Two new phenol derivatives from Stereum hirsutum FP-91666

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Two new phenol derivatives from *Stereum hirsutum* FP-91666

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Two new phenol derivatives, 2-(3-methyl-2-buten-1-yl)-4-methoxyethyl-phenol (1) and 5-hydroxy-4-(hydroxymethyl)-2-(3-methylbut-2-en-1-yl)cyclohex-4-en-1-one (2), together with eight known compounds consisting of phenol derivatives (3 and 4), niacinamide (5), and five ergosta type compounds (6–10), were isolated from solid fermentation products of *Stereum hirsutum* FP-91666. Two new structures were elucidated by extensive spectroscopic methods, including 1D NMR and 2D NMR, and HR-EI-MS experiments.

**Keywords:** Stereaceae; *Stereum hirsutum* FP-91666; 2-(3-methyl-2-buten-1-yl)-4-methoxyethyl-phenol; 5-hydroxy-4-(hydroxymethyl)-2-(3-methylbut-2-en-1-yl)cyclohex-4-en-1-one

1. Introduction

The fungus of *Stereum* belongs to the Stereaceae family (basidiomycetes), and can produce diversiform secondary metabolites [1–3], especially produce structurally diverse sesquiterpenes [4]. In process of studying on the biosynthesis of vibralactone [5], which was produced by *Stereum vibrans* [6], we had searched analogous genes of biosynthetic vibralactone and found that *Stereum hirsutum* (*S. ostrea*) can produce vibaralactone type compounds [7,8]. According to genome data analysis, *S. hirsutum* would produce more secondary metabolites [9], so we investigated the chemical constituent of *S. hirsutum* FP-91666. And two new phenol derivatives, 2-(3-methyl-2-buten-1-yl)-4-methoxyethyl-phenol (1) and 5-hydroxy-4-(hydroxymethyl)-2-(3-methylbut-2-en-1-yl)cyclohex-4-en-1-one (2), together with eight known compounds were isolated from solid fermentation products of *S. hirsutum* FP-91666. This report describes the isolation and structural elucidation of these compounds.

2. Results and discussion

Compound 1 was obtained as colorless amorphism. The HR-EI-MS data indicated a molecular formula of C\(_{14}\)H\(_{20}\)O\(_2\) based on the [M]\(^+\) ion signal at m/z 220.1456. The \(^{13}\)C NMR data (Table 1) revealed four quaternary carbons at \(\delta_C\) 153.8, 135.6, 134.9, and 126.7, five methines at \(\delta_C\) 127.9, 125.5, 121.8, 115.6, and 79.2, and one methylene (\(\delta_C\) 30.1) and four methyls, and from \(^1\)H NMR spectrum, three aromatic protons (\(\delta_H\) 7.06 (brs), 7.07 (dd, 8.0, 2.1), and 6.81 (d, 8.0)) indicated the presence of three-substituted benzene ring; and two methyl singlets (\(\delta_H\) 1.80 (s) and 1.81 (s)) and one sp\(^2\) proton (\(\delta_H\) 5.33–5.36 (m)) suggested compound 1 was prenylated phenol derivatives (Figure 1) [10].

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The HMBC experiment (Table 1) showed correlations between the proton at \( \delta^H 4.24 \) (H-12) and carbons at \( \delta^C 125.5 \) (C-5), \( 127.9 \) (C-3), \( 23.8 \) (C-13), \( 56.2 \) (12-OCH₃), and \( 135.6 \) (C-4), between the proton at \( \delta^H 1.44 \) (H-13) and the carbons at \( \delta^C 79.2 \) (C-12) and \( 135.6 \) (C-4), which indicated that one methoxyethyl group connected with prenylated phenol at position C-4 (\( \delta^C 135.6 \)) (Figure 2). C-12 was a chiral center, but its configuration cannot be determined by current data. Together with other data (Table 1), compound 1 was elucidated to be 2-(3-methyl-2-buten-1-yl)-4-methoxyethyl-phenol (Figure 1).

Compound 2 was obtained as colorless amorphism. The HR-EI-MS data indicated a molecular formula of \( C_{12}H_{18}O_3 \) based on the [M]+ ion signal at \( m/z \) 210.1250. The \( ^{13}C \) NMR data (Table 1) revealed four quaternary carbons at \( \delta^C 212.7 \) (C-11), \( 138.4 \) (C-4), \( 46.5 \) (C-10), and \( 34.5 \) (C-9), two methines at \( \delta^C 177.8 \) and \( 121.8 \) (C-12), and two methyls, which

Table 1. \(^1H\) and \(^{13}C\) NMR spectral data of compounds 1 and 2.

<table>
<thead>
<tr>
<th>Position</th>
<th>(^1H)</th>
<th>(^{13}C)</th>
<th>(^1H)</th>
<th>(^{13}C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>153.8, s</td>
<td>–</td>
<td>212.7, s</td>
</tr>
<tr>
<td>2</td>
<td>–</td>
<td>126.7, s</td>
<td>2.38–2.44 (m)</td>
<td>46.5, d</td>
</tr>
<tr>
<td>3</td>
<td>7.06 (brs)</td>
<td>127.9, d</td>
<td>2.78–2.82 (m); 2.36 (d, 16)</td>
<td>34.5, t</td>
</tr>
<tr>
<td>4</td>
<td>–</td>
<td>135.6, s</td>
<td>–</td>
<td>138.4, s</td>
</tr>
<tr>
<td>5</td>
<td>7.07 (dd, 8.0, 2.1)</td>
<td>125.5, d</td>
<td>–</td>
<td>177.8, s</td>
</tr>
<tr>
<td>6</td>
<td>6.81 (d, 8.0)</td>
<td>115.6, d</td>
<td>4.24 (s)</td>
<td>54.0, t</td>
</tr>
<tr>
<td>7</td>
<td>3.39 (d, 7.2)</td>
<td>30.1, t</td>
<td>2.38–2.44 (m); 2.10–2.16 (m)</td>
<td>30.3, t</td>
</tr>
<tr>
<td>8</td>
<td>5.33–5.36 (m)</td>
<td>121.8, d</td>
<td>5.06–5.09 (m)</td>
<td>121.8, d</td>
</tr>
<tr>
<td>9</td>
<td>–</td>
<td>134.9, s</td>
<td>–</td>
<td>134.9, s</td>
</tr>
<tr>
<td>10</td>
<td>1.80 (s)</td>
<td>25.8, q</td>
<td>1.68 (s)</td>
<td>25.9, q</td>
</tr>
<tr>
<td>11</td>
<td>1.81 (s)</td>
<td>17.9, q</td>
<td>1.63 (s)</td>
<td>17.9, q</td>
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<tr>
<td>12</td>
<td>4.24 (q, 6.4)</td>
<td>79.2, d</td>
<td>4.56–4.60 (m)</td>
<td>61.3, t</td>
</tr>
<tr>
<td>13</td>
<td>1.44 (d, 6.4)</td>
<td>23.8, q</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>12-OCH₃</td>
<td>3.22 (s)</td>
<td>56.2, q</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>– OH</td>
<td>5.12 (s)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

\(^a\)The NMR data are obtained on Avance III 600 in CDCl₃.
\(^b\)The NMR data are obtained on Bruker AV-800 in CD₃OD.

The compound structures from S. hirsutum FP-91666.

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indicated that compound 2 was also prenylated phenol derivatives except the phenol was oxidized [10]. The detail structure was confirmed by 2D NMR. The HMBC experiment (Table 1) showed the proton at δ_H 5.06–5.09 (H-8) correlated with carbons at δ_C 17.9 (C-11), 25.9 (C-10), 30.3 (C-7), and the protons of methylene at δ_H 2.38–2.44 and 2.10–2.16 (H-7) with carbons at δ_C 121.8 (C-8) and 134.9 (C-9), and two methyl group protons at δ_H 1.68 (H-10) and 1.63 (H-11) with carbons at δ_C 121.8 (C-8) and 134.9 (C-9), which indicated the existence of an isopentenyl group. H-12 at δ_H 4.60 correlated with C-4, C-5, C-3, and H-2 correlated with C-1 and C-3, H-6 correlated with the C-1, C-4, and C-5, and H-3 correlated with the C-1, C-2, C-4 and C-5, which indicated compound 2 contained 5-hydroxy-4-(hydroxymethyl)cyclohex-4-en-1-one, which would come from oxidized phenol. These two units connected by C–C bond based on the correlations between protons of methylene at δ_H 2.38–2.44 and 2.10–2.16 (H-7) and C-2 (Figure 2). The configuration of C-2 is uncertain because H-2 was overlapped with H-7, and there is no NOE correlation between H-3 and H-7. Based on above data, compound 2 was determined to be 5-hydroxy-4-(hydroxymethyl)-2-(3-methylbut-2-en-1-yl)cyclohex-4-en-1-one (Figure 1).

In addition to the above-mentioned new phenol derivatives, eight known compounds including 3-(hydroxymethyl)-4-methoxy-2-(3-methylbut-3-en-1-yn-1-yl)phenol (3) [2], 4-methoxy-benzoic acid methyl ester (4) [11], niacinamide (5) [11], ergosterol peroxid (6) [11], (22E,24R)-ergosta-5,7,22-trien-3β-ol (7) [12], 3β,5α,6β-triol-ergosta-7,22-diene (8) [13], 3β,5α-diol-6β-methoxy-ergosta-7,22-diene (9) [14], and 3β,5α,9α-trihydroxy-ergosta-7,22-dien-6-one (10) [15] were also isolated and identified by comparing their NMR and MS data with those reported in the literatures.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured on a Jasco DIP-370 digital polarimeter (JASCO, Tokyo, Japan). UV spectra were measured on a Shimadzu UV-2401PC spectrophotometer (Shimadzu, Tokyo, Japan), λ_max (log ε) in nm. IR spectra were scanned with Bruker Tensor-27 infrared spectrometer with a KBr disk (Bruker, Karlsruhe, Germany). NMR experiments were carried out on a Finnigan LCQ Advantage mass spectrometer (Thermo, San Jose, CA, USA) and a VG Auto-Spec-3000 mass spectrometer (VG, Manchester, England). ESI-MS and HR-EI-MS were recorded on a Finnigan LCQ Advantage mass spectrometer and a VG Auto-Spec-3000 mass spectrometer (VG, Manchester, England). Column chromatography was carried out on silica gel (G, 200-300 mesh and H, Qingdao Marine Chemical Factory, Qingdao, China) and Sephadex LH-20 (Pharmacia Fine Chemicals, Uppsala, Sweden). Precoated silica gel GF254 plates (Qingdao Marine Chemical Factory) were used for thin-layer chromatography.

3.2 Fungal material

S. hirsutum FP-91666, stored in glycerol at −80°C in State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, was used to inoculate on YMG (yeast extract 4.0 g/l, malt extract 10.0 g/l,
glucose 4.0 g/l, agar 15.0 g/l, pH 7.3 before sterilization) media in plate at 26°C for 14 days to afford seed cultures. The S. hirsutum (151) was cultured on YMG dish at temperature of 26°C for 14 days.

3.3 Extraction and isolation

Solid fermentation products of S. hirsutum (151) was cut into small pieces and extracted exhaustively with mixture solution (EtOAc/MeOH/HAc, 80:15:5, v/v/v) by three times to obtain the rude extract. The extracts were dissolved in water, and extracted with EtOAc, and then with n-butanol three times, respectively. The extract of EtOAc section residue (6.85 g) was subjected to a column of silica gel G (200–300 mesh) using petroleum ether (PE)–EtOAc (10:1 → 6:4) and CHCl3–MeOH (10:1 → 0:100) gradient solvent system to give 10 fractions (Fr. 1–Fr. 10). The fraction Fr. 1 (1.10 g) was placed in a column of silica gel (200–300 mesh) and eluted with PE–acetone (100:1 → 6:4) gradient solvent system to produce compound 1 (3 mg). The fraction Fr. 2 (0.55 g) was placed to a column of silica gel (200–300 mesh) using PE–acetone (9:1 → 6:4) gradient solvent system to provide fractions of Fr. 2.1–Fr. 2.6. Then Fr. 2.5 (10 mg) was subjected to Sephadex LH-20 CHCl3–MeOH (1:1) and a column of silica gel (GF254) with CHCl3–MeOH (30:1) isocratic solvent system to produce compound 5 (5 mg).

3.3.1 2-(3-Methyl-2-buten-1-yl)-4-methoxyethyl-phenol (1)

Colorless amorphism, [α]_{D}^{22} = −12.9 (c = 0.70, CHCl3); UV (MeOH) λ_{max} (log ε): 277 (3.17), 239 (3.04), 209
(2.85), 201 (2.85) nm; IR (KBr) \( \nu_{\text{max}} \): 3440, 2923, 1621, 1111, 1036 cm\(^{-1}\); \(^1\)H and \(^{13}\)C NMR spectral data see Table 1; EI-MS: \( m/z \) 220 [M]\(^+\); HR-EI-MS: \( m/z \) 220.1456 [M]\(^+\) (calcd for C\(_{14}\)H\(_{20}\)O\(_2\), 220.1463).

3.3.2 3-Hydroxy-4-(hydroxymethyl)-6-(3-methylbut-2-en-1-yl)cyclohex-3-en-1-one (2)

Colorless amorphism, \( [\alpha]^{22}_{D} \) – 6.6 (c = 0.70, MeOH); UV (MeOH) \( \lambda_{\text{max}} \) (log \( \varepsilon \)): 202 (2.54) nm; \(^1\)H and \(^{13}\)C NMR spectral data see Table 1; EI-MS: \( m/z \) 210 [M]\(^+\); HR-EI-MS: \( m/z \) 210.1250 [M]\(^+\) (calcd for C\(_{12}\)H\(_{18}\)O\(_3\), 210.1256).

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