SHORT REPORT

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Two New Compounds from the Deep-Sea-Derived Fungus *Aspergillus* sp. YPGA8

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Abstract: Chemical examination of a fraction of the EtOAc extract of a marine-derived fungus *Aspergillus* sp. YPGA8 resulted in the isolation of two new compounds, namely aspertriols A–B (**1**–**2**). Compounds **1**–**2** possess an identical 2,3,4-trihydroxybutoxy moiety, which is rarely found in natural products. Their structures were determined by extensive analyses of spectroscopic data (1D and 2D NMR, HRESIMS). The bioassay study revealed that compounds **1** and **2** were inactive toward α-glucosidase.

Keywords: *Aspergillus* sp.; aspertriols A–B; isolation; identification.

1. Plant Source

In our continuous efforts to characterize bioactive natural products from deep-sea-derived *Aspergillus* strains [1, 2], chemical examination of the fermentation broth of a deep-sea derived fungus *Aspergillus* sp. YPGA8 led to the isolation of two new compounds **1**–**2** (Figure 1).

Fungus YPGA8 was isolated from a deep-sea sediment sample that was collected at a depth of 4993 m in the Yap Trench of West Pacific Ocean. The strain was identified as *Aspergillus* sp. based on microscopic examination and by internal transcribed spacer (ITS) sequencing. The ITS sequence has been deposited in GenBank (http://www.ncbi.nlm.nih.gov) with accession number MG835905. The strain YPGA8 (MCCC 3A01017) was deposited at the Marine Culture Collection of China.

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2. Previous Studies

Marine-derived fungi have been recognized as a new source for producing secondary metabolites possessing fascinating structures and versatile biological activities. Many metabolites have been used in pharmaceuticals to exploit lead compounds or have become attractive targets for medicinal or synthetic chemists. The *Aspergillus* species, frequently isolated from marine marine organisms or sediments, have been proved to be highly prolific, previous chemical study of marine-derived *Aspergillus* strains resulted in many structurally unique and bioactive metabolites, including alkaloids [3, 4], cyclopeptides [5], butenolide derivatives [6], nortritterpenoids [7], nitrobenzoyl sesquiterpenoids [8], diphenyl ethers [9], and pentaketides [10], some exhibited pronounced biological activities, such cytotoxic, antibacterial, lipid-lowering, and α-glucosidase inhibitory effects.

3. Present Study

The fermentation was carried out in 10 Fernbach flasks (10 × 500 mL), each containing 60 g of rice. Distilled H_2O (100 mL) was added to each flask, and the contents were soaked overnight before autoclaving at 15 psi for 30 min. After cooling to room temperature, each flask was inoculated with 5.0 mL of the spore inoculum and incubated at 25 °C for 25 days. The fermented material was extracted with EtOAc for three times (3 × 5000 mL). After evaporation under vacuum, the extract (1.0 g) was chromatographed over ODS silica gel column chromatography (CC) (MeOH/H_2O: 20:80→100:0) to give ten fractions (F1 to F10). Fraction F3 was again purified on an ODS silica gel CC eluted with MeOH/H_2O (40:60→70:30) as a mobile phase to afford four fractions (F3c1−F3c4). F3c2 was subjected to RP-HPLC with a mobile phase of MeOH/H_2O (45:55, 2 mL/min) to yield **1** (2.6 mg) and **2** (1.7 mg).

*Aspertriol A (**1**):* colorless oil; $[\alpha]^{25}_{D}$ −4 (*c* 0.2, MeOH); UV (MeOH) λ_{max} 223, 294 nm; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* 287.1132 $[M + HCOO]^-$ (calcd. for $C_{13}H_{19}O_7$, 287.1131).

*Aspertriol B (**2**):* colorless oil; $[\alpha]^{25}_{D}$ −12 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 222, 295 nm ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* 265.1057 $[M + Na]^+$ (calcd. for $C_{12}H_{18}O_5Na$, 265.1052).

α-Glucosidase Assay: The α-glucosidase inhibitory effect was assessed as described in the literature [1, 11].

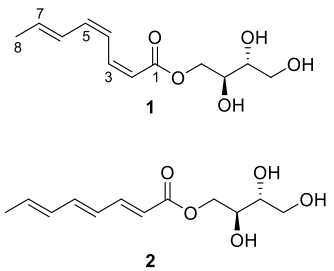

Figure 1. Structures of compounds **1** and **2** from *Aspergillus* sp. YPGA8.

Compund **1** had a molecular formula of $C_{12}H_{18}O_5$, as established by the HRESIMS and NMR data (Table 1), requiring four degrees of unsaturation. The ^{1}H NMR and HSQC spectra showed six olefinic protons (δ_H 5.70, 6.00, 6.39, 6.78, 7.08, 7.25), an olefinic methyl (δ_H 1.82), two oxygenated methylenes (δ_H 4.23, 4.01; 3.54, 3.37,), and two oxygenated methines (δ_H 3.59, 3.37), while the ^{13}C NMR resonances exhibited six olefinic carbons for three double bonds (δ_C 116.9, 121.8, 126.6, 135.8, 138.1, 139.1), one carbonyl carbon for an ester group (δ_C 166.0). All the four degrees of unsaturation

were fully covered by three double bonds and a carbonyl carbon, suggesting compound **1** was acyclic. The ^{1}H-^{1}H COSY relationship (Figure 2) from H-2 (δ_c 5.70) to H-8 (δ_H 1.82) established the spin system from C-2 (δ_c 116.9) to C-8 (δ_c 18.5) (unit A), in which three disubstituted double bonds were found to be located at C-2/C-3, C-4/C-5, C-6/C-7. Additional COSY correlations from H_2-1′ (δ_H 4.23, 4.01) to H_2-4′ (δ_H 3.37, 3.54) established a 2,3,4-trihydroxybutoxy moiety (unit B). The coupling constant between H-2′ and H-3′ (6.8 Hz) of compound **1** was identical with those of reported analogues erythrin and montagnetol [12], suggesting that the 2,3,4-trihydroxybutoxyl moiety in **1** had a 2*S**, 3 *R**-configuration. The above two frament (units A and B) were further connected by HMBC correlations from H-2 (δ_H 5.70), H-3 (δ_H 7.25), H_2-1′ (δ_H 4.23, 4.01) to the ester carbon C-1 (δ_C 166.0). The configurations of the double bonds at Δ^2, Δ^4, and Δ^6 were assigned to be *Z*, *Z*, and *E* configurations by the coupling constants $J_{2,3}$ (11.3 Hz), $J_{4,5}$ (11.5 Hz), and $J_{6,7}$ (13.9 Hz), respectively, which were also supported by the NOESY correlations of H-2 (δ_H 5.70)/H-3 (δ_H 7.25), H-4 (δ_H 7.08)/H-5 (δ_H 6.39), H-6 (δ_H 6.78)/H-8 (δ_H 1.82) (Figure 1). Thus, the structure of **1** was determined as depicted and was named aspertriol A.

Table 1. ^{1}H (400 Hz) and ^{13}C NMR (100 Hz) Data of **1** and **2** in DMSO-d_6 (δ in ppm)

No.	**1**		**2**	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1		166.0		166.4
2	5.70, d (11.3)	116.9	5.94, d (15.1)	120.0
3	7.25, dd (11.8, 11.3)	139.1	7.28, dd (15.1, 11.6)	144.8
4	7.08, dd (11.8, 11.5)	121.8	6.34, dd (14.4, 11.6)	127.6
5	6.39, dd (11.5, 11.1)	138.1	6.70, dd (14.4,11.4)	141.3
6	6.78, dd (13.9, 11.1)	126.6	6.21, dd (14.6, 11.4)	131.3
7	6.00, dq (13.9, 6.8)	135.8	6.01, dd (14.6, 7.0)	135.2
8	1.82, d (6.8)	18.5	1.80, d (7.0)	18.3
1′	4.23, dd (11.4, 2.4) 4.01, dd (11.3, 7.1)	66.1	4.24, dd (11.0, 2.0) 4.01, dd (10.9, 7.2)	66.2
2′	3.59, ddd (7.1, 6.9, 2.4)	69.4	3.58, ddd (7.2, 6.9, 2.4)	69.5
3′	3.37, m	72.4	3.38, m	72.3
4′	3.54, m 3.37, m	63.1	3.55, m 3.38, m	63.1

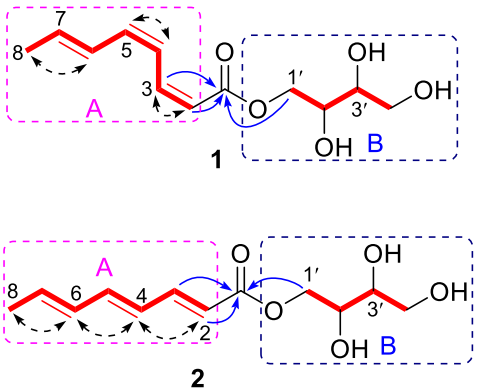

Figure 2. ^{1}H-^{1}H COSY (▬), HMBC (⤻), and NOE (↖-↗) correlations of **1** and **2**.

Compound **2**, a colorless oil, had a molecular formula of $C_{12}H_{18}O_5$ as determined by the HRESIMS and NMR data. The ^{1}H NMR, ^{13}C NMR, and HSQC spectra exhibited signals for three disubstituted double bonds (δ_H 5.94, 6.01, 6.21, 6.34, 6.70, 7.28; δ_C 120.0, 127.6, 131.3, 135.2, 141.3, 144.8), an olefinic methyl (δ_H 1.80; δ_C 18.3), an ester carbon (δ_C 166.4), two oxygenated methylenes (δ_H 3.38, 3.55, 4.01, 4.24; δ_C 66.2, 63.1), and two oxygenated methines (δ_H 3.58, 3.38; δ_C 69.5, 72.3). The aforementioned information was almost identical with that of **1**. The different chemical shifts and coupling constants of the double bonds suggested that **2** was an olefinic isomer of **1**, the structure of **2** was further established by detailed analyses of the 2D NMR data (Figure 1). The coupling constants $J_{2,3}$ (15.1), $J_{4,5}$ (14.4), and $J_{6,7}$ (14.6) defined the double bonds Δ^2, Δ^4, and Δ^6 all to be *E* configurations, which were also supported by the NOESY correlations of H-4 (δ_H 6.34)/H-2 (δ_H 5.94), H-6 (δ_H 6.21)/H-4, and H_3-8 (δ_H 1.80)/H-6 (Figure 2). The NMR data of C-1′ to C-4′ and the coupling constant between 2′ and H-3′ (6.9 Hz) implied that the 2,3,4-trihydroxybutoxy moiety in **2** was the same as that of **1**. Thus, the structure of compound **2** was determined as depicted and was given the trivial name aspertriol B.

Compounds **1** and **2** were screened for their inhibitory activities against α-glucosidase. As results, compounds **1** and **2** exhibited inhibition rate less than 30% at the concentration of 200 μM, while the positive control acarbose exhibited an IC_{50} values of 190.2 μM.

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Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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