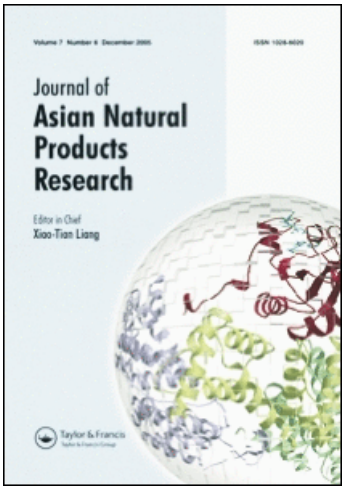

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Two new compounds from the marine *Nigrospora sphaerica*

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Two new compounds, 1-(5-oxotetrahydrofuran-2-yl)ethyl 2-phenylacetate (**1**) and 3-hydroxybutan-2-yl 2-hydroxy-3-phenylpropanoate (**2**), along with three known compounds, harzialactone A (**3**), benzeneethanol 4-hydroxy-1-acetate (**4**), and 1,4-dioxane-2,5-dione-3,6-bis(penylmethyl)-homopolymer (**5**), have been isolated from the fungus *Nigrospora sphaerica*. Their structures were determined on the basis of chemical and spectroscopic methods.

Keywords: *Nigrospora sphaerica*; fungus; 3-hydroxybutan-2-yl 2-hydroxy-3-phenylpropanoate; 1-(5-oxotetrahydrofuran-2-yl)ethyl 2-phenylacetate

1. Introduction

During early chemical investigation, the fungus *Nigrospora sphaerica* has been reported as an endophyte or a pathogen in several plants, but as a marine product it is reported for the first time. Many kinds of compounds such as fatty acids, triglycerides, mannitol, aphidicolin, pectolytic enzymes, epoxyexserohilone, nigrosporolide, and phomolactone have been isolated from it [1–9]. In this paper, we report the isolation and structural elucidation of two new and three known compounds from the marine-derived fungus *N. sphaerica* (Figure 1).

2. Results and discussion

Compound **1** was obtained as a colorless oil, with $[\alpha]_D^{20} -2.4$ ($c = 1.5$, MeOH). The molecular formula was determined to be $C_{14}H_{16}O_4$ by HR-TOF-MS at *m/z* 249.1123 $[M+H]^+$. The ^{1}H NMR spectrum showed five proton signals at δ 7.23–7.35 (5H, m). Correspondingly, the ^{13}C NMR spectrum showed six aromatic carbon signals at δ 134.3, 128.5 × 2, 129.3 × 2, and 126.9. Hence, compound **1** was considered to contain a monosubstituted benzene moiety, which was supported by the IR absorption bands (1614, 1516, and 1450 cm^{-1}) and UV absorption maxima (λ_{max} 276 and 229 nm). Also, a methylene signal was observed at δ 3.69 (2H, s) in the ^{1}H NMR spectrum, and a carbonyl signal at δ 170.6 in the ^{13}C NMR spectrum. In the HMBC spectrum, H-7 (δ 3.69, s) showed correlations with C-6 (δ 134.3), C-1, C-5 (δ 128.5), and C-8 (δ 170.6), so the presence of the phenylacetate substructure was indicated. Furthermore, the ^{1}H NMR

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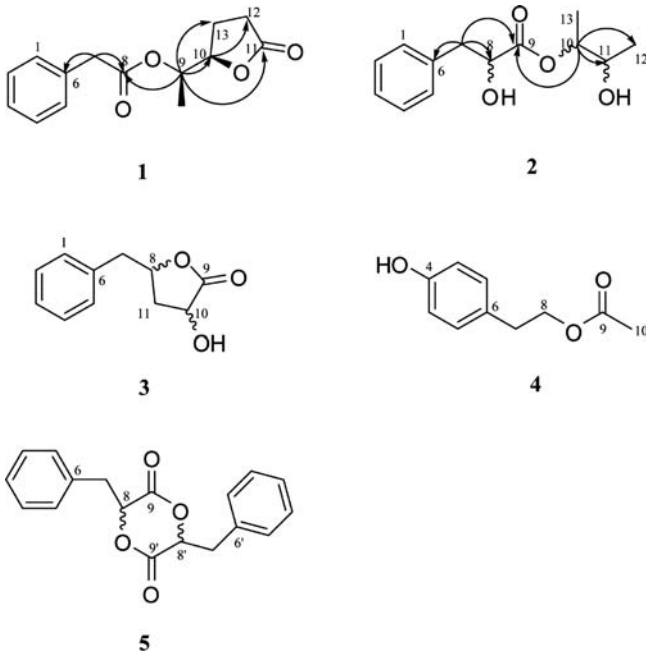


Figure 1. The structures of compounds **1**–**5**.

spectrum showed a methyl signal at δ 1.18 (3H, d, $J = 6.5$ Hz, 14-CH_3) and a methenyl at δ 4.91 (1H, m, 9-CH); in the ^{13}C NMR spectrum, there were two corresponding signals at δ 15.9 (C-14) and 71.6 (C-9), so the ethoxy substructure was confirmed. The butyrolactone substructure was deduced from the proton signals at δ 1.79 (1H, m, 13-H), 2.16 (1H, m, 13-H), 2.29 (1H, m, 12-H), 2.42 (1H, m, 12-H), and 4.55 (1H, m, 10-H) in the ^{1}H NMR spectrum and the corresponding carbon signals at δ 23.4 (C-13), 27.7 (C-12), and 80.7 (C-10), together with an ester carbonyl signal at δ 176.8 (C-11). Meanwhile, in the HMBC experiment, the correlations of H-9 (δ 4.91, m) with C-8 (δ 170.6), C-10 (δ 80.7), C-13 (δ 23.4), and C-14 (δ 15.9); H-10 (δ 4.55, m) with C-9 (δ 71.6), C-13 (δ 23.4), C-12 (δ 27.7), and C-11 (δ 176.8); H-12 (δ 2.29/2.42, m) with C-11 (δ 176.8), C-13 (δ 23.4), and C-10 (δ 80.7) showed that the ethoxy substructure could be connected with the phenylacetate and butyrolactone substructure at C-8 and C-10. By comparing the NMR spectral data and optical rotation values with those in the literature [10], the absolute configurations of C-9 and 10 may be confirmed to be 9 (*R*) and 10 (*S*). On the basis of the above evidence, compound **1** was identified as (9*R*, 10*S*)-1-(5-oxotetrahydrofuran-2-yl)ethyl 2-phenylacetate.

Compound **2** was obtained as a colorless oil, with $[\alpha]_D^{20}$ +6.6 ($c = 2.5$, MeOH). The molecular formula was determined to be $C_{13}H_{18}O_4$ by HR-FAB-MS at *m/z* 239.1279 $[M+H]^+$. The IR spectrum of **2** showed absorption bands at 1614, 1516, and 1450 cm^{-1}, indicating the presence of an aromatic ring, which was supported by the UV absorption maxima at 276 and 229 nm. The ^{1}H NMR spectrum of compound **2** showed aromatic proton signals at δ 7.17–7.29 (5H, m). Correspondingly, the ^{13}C NMR spectrum showed six aromatic carbon signals at δ 37.8, 129.5 × 2, 128.1 × 2, and 126.3. Hence, compound **2** was also considered to contain a monosubstituted benzene moiety. Moreover, the ^{1}H NMR spectrum showed one hydroxyl proton signal at δ

5.45 (1-OH, d, $J = 6.1$ Hz), one methenyl signal at δ 4.22 (1H, m), one methylene signal at δ 2.92 (2H, ddd, $J = 5.2$, 5.4, and 12.1 Hz), and the corresponding carbon signals of methenyl and methylene, together with an ester carbonyl, were shown at δ_C 71.5, 40.3, and 173.2 in the ^{13}C NMR spectrum. On the basis of the above evidence, compound **2** was considered to contain a substructure of α-hydroxy phenylpropionate, which was confirmed by the correlations of H-7 (δ 2.92) with C-1, 5 (δ 129.5), C-6 (δ 137.8), C-8 (δ 71.5), and C-9 (δ 173.2) in the HMBC experiment of **2** (Figure 2). Moreover, the ^{1}H NMR spectrum showed two methyl signals at δ 1.10 (3H, d, $J = 4.5$ Hz) and 0.89 (3H, d, $J = 4.1$ Hz), two methenyls at δ 4.66 (1H, m, H-10) and 3.55 (1H, m, H-11), and a hydroxyl signal at δ 4.72 (1-OH, d, $J = 5.2$ Hz); the HMQC experiment showed the carbon chemical shifts of two methyls at δ 15.1 and 18.3; two methenyls at δ 73.9 and 67.2, respectively. Hence, the substructure was considered to be butanediol. Furthermore, in the HMBC experiment of **2** (Figure 2), the correlations of H-10 (δ 4.66) with C-9 (δ 173.2), C-11 (δ 67.2), C-12 (δ 18.3), and C-13 (δ 15.1) were shown, and thus the substructure of butanediol was connected with the substructure of α-hydroxy phenylpropionate. On the basis of the above evidence, compound **2** was identified as 3-hydroxybutan-2-yl 2-hydroxy-3-phenylpropanoate.

Three known compounds, harzialactone A (**3**) [11], benzeneethanol 4-hydroxy-1-acetate (**4**) [12], and 1,4-dioxane-2,5-dione-3,6-bis(penylmethyl)-homopolymer (**5**) [13], were identified by comparison of their spectral data (^{1}H NMR and ^{13}C NMR) with those reported in the literature.

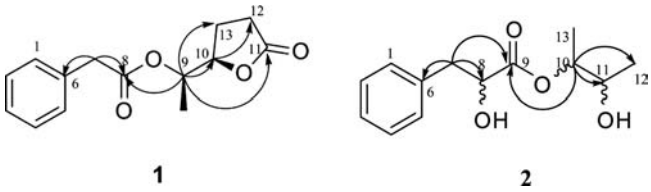
3. Experimental

3.1 General experimental procedures

Optical rotations were measured on a Perkin-Elmer 241 polarimeter. UV spectra were measured on a Shimadzu UV-1601. IR spectra were taken on a Bruker IFS-55 infrared spectrophotometer. The NMR spectral data were recorded on Bruker AV-600 (600 MHz for ^{1}H and 150 MHz for ^{13}C) in DMSO-d_6 with TMS as the internal standard. The HR-FAB-MS data were obtained on the Micross Mass Autospec-Ultima ETOF mass spectrophotometer. Chromatography was performed on silica gel (200–300 mesh; Qingdao Haiyang Chemical Factory, Qingdao, China), Sephadex LH-20 (Pharmacia, San Francisco, CA, USA), and reversed-phase HPLC (Shimadzu LC-8A vp, Kyoto, Japan).

3.2 Fungus material

The accession number (No. HTTM-Z05004) was identified by researcher Li Tian and has been deposited in the Idioplasm Bank of Pharmaceutical Microorganism, First Institute of Oceanography State Oceanic Administration. The fungus *N. sphaerica* was obtained from marine mud in the intertidal zone of Nanhai Sea, China. The hyphostroma was brownish-black.



1 **2**

Figure 2. The key HMBC correlations of compounds **1** and **2**.

3.3 Extraction and isolation

The mycelium and fermentation broth were extracted with acetone and EtOAc, respectively. Both crude extracts (32 g) were subjected to silica gel column, eluted with $CHCl_3$–CH_3OH (100:1 → 0:1), yielding 10 fractions. Fraction 5 (0.9 g) was purified by Sephadex LH-20 column chromatography (CH_3OH) and preparative HPLC (CH_3OH–H_2O 30:100, flow rate 4 ml/min, wavelength 210 nm) to obtain **1** (6 mg, retention time 32 min). Fraction 6 (0.75 g) was purified by Sephadex LH-20 column chromatography (CH_3OH) and preparative HPLC (CH_3OH–H_2O 25:100, flow rate 4 ml/min, wavelength 210 nm) to obtain **2** (5 mg, retention time 44 min), **3** (3 mg, retention time 56 min), **4** (3 mg, retention time 62 min), and **5** (5 mg, retention time 72 min).

3.3.1 1-(5-Oxotetrahydrofuran-2-yl) ethyl 2-phenylacetate (*1*)

Colorless oil, $[\alpha]_D^{20}$ −2.4 ($c = 1.5$, MeOH); UV (MeOH) λ_{max}: 276, 229 nm; IR (KBr) ν_{max} (cm^{-1}): 1614, 1516, 1450; ^1H NMR (DMSO-d_6) δ: 1.18 (3H, d, $J = 6.5$ Hz, 14-CH_3), 1.79 (1H, m, 13-H), 2.16 (1H, m, 13-H), 2.29 (1H, m, 12-H), 2.42 (1H, m, 12-H), 3.69 (2H, s, H-7), 4.55 (1H, m, 10-H), 4.91 (1H, m, 9-H), 7.23–7.35 (5H, m, H-1–5); ^{13}C NMR spectral data, see Table 1; HR-FAB-MS *m/z*: 249.1123 $[M+H]^+$ (calcd for $C_{14}H_{17}O_4$, 249.1121).

3.3.2 3-Hydroxybutan-2-yl 2-hydroxy-3-phenylpropanoate (*2*)

Colorless oil, $[\alpha]_D^{20}$ +6.6 ($c = 2.5$, MeOH); UV (MeOH) λ_{max}: 277, 226 nm; IR (KBr) ν_{max} (cm^{-1}): 1617, 1513, 1454; ^1H NMR (DMSO-d_6) δ: 0.89 (3H, d, $J = 4.1$ Hz, H-12), 1.10 (3H, d, $J = 4.5$ Hz, H-13), 2.92 (2H, ddd, $J = 5.2$, 5.4, and 12.1 Hz, H-7), 3.55 (1H, m, H-11), 4.22 (1H, m, H-8), 4.66 (1H, m, H-10), 4.72 (1H, d, $J = 5.2$ Hz, 11-OH), 5.45 (1H, d, $J = 6.1$ Hz, 8-OH), 7.18–7.29 (5H, m, H-1–5); ^{13}C NMR spectral data, see Table 1; HR-FAB-MS *m/z*: 239.1279 $[M+H]^+$ (calcd for $C_{13}H_{19}O_4$, 239.1277).

Table 1. ^{13}C NMR spectral data of compounds **1** and **2** in DMSO-d_6 (150 MHz).

Position	**1**	**2**
1/5	128.5	129.5
2/4	129.3	128.1
3	126.9	126.3
6	134.3	137.8
7	40.1	40.3
8	170.6	71.5
9	71.6	173.2
10	80.7	73.9
11	176.8	67.2
12	27.7	18.3
13	23.4	15.1
14	15.9	

Acknowledgements

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