Indole Alkaloids from *Cephalanceropsis gracilis*

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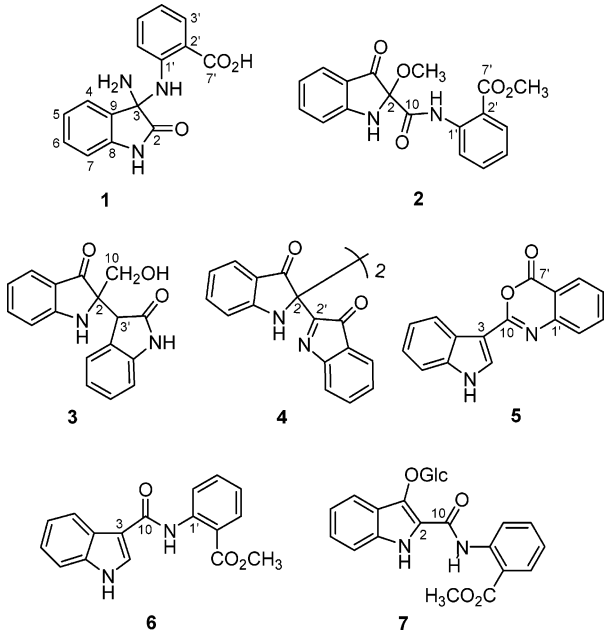
Purification of $CHCl_3$ and EtOAc solubles of the MeOH extract of *Cephalanceropsis gracilis* afforded seven new indole alkaloids, cephalinones A (**1**), B (**2**), C (**3**), and D (**4**) and cephalandoles A (**5**), B (**6**), and C (**7**), besides eight known compounds. The structures of the new compounds were determined by spectroscopic analysis. All 15 indole alkaloids were evaluated for their cytotoxic effects on MCF-7, NCI-H460, and SF-268 cell lines by the MTT method. Only cephalinone-F (**6**) showed significant cytotoxicity.

Cephalanceropsis gracilis (Orchidaceae) is a native orchid of Taiwan.[1] Thus far, there have been no literature reports on the chemistry and biological activity of this species. In our ongoing search for plant-derived anticancer agents, we had the chance to analyze *C. gracilis*. Its crude MeOH extract showed significant cytotoxicity against human breast carcinoma (MCF-7), lung carcinoma (NCI-H460), and central nervous system carcinoma (SF-268) cell lines. Thus, successive column and preparative thin-layer chromatographic separations of the $CHCl_3$ and EtOAc solubles yielded 15 indole alkaloids, including seven new compounds, cephalinones A (**1**), B (**2**), C (**3**), and D (**4**) and cephalandoles A (**5**), B (**6**), and C (**7**), as well as eight known compounds, isatin,[2] methyl dioxindole-3-acetate,[3] indigo,[4] indirubin,[4] indole-3-carbaldehyde,[5] indole-3-carboxylic acid,[5] (*S*)-3-(2-oxopropyl)-3-hydroxyindolin-2-one,[6,7] and isatan.[8,9] Herein we describe the isolation and structural elucidation of the new compounds and the results of their cytotoxicities toward a panel of human cancer cell lines.



Results and Discussion

Cephalinone A (**1**), isolated as an optically active white, amorphous powder, was determined to have the molecular formula $C_{15}H_{12}N_3O_3$ by the pseudomolecular ion at *m*/*z* 284.1037 in the HRFABMS. The ^{1}H NMR and COSY spectra revealed two sets of *o*-disubstituted benzene rings, one at δ 6.93 (1H, d, J = 8.0 Hz, H-7), 7.03 (1H, t, J = 8.0 Hz, H-5), 7.29 (1H, t, J = 8.0 Hz, H-6), and 7.38 (1H, d, J = 8.0 Hz, H-4) and the other at δ 7.11 (1H, t, J = 8.0 Hz, H-4′), 7.39 (1H, t, J = 8.0 Hz, H-5′), 8.07 (1H, d, J = 8.0 Hz, H-3′), and 8.47 (1H, d, J = 8.0 Hz, H-6′). From HMBC and HMQC spectra, it was apparent that carbons corresponding to the former benzene ring as well as an amidic C-2 (δ 170.3) and an oxygenated quaternary C-3 (δ 80.8) were very close to the 3,3-disubstituted indolin-2-one moiety similar to that in 3-(2-oxopropyl)-3-hydroxyindolin-2-one and isatan, which were also isolated from this plant. The carbon signals of the latter benzene ring at δ 116.2 (C-2′), 120.9 (C-6′), 124.2 (C-4′), 132.4 (C-3′), 132.7 (C-5′), and 140.5 (C-1′) and a carbonyl signal at δ 179.0 (C-7′) along with very broad IR carboxylic OH absorption at 3000 cm^{-1} indicated a benzoic acid moiety. The HMBC correlations between H-4 and C-3 as well as H-3′ and C-7′ supported these partial structures. The relative downfield shift of aliphatic C-3 was attributed to the attachment of two amino groups directly to C-3. Subsequently, the downfield shift of aromatic C-1′ inferred that a NH group connected the indolinone and benzoic acid together through C-3 and C-1′. Hence, compound **1** possessed the structure 2-(3-amino-2-oxoindolin-3-yl)aminobenzoic acid and was named cephalinone A. This structure was further supported by the strong MS fragment ion at *m*/*z* 147 ($C_8H_7N_2O$, 3-aminoindolinone cation), representative of the molecular ion minus an aminobenzoic acid.

Cephalinone B (**2**) was isolated as an optically active yellow, amorphous powder. The molecular formula was established as $C_{18}H_{16}N_2O_5$ by HRFABMS, which showed the pseudomolecular ion at *m*/*z* 341.1139. Two sets of *o*-disubstituted benzene rings at δ 6.94 (1H, t, J = 8.4 Hz, H-5), 7.05 (1H, d, J = 8.4 Hz, H-7), 7.53 (1H, t, J = 8.4 Hz, H-6), 7.59 (1H, d, J = 8.4 Hz, H-4) and 7.13 (1H, t, J = 7.8 Hz, H-4′), 7.50 (1H, t, J = 7.8 Hz, H-5′), 8.07 (1H, d, J = 7.8 Hz, H-3′), 8.59 (1H, d, J = 7.8 Hz, H-6′) were clearly observed in the ^{1}H NMR spectrum and were assigned with the aid of COSY correlations. Along with the first set of *o*-disubstituted benzene ring signals, the HMBC correlations of H-4 and a NH (δ 5.34, H-1) with the ketonic carbon C-3 (δ 195.6) and between the methoxyl protons (δ 3.45, 2-OCH_3) and a quaternary carbon C-2 (δ 93.2) inferred the 2-substituted-2-methoxyindolin-3-one skeleton for **2**. Similarly, in addition to the second set of benzene ring signals, the HMBC cross-peaks of both H-3′ and a methoxyl (δ 4.02, 7′-OCH_3) with a carboxylic C-7′ (δ 167.9) and the value of the chemical shift of C-1′ at δ 140.1 indicated the presence of an *o*-aminobenzoic acid methyl ester moiety. The HMBC correlation from NH of the indolinone moiety to an amidic C-10 (δ 164.4) and the NOE correlation between two NH and

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2-OCH_3 indicated an amide bond between these two moieties. Consequently, the structure **2** was assigned for cephalinone B.

Cephalinone C (**3**) was isolated as an optically active yellow, amorphous powder. The HREIMS showed a molecular ion at *m*/*z* 294.1002, consistent with the molecular formula $C_{17}H_{14}N_2O_3$. Comparison of the ^{1}H and ^{13}C NMR spectra of **3** with those of **2**, and HMBC correlations of H-4 (δ 7.26) with C-3 (δ 201.0) and NH (δ 7.14, H-1) with C-2 (δ 71.1), C-3, and C-9 (δ 121.2), indicated the presence of a 2,2-disubstituted indolin-3-one unit in **3**. The remaining proton signals at δ 6.74 (1H, d, J = 7.5 Hz, H-7′), 6.81 (1H, t, J = 7.5 Hz, H-5′), 7.12 (1H, t, J = 7.5 Hz, H-6′), and 7.29 (1H, d, J = 7.5 Hz, H-4′) together with an amidic C-2′ (δ 175.1) and a methine C-3′ (δ 48.4) were indicative of a 3′-substituted indolin-2′-one unit. This was further substantiated by the HMBC correlations of H-3′ (δ 3.90) with C-2′ (δ 175.1), C-4′ (δ 125.8), C-8′ (δ 143.5), and C-9′ (δ 125.6) and NH (δ 10.29, H-1′) with C-2′, C-3′ (δ 48.4), C-8′, and C-9′. H-3′ also showed HMBC correlations with C-2 and C-3, indicating that the two units were linked via C-2 and C-3′. The other substituent on C-2 was determined to be CH_2OH due to the HMBC correlation of the oxygenated methylene H-10 (δ 3.82) with C-2 and the hydroxyl 10-OH (δ 5.04) with C-2 and C-10 (δ 62.7). Thus, the structure of 2-hydroxymethyl-2-(2-oxoindolin-3-yl)indolin-3-one was established for cephalinone C (**3**).

Cephalinone D (**4**) was isolated as an optically active red, amorphous powder. The HRFABMS showed a pseudomolecular ion at *m*/*z* 523.1404, corresponding to the molecular formula $C_{32}H_{18}N_4O_4$. A set of *o*-disubstituted benzene ring signals in the ^{1}H and ^{13}C NMR spectra and the HMBC correlations from H-4 (δ 7.46) to C-3 (δ 195.6) and from NH (δ 8.52, H-1) to C-2 (δ 75.5), C-3, C-8 (δ 162.0), and C-9 (δ 119.5) indicated a 2,2-disubstituted indolin-3-one unit for **4**. Another set of four mutually coupled proton signals assignable to an *o*-disubstituted benzene ring together with an imino carbon C-2′ (δ 162.0) and a carbonyl C-3′ (δ 179.6) as well as the HMBC correlation between H-4′ (δ 7.70) and C-3′ indicated the existence of a 2-substituted 3*H*-indol-3-one unit. A carbon−carbon bond via C-2 and C-2′ between these two units was proved by the HMBC correlation between NH (H-1) and C-2′. From the aforementioned spectroscopic analysis, a 2-(3-oxoindolin-2-yl)indol-3-one ($C_{16}H_9N_2O_2$) skeleton was deduced. Thus, the ^{1}H and ^{13}C NMR spectra showed only half of the total signals for the protons and carbons available in its molecular formula, indicating that this compound was a symmetrical dimer of 2-(3-oxoindolin-2-yl)indol-3-one with the linkage occurring at C-2. Consequently, the C-2 carbon−carbon linkage between two identical indolinone moieties completed the structure **4** for cephalinone D.

The absolute configurations of the indolinone moiety of **1**−**4** could not be determined due to insufficient amounts of these materials.

Cephalandole A (**5**) was isolated as a yellow, amorphous powder and was determined to have the molecular formula $C_{16}H_{10}N_2O_2$ by HREIMS data (*m*/*z* 262.0742). The ^{1}H NMR spectrum showed two sets of signals for two *o*-disubstituted benzene rings. One set at δ 7.27 (2H, m, H-5 and -6), 7.56 (1H, d, J = 8.1 Hz, H-7), and 8.88 (1H, d, J = 8.1 Hz, H-4) together with a doublet at δ 8.81 (1H, J = 3.0 Hz, H-2) and a broad signal at δ 11.11 (1H, NH) indicated a 3-substituted indole moiety. This was confirmed by the HMBC correlations of H-2 with C-3 (δ 112.3), C-8 (δ 137.9), and C-9 (δ 127.3) and the NOE correlations of NH with H-2 and H-7. The other set of benzene ring signals resonating at δ 7.35 (1H, d, J = 7.8 Hz, H-6′), 7.43 (1H, t, J = 7.8 Hz, H-4′), 7.49 (1H, t, J = 7.8 Hz, H-5′), and 7.89 (1H, d, J = 7.8 Hz, H-3′) combined with signals of C-7′ at δ 153.0 and C-10 at δ 149.0 were attributed to a 10-substituted benzooxazinone moiety. The connectivity between these two moieties by a carbon−carbon bond between C-3 and C-10 was inferred by the HMBC correlation of H-2 with C-10. Thus, the structure 2-(1*H*-indol-3-yl)-4*H*-benzo[*d*][1,3]oxazin-4-one was deduced for cephalandole A (**5**).

Cephalandole B (**6**) was isolated as a yellowish, amorphous powder. The HREIMS determined its molecular formula as $C_{17}H_{14}N_2O_3$ due to the molecular ion at *m*/*z* 294.1005. The ^{1}H NMR spectrum of **6** also showed signals for two *o*-disubstituted benzene rings in the molecule. The ^{1}H and ^{13}C NMR spectra of **6** showed resemblance to compound **5** with signals attributable to a 3-substituted indole skeleton. The remaining proton and carbon signals were identical to those of the *o*-aminobenzoic acid methyl ester moiety in **2**. The linkage between these two moieties through an amide bond between C-3 (δ 113.4) and C-1′ (δ 142.5) was inferred by the presence of an amidic C-10 at δ 163.6 and the HMBC correlations from H-2 (δ 7.96) and 1′-NH (δ 11.73) to C-10. The above analysis led us to conclude that methyl *o*-(indole-3-carboxamido)benzoate (**6**) is the structure of cephalandole B.

Cephalandole C (**7**) was isolated as an optically active yellowish, amorphous powder. The HREIMS of this compound showed the molecular ion at *m*/*z* 472.1484 corresponding to the molecular formula $C_{23}H_{24}N_2O_9$. The strong peak at *m*/*z* 310 produced by the loss of 162 amu from the molecular ion indicated that compound **7** was a monoglycoside. The anomeric proton H-1″ at δ 4.91 (1H, d, J = 7.7 Hz) and ^{13}C signals at δ 61.1 (C-6″), 69.9 (C-4″), 73.2 (C-2″), 76.5 (C-3″), 77.4 (C-5″), and 105.4 (C-1″) indicated that the sugar moiety was glucose. The ^{1}H and ^{13}C resonances corresponding to the aglycon moiety consisted of indole and methyl *o*-carboxamidobenzoate and were similar to those of **6** except that the H-2 resonance was absent in the ^{1}H NMR spectrum and the ^{13}C chemical shifts associated with C-2 and C-3 were shifted significantly, indicating a difference in the substitution of the 2,3-disubstituted indole. The linkage of the glucose unit to C-3 was supported by the HMBC correlation observed between H-1″ and C-3 and NOE correlation between H-1″ and H-4 (δ 7.99). Consequently, the *o*-carboxamidobenzoate substituent replaced the C-2 proton of **6**. This was accompanied by a upfield shift of C-2 (δ 118.6) and a downfield shift of C-3 (δ 137.6) resonances. Therefore, structure **7** was assigned for cephalandole C.

All of the indoles isolated from $CHCl_3$ and EtOAc extracts of *C. gracilis* were subjected to cytotoxic evaluation against MCF-7, NCI-H460, and SF-268 cell lines. Only cephalinone D (**4**) showed significant cytotoxicity against MCF-7, NCI-H460, and SF-268 cell lines with IC_{50} values of 7.57, 7.8, and 12.2 μM, respectively.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. UV spectra were recorded on an Agilent 8453 spectrophotometer. IR spectra were recorded on a Nicolet Magna FT-IR spectrophotometer. NMR spectra were recorded on Bruker Avance-300, AMX-400, and Avance-500 FT-NMR spectrometers; all chemical shifts were given in ppm from tetramethylsilane as an internal standard. Mass spectra were obtained on a VG 70-250S spectrometer by a direct inlet system.

Plant Material. Whole plants of *Cephalantheropsis gracilis* were collected from Pingtung Hsien, Taiwan, in December 2004. The collection was authenticated by Professor C. S. Kuoh, Department of Life Sciences, National Cheng Kung University, Tainan, Taiwan. A voucher specimen (No. PLW-0401) was deposited in the Herbarium of National Cheng Kung University, Tainan, Taiwan.

Extraction and Isolation. The dried *C. gracilis* plants (2.4 kg) were extracted with MeOH (7 × 5 L) under reflux. The combined extracts were concentrated under reduced pressure to a dark brown syrup. The syrup was suspended in H_2O and then partitioned successively with hexane, $CHCl_3$, and EtOAc. The $CHCl_3$ extract (30 g) was chromatographed on a silica gel column by eluting with a gradient of hexane−$CHCl_3$ (1:2 to $CHCl_3$) to yield 12 fractions. After repeated chromatography on silica gel followed by preparative TLC purification, cephalandole A (**5**) (7 mg), cephalinone B (**2**) (6 mg), cephalandole C (**7**) (20 mg), indirubin (48 mg), cephalinone D (**4**) (30 mg), isatin (7 mg), indole-3-carbaldehyde (3 mg), cephalinone C (**3**) (6 mg), indole-

Table 1. ^{1}H NMR Data of Indoles **1**−**7** (δ, multiplicity, *J*, Hz in parentheses)

	1 (CD_3OD)	**2** ($CDCl_3$)	**3** (DMSO-d_6)	**4** (DMSO-d_6)	**5** (acetone-d_6)	**6** ($CDCl_3$)	**7**[a] (DMSO-d_6)
H-1		5.34 s	7.14 s	8.52 s	11.11 br s	8.64 br s	11.39 s
H-2					8.81 d (3.0)	7.96 d (2.9)	
H-4	7.38 d (8.0)	7.59 d (8.4)	7.26 d (7.5)	7.46 d (8.4)	8.88 d (8.1)	8.41 d (8.0)	7.99 d (8.0)
H-5	7.03 t (8.0)	6.94 t (8.4)	6.62 t (7.5)	6.82 t (8.4)	7.27 m	7.31 m	7.02 t (8.0)
H-6	7.29 t (8.0)	7.53 t (8.4)	7.35 t (7.5)	7.56 t (8.4)	7.27 m	7.31 m	7.22 t (8.0)
H-7	6.93 d (8.0)	7.05 d (8.4)	6.82 d (7.5)	6.87 d (8.4)	7.56 d (8.1)	7.43 d (8.0)	7.39 d (8.0)
H-10			3.82 m				
H-1′			10.29 s				
H-3′	8.07 d (8.0)	8.07 d (7.8)	3.90 s		7.89 d (7.8)	8.07 d (8.0)	7.92 d (8.0)
H-4′	7.11 t (8.0)	7.13 t (7.8)	7.29 d (7.5)	7.70 d (7.9)	7.43 t (7.8)	7.08 t (8.0)	7.20 t (8.0)
H-5′	7.39 t (8.0)	7.50 t (7.8)	6.81 t (7.5)	7.08 t (7.9)	7.49 t (7.8)	7.59 t (8.0)	7.61 t (8.0)
H-6′	8.47 d (8.0)	8.59 d (7.8)	7.12 t (7.5)	7.41 t (7.9)	7.35 d (7.8)	8.93 d (8.0)	8.48 d (8.0)
H-7′			6.74 d (7.5)	6.91 d (7.9)			
1′-NH		12.04 br s				11.73 br s	11.11 s
2-OCH_3		3.45 s					
7′-OCH_3		4.02 s				3.95 s	3.86 s
3- or 10-OH			5.04 t (5.4)				

[a] The glucose signals at δ 3.17 (1H, t, J = 7.7 Hz, H-4″), 3.25 (1H, m, H-5″), 3.27 (1H, m, H-3″), 3.37 (1H, m, H-6″a), 3.57 (1H, m, H-2″), 3.70 (1H, dd, J = 11.1, 4.5 Hz, H-6″b), 4.49 (1H, t, J = 5.3 Hz, 6″-OH), 4.91 (1H, d, J = 7.7 Hz, H-1″), 5.01 (1H, d, J = 4.9 Hz, 4″-OH), 5.09 (1H, d, J = 4.3 Hz, 3″-OH), 5.36 (1H, d, J = 5.8 Hz, 2″-OH).

Table 2. ^{13}C NMR Data of Indoles **1**−**7**

	1 (CD_3OD)	**2** ($CDCl_3$)	**3** (DMSO-d_6)	**4** (DMSO-d_6)	**5** (acetone-d_6)	**6** ($CDCl_3$)	**7**[a] (DMSO-d_6)
C-2	170.3	93.2	71.1	75.5	134.6	127.3	118.6
C-3	80.8	195.6	201.0	195.6	112.3	113.4	137.6
C-4	125.2	125.1	123.3	124.7	124.1	121.5	120.7
C-5	123.8	121.2	117.2	119.3	122.5	122.0	119.6
C-6	131.4	138.5	136.3	139.5	124.1	123.4	124.7
C-7	111.5	113.9	112.1	112.2	112.8	111.4	112.6
C-8	144.3	161.9	161.6	162.0	137.9	136.3	134.1
C-9	131.7	120.2	121.2	119.5	127.3	125.7	118.8
C-10		164.4	62.7		149.0	163.6	159.1
C-1′	140.5				146.2	142.5	139.2
C-2′	116.1	116.5	175.1	162.0	133.2	114.6	119.2
C-3′	132.4	131.1	48.4	179.6	128.9	130.9	130.5
C-4′	124.2	123.4	125.8	124.4	126.1	121.8	123.2
C-5′	132.7	134.3	120.9	122.7	129.6	134.8	133.3
C-6′	120.9	120.4	128.1	136.0	116.7	120.5	122.2
C-7′	179.0	167.9	109.1	112.8	153.0	169.1	166.7
C-8′			143.5	147.9			
C-9′			125.6	123.8			
2-OCH_3		52.3					
7′-OCH_3		52.9				52.3	52.2

[a] The glucose signals at δ 61.1 (C-6″), 69.9 (C-4″), 73.2 (C-2″), 76.5 (C-3″), 77.4 (C-5″), 105.4 (C-1″).

3-carboxylic acid (3 mg), and indigo (328 mg) were isolated successively. The EtOAc extract (20 g) was subjected to column chromatography on Cosmosil 75 C18 and eluted with a gradient of H_2O−MeOH (from H_2O to MeOH) to give seven fractions. After repeated chromatography on silica gel and preparative TLC purification, methyl dioxindole-3-acetate (4 mg), cephalinone A (**1**) (3 mg), isatan (51 mg), cephalandole B (**6**) (23 mg), and (*S*)-3-(2-oxopropyl)-3-hdyroxyindolin-2-one (21 mg) were obtained.

Cephalinone A (1): white, amorphous powder; $[\alpha]_D$ −7.6 (*c* 0.18, MeOH); UV (CH_3OH) λ_{max} (log ϵ) 207 (3.8), 255 (3.2), 293 (3.0), 358 (2.7) nm; IR (KBr) ν_{max} 3700−2600 (br), 1720, 1655, 1619, 1586 cm^{-1}; ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; FABMS *m*/*z* (rel int) 284 ([M + H]$^+$, 25), 147 (48); HRFABMS *m*/*z* 284.1037 [M + H]$^+$ (calcd for $C_{15}H_{14}N_3O_3$, 284.1035).

Cephalinone B (2): yellow, amorphous powder; $[\alpha]_D$ −92.5 (*c* 0.040, $CHCl_3$); UV ($CHCl_3$) λ_{max} (log ϵ) 263 (3.6), 315 (3.5), 385 (3.1) nm; IR (KBr) ν_{max} 3334, 2953, 2853, 1702, 1699, 1617, 1587, 1525 cm^{-1}; ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; FABMS *m*/*z* (rel int) 341 ([M + H]$^+$, 9), 221 (100); HREIMS *m*/*z* 341.1139 [M + H]$^+$ (calcd for $C_{18}H_{17}N_2O_5$, 341.1138).

Cephalinone C (3): yellow, amorphous powder; $[\alpha]_D$ −8.4 (*c* 0.095, $CHCl_3$); UV (CH_3OH) λ_{max} (log ϵ) 265 (2.7), 314 (2.6) nm; IR (KBr) ν_{max} 3307, 2924, 2853, 1716, 1622, 1514 cm^{-1}; ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; EIMS *m*/*z* (rel int) 294 (M$^+$, 33), 262 (49), 234 (29), 205 (18), 84 (100); HREIMS *m*/*z* 294.1002 [M]$^+$ (calcd for $C_{17}H_{14}N_2O_3$, 294.1005).

Cephalinone D (4): red, amorphous powder; $[\alpha]_D$ −191.7 (*c* 0.045, CH_3OH); UV (CH_3OH) λ_{max} (log ϵ) 228 (4.0), 174 (3.7), 308 (3.6), 424 (3.3), 546 (3.5) nm; IR (KBr) ν_{max} 3316, 1711, 1611 cm^{-1}; ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; FABMS *m*/*z* (rel int) 523 ([M + H]$^+$, 4), 262 (100); HRFABMS *m*/*z* 523.1404 [M + H]$^+$ (calcd for $C_{32}H_{19}N_4O_4$, 523.1406).

Cephalandole A (5): yellow, amorphous powder; UV (CH_3OH) λ_{max} (log ϵ) 255 (3.0), 282 (2.9), 394 (3.0) nm; IR (KBr) ν_{max} 3298, 2921, 1719, 1605, 1533 cm^{-1}; EIMS *m*/*z* (rel int) 262 (M$^+$, 73), 234 (100), 205 (13), 175 (12); ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; HREIMS *m*/*z* 262.0742 [M]$^+$ (calcd for $C_{16}H_{10}N_2O_2$, 262.0743).

Cephalandole B (6): yellowish, amorphous powder; UV ($CHCl_3$) λ_{max} (log ϵ) 263 (2.9), 347 (2.8) nm; IR (KBr) ν_{max} 3264, 1650, 1587, 1530 cm^{-1}; EIMS *m*/*z* (rel int) 294 (M$^+$, 30), 281 (35), 248 (43), 151 (49), 144 (57), 72 (100); ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; HREIMS *m*/*z* 294.1002 [M]$^+$ (calcd for $C_{17}H_{14}N_2O_3$, 294.1005).

Cephalandole C (7): yellowish, amorphous powder; $[\alpha]_D$ +39.1 (*c* 0.070, CH_3OH); UV (CH_3OH) λ_{max} (log ϵ) 207 (4.2), 260 (3.5), 297 (3.4), 351 (3.3) nm; IR (KBr) ν_{max} 3393, 1681, 1649, 1589 cm^{-1}; ^{1}H NMR data, Table 1; ^{13}C NMR data, Table 2; EIMS *m*/*z* (rel int) 472

(M^+, 0.1), 310 (53), 278 (100); HREIMS *m*/*z* 472.1484 $[M]^+$ (calcd for $C_{23}H_{24}N_2O_9$, 472.1482).

Cytotoxicity Assay. The cytotoxicity assay was carried out according to the procedure described previously.[10]

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References and Notes

(1) Su, H. J. *Flora of Taiwan*, 2nd ed.; Editorial Committee of the Flora of Taiwan: Taipei, Taiwan, 2000; Vol. 5, pp 795−796.
(2) Yoshikawa, M.; Murakami, T.; Kishi, A.; Sakurama, T.; Matsuda, H.; Nomura, M.; Matsuda, H.; Kubo, M. *Chem. Pharm. Bull.* **1998**, *46*, 886−888.
(3) Kinashi, H.; Suzuki, Y.; Takeuchi, S.; Kawarada, A. *Agr. Biol. Chem.* **1976**, *40*, 2465−2470.
(4) Guengerich, F. P.; Sorrells, J. L.; Schmitt, S.; Krauser, J. A.; Aryal, P.; Meijer, L. *J. Med. Chem.* **2004**, *47*, 3236−3241.
(5) Wu, P. L.; Lin, F. W.; Wu, T. S.; Kuoh, C. S.; Lee, K. H.; Lee, S. J. *Chem. Pharm. Bull.* **2004**, *52*, 345−349.
(6) Kawasaki, T; Nagaoka, M.; Satoh, T.; Okamoto, A.; Ukon, R.; Ogawa, A. *Tetrahedron* **2004**, *60*, 3493−3503.
(7) Luppi, G.; Cozzi, P. G.; Monari, M.; Kaptein, B.; Broxterman, Q. B.; Tomasini, C. *J. Org. Chem.* **2005**, *70*, 7418−7421.
(8) Lefevre, L. *Bull. Soc. Chim. Fr.* **1916**, *19*, 113−116.
(9) Teuber, H. J.; Hohn, J. *Chem. Ber.* **1982**, *115*, 90−98.
(10) Chuang, T. H.; Lee, S. J.; Yang, C. W.; Wu, P. L. *Org. Biomol. Chem.* **2006**, *4*, 860−867.

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