# Aspergillusol A, an α-Glucosidase Inhibitor from the Marine-Derived Fungus *Aspergillus aculeatus*

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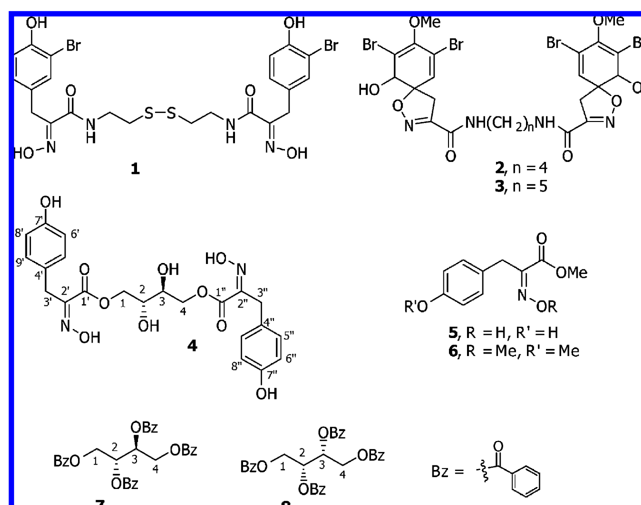
A new tyrosine-derived metabolite, aspergillusol A (**4**), was isolated on a gram scale, together with a methyl ester of 4-hydroxyphenylpyruvic acid oxime (**5**) and secalonic acid A, from the marine-derived fungus *Aspergillus aculeatus* CRI323-04. The tetraol in **4** was identified as erythritol by comparison of the $^1$H NMR spectrum of its benzoylated derivative with those of benzoylated erythritol (**7**) and D-threitol (**8**), as well as by cellulose-based chiral HPLC analysis. Aspergillusol A (**4**) selectively inhibited α-glucosidase from the yeast *Saccharomyces cerevisiae*, but it was inactive toward the α-glucosidase from the bacterium *Bacillus stearothermophilus*.

Brominated tyrosine-derived metabolites, psammaplin A (**1**), aerothionin (**2**), and homoaerothionin (**3**), are isolated from marine sponges.[1−4] These and related tyrosine-derived metabolites often contain hydroxyphenylpyruvic acid oxime in their molecules, and they are found in various marine sponges including *Aplysinella rhax*, *Psammaplinaplysilla* sponges, *Poecillastra* sp., *Jaspis* sp., *Verongia aerophoba*, *Hymeniacidon sanguinea*, *Ianthella basta*, and *Suberea clavata*.[1−10] In 1975, Cimino and colleagues reported the occurrence of 4-hydroxyphenylpyruvic acid oxime in marine sponges and proposed that it was the biogenetic precursor of aerothionin (**2**), homoaerothionin (**3**), and aeroplysinin-1.[4] We have recently isolated the marine-derived fungus *Aspergillus aculeatus* CRI323-04 from a marine sponge, *Xestospongia testudinaria*. Surprisingly, chemical exploration of the fungus *A. aculeatus* CRI323-04 led to the isolation of tyrosine-derived metabolites **4** and **5**. Aspergillusol A (**4**) has structural similarities to psammaplin A (**1**), a metabolite of marine sponges.[1] α-Glucosidase and aromatase inhibitory activities as well as cytotoxicity of the isolated compounds **4** and **5** are also presented in this paper.




Separation of a cell extract by Sephadex LH-20 column chromatography and $C_{18}$ reversed-phase HPLC yielded aspergillusol A (**4**), a methyl ester of 4-hydroxyphenylpyruvic acid oxime (**5**), and secalonic acid A.[11] Although **5** is synthetically known,[12] its NMR data have never been well documented; the assignments of $^1$H and $^{13}$C resonances in **5** are listed in the Experimental Section. Compound **5** was possibly an artifact derived from the methanolysis of aspergillusol A (**4**) during extraction and separation.

A 10 L culture of *A. aculeatus* CRI323-04 provided greater than one gram (1262 mg) of aspergillusol A (**4**), which is a relatively high yield. Compound **4** had, as revealed by the ESITOF-MS, a molecular formula of $C_{22}H_{24}N_2O_{10}$. However, the $^{13}$C NMR spectrum of **4** showed only 11 carbon signals; therefore **4** had symmetry based on its molecular formula. The $^1$H NMR of **4** showed signals of a half-molecule including those of three exchangeable protons ($\delta_H$ 12.38, 9.22, and 5.16), two pairs of protons on a 1,4-disubstituted benzene ($\delta_H$ 7.00 and 6.63), two methylene protons ($\delta_H$ 4.29 and 4.10; and 3.70), and one oxygenated sp$^3$ methine ($\delta_H$ 3.64). DEPT and HMQC spectra revealed that a half-molecule of **4** contained two methylenes, five methines, and four nonprotoned carbons. The $^{13}$C NMR spectrum implied that C-1/C-4 and C-2/C-3 are an oxygenated sp$^3$ methylene ($\delta_C$ 67.1) and an oxygenated methine ($\delta_C$ 69.4), respectively. A downfield shift ($\delta_H$ 4.29 and 4.10) of $H_2$-1/$H_2$-4 implied that this methylene was part of either an ester or an ether linkage. The $^1$H−$^1$H COSY spectrum of **4** demonstrated the connectivity of $H_2$-1/H-2/2-OH, establishing the fragment [−O−$CH_2$−CH(OH)−]. Because the molecule of **4** had symmetry, it possessed the fragment of a tetraol moiety, [−O−$CH_2$−CH(OH)−CH(OH)−$CH_2$−O−]. The HMBC spectrum of aspergillusol A (**4**) provided evidence of a 4-hydroxyphenylpyruvic acid oxime unit as a partial structure, showing correlations (of a half-molecule) from ═N-O*H* to C-2′; H-3′ to C-1′, C-2′, C-4′, and C-5′ (or C-9′); H-5′ (or H-9′) to C-3′ and C-7′; H-6′ (or H-8′) to C-4′ and C-7′; and Ar-O*H* to C-7′ and C-6′ (or C-8′). In the NOESY spectrum of aspergillusol A (**4**), there were correlations between H-5′/H-9′ (or H-5″/H-9″) and $H_2$-3′ (or $H_2$-3″) and between an aromatic hydroxy group (Ar-O*H*) and H-6′/H-8′ (or H-6″/H-8″), suggesting the proximity among these protons. However, there was no NOESY correlation observed between ═N-O*H* and $H_2$-3′ (or $H_2$-3″), implying the presence of a (*Z*)-oxime in **4**. It should be noted that, as in the case of an oxime with an amide

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linkage, e.g., psammaplin A (**1**), the benzylic C-3′ (or C-3″) of a (*E*)-oxime resonates upfield ($\delta_C$ 26−27), while that of a (*Z*)-oxime exhibits downfield shifts ($\delta_C$ 35).[1] Previous studies employed the chemical shifts of the benzylic carbon to address the oxime geometry.[1,2,5,7−10] However, such carbon chemical shifts may not be applicable for the oxime with an ester linkage as present in aspergillusol A (**4**). The intermediate resonance ($\delta_C$ 29.6) observed for the benzylic C-3′ (or C-3″) in **4** is inconclusive with regard to the oxime geometry. Further experiments were carried out in order to secure the oxime geometry in **4**. Aspergillusol A (**4**) was subjected to methylation under basic conditions (MeI, $K_2CO_3$, and DMF), yielding the tri-*O*-methyl product **6**. The NOESY spectrum of **6** showed a cross-peak between the =N-OMe and COOMe protons, indicating the proximity of these *O*-methyl groups and, thus, the presence of a (*Z*)-oxime in **4**. The linkage between the tetraol moiety and the 4-hydroxyphenylpyruvic acid oxime unit was evident from the HMBC correlation from H-1/H-4 to C-1′/C-1″. On the basis of these spectroscopic data, a gross structure of aspergillusol A (**4**) was successfully established as shown. However, the two stereogenic centers of the tetraol unit in **4** have to be clarified. There are two natural tetraols, known as sugar alcohols, threitol ((2*R*,3*R*)-butane-1,2,3,4-tetrol) and erythritol ((2*R*,3*S*)-butane-1,2,3,4-tetraol), and the latter is widely found in microorganisms. While threitol is optically active, erythritol is optically inactive because it has a plane of symmetry (or *meso* forms).[13] The specific rotation for aspergillusol A (**4**) measured in MeOH was +3.1 (*c* 1.06), and the tetraol product obtained by enzymatic hydrolysis with lipase also had a small positive specific rotation ($[\alpha]^{27}_D$ +3.7 (*c* 2.15, MeOH)), which possibly suggested threitol as the tetraol core of **4**. However, the specific rotations for D-threitol previously reported were +4.5 ($H_2O$)[14] and −14.0 (EtOH),[15] indicating that the sign and magnitude of rotation can vary in different solvents. In order to obtain additional information regarding the nature of the tetraol, $^1$H and $^{13}$C NMR spectra of the tetraol were compared with those of authentic erythritol and D-threitol. Unfortunately, these comparisons did not unambiguously assign the identity of the tetraol. Subsequently, erythritol and D-threitol were benzoylated, and the $^1$H NMR spectrum of benzoylated erythritol (**7**) could be clearly distinguished from that of a benzoylated D-threitol (**8**) (Supporting Information). Accordingly, benzoylation of the tetraol in aspergillusol A (**4**) was carried out to yield the corresponding benzoylated product, whose $^1$H NMR spectrum was identical to that of **7**, indicating the presence of erythritol in **4**. Furthermore, the benzoylated products **7** and **8** behaved differently on a cellulose-based chiral HPLC column; compounds **7** and **8** had respective retention times ($t_R$) of 10.57 and 3.83 min. The benzoylated tetraol showed a $t_R$ similar to that of **7** (10.60 min), thus confirming the presence of erythritol in **4**. On the basis of these data, the stereogenic centers in aspergillusol A (**4**) were conclusively assigned. With the tetraol linker firmly established as erythritol, it seems likely that the small optical rotations measured for **4** and the tetraol were due to minor optically active impurities.

Aspergillusol A (**4**) inhibited α-glucosidase with $IC_{50}$ values of 465 ± 2 ($n$ = 3) and 1060 ± 20 ($n$ = 3) μM toward α-glucosidases from *Saccharomyces cerevisiae* and *Bacillus stearothermophilus*, respectively. The reference drug, 1-deoxynojirimycin, inhibited α-glucosidases from *S. cerevisiae* and *B. stearothermophilus* with respective $IC_{50}$ values of 222 ± 8 and 0.45 ± 0.01 μM. Therefore, aspergillusol A (**4**) was ca. 2 times less active than the standard drug toward α-glucosidase from the yeast *S. cerevisiae*; however, it was 2300 times less active for α-glucosidase from the bacterium *B. stearothermophilus*. These results indicated that the yeast α-glucosidase was more susceptible to aspergillusol A (**4**) than the bacterial α-glucosidase. Compound **4** was inactive toward aromatase enzyme ($IC_{50}$ > 100 μM). Aspergillusol A (**4**) was inactive (at 105 μM) against the HepG2 (human hepatocellular liver carcinoma) cell line, while it showed weak cytotoxic activity toward HuCCA-1 (human lung cholangiocarcinoma), A549 (human lung carcinoma), and MOLT-3 (acute lymphoblastic leukemia) cell lines with respective the $IC_{50}$ values of 50, 74, and 19 μM. Interestingly, compound **8** selectively inhibited the growth of HepG2 and HL-60 (human promyelocytic leukemia) cancer cells with respective $IC_{50}$ values of 29 and 44 μM, while it was inactive (at 240 μM) against HuCCA-1 and A549 cancer cells.

The fungus *A. aculeatus* CRI323-04 produces large quantities of aspergillusol A (**4**), whose structure is similar to that of a brominated tyrosine-derived metabolite, psammaplin A (**1**), a metabolite of marine sponges. Brominated tyrosine-derived metabolites are found in various classes of marine sponges,[1−10] indicating that there is no chemotaxonomic significance of these compounds in marine sponges. As particular secondary metabolites in marine sponges originate from symbiotic cyanobacteria, bacteria, and dinoflagellates,[16] it is possible that marine sponges could utilize a microbial tyrosine-derived metabolite similar to **4** for the production of toxic brominated tyrosine-derived metabolites that may act as chemical defenses in the sponge hosts. It should be noted that the oxime unit in sponge metabolites has an *E*-geometry, while that in the fungal metabolite (**4**) possesses a *Z*-geometry. Because marine sponges and the fungus produce different geometries of the oxime unit, their tyrosine-derived metabolites may not be biogenetically related. In addition, there have been no reports on the presence of brominated tyrosine-derived metabolites in the sponge host *Xestospongia testudinaria*, from which the marine-derived funungus was isolated. However, despite the inconsistencies in the oxime geometries and the isolation of the fungus from a nonproducing host sponge, the isolation of **4** does demonstrate that fungi have the ability to synthesize tyrosine-derived oximes and should be considered as potential sources of precursors for the brominated tyrosine-derived sponge metabolites. A few natural tyrosine derivatives have previously been isolated from fungi including tyrosol carbamate from an *Arthrinium* sp. isolated from a deep-water sediment,[17] compound OF4949 from *Penicillium rugulosum*,[18] and the gymnastatins from a sponge-derived fungus *Gymnasella dankaliensis*.[19] However, these metabolites do not contain an oxime unit in their molecules, and the present work is the first report on a fungal tyrosine derivative with an oxime moiety.

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured with the sodium D line (590 nm) on a JASCO DIP-370 digital polarimeter. UV spectra were recorded on a Shimadzu UV−vis spectrometer (UV-1700 Pharma Spec). FTIR were obtained using a universal attenuated total reflectance (UATR) attached on a Perkin-Elmer Spectrum One spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker AM 400 instrument (operating at 400 MHz for $^1$H and 100 MHz for $^{13}$C). ESITOF-MS were determined using a Bruker MicroTOF$_{LC}$ spectrometer.

**Fungal Material and Identification.** *Aspergillus aculeatus* CRI323-04 was isolated from the marine sponge *Xestospongia testudinaria* (specimen no. CRI323), which was collected in November 2006, by scuba diving at 35−40 feet, from Ton Sai Bay, Phi Phi Islands, Krabi Province. The marine-derived fungus isolate CRI323-04 was identified on the basis of both morphology on Czapek solution agar (CzA) and analysis of the DNA sequences of the ITS1-5.8S-ITS2 rRNA gene region and the calmodulin gene (Supporting Information). The ITS1-5.8S-ITS2 and partial *cmd*A gene DNA sequences of the CRI323-04 fungus have been submitted to GenBank with the accession numbers FJ525443 and FJ525444, respectively. A culture of the CRI323-04 strain has been deposited at Chulabhorn Research Institute (CRI) and MIM Laboratory, Department of Microbiology, Mahidol University, Thailand.

**Extraction and Isolation.** The fungus CRI323-04 was cultured in potato dextrose broth (PDB) using seawater (Andaman Sea, Krabi Province) instead of distilled water. The fungus was inoculated into 1 L Erlenmeyer flasks, each containing 250 mL of PDB, and further incubated under static condition for 30 days. Fungal cells were separated from broth (10 L) by filtration. Fungal cells were macerated sequentially in MeOH and $CH_2Cl_2$, each for two days. The $CH_2Cl_2$ extract contained,

as revealed by a $^1$H NMR spectrum, triglycerides and fatty acids, while the MeOH extract was partitioned with $H_2O$ and hexane in order to remove triglycerides. A $H_2O$ layer was then extracted with EtOAc (10 times) to yield a crude extract (3.1 g), which was chromatographed on Sephadex LH-20, eluted with MeOH, and nine fractions (F1−F9) were obtained. Fraction F-6 contained aspergillusol A (**4**; 523 mg). Fraction 5 (1.37 g) was washed with a mixture of MeOH/$H_2O$ (40:60); the residue obtained was aspergillusol A (**4**; 739 mg). Therefore, the total amount of aspergillusol A (**4**) was 1262 mg. Fraction 4 was separated by preparative HPLC, eluting with a mixture of MeOH/$H_2O$ (30:70), to yield 73.6 mg of a methyl ester of 4-hydroxyphenylpyruvic acid oxime (**5**). The residue that did not dissolve in the HPLC solvent system was recrystallized from $CH_2Cl_2$ to afford secalonic acid A (1.9 mg).[11]

**Aspergillusol A (4):** yellow, amorphous solid; UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 221 (2.7) and 278 (1.9) nm; FTIR (UATR) $\nu_{max}$ 3404, 3185, 1708, 1612, 1513, 1414, 1307, 1257, 1201, 1096, 995, 800 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 12.38 (1H, s, N-O*H*), 9.22 (1H, s, Ar-O*H*), 7.00 (2H, d, $J$ = 8.5 Hz, H-5′/H-9′ or H-5″/H-9″), 6.63 (2H, d, $J$ = 8.5 Hz, H-6′/H-8′ or H-6″/H-8″), 5.16 (1H, br d, $J$ = 5.1 Hz, 2-OH/3-OH), 4.29 (1H, br d, $J$ = 10.7 Hz, H-1a/H-4a), 4.10 (1H, dd, $J$ = 11.2, 5.3 Hz, H-1b/H-4b), 3.70 (2H, s, $H_2$-3′/$H_2$-3″), 3.64 (1H, m, H-2/H-3); $^{13}$C NMR (DMSO-$d_6$,100 MHz) $\delta$ 164.2 (qC, C-1′/C-1″), 156.1 (qC, C-7′/C-7″), 150.5 (qC, C-2′/C-2″), 130.1 (CH, C-5′/C-9′ or C-5″/C-9″), 126.8 (qC, C-4′/C-4″), 115.5 (CH, C-6′/C-8′ or C-6″/C-8″), 69.4 (CH, C-2/C-3), 67.1 ($CH_2$, C-1/C-4), and 29.6 ($CH_2$, C-3′/C-3″); ESITOF-MS $m/z$ 477.1513 $[M + H]^+$ (calcd for $C_{22}H_{25}N_2O_{10}$, 477.1509).

**Methyl Ester of 4-Hydroxyphenylpyruvic Acid Oxime (5):** $^1$H NMR (acetone-$d_6$, 400 MHz) $\delta$ 7.10 (2H, d, $J$ = 8.5 Hz, H-5/H-9), 6.73 (2H, d, $J$ = 8.5 Hz, H-6/H-8), 3.82 (2H, s, $H_2$-3), 3.72 (3H, s, OMe); $^{13}$C NMR (acetone-$d_6$,100 MHz) $\delta$ 164.3 (qC, C-1), 155.8 (qC, C-7), 150.8 (qC, C-2), 129.9 (CH, C-5/C-9), 127.0 (qC, C-4), 115.0 (CH, C-6/C-8), 51.4 ($OCH_3$), and 29.1 ($CH_2$, C-3); ESITOF-MS $m/z$ 210.0753 $[M + H]^+$ (calcd for $C_{10}H_{12}NO_4$, 210.0766).

**Hydrolysis of Aspergillusol A (4) by Lipase.** A reaction mixture containing compound **4** (102 mg), 2.15 mL of acetone, 2.15 mL of 73.5 mM $KH_2PO_4$/$K_2HPO_4$ buffer (pH 6.8), and 6.1 mg of lipase was stirred at 36 °C for 21 h. The mixture was evaporated to dryness, and the dried material was extracted several times with EtOAc in order to remove nonpolar compounds. The resulting residue was further extracted twice with MeOH/$H_2O$ (3:1) to yield 27.4 mg of erythritol.

**Preparation of Tri-*O*-methyl Derivative 6.** A reaction mixture containing aspergillusol A (**1**) (70 mg), $K_2CO_3$ (101 mg), DMF (1 mL), and MeI (1.5 mL) was left stirring overnight at room temperature. After removing DMF and MeI under vacuum, the reaction mixture was washed several times with a mixture of MeOH/$H_2O$ (40:60). The insoluble oily residue (8.1 mg) was the tri-*O*-methyl product **6**: $^1$H NMR ($CDCl_3$, 600 MHz) $\delta_H$ 7.18 (2H, d, $J$ = 8.66 Hz, H-5/H-9), 6.81 (2H, d, $J$ = 8.66 Hz, H-6/H-8), 4.10 (3H, s, N-$OCH_3$), 3.87 (2H, s, H-3), 3.83 (3H, s, $COOCH_3$), 3.78 (3H, s, 7-$OCH_3$); $^{13}$C NMR ($CDCl_3$, 150 MHz) $\delta_C$ 163.87 (−*C*OO, C-1), 158.34 (qC, C-7), 150.83 (*C*=N, C-2), 130.07 (CH, C-5/C-9), 127.81 (qC, C-4), 113.93 (CH, C-6/C-8), 63.32 ($CH_3$, N-O*C*$H_3$), 55.22 ($CH_3$, 7-O*C*$H_3$), 52.73 ($CH_3$, COO*C*$H_3$), 30.33 ($CH_2$, C-3); ESITOF-MS $m/z$ 238.1082 $[M + H]^+$ (calcd for $C_{12}H_{16}NO_4$, 238.1079).

**Benzoylation of *meso*-Erythritol and D-Threitol.** A reaction mixture consisting of the tetraol, pyridine (0.2 mL), and benzoyl chloride (0.4 mL) was stirred overnight at room temperature. After removing pyridine under vacuum, the reaction mixture was dissolved in EtOAc and extracted sequentially with 0.5 M HCl (3 times) and saturated $Na_2CO_3$ (3 times) and finally washed with $H_2O$ (3 times) to give the benzoylated tetraol. With this procedure, *meso*-erythritol (52.1 mg) and D-threitol (50.6 mg) gave the benzoylated products **7** and **8** with respective yields of 129.9 and 132.0 mg. The tetraol (21.5 mg) obtained from lipase hydrolysis of aspergillusol A (**4**) was benzoylated in the same manner as that of authentic compounds to afford 6.9 mg of the product, whose $^1$H NMR spectrum was identical to that of **7**. Benzoylated *meso*-erythritol (**7**): white powder; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta_H$ 8.04 (4H, dd, $J$ = 8.49 and 1.34 Hz), 8.01 (4H, dd, $J$ = 8.48 and 1.33 Hz), 7.57 (2H, t, $J$ = 7.44 Hz), 7.55 (2H, t, $J$ = 7.44 Hz), 7.44 (4H, t, $J$ = 8.27 Hz), 7.40 (4H, t, $J$ = 7.84 Hz); 5.97 (2H, m); 4.89 (2H, dd, $J$ = 12.23 and 2.74 Hz); 4.65 (2H, dd, $J$ = 12.19 and 5.42 Hz); ESITOF-MS $m/z$ 561.1511 $[M + Na]^+$ (calcd for $C_{32}H_{26}NaO_8$, 561.1525). Benzoylated D-threitol (**8**): white solid; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta_H$ 8.06 (4H, dd, $J$ = 8.46 and 1.33 Hz), 7.99 (4H, dd, $J$ = 8.41 and 1.31 Hz), 7.56 (2H, t, $J$ = 7.54 Hz), 7.54 (2H, t, $J$ = 7.54 Hz), 7.43 (4H, t, $J$ = 7.90 Hz), 7.40 (4H, t, $J$ = 7.45 Hz); 6.00 (2H, m); 4.78 (2H, dd, $J$ = 12.02 and 3.98 Hz); 4.69 (2H, dd, $J$ = 12.00 and 5.89 Hz); ESITOF-MS $m/z$ 561.1519 $[M + Na]^+$ (calcd for $C_{32}H_{26}NaO_8$, 561.1525).

**Analysis of Benzoylated Tetraols by Chiral HPLC.** Benzoylated tetraols were analyzed by HPLC (SpectraSYSTEM P4000) equipped with a UV detector (SpectraSYSTEM UV1000). The chiral column was Lux Cellulose-1, 5 $\mu$m, 250 × 4.60 mm (solvent system 2-propanol/hexane (20:80); flow rate 1 mL/min). The benzoylated tetraol in **4** showed $t_R$ = 10.60 min, which was similar to that of a benzoylated erythritol ($t_R$ = 10.57 min), but significantly different from that of a benzoylated threitol ($t_R$ = 3.83 min).

**Inhibition of Aromatase (CYP19).** Inhibition of aromatase was assayed following the method described by Stresser et al.[20] Ketoconazole was a positive control exhibiting an $IC_{50}$ value of 2.4 $\mu$M.

**Inhibition of α-Glucosidase.** An assay for α-glucosidase (Sigma, G5003 from *Saccharomyces cerevisiae*; Sigma, G3651 from *Bacillus stearothermophilus*) was performed in triplicate ($n$ = 3) using a colorimetric method described by Wu et al.[21] The substrate was *p*-nitrophenyl α-D-glucoside (1.0 mM final concentration). α-Glucosidase from the yeast *S. cerevisiae* and the bacterial *B. stearothermophilus* was prepared at 0.1 and 0.3 U/mL (final concentration), respectively. In our assay system, a standard drug, 1-deoxynojirimycin, showed $IC_{50}$ values of 222 ± 8 and 0.45 ± 0.01 $\mu$M toward α-glucosidases from *S. cerevisiae* and *B. stearothermophilus*, respectively.

**Cytotoxicity Assay.** Cytotoxic activity for HepG2, HuCCA-1, and A549 cancer cell lines was evaluated with the MTT assay,[22] while that for MOLT-3 and HL-60 cell lines was assessed using the XTT assay.[23] Doxorubicin was used as the reference drug, and respective $IC_{50}$ values of 0.37, 0.64, 0.40, and 0.04 $\mu$M were observed for HepG2, HuCCA-1, A549, and MOLT-3 cell lines.

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**Supporting Information Available:** $^1$H, $^{13}$C, HMQC, HMBC, and NOESY spectra of **4**; $^1$H and $^{13}$C NMR spectra of **6**; $^1$H NMR spectra of **7** and **8**; and details of fungal identification. This material is available free of charge via the Internet at http://pubs.acs.org.

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