Chaetopyranin, a Benzaldehyde Derivative, and Other Related Metabolites from *Chaetomium globosum*, an Endophytic Fungus Derived from the Marine Red Alga *Polysiphonia urceolata*

Song Wang,[†,‡] Xiao-Ming Li,[†] Franka Teuscher,[§] Dong-Li Li,[†,‡] Arnulf Diesel,[§] Rainer Ebel,[§] Peter Proksch,[§] and Bin-Gui Wang*[,†]

Key Laboratory of Experimental Marine Biology, Institute of Oceanology, Chinese Academy of Sciences, Qingdao 266071, People's Republic of China, Graduate School of Chinese Academy of Sciences, Beijing 100039, People's Republic of China, and Institut für Pharmazeutische Biologie und Biotechnologie, Heinrich-Heine-Universität Düsseldorf, Universitätsstrasse 1, Geb. 26.23, 40225 Düsseldorf, Germany

Received June 1, 2006

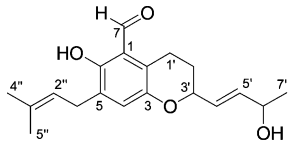
Cultivation of the endophytic fungus *Chaetomium globosum*, which was isolated from the inner tissue of the marine red alga *Polysiphonia urceolata*, resulted in the isolation of chaetopyranin (**1**), a new benzaldehyde secondary metabolite. Ten known compounds were also isolated, including two benzaldehyde congeners, 2-(2′,3-epoxy-1′,3′-heptadienyl)-6-hydroxy-5-(3-methyl-2-butenyl)benzaldehyde (**2**) and isotetrahydroauroglaucin (**3**), two anthraquinone derivatives, erythroglaucin (**4**) and parietin (**5**), five asperentin derivatives including asperentin (**6**, also known as cladosporin), 5′-hydroxy-asperentin-8-methylether (**7**), asperentin-8-methyl ether (**8**), 4′-hydroxyasperentin (**9**), and 5′-hydroxyasperentin (**10**), and the prenylated diketopiperazine congener neoechinulin A (**11**). The structures of these compounds were determined on the basis of their spectroscopic data analysis (^{1}H, ^{13}C, ^{1}H−^{1}H COSY, HMQC, and HMBC NMR, as well as low- and high-resolution mass experiments). To our knowledge, compound **1** represents the first example of a 2*H*-benzopyran derivative of marine algal-derived fungi as well as of the fungal genus *Chaetomium*. Each isolate was tested for its DPPH (1,1-diphenyl-2-picrylhydrazyl) radical-scavenging property. Compounds **1**−**4** were found to have moderate activity. Chaetopyranin (**1**) also exhibited moderate to weak cytotoxic activity toward several tumor cell lines.

Marine microorganisms have recently gained prominence as an important source of biologically active secondary metabolites.[1−4] Among marine microorganisms, marine fungi represent an important resource for the discovery of structurally unique marine natural products with anticipated biomedical potential.[5] Among marine fungi, those living associated with marine algae are a particularly promising source of novel natural products due to the unique ecological niche in which they exist. Recently, numerous biologically active metabolites have been discovered and reported from marine algal-derived endophytic fungi.[6−11]

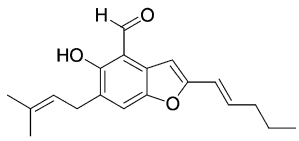
As part of our studies on secondary metabolites from marine organisms from the Chinese sea coast, we have investigated the chemical constituents obtained from fermentation of the marine endophytic fungus *Chaetomium globosum*, which was isolated from the inner tissue of the marine red alga *Polysihonia urceolata* collected from the Qingdao coastline. This paper describes the isolation and structure elucidation of the new benzaldehyde derivative chaetopyranin (**1**). In addition, 10 known compounds (**2**−**11**) were also isolated and identified. The complete ^{1}H and ^{13}C NMR spectral data for **2** are reported here for the first time.

The fungus *C. globosum* was grown in liquid malt-extract medium. The combined extracts from the culture broth and from the mycelium were fractionated by column chromatography on silica gel and Sephadex LH-20, respectively, as well as by preparative TLC, to afford 11 metabolites.

Compound **1**, obtained as a yellowish powder, displayed a molecular ion peak at *m*/*z* 316 $[M]^+$ in the EIMS, which in conjunction with NMR data (Table 1) suggested the molecular formula $C_{19}H_{24}O_4$, thus implying eight degrees of unsaturation. The molecular formula was subsequently confirmed by the analysis of high-resolution ESIMS (*m*/*z* 339.1580 $[M + Na]^+$, calcd for $C_{19}H_{24}O_4Na$, 339.1572). The IR spectrum displayed strong absorptions for hydroxyl groups (3374 and 3261 cm^{-1}), a carbonyl carbon



1



2

(1725 cm^{-1}), a double bond (1643 cm^{-1}), and an aromatic ring (1615 and 1592 cm^{-1}). In the ^{1}H NMR spectrum, the well-dispersed signals were displayed over a broad range, thereby disclosing the presence of a phenolic hydroxyl proton at δ_H 12.07 (OH-6) and an aldehyde proton at δ_H 10.29 (H-7) in the lower field. Furthermore, an aromatic singlet at δ_H 6.92 (H-4), a *trans*-fused double bond as indicated by a pair of double doublets at δ_H 5.81 (J = 15.6, 5.3 Hz, H-4′) and 5.86 (J = 15.6, 5.6 Hz, H-5′), and a further olefinic triplet at δ_H 5.31 (H-2″) were present in the aromatic and olefinic regions. In addition, the presence of two oxygenated proton signals at δ_H 4.49 (H-3′) and 4.29 (H-6′), two methyl singlets at δ_H 1.73 (H-4″) and 1.70 (H-5″), and an aliphatic methyl doublet at δ_H 1.21 (H-7′) were also present in the ^{1}H NMR spectrum (Table 1). The ^{13}C NMR spectrum exhibited 19 carbon signals attributable to three methyls, three methylenes, seven methines, and six quaternary carbon atoms according to the DEPT spectrum. The ^{1}H, ^{13}C, and DEPT NMR spectra enabled all but two hydrogen atoms of **1** to be accounted for; thus, it was evident that the remaining doublet observed at δ_H 3.81 (OH-6′) besides the signal already mentioned above (δ_H 12.07, OH-6) were both due to OH groups.

Detailed analysis of the one- and two-dimensional NMR spectral data resulted in the elucidation of three substructures for chaetopyranin (**1**). In the ^{1}H−^{1}H COSY, one of the olefinic protons (H-4′) correlated to an oxygenated methine proton resonating at δ_H 4.49 (H-3′). The latter was revealed by COSY to be connected to a four-proton coupling system of two methylene groups (CH_2-2′ at

* To whom correspondence should be addressed. Tel: 0086-532-82898553. Fax: 0086-532-82880645. E-mail: wangbg@ms.qdio.ac.cn.
† Institute of Oceanology.
‡ Graduate School of Chinese Academy of Sciences.
§ Heinrich-Heine-Universität Düsseldorf.

10.1021/np060248n CCC: $33.50
Published on Web 10/18/2006

Table 1. NMR Spectral Data of Compounds **1** and **2**

	1[a]			**2**[b]		
	δ_H (*J* in Hz)	δ_C	HMBC	δ_H (*J* in Hz)	δ_C	HMBC
1		117.7 C			110.8 C	
2		121.5 C			128.7 C	
3		147.7 C			148.5 C	
4	6.92 s	127.7 CH	1″, 2, 3, 6	7.46 s	119.4 CH	1″, 2, 3, 6
5		130.1 C			126.4 C	
6		156.5 C			157.6 C	
7	10.29 s	196.7 CH	1, 5, 6	10.24 s	193.0 CH	1, 5, 6
1′	3.24, 3.16 m	20.7 CH_2	2, 2′, 3, 3′	6.73 br s	98.9 CH	2, 2′, 3, 3′
2′	2.13, 1.81 m	28.2 CH_2			157.6 C	
3′	4.49 br t (7.2)	75.8 CH		6.31 dd (17.2, 1.4)	118.4 CH	2′, 5′
4′	5.81 dd (15.6, 5.3)	128.5 CH	2′, 5′	6.51 m	135.4 CH	2′, 5,′
5′	5.86 dd (15.6, 5.6)	138.0 CH	3′, 4′, 6′, 7′	2.25 m	35.1 CH_2	3′, 4′, 6′, 7′
6′	4.29 m	67.7 CH		1.55 m	22.1 CH_2	4′, 5′, 7′
7′	1.21 d (6.4)	24.0 CH_3	5′, 6′	0.98 t (7.4)	13.7 CH_3	5′, 6′
1″	3.26 d (7.3)	27.6 CH_2	2″, 3″, 4, 5	3.41 d (7.3)	27.5 CH_2	2″, 3″, 4, 5, 6
2″	5.31 br t (7.3)	122.4 CH	1″, 4″	5.35 t (7.3)	121.3 CH	1″, 4″
3″		133.8 C			134.0 C	
4″	1.73 s	25.9 CH_3	2″, 3″, 5″	1.78 s	25.8 CH_3	2″, 3″, 5″
5″	1.70 s	17.8 CH_3	2″, 3″, 4″	1.72 s	17.8 CH_3	2″, 3″, 4″
6-OH	12.07 s		1, 5, 6	11.70 s		1, 5, 6
6′-OH	3.81 d (4.4)					

[a] Measured in acetone-d_6. [b]Measured in $CDCl_3$.

δ_H 2.13 and 1.81 and CH_2-1′ at δ_H 3.24 and 3.16, respectively). The second olefinic proton (H-5′) also displayed a correlation to an oxygenated methine proton appearing at δ_H 4.29 (m, H-6′). The latter displayed two further cross-peaks with the doublet methyl signal at δ_H 1.21 (H-7′) and with the hydroxyl proton signal at δ_H 3.81 (OH-6′). This led to the elucidation of the first substructure comprised of C-1′ through C-7′ with a hydroxyl substitution at C-6′. The presence of this substructure was further confirmed by HMBC correlations. In addition, the cross-peak between a two-proton doublet at δ_H 3.26 (J = 7.3 Hz, H-1″) and a one-proton broad olefinic triplet at δ_H 5.31 (J = 7.3 Hz, H-2″) in the $^1H-^1H$ COSY revealed the presence of a second coupling system containing only CH_2-1″ and CH-2″. Furthermore, HMBC correlations from H-1″ to the olefinic quaternary carbon signal appearing at δ_C 133.8 (C-3″) and from H-2″ to a methyl carbon signal at δ_C 25.9 (C-4″) as well as from both H-4″ and H-5″ to C-2″ (δ_C 122.4, CH) clearly indicated the presence of a 3-methyl-2-butenyl substructure in **1**. Finally, the remaining proton signal in the aromatic region, δ_H 6.92 (s), as a singlet as well as the remaining six carbon NMR signals resonating at δ_C 117.7 (C, C-1), 121.5 (C, C-2), 147.7 (C, C-3), 127.7 (CH, C-4), 130.1 (C, C-5), and 156.5 (C, C-6) revealed the presence of a pentasubstituted benzene ring system. Since the above-mentioned three substructures together with the aldehyde group accounted for seven of the eight degrees of unsaturation, compound **1** had to contain a further ring, presumably a cyclic ether system according to the number of oxygen atoms and oxygenated carbons as indicated by HRESIMS and NMR data, respectively.

The connection of the substructures in **1** was accomplished by the analysis of key HMBC correlations. The cross-peaks observed from the aldehyde proton (H-7) to C-1 and C-6 and from the 6-OH proton to C-1, C-5, and C-6 enabled placement of the aldehyde and one hydroxyl group at C-1 and C-6, respectively. The HMBC correlations between H-1″ and C-4, C-5, and C-6 indicated the connection of the 3-methyl-2-butenyl substituent to C-5. The HMBC correlations from H-1′ to C-2 and C-3 indicated the connection of C-1′ (δ_C 20.7) at C-2. The final substitution in the benzene ring system was assigned to C-3. The lower field carbon signal appearing at δ_C 147.7 (C) for C-3 suggested that this carbon was oxygenated. Considering that three of the four oxygen atoms were already accounted for by one aldehyde and two hydroxyl groups, the remaining oxygen atom had to be connected both to C-3 and to the oxymethine carbon C-3′ (δ_C 75.8), which confirmed the presence of an ether-ring system. The possibility of the ring closure at C-6′ could be excluded by the fact that the hydroxyl proton at C-6′ appeared as a doublet at δ_H 3.81 (d, J = 4.4 Hz, 6′-OH), which displayed a COSY correlation with the methine proton at δ_H 4.29 (m, H-6′), and the latter exhibited a further correlation to a doublet methyl group at δ_H 1.21 (d, J = 6.4 Hz, H-7′).

The relative configuration of **1** was investigated by the analysis of proton coupling constants. The observed coupling constant for H-3′ (J = 7.2 Hz) at δ_H 4.49 most likely supports the substitution at C-3′ to be equatorial, rather than axial. This is largely in agreement with the literature reports that in benzopyrans an equatorial orientation is preferred for the C-2 (in the case for **1**, C-3′) substitution.[12,13] However, the relative configuration at C-6′ remains unknown.

From the above deductions, the structure of compound **1** was assigned as (*E*)-6-hydroxy-2-(3-hydroxybut-1-enyl)-7-(3-methylbut-2-enyl)chroman-5-carbaldehyde, for which we propose the trivial name chaetopyranin. To the best of our knowledge, compound **1** represents the first example of a 2*H*-benzopyran derivative from a marine algal-derived fungus or from the fungal genus *Chaetomium*.

Compound **2** was also obtained as a yellowish powder, and its structure was determined by the analysis of HRESIMS and 1D and 2D NMR data. This compound has previously been isolated from the mycelium of *Aspergillus amstelodami*. However, only limited proton NMR data have been reported for this compound.[14] Therefore, the complete ^1H and ^{13}C NMR data have been assigned as listed in Table 1.

In addition to compounds **1** and **2**, nine other compounds (**3**−**11**) were also isolated in this study. By comparison of their NMR and MS data with those reported in the literature, the structures of these compounds were identified as the benzaldehyde congener isotetrahydroauroglaucin (**3**),[15] the two anthraquinone derivatives erythroglaucin (**4**) and parietin (**5**),[16,17] five asperentin derivatives, asperentin (**6**), 5′-hydroxy-asperentin-8-methyl ether (**7**), asperentin-8-methyl ether (**8**), 4′-hydroxyasperentin (**9**), and 5′-hydroxyasperentin (**10**),[18,19] and the prenylated diketopiperazine derivative neoechinulin A (**11**).[20]

All isolated compounds were tested for their DPPH (1,1-diphenyl-2-picrylhydrazyl) radical-scavenging property, and compounds **1**−**4** showed moderate activity with IC_{50} values of 35, 88, 26, and 62 μg/mL, respectively. The IC_{50} of the positive control, butylated hydroxytoluene (BHT), was 18 μg/mL. The other compounds (including **11**, for which radical-scavenging properties had previously been described) showed no or only weak activity.

Chaetopyranin (**1**) also displayed moderate or weak cytotoxic activities against three tumor cell lines, with IC_{50} values of 15.4

(human microvascular endothelial cells, HMEC), 28.5 (hepatocellular carcinoma cells, SMMC-7721), and 39.1 μg/mL (human lung epithelial cells, A549).

Experimental Section

General Experimental Procedures. Melting points were determined by a SGW X-4 micromelting apparatus (uncorrected). Optical rotations were measured on a JASCO P-1020 digital polarimeter. IR spectra were performed on a Nicolet NEXUE 470 infrared spectrophotometer. UV spectra were measured on a PuXi TU-1810 UV−visible spectrophotometer. 1D and 2D NMR were recorded on a Bruker Avance 500 MHz spectrometer with TMS as internal standard. Mass spectra were performed on a VG Autospec 3000 mass spectrometer. HPLC analysis was carried out on a Dionex HPLC system (P680 HPLC pump, UVD 340U UV−visible detector) using a C18 (5 μm, 8.0 × 250 mm) column. Silica gel (200−300 and 300−400 mesh, Qingdao Haiyang Chemical Co., Qingdao, China) and Sephadex LH-20 (Merck, Darmstadt, Germany) were used for open CC.

Origin of the Algal Sample. The fresh algal sample was collected in April 2003 from the Qingdao coastline and was identified as *Polysiphonia urceolata* (Lightfoot ex Dillwyn) Greville (family Rhodomelaceae) by Prof. B.-M. Xia and Dr. L.-P. Ding at the Institute of Oceanology, Chinese Academy of Sciences (IOCAS). A voucher specimen (no. HZ03047) has been deposited in the Herbarium of Marine Organisms at IOCAS.

Isolation and Microscopic Identification of the Fungus. The isolation of the fungus was carried out using an indirect isolation method. After surface sterilization with 70% EtOH for 15 s the alga was rinsed in sterile water. To distinguish remaining epiphytic fungi from endophytic fungi, an imprint of the algal surface on biomalt agar was done. The alga was then aseptically cut into small pieces and pressed onto agar plates containing isolation medium: 15 g/L agar, artificial seawater (contained sea salt 24.4 g/L), and chloramphenicol (200 mg/L) to suppress bacterial growth. The fungal strain under investigation was found to grow exclusively out of the algal tissue, but not on the agar plates taken from the imprint of the algal surface (agar medium: 15 g/L agar, 15 g of sterile mashed alga, and 1 L of artificial seawater). For sporulation the fungus was inoculated on malt/agar medium (15 g/L agar, 15 g/L malt extracts). By classical microscopic analysis, the fungus was identified as a member of the genus *Chaetomium* and was further identified as *C. globosum* by using the molecular taxonomic method (see below). The strain is preserved at the China Center for Type Culture Collection (CCTCC) under the patent depository number CCTCC AF 206003.

Molecular Taxonomy of the Fungus. A piece (0.5 cm^2) of fungal culture was cut from the culture agar dish and lyophilized in a sample tube (2 mL) closed with a hydrophobic membrane (LidBac, Eppendorf, Hamburg, Germany). The sample was powderized in a MixerMill MM300 (Retsch, Haan, Germany) after adding a tungsten carbide bead (Qiagen, Hilden, Germany). DNA isolation was performed using the DNeasy plant mini kit (Qiagen, Hilden, Germany) according to the manufacturer's protocol. The procedure includes cell lysis, digestion of RNA by RNase A, removal of precipitates and cell debris, DNA shearing, DNA precipitation, and purification. The DNA obtained was dissolved in 50 μL of elution buffer supplied by the manufacturer. PCR was then performed using Hot Star Taq master mix (Qiagen, Hilden, Germany) Taq polymerase and the primer (Invitrogen, Karlsruhe, Germany) pair ITS1 and ITS4 in an iCycler (Bio-Rad, Hercules, CA) thermal cycler according to the following protocol: (1) initial denaturation 95 °C 15 min; (2) denaturation 95 °C 1 min; (3) annealing 56 °C 0.5 min; (4) extension 72 °C 1 min; (5) final extension 72 °C 10 min. Steps 2−4 were repeated 35 times.[21] Each sample consisted of 25 μL of Taq polymerase master mix, 3 μL of primer mix (10 pmol/μL each), 3 μL of template DNA, and 19 μL of water. From this, 20 μL was loaded onto an agarose gel (2% agarose in 1 × TBE, 5 μL of ethidium bromide 1% m/V solution per 100 mL of gel). After electrophoresis at 70 V for 60 min, the band due to the PCR product (approximate size 550 bp) was isolated from the gel slice using the PerfectPrep gel cleanup kit (Eppendorf, Hamburg, Germany) according to the manufacturer's protocol. The PCR product was then submitted for sequencing (SeqLab, Goettingen, Germany) with the primer ITS1. The sequence data have been submitted to and deposited at GenBank (accession no. bankit823609, DQ854987). BLAST search of the FASTA sequence was performed with the option "nr", including GenBank, RefSeq Nucleotides, EMBL, DDBJ, and PDB sequences on the BLAST homepage, NCBI, Bethesda, MD. The search result showed that the sequence was the most similar (98%) to the sequence of *Chaetomium globosum* (compared to gi 38503532 gb AY429056.1).

Cultivation. The fungal strain was cultivated in 1 L flasks, each filled with 300 mL of liquid biomalt medium containing malt extract 3 g/L, yeast extract 3 g/L, peptone 5 g/L, sea salt 24.4 g/L, and glucose 20 g/L. Each flask was inoculated with a piece of fungal biomass (1 cm^2), and after a growth period of 40 days in static culture at room temperature, 20 vol % EtOAc was added and the mixture was kept for the next extraction procedure.

Extraction and Isolation. Mycelium and culture broth of *C. globosum* (20 L) were homogenized using a Waring blender and exhaustively extracted with MeOH and EtOAc, respectively. The MeOH and EtOAc extracts were filtered, and the filtrates were evaporated under reduced pressure at 40 °C to yield MeOH (15 g) and EtOAc (25 g) soluble crude extracts. Since the HPLC profiles of the two extracts were nearly identical, they were combined before further separation. Initial chromatographic separation of the combined extracts was performed using Si gel (200−300 mesh) CC with a gradient solvent system from 3% acetone/petroleum ether to 100% acetone to yield 27 fractions (800 mL for each fraction). The fractions were monitored by TLC. Fraction 21 was further purified by repeated preparative TLC on Si gel and developed with a mixture of EtOAc/petroleum ether (1:4) to give compounds **1** (7.2 mg), **2** (7.5 mg), and **3** (12.5 mg). Fraction 27 (4.5 g) was further fractionated by CC on Si gel (300−400 mesh) with a gradient solvent system from $CHCl_3$/MeOH (30:1) to $CHCl_3$/MeOH (1:1) to yield five subfractions (150 mL for each fraction). Subfraction 27-1 (500 mg) was further purified by repeated preparative TLC on Si gel with a mixture of $CHCl_3$/MeOH (30:1) as developing solvent and then subjected to CC on Sephadex LH-20 using $CHCl_3$/MeOH (1:1) as solvent system to give compounds **4** (17.5 mg) and **5** (7.2 mg). Subfraction 27-4 (1.5 g) was separated by repeated preparative TLC on $CHCl_3$ gel developed with a mixture of $CHCl_3$/MeOH (15:1) and further purified by CC on Sephadex LH-20 using $CHCl_3$/MeOH (1:1) as solvent system to yield compounds **6** (22.5 mg), **7** (16.5 mg), **8** (12.5 mg), and **9** (10.5 mg).

(*E*)-6-Hydroxy-2-(3-hydroxybut-1-enyl)-7-(3-methylbut-2-enyl)-chroman-5-carbaldehyde (chaetopyranin, 1): yellow solid (acetone); mp 136−138 °C; $[\alpha]_D^{22}$ +8.0 (*c* 0.50, MeOH); UV (MeOH) λ_{max} (log ϵ) 268 (3.21), 261 (3.15) nm; IR (KBr) γ_{max} 3374, 3261, 2967, 2923, 1725, 1643, 1615, 1592, 1435, 1375, 1298, 1263, 1217, 1193, 1107, 1073, 972, and 800 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 316 $[M]^+$ (94), 243 (63), 215 (43), 199 (62), 189 (41), 175 (84), 163 (100), 91 (56), 81 (55), and 77 (53); HRESIMS, *m*/*z* 339.1580 $[M + Na]^+$ (calcd for $C_{19}H_{24}O_4Na$, 339.1572).

(*E*)-5-Hydroxy-6-(3-methylbut-2-enyl)-2-(pent-1-enyl)benzofuran-4-carbaldehyde (2): yellow solid ($CHCl_3$); mp 142−143 °C; IR (KBr) γ_{max} 3444, 2928, 2855, 2923, 1740, 1645, 1459, 1433, 1262, 1194, 1104, 1020, 799, and 495 cm^{-1}; ^1H and ^{13}C NMR, see Table 2; EIMS *m*/*z* 298 $[M]^+$ (97), 283 $[M - Me]^+$ (35), 255 (30), 243 (100), 213 (74), 201 (31), 149 (47), and 128(31); positive HRESIMS, *m*/*z* 321.1466 $[M + Na]^+$ (calcd for $C_{19}H_{22}O_3Na$, 321.1466).

Assay for DPPH-Radical-Scavenging Property. The DPPH-radical-scavenging properties of all isolated compounds were determined as described in a previous report.[22]

Cytotoxicity Assays. Cytotoxicity assays toward tumor cell lines SMMC-7721, A549, and HMEC were carried out as previously reported.[23]

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (No. 30530080) and by the innovation program of the Institute of Oceanology of the Chinese Academy of Sciences (IOCAS, L79032432). The program Bairen Jihua from the Chinese Academy of Sciences (awarded to B.-G.W.) and financial support by the BMBF to P.P. and R.E. are also gratefully acknowledged. The authors are grateful to B.-M. Xia and L.-P. Ding at the Institute of Oceanology, Chinese Academy of Sciences, for identifying the algal material. We would also like to acknowledge two anonymous referees for the critical comments and suggestions to our manuscript.

Supporting Information Available: The sequence data for the molecular taxonomic identification of the fungal strain *Chaetomium globosum*; 1D and 2D NMR, IR, EIMS, and HRESIMS spectra of compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Lindel, T.; Jensen, P. R.; Fenical, W. *Tetrahedron Lett.* **1996**, *37*, 1327−1330.
(2) König, G. M.; Wright, A. D. *Planta Med.* **1996**, *62*, 193−211.
(3) Needham, J.; Kelly, M. T.; Ishige, M.; Andersen, R. J. *J. Org. Chem.* **1994**, *59*, 2058−2069.
(4) Jayatilake, G. S.; Thornton, M. P.; Leonard, A. C.; Grimwade, J. E.; Baker, B. J. *J. Nat. Prod.* **1996**, *59*, 293−296.
(5) Bugni, T. S.; Ireland, C. M. *Nat. Prod. Rep.* **2004**, *21*, 143−163.
(6) Krohn, K.; Dai, J.; Flörke, U.; Aust, H. J.; Dräger, S.; Schulz, B. *J. Nat. Prod.* **2005**, *68*, 400−405.
(7) Komatsu, K.; Shigemori, H.; Kobayashi, J. *J. Org. Chem.* **2001**, *66*, 6189−6192.
(8) Shigemort, H.; Konmotsu, K.; Mikami, Y.; Kobayashi, J. *Tetrahedron* **1999**, *55*, 14925−14930.
(9) Cueto, M.; Jensen, P. R.; Kauffman, C.; Fenical, W.; Lobkovsky, E.; Clardy, J. *J. Nat. Prod.* **2001**, *64*, 1444−1446.
(10) Iwaoto. C.; Yamada, T.; Ito, Y.; Minoura, K.; Numata, A. *Tetrahedron* **2001**, *57*, 2997−3004.
(11) Belofsky, G. N.; Jensen, P. R.; Renner, M. K.; Fenical, W. *Tetrahedron* **1998**, *54*, 1715−1724.
(12) Teles, H. L.; Silva, G. H.; Castro-Gamboa, I.; da Silva, Bolzani, V.; Pereira, J. O.; Costa-Neto, C. M.; Haddad, R.; Eberlin, M. N.; Young, M. C. M.; Araujo, A. R. *Phytochemistry* **2005**, *66*, 2363−2367.
(13) Joshi, V.; Merchant, J. R. *Indian J. Chem.* **1984**, *23*, 266−267.
(14) Inoue, S.; Hashizume, K.; Takamatsu, N.; Nagano, H.; Kishi, Y. *Yakugaku Zasshi* **1977**, *97*, 569−575.
(15) Sokolov, L. B.; Alekseeva, L. E.; Kul'bakh, V. O.; Kuznetsova, N. A.; Nyn'vs. *Antibiotiki* **1971**, *16*, 504−510.
(16) Podojil, M.; Sedmer, P.; Vokoun, J.; Betina, V.; Barathova, Z.; Horakova, K.; Memec, P. *Folia Microbiol. (Praha)* **1978**, *23*, 438−443.
(17) Sargent, M. V.; Smith, D. O. N.; Elix, J. A. *J. Chem. Soc.* **1970**, 307−311.
(18) Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1972**, *19*, 2400−2406.
(19) Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1973**, *19*, 2704−2706.
(20) Yagi, R.; Doi, M. *Biosci. Biotechnol. Biochem.* **1999**, *63*, 932−933.
(21) White, T. J.; Bruns, T.; Lee, S.; Taylor, J. In *PCR Protocols: A Guide to Methods and Applications*; Innis, M. A., Gelfand, D. H., Sninsky, J. J., White, T. J., Eds.; Academic Press: San Diego, 1990; pp 315−322.
(22) Duan, X. J.; Zhang, W. W.; Li, X. M.; Wang, B. G. *Food Chem.* **2006**, *95*, 37−43.
(23) Berengeron, R. I.; Davanaugh, P. F., Jr.; Kline, S. J.; Hughes, R. G., Jr.; Elliot, G. T.; Porter, C. W. *Biochem. Biophys. Res. Commun.* **1984**, *121*, 848−854.

NP060248N