JOURNAL OF NATURAL PRODUCTS

ARTICLE

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Prenylated Polyhydroxy-*p*-terphenyls from *Aspergillus taichungensis* ZHN-7-07

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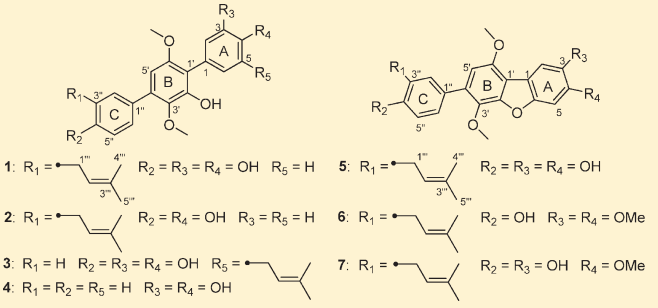
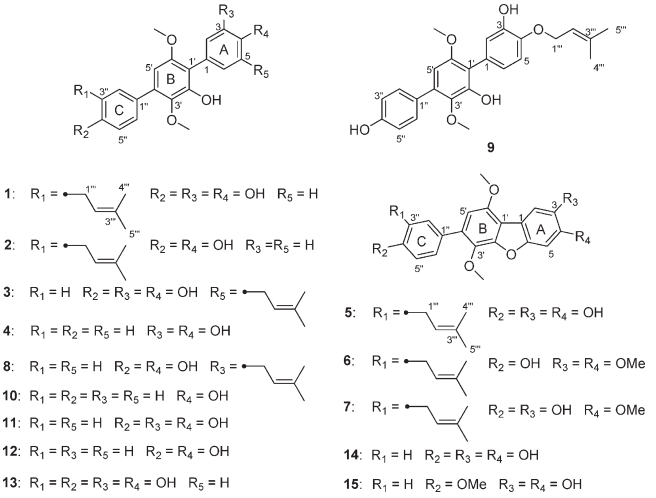
Supporting Information

ABSTRACT: Six new prenylated polyhydroxy-*p*-terphenyl metabolites, named prenylterphenyllins A−C (**1**−**3**) and prenylcandidusins A−C (**5**−**7**), and one new polyhydroxy-*p*-terphenyl with a simple tricyclic C-18 skeleton, named 4″-dehydro-3-hydroxyterphenyllin (**4**), were obtained together with eight known analogues (**8**−**15**) from *Aspergillus taichungensis* ZHN-7-07, a root soil fungus isolated from the mangrove plant *Acrostichum aureum*. Their structures were determined by spectroscopic methods, and their cytotoxicity was evaluated using HL-60, A-549, and P-388 cell lines. Compounds **1** and **8** exhibited moderate activities against all three cell lines (IC_{50} 1.53−10.90 μM), whereas compounds **4** and **6** displayed moderate activities only against the P-388 cell line (IC_{50} of 2.70 and 1.57 μM, respectively).



Fungi have proven to be a valuable source of promising natural products.[1] Specifically, those metabolites reported from specimens of the genus *Aspergillus* sp. have continually attracted the interest of the scientific community due to their structural diversity and potent biological activities.[1,2] This fungal genus has been subdivided into several subgenera and sections on the basis of conidial color and morphology. Members of the *Aspergillus* section *Candidi*, namely, *A. candidus*, *A. campestris*, *A. taichungensis*, and *A. tritici*,[3] are known to produce a host of secondary metabolites including the terphenyllins,[3b,c] candidusins,[3b,c] chlorflavonins,[3b,c] and xanthoascins.[3b,c] Most of these compounds are exclusive to this section, and in recent communications the terphenyllins and candidusins are regarded as chemotaxonomical indicators of the monotypic *Aspergillus* section *Candidi*.[3] Their biological activities include antioxidant, cytotoxic, antimicrobial, and immunosuppressive properties.[4]

In our continued search for new anticancer compounds from fungi associated with mangrove plants,[1b,2c,5] we observed that the ethyl acetate extract derived from the fungus strain ZHN-7-07 exhibited intriguing UV profiles and cytotoxicity against the P-388 (mice lymphocytic leukemia) cell line. This strain was isolated from the root soil of the mangrove plant *Acrostichum aureum* and identified as *Aspergillus taichungensis*. Studies on the bioactive constituents of the extract led to the isolation of seven new polyhydroxy-*p*-terphenyl-type metabolites including six prenylated ones, prenylterphenyllins A−C (**1**−**3**) and prenylcandidusins A−C (**5**−**7**), and one exhibiting a more basic tricyclic C-18 skeleton, 4″-dehydro-3-hydroxyterphenyllin (**4**), together with the known analogues prenylterphenyllin (**8**),[6] terprenin (**9**),[7] deoxyterhenyllin (**10**),[8] 3-hydroxyterphenyllin (**11**),[9,10] terphenyllin (**12**),[7] 3,3-dihydroxyterphenyllin (**13**),[9,10] candidusin A (**14**),[11] and candidusin C (**15**).[3b] The cytotoxicity of compounds **1**−**8** and **11**−**15** was evaluated using HL-60, A-549, and P-388 cell lines. Herein, we report the isolation and structure elucidation of the seven new metabolites (**1**−**7**), as well as cytotoxic activities for compounds **1**−**8** and **11**−**15**.



RESULTS AND DISCUSSION

The isolated fungus *A. taichungensis* ZHN-7-07 was grown in a static liquid media. The culture broth was extracted with EtOAc,

Received: January 17, 2011
Published: April 12, 2011

Table 1. ^{1}H NMR Data for Compounds 1−7 (recorded in DMSO-d_6)[a]

	1	2	3	4	5	6	7
position	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)
2	6.69, d (1.9)	7.09, brd (8.7)	6.43, d (1.8)	6.70, brd (1.8)	7.39, s	7.46, s	7.42, s
3		6.75, brd (7.8)					
5	6.71, d (8.2)	6.75, brd (7.8)		6.72, brd (8.3)	7.09, s	7.45, s	7.39, s
6	6.54, dd (8.2, 1.9)	7.09, brd (8.7)	6.57, d (1.8)	6.56, dd (8.3, 1.8)			
3-OH/OMe	8.75, brs		9.06, brs	8.78, brs	9.11, brs	3.87, s	9.05, brs
4-OH/OMe	8.75, brs	9.31, brs	9.06, brs	8.78, brs	9.45, brs	3.88, s	3.89, s
5′	6.35, s	6.36, s	6.37, s	6.43, s	6.70, s	6.74, s	6.72, s
2′-OH	8.42, brs	8.50, brs	8.41, brs	8.55, brs			
3′-OMe	3.30, s	3.29, s	3.29, s	3.30, s	3.78, s	3.80, s	3.80, s
6′-OMe	3.63, s	3.63, s	3.63, s	3.65, s	3.98, s	4.00, s	3.99, s
2″	7.31, d (2.3)	7.31, d (1.9)	7.43, d (8.2)	7.62, brd (8.3)	7.29, d (2.3)	7.30, d (2.3)	7.30, d (1.9)
3″			6.84, d (8.2)	7.46, dd (7.8, 7.8)			
4″				7.39, dd (7.3, 7.3)			
5″	6.86, d (8.2)	6.85, d (7.8)	6.84, d (8.2)	7.46, dd (7.8, 7.8)	6.88, d (8.2)	6.88, d (8.3)	6.89, d (8.6)
6″	7.25, dd (8.2, 2.3)	7.24, dd (7.8, 1.9)	7.43, d (8.2)	7.62, brd (8.3)	7.25, dd (8.5, 2.3)	7.24, dd (8.2, 2.3)	7.25, dd (8.2, 2.3)
4″-OH	9.45, brs	9.45, brs	9.48, brs		9.45, brs	9.45, brs	9.48, brs
1‴	3.27, d (7.3)	3.26, d (7.3)	3.22, d (7.3)		3.29, d (7.4)	3.29, d (7.4)	3.30, d (7.3)
2‴	5.34, t (7.3)	5.33, t (7.3)	5.29, t (7.3)		5.36, t (6.9)	5.36, t (6.9)	5.36, t (6.9)
4‴	1.70, s	1.70, s	1.67, s		1.71, s	1.70, s	1.71, s
5‴	1.69, s	1.69, s	1.66, s		1.71, s	1.70, s	1.71, s

[a] Spectra were recorded at 600 MHz for ^{1}H NMR using TMS as internal standard.

and the organic extract was separated using normal-phase silica gel followed by Sephadex LH-20, to be finally purified by semipreparative HPLC to yield compounds **1**−**15**.

Prenylterphenyllin A (**1**) was obtained as a colorless, amorphous solid, and its molecular formula was established as $C_{25}H_{26}O_6$ on the basis of HRESIMS data {$[M + H]^+$ ion at m/z 423.1814, calcd 423.1808; Δ +1.5 ppm}. The formula above was consistent with the ^{1}H and ^{13}C NMR data and indicated 13 degrees of unsaturation. The ^{1}H and ^{13}C NMR data of compound **1** displayed resonances that were assigned to 12 quaternary carbons, eight methines, one methylene, two methyliums, and two methoxyl groups (Tables 1 and 2). These data were very similar to those of the known metabolite 3-hydroxyterphenyllin (**11**),[9,10] except for the lack of one aromatic proton and the appearance of an additional isoprene unit. The basic polyhydroxy-*p*-terphenyl skeleton in **1** was confirmed by ^{1}H−^{1}H COSY and HMBC correlations (Figure 1). The isoprene moiety was elucidated via HMBC correlations from H-4‴ and H-5‴ to C-2‴ and was assigned at C-3″ on the basis of HMBC correlations from H-1‴ to C-4″ and from H-2″ to C-1‴ (Figure 1). Thus, we concluded the structure elucidation of compound **1** and named it prenylterphenyllin A.

Prenylterphenyllin B (**2**) was separated as a colorless, amorphous solid. An $[M + H]^+$ molecular ion at m/z 407.1850 (calcd 407.1858; Δ −2.1 ppm) in the HRESIMS spectrum was in agreement with the molecular formula $C_{25}H_{26}O_5$. Their similar UV absorptions suggested that **2** was an analogue of **1**. Comparison of the NMR data for the two compounds suggested that they had the same substructures of rings B and C, with the main differences located on ring A. Specifically, analogue **2** showed the absence of one hydroxyl group and the presence instead of one additional hydrogen to outline a 1,4-disubstituted benzene ring in compound **2** (Table 1). Thus, compound **2** was elucidated as a dehydroxyl analogue of prenylterphenyllin A (**1**).

Prenylterphenyllin C (**3**) was a colorless, amorphous solid, and HRESIMS indicated the molecular formula $C_{25}H_{26}O_6$. Compound **3** displayed similar NMR resonances to the already reported metabolite **8**,[6] and their comparison suggested that they shared the same substructures of rings B and C. However, the absence of three signals for several aromatic protons in **8** (δ_H 6.77, d, J = 8.3 Hz, δ_H 6.91, dd, J = 8.2, 2.3 Hz, and δ_H 6.95, d, J = 2.3 Hz) and the presence of an additional deshielded hydroxyl group singlet (δ_H 9.06, brs), as well as two new aromatic protons (δ_H 6.43, d, J = 1.8 Hz, and δ_H 6.57, d, J = 1.8 Hz) in **3**, suggested that the latter compound exhibited a 1,2,3,5-tetrasubstituted ring A. Therefore, the structure of compound **3** was determined as prenylterphenyllin C.

The molecular formula of **4** was determined as $C_{20}H_{18}O_5$ on the basis of an $[M + H]^+$ ion at m/z 339.1230 (calcd 339.1232; Δ −0.7 ppm) in the HRESIMS. Similarities in the NMR data (Tables 1 and 2) of compound **4** and known deoxyterhenyllin (**10**)[8] showed that their structure was closely related with the exception of ^{1}H NMR data for ring A in **10** (δ_H 6.77, 2H, brd, J = 8.4 Hz and δ_H 7.06, 2H, brd, J = 7.9 Hz), which were replaced in **4** by resonances consistent with a 1,2,4-trisubstituted benzene (Table 1). Additionally, this new entity exhibited the presence of a second deshielded hydroxyl group (δ_H 8.78), suggesting the replacement of an aromatic proton in **10** by a hydroxyl group in **4**. The structure of **4** was further confirmed by the HMBC correlations shown in Figure 1. Thus, the structure of **4** was elucidated as 4″-dehydro-3-hydroxyterphenyllin.

Prenylcandidusin A (**5**) was found to possess the molecular formula $C_{25}H_{24}O_6$ as determined by HRESIMS and consistent with 14 degrees of unsaturation. Careful comparison of the NMR data for **1** and **5** (Tables 1 and 2) revealed that they had almost identical ^{1}H and ^{13}C resonances except for the absence of one hydroxyl group peak at δ_H 8.42 (brs), the H-6 proton at δ_H 6.54 (dd, J = 8.2, 1.9 Hz), and a noticeable downfield chemical shift for

dx.doi.org/10.1021/np2000478 |J. Nat. Prod. 2011, 74, 1106–1110

Table 2. ^{13}C NMR Data for Compounds 1−7 (recorded in DMSO-d_6)[a]

	1	2	3	4	5	6	7
position	δ_C, mult	δ_C, mult	δ_C, mult	δ_C, mult	δ_C, mult	δ_C, mult	δ_C, mult
1	125.5, qC	125.1, qC	124.8, qC	125.3, qC	114.2, qC	114.8, qC	115.2, qC
2	119.0, CH	114.8, CH	115.6, CH	118.9, CH	107.6, CH	104.6, CH	107.5, CH
3	144.4, qC	132.4, CH	142.1, qC	144.5, qC	143.1, qC	146.7, qC	144.1, qC
4	144.8, qC	156.4, qC	144.5, qC	144.8, qC	149.8, qC	150.5, qC	148.5, qC
5	115.3, CH	132.4, CH	127.4, qC	115.4, CH	99.0, CH	96.9, CH	96.7, CH
6	122.4, CH	114.8, CH	131.0, CH	122.4, CH	146.4, qC	149.2, qC	149.7, qC
3-OMe						56.7, CH_3	
4-OMe						56.5, CH_3	56.6, CH_3
1′	117.7, qC	117.4, qC	118.0, qC	118.6, qC	114.5, qC	114.2, qC	114.2, qC
2′	148.7, qC	148.6, qC	148.6, qC	148.7, qC	149.0, qC	149.7, qC	149.2, qC
3′	139.8, qC	139.8, qC	139.8, qC	140.0, qC	136.5, qC	136.5, qC	136.5, qC
4′	132.9, qC	133.1, qC	132.7, qC	132.9, qC	131.3, qC	131.9, qC	131.9, qC
5′	103.5, CH	103.5, CH	103.5, CH	103.8, CH	106.1, CH	106.3, CH	106.1, CH
6′	153.6, qC	153.6, qC	153.6, qC	153.8, qC	149.9, qC	150.0, qC	150.1, qC
3′-OMe	60.5, CH_3	60.5, CH_3	60.5, CH_3	60.9, CH_3	61.1, CH_3	61.1, CH_3	61.1, CH_3
6′-OMe	56.1, CH_3	56.2, CH_3	56.1, CH_3	56.2, CH_3	56.4, CH_3	56.6, CH_3	56.4, CH_3
1″	129.3, qC	129.3, qC	129.3, qC	138.8, qC	129.2, qC	129.0, qC	129.1, qC
2″	130.2, CH	130.2, CH	130.2, CH	129.2, CH	130.9, CH	130.9, CH	130.9, CH
3″	127.7, qC	127.7, qC	115.7, CH	128.9, CH	127.6, qC	127.7, qC	127.6, qC
4″	154.9, qC	154.9, qC	157.2, qC	127.7, CH	154.9, qC	154.9, qC	154.9, qC
5″	115.3, CH	115.3, qC	115.7, CH	128.9, CH	115.3, CH	115.3, CH	115.1, CH
6″	127.4, CH	127.4, CH	130.2, CH	129.2, CH	128.1, CH	128.1, CH	128.1, CH
1‴	28.6, CH_2	28.6, CH_2	26.1, CH_2		28.7, CH_2	28.7, CH_2	28.7, CH_2
2‴	123.4, CH	123.4, CH	123.8, CH		123.5, CH	123.5, CH	123.5, CH
3‴	131.9, qC	131.9, qC	131.3, qC		131.9, qC	131.9, qC	131.7, qC
4‴	26.1, CH_3	26.1, CH_3	28.7, CH_3		26.1, CH_3	26.1, CH_3	26.1, CH_3
5‴	18.2, CH_3	18.2, CH_3	18.2, CH_3		18.2, CH_3	18.2, CH_3	18.2, CH_3

[a] Spectra were recorded at 150 MHz for ^{13}C NMR using TMS as internal standard.

C-6 (δ_C +24.0 ppm). Considering the molecular formula above and the additional degree of unsaturation in relation to **1**, the structure of compound **5** was found to be a cyclization product of **1** between C-6 and C-2′ via an oxygen atom. This ether bridge was further confirmed by $^1H-^1H$ COSY and HMBC data (Figure 1) and also supported by the chemical shift comparison with candidusin A (**14**)[11] and candidusin C (**15**).[3b]

The molecular formulas for compounds **6** and **7** were determined by HRESIMS as $C_{27}H_{28}O_6$ and $C_{26}H_{26}O_6$, respectively. Their UV and IR spectra were almost identical to those obtained for prenylcandidusin A (**5**), which suggested that these two metabolites were analogues of **5**. Comparison of the NMR data of **6** and **7** with those obtained for **5** indicated that both hydroxyl groups at δ_H 9.45 (brs) and δ_H 9.11 (brs) were replaced by methoxy resonances at δ_H 3.99 (s)/δ_C 56.5 (CH_3) and δ_H 3.80 (s)/δ_C 56.7 (CH_3) in **6**, whereas for compound **7** only one of the hydroxy signals (δ_H 9.45) was found to be methylated [methoxy group at δ_H 3.98 (s)/δ_C 56.0 (CH_3)]. The positions of the methoxy moieties were assigned at C-3 and C-4 for **6** and at C-4 for **7** via HMBC correlations (Figure 1). Further confirmation of the methoxy location in **7** was provided by a NOESY correlation between 4-OMe and H-5. Thus, the structures of **6** and **7** were elucidated as prenylcandidusins B and C.

The cytotoxicity of compounds **1**−**8** and **11**−**15** was evaluated on HL-60, A-549, and P-388 cell lines using the SRB[12,13] and MTT[12,14] methods with adriamycin (ADM) as positive control. Compounds **1** and **8** exhibited moderate activities against these three cell lines with IC_{50} values of 1.53, 8.32, 10.90 and 2.75, 3.62, 1.99 μM, respectively. Metabolites **4** and **6** displayed moderate activities only against the P-388 cell line, with IC_{50} values of 2.70 and 1.57 μM, respectively. All other compounds showed weak cytotoxic activity against these cell lines (Table 3). Biological evaluation of compounds **9** and **10** was hindered by the small quantities of material available.

In summary, we have isolated and determined the structures of seven new polyhydroxy-*p*-terphenyl metabolites (**1**−**7**) together with eight known analogues (**8**−**15**). Polyhydroxy-*p*-terphenyl-type chemical entities, mainly found in mycomycetes, include scaffolds with a C-18 tricyclic or polycyclic C-18 skeleton and those exhibiting alkylated (methylate or prenylate) side chains.[4] To date, less than 20 polyhydroxy-*p*-terphenyl metabolites have been isolated from lower fungi, with the majority reported from *Aspergillus* section *Candidi*.[4,6] Members of this family of natural products, with terprenin (**9**) the first example isolated from *A. candidus*, have displayed various degrees of cytotoxicity.[4,7] Prenylation is known to play an important role in the diversification of natural products, such as propanoids, flavonoids, coumarins, and alkaloids, and prenylated examples within these compound families have been shown to exert valuable *in vitro* and *in vivo* biological activities (anticancer, anti-inflammatory, antibacterial,

antiviral, antifungal) often quite different from those of their non-prenylated precursors.[15−17] Prenylation in polyhydroxy-*p*-terphenyl metabolites is rare, and to the best of our knowledge, only two compounds, prenylterphenyllin (**8**) and 4-deoxyprenylterphenyllin, have been reported to have this modification and exibited strong cytotoxicity.[6] In our case, six of the seven new isolated compounds are prenylated and the prenylation seemed to influence the cytotoxicity of this compound family. However our SAR data are not conclusive, and further investigation is required to clarify this aspect.

EXPERIMENTAL SECTION

General Experimental Procedures. IR spectra were recorded on a Nicolet NEXUS 470 spectrophotometer in KBr discs. UV spectra were recorded on a Beckman DU640 spectrophotometer. ^{1}H NMR, ^{13}C NMR, and DEPT spectra and 2D NMR were recorded on a JEOL JNM-ECP 600 spectrometer using TMS as internal standard, and chemical shifts were recorded as δ values. ESIMS was measured on a Micromass Q-TOF Ultima Global GAA076 LC mass spectrometer. Semipreparative HPLC was performed using an ODS column [YMC-Pack ODS-A, 10 × 250 mm, 5 μm, 4 mL/min].

Fungal Material. The fungal strain *A. taichungensis* ZHN-7-07 was isolated from the root soil of the mangrove plant *Acrostichum aureum* and was identified by ITS sequence. The voucher specimen is deposited in our laboratory at −20 °C. Working stocks were prepared on potato dextrose agar slants stored at 4 °C.

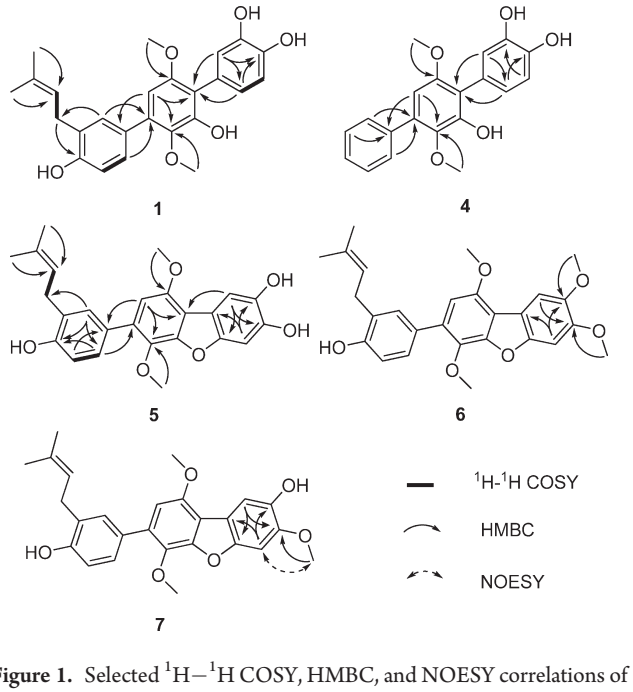


Figure 1. Selected ^{1}H−^{1}H COSY, HMBC, and NOESY correlations of compounds **1** and **4**−**7**.

Fermentation and Extraction. Fermentation was carried out as follows. *A. taichungensis* ZHN-7-07 was cultured under static conditions at 28 °C in 1000 mL Erlenmeyer flasks containing 300 mL of fermentation media (mannitol 20 g, maltose 20 g, glucose 10 g, monosodium glutamate 10 g, KH_2PO_4 0.5 g, $MgSO_4 \cdot 7H_2O$ 0.3 g, yeast extract 3 g, and corn steep liquor 1 g, dissolved in 1 L seawater, pH 6.5). After 30 days of cultivation, 30 L of whole broth was filtered through cheesecloth to separate the broth supernatant and mycelia. The former was extracted with ethyl acetate, while the latter was extracted with acetone. The acetone extract was evaporated under reduced pressure to afford an aqueous solution and then extracted with ethyl acetate. The two ethyl acetate extracts were combined and concentrated under reduced pressure to give a crude extract (40.0 g).

Purification. The crude extract (40.0 g) was applied to a silica gel (300−400 mesh) column and was separated into five fractions (Fr.1−Fr.5) using a step gradient elution of petroleum ether/acetone. Fr.3, eluted with 9:1 petroleum ether/acetone, was fractionated on a C-18 ODS column using a step gradient elution of MeOH/H_2O and was separated into 10 subfractions (Fr.3.1−Fr.3.10). Fr.3.7 was further purified by semipreparative HPLC (80:20 MeOH/H_2O, 4 mL/min) to give compound **7** (50 mg, t_R 9.8 min). Fr.3.8 was applied on semipreparative HPLC (80:20 MeOH/H_2O, 4 mL/min) to afford compound **6** (5.0 mg, t_R 15.0 min). Fr.4, eluted with 8:2 petroleum ether/acetone, was fractionated on a C-18 ODS column using a step gradient elution of MeOH/H_2O and was separated into 10 subfractions (Fr.4.1−Fr.4.10). Fr.4.5 was separated on Sephadex LH-20 using $CHCl_3$/MeOH (50:50) and further purified by semipreparative HPLC (70:30 MeOH/H_2O, 4 mL/min) to afford compounds **1** (9.5 mg, t_R 9.5 min), **3** (1.8 mg, t_R 11.0 min), **10** (1.5 mg, t_R 12.0 min), and **14** (20.0 mg, t_R 6.36 min), respectively. Compounds **4** (10.0 mg, t_R 17 min), **11** (25.0 mg, t_R 5.5 min), and **12** (20.0 mg, t_R 17.7 min) were also obtained from Fr.4.5, which was applied on Sephadex LH-20 using $CHCl_3$/MeOH (50:50) and purified by semipreparative HPLC (60:40 MeOH/H_2O, 4 mL/min). Fr.4.7 was applied on Sephadex LH-20 using $CHCl_3$/MeOH (50:50) and further purified by semipreparative HPLC (70:30 MeOH/H_2O, 4 mL/min) to yield **2** (2.0 mg, t_R 14.0 min), **5** (11.0 mg, t_R 15.0 min), **8** (3.0 mg, t_R 14.5 min), **9** (1.2 mg, t_R 13.0 min), and **15** (5.0 mg, t_R 9.9 min), respectively. Fr.5, eluted with 7:3 petroleum ether/acetone, was fractionated on a C-18 ODS column using a step gradient elution of MeOH/H_2O and was further purified by semipreparative HPLC (50:50 MeOH/H_2O, 4 mL/min) to give compound **13** (30 mg, t_R 9.8 min).

Cytotoxicity Assay. Cytotoxic activities of **1**−**8** and **11**−**15** were evaluated by the MTT method using P388 and HL-60 cell lines and the SRB method using the A-549 cell line with ADM as positive control.[12]

Prenylterphenyllin A (***1***)*:* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 216 (4.68), 282 (4.35) nm; IR (KBr) ν_{max} 3397, 2965, 2935, 2841, 1672, 1608, 1486, 1460, 1398, 1125, 1108, 1069, 820 cm^{-1}; ^{1}H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m*/*z* 423.1814 (calcd for $C_{25}H_{27}O_6$, 423.1808; Δ +1.5 ppm).

Prenylterphenyllin B (***2***)*:* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 210 (4.65), 277 (4.39) nm; IR (KBr) ν_{max} 3356, 2961, 2931, 2849, 1608, 1521, 1485, 1459, 1399, 1263, 1172, 1105, 1071, 1019, 823 cm^{-1}; ^{1}H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m*/*z* 407.1850 (calcd for $C_{25}H_{27}O_5$, 407.1858; Δ −2.1 ppm).

Table 3. Cytotoxicities against HL-60, A-549, and P-388 Cell Lines of Compounds 1−8 and 11−15 (IC_{50} (μM))[a]

	1	2	3	4	5	6	7	8	11	12	13	14	15
HL-60	1.53	38.46	28.24	9.89	11.83	76.65	10.12	2.75	9.86	10.98	11.04	77.56	16.52
A-549	8.32	>100	>100	40.71	53.2	8.61	12.26	3.62	34.68	12.17	14.32	19.34	83.60
P-388	10.89	12.57	86.16	2.70	16.5	1.57	75.72	1.99	28.06	17.76	9.13	46.83	96.89

[a] Data represent mean values of three independent experiments and were determined by the SRB method using the A-549 cell line and the MTT method using P388 and HL-60 cell lines.

dx.doi.org/10.1021/np2000478 |*J. Nat. Prod.* 2011, 74, 1106–1110

*Prenylterphenyllin C (**3**):* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 215 (4.66), 282 (4.33) nm; IR (KBr) ν_{max} 3397, 2965, 2933, 2845, 1672, 1608, 1524, 1487, 1435, 1397, 1225, 1107, 1069, 819 cm^{-1}; ^1H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m/z* 423.1815 (calcd for $C_{25}H_{27}O_6$, 423.1808; Δ +1.7 ppm).

*4-Dehydro-3-hydroxyterphenyllin (**4**):* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 209 (4.39), 273 (4.04) nm; IR (KBr) ν_{max} 3492, 3411, 2933, 1682, 1604, 1561, 1519, 1480, 1403, 1360, 1200, 1118, 1071, 836, 773 cm^{-1}; ^1H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m/z* 339.1230 (calcd for $C_{20}H_{19}O_5$, 339.1232; Δ −0.7 ppm).

*Prenylcandidusin A (**5**):* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 221 (4.62), 283 (4.32), 296 (4.30), 334 (4.44) nm; IR (KBr) ν_{max} 3383, 2933, 1607, 1518, 1469, 1393, 1327, 1233, 1121, 1064, 819 cm^{-1}; ^1H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m/z* 421.1652 (calcd for $C_{25}H_{25}O_6$, 421.1651; Δ +0.2 ppm).

*Prenylcandidusin B (**6**):* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 221 (4.47), 282 (4.14), 296 (4.16), 331 (4.27) nm; IR (KBr) ν_{max} 3425, 2932, 2836, 1602, 1519, 1442, 1430, 1382, 1328, 1240, 1205, 1132, 1097,1017, 808 cm^{-1}; ^1H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m/z* 449.1960 (calcd for $C_{27}H_{29}O_6$, 449.1964; Δ −0.9 ppm).

*Prenylcandidusin C (**7**):* colorless, amorphous solid; UV (MeOH) λ_{max} (log ε) 221 (4.38), 283 (4.05), 296 (4.06), 333 (4.19) nm; IR (KBr) ν_{max} 3426, 2966, 2930, 2483, 1604, 1519, 1479, 1438, 1391, 1234, 1184, 1129, 1022, 817 cm^{-1}; ^1H and ^{13}C NMR see Tables 1 and 2; HRESIMS $[M + H]^+$ *m/z* 435.1806 (calcd for $C_{26}H_{27}O_6$, 435.1808; Δ −0.4 ppm).

■ ASSOCIATED CONTENT

Supporting Information. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

This work was financially supported by the Chinese National Science Fund (No. 30973627), the Shandong Provincial Natural Science Fund (No. ZR2009CZ016), the Public Projects of State Oceanic Administration (No. 2010418022-3), and the Program for Changjiang Scholars and Innovative Research Team in University (No. IRT0944). The cytotoxicity assays were performed at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences. We also thank Dr. A. R. Pereira (Scripps Institution of Oceanography, La Jolla) for helping with the manuscript preparation.

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