Compounds **5** and **6** were determined as *threo* and *erythro* configurations by the coupling constants between H-11 and H-12 ($J = 4.0$ Hz for **5**; $J = 7.2$ Hz for **6**) as well as the chemical shifts of 13-methyls [15, 16]. The absolute configuration of the 11,12-diol moieties of compounds **5** and **6** were assigned using the in situ dimolybdenum CD method developed by Snatzke and Frelek [17, 18]. When adding dimolybdenum tetraacetate $[\text{Mo}_2(\text{OAc})_4]$ to solution of **5** and **6** in DMSO, respectively, metal complexes were generated as an auxiliary chromophore. The Cottonogenic diol derivatives are constrained into a chiral, *gauche* arrangement with the bulkier substituents adopt a pseudo-equatorial position pointing away from the remaining

portion of the complex. The signs of band II (310 nm) are same with the O–C–C–O dihedral angle, and are most safely related to the absolute configuration of the diol. As shown in Fig. 4, the positive and negative Cotton effects at 310 nm of compounds **5** and **6** metal complexes corresponding to the clockwise and counter-clockwise of the O–C–C–O dihedral angles, respectively, which led to the unambiguously assign of the absolute configurations of **5** and **6** as 11*R*,12*R* and 11*S*,12*R*, respectively [19, 20]. Therefore, compounds **5** and **6** were elucidated as shown in Fig. 1 and were given the respective names (11*R*,12*R*)- and (11*S*,12*R*)-vibradiol.

The previously described compound vibractone B (**7**) possessing an epoxy ring at C2–C3 was re-encountered in this research with a yield of more than 3 g [6]. Re-examined of the ROESY spectrum suggested that the mis-assignment of configuration of the epoxy ring as supported by the obvious ROESY correlations between H-8/H-2, and H-2/H-13 (Fig. 5), suggestive of α configuration instead of β configuration of the epoxy ring. Finally, crystals of **7** suitable for single crystal X-ray diffraction analysis were cultured via slowly evaporated methanol. As shown in Fig. 5, the X-ray diffraction result unequivocally determined the epoxy ring as α configuration.

In conclusion, six previously undescribed compounds were isolated from the scale-up fermentation of the fungus *B. vibrans*. All these compounds are biosynthetically related. Vibractamide A (**1**) represents the other type of nitrogen-containing vibractone derivative possible originated from different nitrogen atom-introducing pathway comparing with those of vibractoximes A–P. This work provided further evidences for divergent vibractone biosynthesis pathway and expanded the structural diversity of vibractone-related compounds.



Scheme 1 Proposed biosynthetic pathway for compound **1**

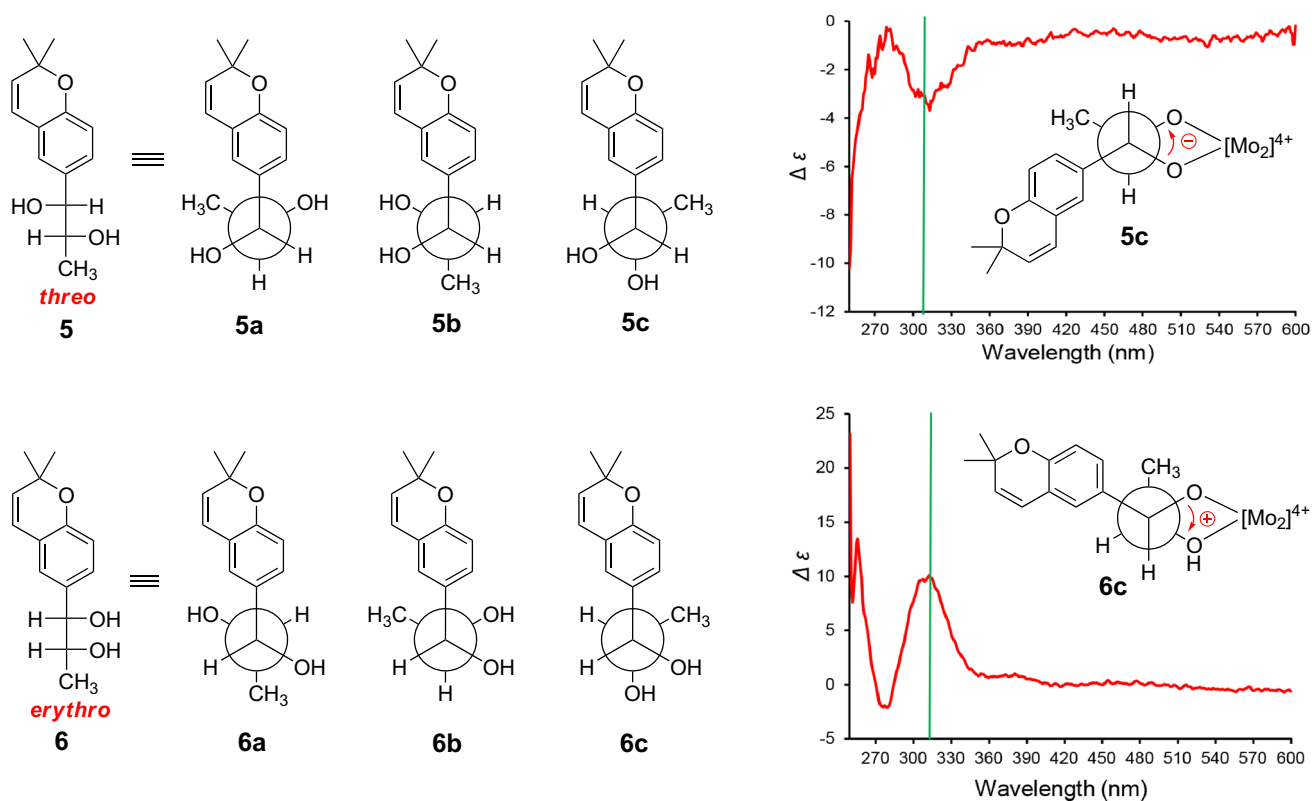


Fig. 4 Fischer projections of compounds **5** and **6**; Newman projections of the possible conformers **5a**, **5b**, **5c** for **5**, and **6a**, **6b**, **6c** for **6**; and CD spectra of in situ formed Mo-complexes of **5** and **6** in DMSO

after 0.5 h from dissolving in the 1:1.2 ligand-to-metal ratio (green lines marked the position of 310 nm)

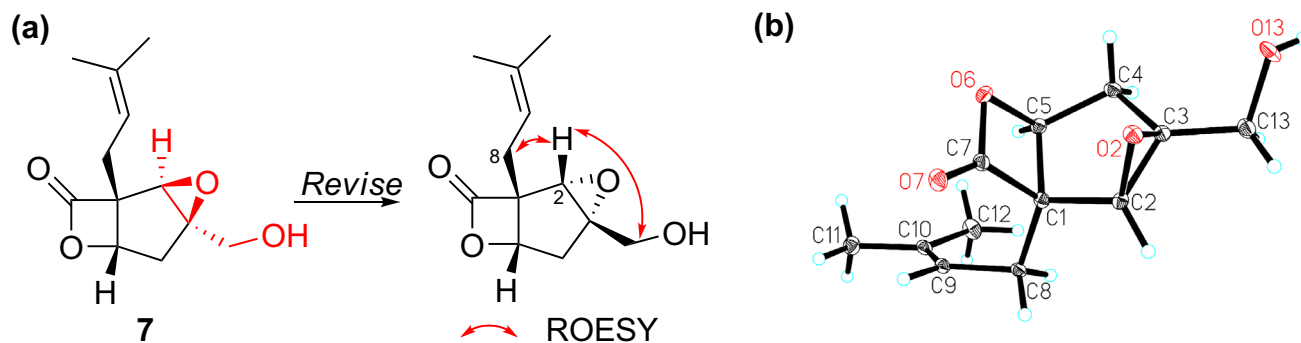


Fig. 5 **a** Structure revision of vibralactone B (**7**); **b** ORTEP drawing of compound **7**

3 Experimental Section

3.1 General Experimental Procedures

Optical rotations were obtained on a JASCO P-1020 digital polarimeter (Horiba, Kyoto, Japan). UV spectra were recorded on a Shimadzu UV-2401PC UV–visible recording spectrophotometer (Shimadzu, Kyoto, Japan). 1D and 2D NMR spectra were obtained on a Bruker Avance III 600 MHz spectrometer (Bruker Corporation, Karlsruhe, Germany). HRESIMS were recorded on an Agilent 6200

Q-TOF MS system (Agilent Technologies, Santa Clara, CA, USA). HREIMS were obtained on a Waters Autospec Premier P776 mass spectrometer. Single crystal X-ray diffraction was performed on an APEX II DUO spectrophotometer (Bruker AXS GmbH, Karlsruhe, Germany). Sephadex LH-20 (Amersham Biosciences, Uppsala, Sweden) and silica gel (Qingdao Haiyang Chemical Co., Ltd) were used for column chromatography (CC). Medium pressure liquid chromatography (MPLC) was performed on a Büchi Sepacore System equipped with pump manager C-615, pump modules C-605 and fraction collector C-660

(Büchi Labortechnik AG, Flawil, Switzerland), and columns packed with Chromatorex C-18 (40–75 μm , Fuji Silysia Chemical Ltd., Kasugai, Japan). Preparative high performance liquid chromatography (prep-HPLC) were performed on an Agilent 1260 liquid chromatography system equipped with Zorbax SB–C18 column (particle size 5 μm , dimension 9.4 mm \times 150 mm, flow rate 8 mL/min, respectively) and a DAD detector (Agilent Technologies, Santa Clara, CA, USA).

3.2 Fungal Material and Cultivation

The fungus *B. vibrans* was collected from the Ailao Mountains of Yunnan Province, P. R. China in August 2005, and identified by Prof. Mu Zang (Kunming Institute of Botany, CAS), who is a mushroom specialist. A voucher specimen of *B. vibrans* was deposited in the Herbarium of KIB. The culture medium to ferment this fungus consist of 5% glucose, 0.15% peptone from porcine meat, 0.5% yeast extract, 0.05% KH_2PO_4 , and 0.05% MgSO_4 . Five hundred 500-mL Erlenmeyer flasks each containing 350 mL of culture medium were inoculated with *B. vibrans* strains. The incubation was carried out on rotary shakers at 24 $^\circ\text{C}$ and 150 rpm for 25 days in dark environment.

3.3 Extraction and Isolation

The culture broth (175 L) of *B. vibrans* was filtered. The filtrate was concentrated under pressure to 10 L and then partition with EtOAc for four times to give a filtrate-originated EtOAc layer (170 g). Meanwhile, the mycelia were extracted by EtOH (95%) for three times. The extraction was concentrated under pressure to remove organic solvent and then dissolve in water and partition with EtOAc for four times to give a mycelium-originated EtOAc layer (183 g). The total EtOAc residue was subjected to CC over silica gel (200–300 mesh) eluting with a gradient of petroleum ether/acetone (100:0 \rightarrow 0:100) to give five fractions (A–E). Fraction D was separated by MPLC eluting with MeOH/ H_2O (20:80 \rightarrow 100:0) to yield ten subfractions D1–D10. Subfraction D4 was subjected to HPLC to give compound **1** (1.5 mg, MeCN/ H_2O , 25–45%, 25 min, 8 mL/min, $t_R = 10.6$ min). Subfraction D5 was subjected to HPLC (MeCN/ H_2O , 30–50%, 25 min, 8 mL/min) to give compounds **2** (20.5 mg, $t_R = 16.5$ min) and **3** (6.5 mg, $t_R = 18.6$ min). Subfraction D6 was separated by HPLC (MeCN/ H_2O , 33–53%, 25 min, 8 mL/min) to afford compounds **5** (30.3 mg, $t_R = 15.6$ min) and **6** (2.0 mg, $t_R = 16.5$ min). Subfraction D8 was purified by HPLC to give compound **4** (3.0 mg, MeCN/ H_2O , 36–56%, 25 min, 8 mL/min, $t_R = 17.5$ min).

Vibrallactamide A (1) colorless oil; $[\alpha]_D^{25} +4.2$ (c 0.11, MeOH); UV (MeOH) λ_{max} (log ϵ) 204.5 (4.80); IR (KBr) ν_{max} 3447, 2975, 2972, 1637, 1383, 1126, 1044 cm^{-1} ; ^1H NMR (600 MHz, acetone- d_6 or DMSO- d_6) and ^{13}C NMR (150 MHz, acetone- d_6 or DMSO- d_6) data, see Tables 1 and 2; HREIMS m/z 253.1672 $[\text{M}]^+$ (calcd for 253.1678, $\text{C}_{14}\text{H}_{23}\text{O}_3\text{N}$).

Vibrallactone T (2) colorless oil; $[\alpha]_D^{25} -61.3$ (c 0.08, MeOH); UV (MeOH) λ_{max} (log ϵ) 204.5 (3.53); IR (KBr) ν_{max} 3423, 2972, 2927, 2863, 1816, 1722, 1630, 1379, 1122, 977 cm^{-1} ; ^1H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, see Tables 1 and 2; HRESIMS m/z 247.0937 $[\text{M} + \text{Na}]^+$ (calcd for 247.0941, $\text{C}_{12}\text{H}_{16}\text{O}_4\text{Na}$).

13-O-Lactyl vibrallactone (3) colorless oil; $[\alpha]_D^{25} -100.8$ (c 0.08, MeOH); UV (MeOH) λ_{max} (log ϵ) 203.6 (3.71), 217.0 (sh, 3.50); IR (KBr) ν_{max} 3427, 2971, 2927, 2858, 1819, 1738, 1631, 1213, 1131, 1035 cm^{-1} ; ^1H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, see Tables 1 and 2; HRESIMS m/z 303.1206 $[\text{M} + \text{Na}]^+$ (calcd for 303.1203, $\text{C}_{15}\text{H}_{20}\text{O}_5\text{Na}$).

10-O-Acetyl vibrallactone G (4) colorless oil; $[\alpha]_D^{25} -10.6$ (c 0.18, MeOH); UV (MeOH) λ_{max} (log ϵ) 206.0 (3.01), 257.0 (sh, 2.53); IR (KBr) ν_{max} 3426, 2973, 2930, 2858, 1746, 1632, 1381, 1245, 1044 cm^{-1} ; ^1H NMR (600 MHz, acetone- d_6) and ^{13}C NMR (150 MHz, acetone- d_6) data, see Tables 1 and 2; HRESIMS m/z 249.1100 $[\text{M} + \text{Na}]^+$ (calcd for 249.1097, $\text{C}_{12}\text{H}_{18}\text{O}_4\text{Na}$).

(11R,12R)-Vibradiol (5) white powder; $[\alpha]_D^{25} +9.3$ (c 0.15, MeOH); UV (MeOH) λ_{max} (log ϵ) 196.5 (4.07), 223.0 (4.51), 264.5 (3.55), 311.5 (3.42); IR (KBr) ν_{max} 3449, 2977, 2925, 1637, 1384, 1262, 1126 cm^{-1} ; ^1H NMR (600 MHz, acetone- d_6) and ^{13}C NMR (150 MHz, acetone- d_6) data, see Tables 1 and 2; HREIMS m/z 234.1264 $[\text{M}]^+$ (calcd for 234.1256, $\text{C}_{14}\text{H}_{18}\text{O}_3$).

(11S,12R)-Vibradiol (6) white powder; $[\alpha]_D^{25} +52.4$ (c 0.15, MeOH); UV (MeOH) λ_{max} (log ϵ) 222.5 (4.45), 264.5 (3.48), 310.5 (3.35); IR (KBr) ν_{max} 3443, 2974, 2926, 2857, 1634, 1383, 1125, 1037 cm^{-1} ; ^1H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, see Tables 1 and 2; HREIMS m/z 234.1255 $[\text{M}]^+$ (calcd for 234.1256, $\text{C}_{14}\text{H}_{18}\text{O}_3$).

Single crystal X-ray diffraction data for vibrallactone B (7, MeOH) Crystal data for Cu_7_0 m: $\text{C}_{12}\text{H}_{16}\text{O}_4$, $M = 224.25$, $a = 10.0771(4)$ \AA , $b = 5.8671(2)$ \AA , $c = 10.3263(4)$ \AA , $\alpha = 90^\circ$, $\beta = 115.1150(10)^\circ$, $\gamma = 90^\circ$, $V = 552.80(4)$ \AA^3 , $T = 100(2)$ K, space group $P21$, $Z = 2$, $\mu(\text{CuK}\alpha) = 0.834$ mm^{-1} , 5458 reflections measured, 1862 independent reflections ($R_{\text{int}} = 0.0365$). The final R_I values were 0.0353 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0961 ($I > 2\sigma(I)$). The final R_I values were 0.0354 (all

data). The final $wR(F^2)$ values were 0.0963 (all data). The goodness of fit on F^2 was 1.113. Flack parameter = 0.07(6). Crystallographic data for compound **7** have been deposited to the Cambridge Crystallographic Data Center (No. CCDC 1580061). These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>.

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Compliance with Ethical Standards

Conflict of interest The authors declare no competing financial interest.

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