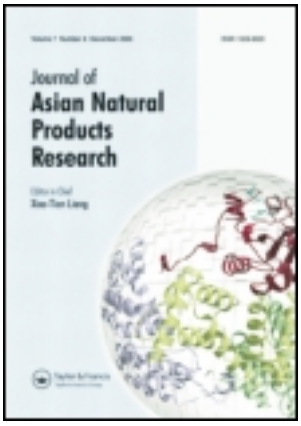

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Vibralactones G–J from cultures of the basidiomycete *Boreostereum vibrans*

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Four new vibralactone derivatives, named vibralactones G–J (**1**–**4**), together with vibralactone (**5**) have been isolated from cultures of the basidiomycete *Boreostereum vibrans*. The new structures were elucidated by means of spectroscopic methods.

Keywords: *Boreostereum vibrans*; basidiomycete; vibralactones G–J

1. Introduction

Vibralactone and its derivatives have been found in the basidiomycete *Boreostereum vibrans* [1–3]. Our previous studies have reported vibralactone, 1,5-secovibralactone, and vibralactones B–F from cultures of *B. vibrans* [1–3]. Of them, vibralactone showed inhibitory activity against pancreatic lipase with an IC_{50} value of 0.4 μg/ml [1]. In addition, these natural products have attracted great interests of synthetic chemists due to structural and bioactive novelty, and total syntheses of vibralactone and vibralactone C have been finished [4,5]. Recently, vibralactone as a tool to study the activity and structure of the ClpP1P2 complex from *Listeria monocytogenes* has been reported [6]. A further search on the cultures of *B. vibrans* led to the isolation of four new vibralactone derivatives, named vibralactones G–J (**1**–**4**), and one known compound vibralactone (**5**) (Figure 1) [1]. The new structures were established by means of spectroscopic methods, while the known compound **5** was identified by comparison with data in the literature. Herein, the isolation and structural elucidation of these compounds have been reported.

2. Results and discussion

Compound **1** was obtained as a colorless oil. Its molecular formula was established as $C_{10}H_{16}O_3$ according to the pseudomolecular ion at *m/z* 207.0996 $[M + Na]^+$ in the HR-ESI-MS. The IR spectrum showed the presence of hydroxy (3431 cm^{-1}) and carbonyl (1767 cm^{-1}) groups. The ^1H and ^{13}C NMR spectroscopic data (Table 1) revealed 10 carbon resonances assigned to one carbonyl carbon, two olefinic carbons, two methines (including one oxygenated at δ_C 75.2), three methylenes (including one oxygenated at δ_C 61.1), and two methyls.

In the ^1H–^1H COSY spectrum, a fragment of CH_3—CH—CH_2—CH—CH_2—CH— was established readily as shown in Figure 2. The HMBC correlation of H-5 at δ_H 4.65 (1H, m,) with C-2 at δ_C 179.3 established a five-membered lactone ring.

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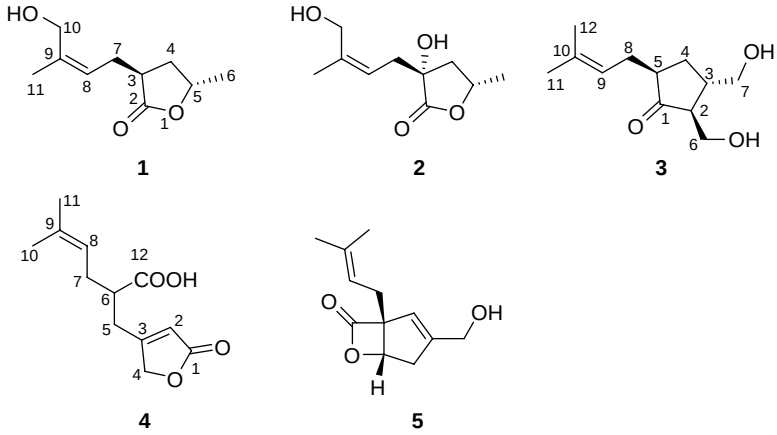

Figure 1. Structures of compounds **1**–**5**.

In addition, the HMBC correlations of a methyl signal at δ_H 1.80 (3H, s, H-11) and an oxygenated methylene signals at δ_H 4.11 (1H, d, $J = 12.0$ Hz, H-10a) and 4.04 (1H, d, $J = 12.0$ Hz, H-10b) with the signal at δ_C 122.9 (d, C-8) suggested the existence of an oxygenated isoprenyl group connected to C-7 (Figure 2).

To establish the relative configuration of **1**, a ROESY experiment was exerted, in which the ROESY correlations of H-5/H-4a and H-4b/H-3 suggested that H-3 and H-5 were in the opposite side. Therefore, compound **1** was established and named as vibralactone G.

Compound **2**, a colorless oil, possesses a molecular formula $C_{10}H_{16}O_4$ as established by the HR-ESI-MS at *m/z* 223.0942 $[M + Na]^+$. The IR spectrum showed the presence of carbonyl (1767 cm^{-1}) and hydroxy (3419 cm^{-1}) groups. The ^1H and ^{13}C NMR data of **2** were very similar to those of **1** except for a sp^3 quaternary carbon at δ_C 76.8 (s, C-3) in **2** instead of a sp^3 methine in **1**. This quaternary carbon was assigned to C-3 as supported by the HMBC correlations of H-4a at δ_H 2.54 (1H, dd, $J = 15.0$, 6.0 Hz), H-4b at δ_H 1.81 (1H, dd, $J = 15.0$, 8.8 Hz), H-7a at δ_H 2.47 (1H, dd, $J = 6.0$, 14.0 Hz), and H-7b at δ_H 2.44 (1H, dd, $J = 6.0$, 14.0 Hz) with C-3 at δ_C 76.8. Detailed analysis of other 2D NMR data (HSQC, HMBC, $^1H-^1H$ COSY, and ROESY) suggested that the other parts were the same as those of **1**. Therefore, compound **2** was established as depicted, and named vibralactone H.

Compound **3** was obtained as a colorless oil. Its molecular formula was established as $C_{12}H_{20}O_3$ by the positive HR-ESI-MS at *m/z* 235.1316 $[M + Na]^+$. The IR spectrum showed absorption bands at 3407 cm^{-1} and 1731 cm^{-1}, corresponding to the hydroxy and carbonyl groups, respectively. The ^{13}C NMR spectral data (Table 1) revealed 12 carbon signals assigned to one carbonyl, one double bond, three sp^3 methines, four sp^3 methylenes (two oxygenated), and two methyls. Of them, signals at δ_C 17.9 (q, C-11), 25.8 (q, C-12), 28.8 (t, C-8), 121.0 (d, C-9), and 134.2 (s, C-10) indicated the presence of an isoprenyl group. In the $^1H-^1H$ COSY spectrum, a partial structure was established as shown in Figure 2. The HMBC correlations of H-3, H-6, and H-8 with the quaternary carbon at δ_C 220.2 (s, C-1) suggested a five-membered keto ring (Figure 2). In addition, the HMBC correlation of H-5 at δ_H 2.42 (1H, m) with C-9 at δ_C 121.0 suggested that the isoprenyl group was connected to C-5 (Figure 2). The ROESY spectrum displayed some similarities to those of **1**

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1**–**4** (J in Hz).

	1[a]		**2**[b]		**3**[a]		**4**[c]	
NO.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1						220.2 s		174.0 s
2		179.3 s		179.0 s	2.27 (m)	56.7 d	5.91 (s)	116.5 d
3	2.74 (m)	39.4 d		76.8 s	2.26 (m)	42.1 d		167.9 s
4a	2.15 (m)	34.1 t	2.54 (dd, 15.0, 6.0)	42.8 t	2.11 (2H, m)	28.3 t	4.77 (2H, s)	73.3 t
4b	2.01 (m)		1.81 (dd, 15.0, 8.8)					
5a	4.65 (m)	75.2 d	4.47 (m)	73.6 d	2.42 (m)	47.3 d	2.70 (dd, 11.6, 7.8)	29.4 t
5b							2.57 (dd, 11.6, 6.4)	
6a	1.34 (3H, d, 6.3)	21.2 q	1.35 (3H, d, 6.1)	21.7 q	3.99 (dd, 11.3, 3.8)	62.1 t	2.73 (m)	43.8 d
6b					3.62 (dd, 11.3, 6.6)			
7a	2.39 (2H, m)	28.0 t	2.44 (dd, 7.5, 14.0)	35.5 t	3.86 (dd, 10.9, 3.2)	66.4 t	2.46 (m)	30.7 t
7b			2.47 (dd, 6.0, 14.0)		3.60 (dd, 10.9, 7.3)		2.33 (m)	
8a	5.26 (t, 7.7)	122.9 d	5.35 (t, 7.5)	120.5 d	1.84 (m)	28.8 t	5.09 (t, 6.8)	119.2 d
8b					1.66 (m)			
9		138.2 s		140.9 s	5.08 (t, 6.8)	121.0 d		135.9 s
10a	4.11 (d, 12.0)	61.1 t	4.07 (d, 12.2)	61.2 t		134.2 s	1.63 (3H, s)	17.9 q
10b	4.04 (d, 12.0)		4.04 (d, 12.2)					
11	1.80 (3H, s)	21.7 q	1.78 (3H, s)	22.2 q	1.62 (3H, s)	17.9 q	1.73 (3H, s)	25.8 q
12					1.70 (3H, s)	25.8 q		179.4 s

[a] At 400 and 100 MHz, in $CDCl_3$.
[b] At 500 and 125 MHz, in Me_2CO-d_6.
[c] At 500 and 125 MHz, in $CDCl_3$.

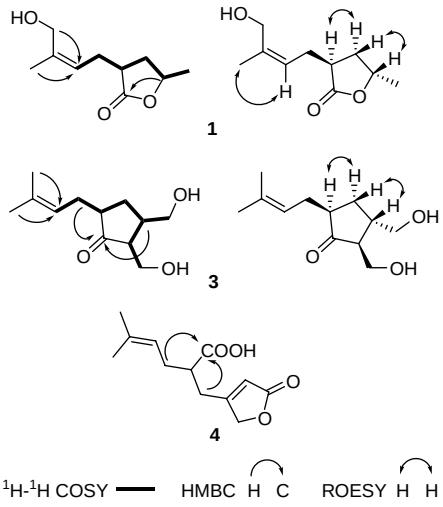

Figure 2. Key 2D NMR correlations of **1**, **3**, and **4**.

including the ROESY correlations of H-5/H-4a and H-4b/H-3 (Figure 2), which suggested that H-3 and H-5 were in the opposite side. Meanwhile, no ROESY signal between H-3 and H-2 suggested that they were also in the opposite side. Therefore, the planar and stereo structure of compound **3** was established and named vibralactone I.

Compound **4** was obtained as a colorless oil. The molecular formula was found to be $C_{12}H_{16}O_4$ by HR-ESI-MS at *m/z* 225.1126 $[M + H]^+$. The IR spectrum showed the presence of a hydroxy (3429 cm^{-1}) and two carbonyls (1781 and 1746 cm^{-1}) groups. The ^{13}C NMR spectrum displayed 12 carbon resonances ascribable to two carbonyls, four double bonds, one methine, three methylenes, and two methyls (Table 1). An isoprenyl group was detected from signals at δ_C 17.9 (q, C-10), 25.8 (q, C-11), 30.7 (t, C-7), 119.2 (d, C-8), and 135.9 (s, C-9). In addition, the signals at δ_C 174.0 (s, C-1), 116.5 (d, C-2), and 167.9 (s, C-3) as well as the UV absorption maximum at 295 nm suggested an α,β-unsaturated ester, while the HMBC correlation of H-4 at δ_H 4.77 (2H, s) with C-1 at δ_C 174.0 established a five-membered lactone ring. The rest of the three carbon signals at δ_C 29.4 (t, C-5), 43.8 (d, C-6), and 179.4 (s, C-12) were constructed according to the HMBC correlations as shown in Figure 2. Therefore, compound **4** was established and named vibralactone J.

To the best of our knowledge, compounds **3** and **4** were novel natural products which might be derived from vibralactone (**5**) [1] and 1,5-secovibralactone [2] via hydrolysis, oxygenation, cyclization, and H migration (Figure 3).

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor 27 spectrophotometer was used for scanning IR spectroscopy using KBr pellets. 1D and 2D spectra were run on Avance III 600,

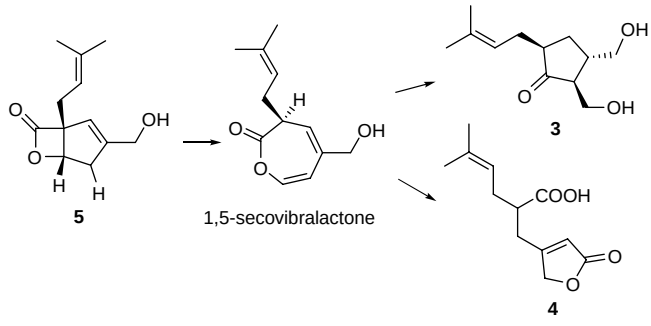

Figure 3. Plausible biogenetic synthetic pathway of **3** and **4**.

Bruker DRX-500, and Bruker AM-400 spectrometers with Tetramethylsilane as an internal standard. Chemical shifts (δ) were expressed in ppm with reference to the solvent signals. HR-ESI-MS were obtained on an API-Qstar-Pulsar-1 spectrometer. Column chromatography (CC) was performed on Silica gel (200–300 mesh, Qingdao Haiyang Chemical Co. Ltd, Qingdao, China) and RP-18 (20–45 μm, Fuji Silysia Chemical Ltd, Kasugai, Aichi, Japan). Fractions were monitored by TLC (GF 254, Qingdao Haiyang Chemical Co., Ltd) and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4.

3.2 Fungal material and cultivation

B. vibrans was provided and fermented by Dr Da-Gan Ji, Kunming Institute of Botany. A voucher specimen has been deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences. The culture medium consisted of glucose 5%; peptone 0.15%; yeast 0.5%; KH_2PO_4 0.05%; and $MgSO_4$ 0.05% in 1 liter of deionized water (pH 6.5 before autoclaving). The fungus was grown in Erlenmeyer flasks (500 with 300 ml of medium). Fermentation was carried out in a rotary shaker at 22°C and 200 rpm for 26 d.

3.3 Extraction and isolation

The whole culture broth (25 liters) of *B. vibrans* was extracted three times with EtOAc (14 liters) after filtration. The organic layer was concentrated under reduced pressure to give a crude extract (15.0 g). The residue was subjected to CC over silica gel (200–300 mesh), eluted with a petroleum ether–EtOAc (20:1, 15:1, 10:1, 5:1, 1:1, 0:1, v/v) gradient, to afford fractions A–F. Fraction D (230 mg) eluted with petroleum ether–EtOAc (2:1, v/v) was separated repeatedly by reverse-phased RP-18 (MeOH–H_2O, 30% → 45%) CC to give **1** (22.3 mg) and **4** (50.0 mg). Fraction E (110 mg) was separated by silica gel CC eluted with petroleum ether–EtOAc (1:1), then purified by RP-18 (MeOH–H_2O, 20% → 30%) CC to afford **3** (3 mg) and **2** (11 mg).

3.3.1 Vibralactone G (**1**)

A colorless oil; $[\alpha]_D^{18}$ −2.7 (*c* 0.53, MeOH). IR (KBr) ν_{max}: 3431, 2964, 2931, 1767, 1736, 1453, 1384, 1287, 1188, 1003 cm^{-1}; ^1H (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectral data see Table 1; Positive HR-ESI-MS *m/z*: 207.0996 $[M + Na]^+$ (calcd for $C_{10}H_{16}O_3Na$, 207.0997).

3.3.2 Vibralactone H (**2**)

A colorless oil; $[\alpha]_D^{11}$ −18.2 (*c* 0.11, MeOH). IR (KBr) ν_{max}: 3421, 2957, 2921, 1767, 1627, 1450, 1385, 1206, 1125, 1048 cm^{-1}; ^1H (500 MHz, Me_2CO-d_6) and ^{13}C NMR (125 MHz, Me_2CO-d_6) spectral data see Table 1; Positive HR-ESI-MS *m/z*: 223.0942 $[M + Na]^+$ (calcd for $C_{10}H_{16}O_4Na$, 223.0946).

3.3.3 Vibralactone I (**3**)

A colorless oil; $[\alpha]_D^{9}$ −26.0 (*c* 0.36, MeOH). IR (KBr) ν_{max}: 3407, 2959, 2919, 1731, 1628, 1452, 1380, 1287, 1053 cm^{-1}; ^1H (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectral data see Table 1; Positive HR-ESI-MS *m/z*: 235.1316 $[M + Na]^+$ (calcd for $C_{12}H_{20}O_3Na$, 235.1310).

3.3.4 Vibralactone J (**4**)

A colorless oil; $[\alpha]_D^{18}$ −4.5 (*c* 0.26, MeOH). UV (MeOH) λ_{max} (log ε): 295 (1.09), 217 (3.24), 198 (2.49) nm; IR (KBr) ν_{max}: 3428, 2969, 2926, 1781, 1746, 1637, 1443, 1177, 1029, 889 cm^{-1}; ^1H (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectral data see Table 1; Positive HR-ESI-MS *m/z*: 225.1126 $[M + H]^+$ (calcd for $C_{12}H_{17}O_4$, 225.1126).

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