

Isomalabaricane-Type Compounds from the Marine Sponge *Rhabdastrella* aff. *distincta*

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Fractionation of the marine sponge *Rhabdastrella* aff. *distincta* led to the isolation and characterization of four new isomalabaricane analogues, isogeoditin A (**1**), 13-(*E*)-isogeoditin A (**2**), isogeoditin B (**3**), and 22,23-dihydrostellettin B (**4**), along with seven known isomalabaricane derivatives (**5**–**11**). Methylation of **10** and **11** afforded methyl esters **12** and **13**. The structures of compounds **1**–**4** were determined on the basis of spectroscopic data analysis. All compounds were tested against a small panel of human tumor cell lines.

The genus *Rhabdastrella* of marine sponges is commonly distributed off Asian tropical oceans, such as the shallow coral reefs in southern mainland China, New Caledonia, and the Philippines.^{1–4} Thus far, only the species *R. globostrella* has been examined chemically, and a series of isomalabaricane-type nortriterpenoids and triterpenoids were isolated.^{1–4} However, the secondary metabolites from the species *R. aff. distincta* (Thiele) (Ancorinidae), collected off the inner reef of Hainan Island in the South China Sea, have not yet been reported. In this paper, we describe the isolation, structural elucidation, and biological activities of new isomalabaricane-type compounds from this sponge.

Results and Discussion

A methanol extract of *R. aff. distincta* was partitioned between CH₂Cl₂ and H₂O. The CH₂Cl₂ fraction was submitted to primary bioassay and exhibited broad cytotoxic activities toward the HL-60, PC-3MIE8, BGC-823, MDA-MB-423, Bel₇₄₀₂, and Hela tumor cell lines. This cytotoxic fraction was then subjected to repeated silica gel chromatographic separation followed by semipreparative HPLC isolation to afford four new compounds (**1**–**4**), together with seven known isomalabaricanes. Compounds **5**–**11** were identified as the nortriterpenoids geoditins A (**5**) and B (**6**) and the triterpenoids stellettins A (**7**), B (**8**), C (**9**), E (**10**), and rhabdastrellic acid A (**11**). Compounds **5** and **6** were obtained previously from the sponge *Geodia japonica*, which was collected from the area close to where our sample was collected.⁵ Compounds **7**–**10** commonly occur in the sponges *Stelletta*^{6–9} and *Jaspis*,^{10–13} but **11** has been reported only from *R. globostrella*.¹ Methylation of **10** and **11** afforded their methyl esters **12** and **13**, respectively, and **13** was identified as a new isomalabaricane derivative. The structures of all the known compounds were identified on the basis of their 1D and 2D NMR spectra, MS data, and optical rotations and by comparison of their spectroscopic data with those reported in the literature.

Compound **1** was obtained as a yellow oil, and its molecular formula was determined as C₂₉H₃₈O₄ by

HREIMS. The IR absorptions at 1698, 1647, 1601, and 1556 cm⁻¹ suggested the presence of conjugated carbonyl groups. The ¹H NMR spectrum displayed signals for five vinylic protons at δ 9.01 (1H, d, *J* = 15.5 Hz, H-15), 6.98 (1H, dd, *J* = 15.5, 11.5 Hz, H-16), 7.22 (1H, d, *J* = 11.5 Hz, H-17), 6.08 (1H, d, *J* = 12.0 Hz, H-23), and 5.78 (1H, d, *J* = 12.0 Hz, H-24) and seven methyl singlets involving four methyls on sp³ quaternary carbons at δ 0.59 (3H, s, CH₃-19), 1.04 (3H, s, CH₃-27), 1.05 (3H, s, CH₃-29), and 1.17 (3H, s, CH₃-28) and three vinylic methyls at δ 1.81 (3H, s, CH₃-26), 1.82 (3H, s, CH₃-18), and 2.21 (3H, s, CH₃-21). The ¹³C NMR spectrum exhibited 29 carbons, of which four were attributed to keto carbons [δ 216.3 (s), 205.4 (s), 197.4 (s), and 195.3 (s)] and eight were assigned to vinylic carbons [δ 148.3 (s), 140.3 (s), 139.3 (d), 129.8 (d), 140.1 (d), 140.8 (s), 137.6 (d), and 134.2 (d)]. The ¹H and ¹³C NMR features were characteristic of isomalabaricane-type compounds^{3,8} and largely in agreement with those of the known nortriterpenoid geoditin A.³ Additionally, compound **1** has the same molecular formula as that of geoditin A. The ¹H NMR spectrum of **1** differed from geoditin A in the side chain, where a *Z*-orientation between protons H-23 (δ 6.08, d, *J* = 12.0 Hz) and H-24 (δ 5.78, d, *J* = 12.0 Hz) was assigned instead of the *E*-geometry in geoditin A. The stereochemistry of the tricyclic ring system and the remaining double bonds in the side chain of **1** were identical to those of geoditin A on the basis of the NOESY and *J* values of vinylic protons. Therefore, the structure of **1** was identified as the 23(*Z*)-isomer of geoditin A and named isogeoditin A. Isogeoditin A (**1**) isomerized to its geometrical isomer, geoditin A, while exposed to air or kept in a NMR tube at high magnetic field.

Their HREIMS spectral data revealed that **2** and **1** have the same molecular formula (C₂₉H₃₈O₄), and the ¹H and ¹³C NMR spectra of **2** were closely comparable to those of **1**. The structure of **2** was determined as the 13(*E*)-isomer of **1** through the evidence of the upfield signal at δ 6.94 (1H, d, *J* = 15.0 Hz, H-15) along with downfield signal at δ 2.37 (3H, s, H-18), by comparison with those of **1**. This was supported by the presence of a NOE correlation between H-15 and the methyl proton signal at δ 1.46 (3H, s, H-29) and the absence of a NOE between H-18 and H₃-29. Further assignment of the NOE correlations confirmed that the remaining relative configuration of **2** is the same

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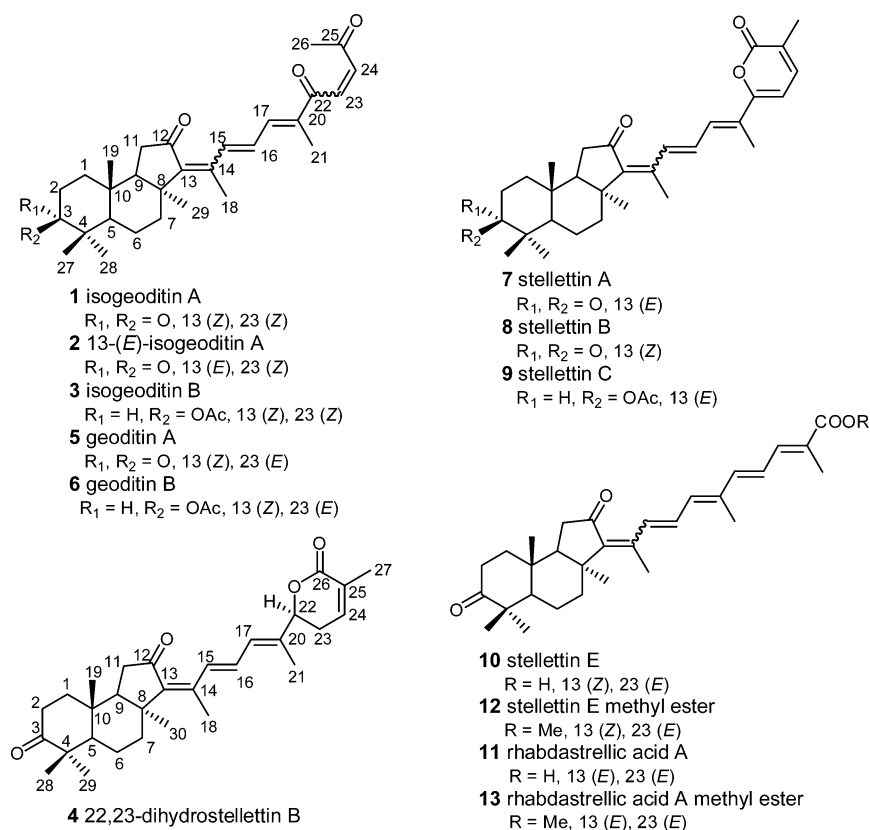
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Chart 1



as that of **1**. The structure of **2** was thus identified as 13-(*E*)-isogeoditin A.

The molecular formula of compound **3** was assigned as C₃₁H₄₂O₅ from the HREIMS, 42 amu higher than that of **1**. A comparison of ¹H and ¹³C NMR data of **3** with those of **1** indicated that **3** possesses the same side chain and tricyclic core as **1**. The NMR spectra of compound **3** differed from **1** in the presence of signals for an additional acetyl group [δ 1.89 (3H, s), 20.6 (q), 169.8 (s)] and an oxygen-bearing methine group [δ 4.83 (1H, dd, J = 5.0, 11.5 Hz, H-3), 80.3 (d, C-3)]. This functionality replaced a keto group at C-3 of **1**. HMBC correlations of the methyl protons at δ 1.00 (3H, s, H-27) and 1.05 (3H, s, H-28) with the methine carbon, C-3, and in turn the methine proton H-3 with carbonyl carbon of acetyl group and two methyl carbons at δ 29.0 (q, C-27) and 16.9 (q, C-28), supported the location of the acetoxy group at C-3. The relative configuration at C-3 was determined as H-3 α according to the NOE correlations between H-3 and H-28. Accordingly, the structure of **3** was determined as the 3 β -acetoxy derivative of **1** and named isogeoditin B.

HREIMS was used to determine the molecular formula of **4** as C₃₀H₄₀O₄, 2 amu higher than that of stellettin B (**8**).⁶ Interpretation of the 2D NMR spectra (COSY, HMQC, and HMBC) of **4** revealed that the tricyclic skeleton and partial side chain were the same as those of stellettin B. However, the DEPT and HMQC spectra of **4** contained signals for a new oxygen-bearing methine group [δ 4.87 (1H, dd, J = 3.5, 12.5 Hz, H-22), 82.6 (d, C-22)] and a new methylene group [δ 2.60 (2H, m, H-23), 28.7 (t, C-23)], while the double bond at C-22 of stellettin B was missing. These changes were deduced to result from hydrogenation of the C-23/C-24 double bond of stellettin B to form the α,β -unsaturated α -methyl- δ -lactone. This conclusion was supported by the COSY cross-peaks between H-22/H-23 and H-23/H-24 (δ 6.65, brs) and the HMBC correlations be-

tween the methyl protons at δ 1.97 (3H, s, 27-H) and carbons at δ 165.8 (s, C-26), 128.5 (s, C-25), and 138.9 (d, C-24), as well as between the methine proton H-22 and C-26, C-24, C-23, C-20 (δ 136.8, s) and C-21 (δ 13.0, q).

Table 1. ¹³C NMR Data of Compounds 1–4

position	1 ^a	2 ^b	3 ^a	4 ^b
1	31.3 t	31.6 t	32.8 t	31.4 t
2	33.5 t	33.4 t	25.3 t	33.5 t
3	216.3 s	218.9 s	80.3 d	219.0 s
4	46.8 s	46.8 s	38.1 s	46.9 s
5	45.5 d	45.5 d	46.6 d	45.4 d
6	19.7 t	19.7 t	18.1 t	19.6 t
7	37.1 t	36.6 t	37.8 t	37.2 t
8	44.9 s	45.1 s	44.5 s	44.8 s
9	47.6 d	47.7 d	49.6 d	47.9 d
10	34.8 s	34.8 s	35.4 s	34.8 s
11	37.0 t	38.6 t	36.5 t	36.8 t
12	205.4 s	207.5 s	205.2 s	206.2 s
13	148.3 s	149.3 s	148.8 s	145.9 s
14	140.3 s	139.4 s	139.9 s	142.4 s
15	139.3 d	140.3 s	139.0 d	133.9 d
16	129.8 d	130.7 d	129.2 d	129.4 d
17	140.1 d	140.3 d	139.8 d	128.7 d
18	15.7 q	15.5 q	15.4 q	16.0 q
19	23.4 q	23.5 q	22.0 q	23.5 q
20	140.8 s	139.4 s	138.7 s	136.8 s
21	12.0 q	12.0 q	11.5 q	13.0 q
22	195.3 s	191.0 s	194.8 s	82.6 d
23	137.6 d	137.5 d	137.0 d	28.7 t
24	134.2 d	134.6 d	133.9 d	138.9 d
25	197.4 s	198.0 s	197.0 s	128.5 s
26	29.7 q	30.0 q	29.1 q	165.8 s
27	29.2 q	29.3 q	29.0 q	17.1 q
28	19.7 q	19.7 q	16.9 q	29.2 q
29	24.5 q	26.2 q	24.3 q	19.4 q
30				24.7 q
CO			169.8 s	
Me (Ac)			20.6 q	

^a Measured in C₆D₆. ^b Measured in CDCl₃.

Table 2. ^1H NMR Data of Compounds 1–4

position	1 ^a	2 ^b	3 ^a	4 ^b
1	ddd, 6.0, 10.0, 12.0 1.61 ddd, 3.5, 10.0, 12.0	1.55 m, 2.18 m	1.00 m, 1.29 m	1.04 m 1.29 m
2	2.40 ddd, 6.0, 10.0, 12.0 2.28 ddd, 3.5, 10.0, 12.0	2.76 m, 2.42 m	1.92 m, 1.68 m	2.39 m 2.74 m
3			4.83 dd, 5.0, 11.5	
5	2.04 dd, 1.5, 11.5	2.40 m	1.60 m	2.37 m
6	1.15 m; 1.26 m	1.52m, 1.55 m	1.51 m, 1.52 m	1.24 m, 1.52 m
7	1.83m; 1.64 m	1.71 m, 1.70 m	1.30 m, 1.53 m	2.23 m
9	1.42 dd, 7.0, 15.0	1.91 m	1.51 m	1.90 m
11	1.97 dd, 16.5, 15.0 2.08 dd, 7.0, 16.5	2.29 m 2.39 m	2.07 m 2.11 m	2.18 m 2.25 m
15	9.01 d, 15.5	6.94 d, 15.0	9.01 d, 15.5	8.08 d, 15.0
16	6.98 dd, 11.5, 15.5	7.09 dd, 15.0, 11.0	6.96 dd, 15.5, 11.5	6.85 dd, 11.0, 15.0
17	7.22 d, 11.5	7.06 d, 11.0	7.22 d, 11.5	6.33 d, 11.0
18	1.82 s	2.37 s	1.78 s	2.07 s
19	0.59 s	0.88 s	0,78 s	0.88 s
21	2.21 s	2.09 s	2.21 s	1.93 s
22				4.87 dd, 3.5, 12.5
23	6.08 d, 12.0	6.75 d, 12.0	6.07 d, 12.0	2.60 m
24	5.78 d, 12.0	6.49 d, 12.0	5.77 d, 12.0	6.65 brs
26	1.81 s	2.30 s	1.83 s	
27	1.04 s	1.15 s	1.00 s	1.97 s
28	1.17 s	1.08 s	1.05 s	1.08 s
29	1.05 s	1.46 s	1.07 s	1.14 s
30				1.41 s
Ac			1.89 s	

^a Measured in C_6D_6 . ^b Measured in CDCl_3 .

Table 3. Cytotoxicity Data of the Active Compounds^{a,b}

compound	IC_{50} ($\mu\text{g/mL}$)					
	HL-60	PC-3MIE8	BGC-823	MDA-MB-423	Bel ₇₄₀₂	Hela
1	0.13	0.07	0.47	1.2	3.7	0.35
3	0.5	3.4	2.2	2.2	3.9	3.0
8	0.2	>5.0	>5.0	>5.0	>5.0	>5.0
9	>5.0	3.1	>5.0	>5.0	>5.0	>5.0
12	4.2	>5.0	>5.0	>5.0	>5.0	>5.0
colchicine	1.6	0.7	0.6	0.2	0.3	0.1

^a Compounds 2, 4–7, 10, 11, and 13 were inactive ($\text{IC}_{50} > 5 \mu\text{g/mL}$) for all cell lines in which they were evaluated. ^b Key to cell lines used: HL-60 (human promyelocytic leukemia); PC-3MIE8 (human prostate carcinoma); BGC-823 (human gastric carcinoma); MDA-MB-423 (human breast carcinoma); Bel₇₄₀₂ (human hepatocellular carcinoma); and Hela (human cervical carcinoma).

The J values of H-22 ($J_{\text{H}-22/\text{H}-23\text{a}} = 12.5 \text{ Hz}$ and $J_{\text{H}-22/\text{H}-23\text{b}} = 3.5 \text{ Hz}$) implied an axial–axial and an axial–equatorial coupling between H-22 and the H₂-23 methylene protons. The absolute stereochemistry of C-22 was assigned as *S* from its negative Cotton effect of the CD spectrum at 247 nm ($n \rightarrow \pi^*$ transition) using the Sznatzke rule.^{14,15} The structure of 4 was thus determined as 22,23-dihydrostellettin B.

Compounds 1–13 were submitted for bioassay against several cultured human tumor cell lines (HL-60, PC-3MIE8, BGC-823, MDA-MB-423, Bel₇₄₀₂, and Hela). Compound 1 showed significant cytotoxicity toward the former three cell lines (Table 3), but 2 had no cytotoxic activity, implying that isomalabaricanes in the *Z*-form at C-13 possess higher inhibition against tumor cell lines than those with the *E*-orientation. While comparing the cytotoxic activities of 4 with those of stellettin B as described in the literature,^{6–9} it was observed that the double bond between C-23/C-24 in the δ -lactone ring is a required functionality.

Experimental Section

General Experimental Procedures. Optional rotations were measured with a Perkin-Elmer 243B polarimeter. The IR spectra were determined on a Thermo Nicolet Nexus 470 FT-IR spectrometer. The CD spectrum was recorded on a JASCO J-720 spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-500 FT NMR spectrometer using TMS as internal standard. Chemical shifts are expressed in

parts per million (ppm), and coupling constants are reported in hertz (Hz). EIMS were performed with a Bruker APEX II mass spectrometer, and ESIMS were recorded in the Q-STAR ESI-TOF-MS/MS spectrometer. HREIMS were obtained on a GCT-MS instrument. Column chromatography was carried out with silica gel (200–300 mesh), and HF₂₅₄ silica gel for TLC was provided by Qingdao Marine Chemistry Co. Ltd., Qingdao, People's Republic of China. Sephadex LH-20 (18–110 μm) was obtained from Pharmacia Co. HPLC was performed on an Alltech 426 apparatus using a Kromasil prepack column (ODS, 10 mm \times 250 mm, for reversed phase).

Animal Material. The marine sponge *Rhabdastrella* aff. *distincta* (Thiele) was collected off an inner coral reef (10 m depth) at Hainan Island in the South China Sea, in June 2002. The fresh sample was frozen after keeping small pieces in alcohol for taxonomy. The species was identified by one of the authors, R.W.M.v.S. A voucher specimen (HS-14) is deposited at the State Key Laboratory of Natural and Biomimetic Drugs, Peking University.

Extraction and Isolation. The frozen sponge (4.2 kg, wet wt) was homogenized and then extracted with MeOH. The concentrated total extract was partitioned between H₂O and CH₂Cl₂. The CH₂Cl₂ extract (5.0 g) was subjected to silica gel column chromatography using a mixture of CH₂Cl₂–Et₂OAc (2:1) as eluent to obtain six fractions (A–F). Fraction A (0.8 g) was further subjected to silica gel column chromatography, eluting with petroleum ether–acetone (6:1), to yield stellettin A (7, 50 mg), stellettin B (8, 30 mg), stellettin C (9, 15 mg), and geoditins A (5, 2.5 mg) and B (6, 3 mg). Part of fraction B (0.1 g) was purified in the same manner as fraction A by

eluting with petroleum ether–acetone (1:1) to afford stellettin E (**10**, 20 mg) and rhabdastrellic acid A (**12**, 10 mg), and the remaining fraction B (0.4 g) was treated with excess CH_2N_2 and then purified on a silica gel column with petroleum ether–acetone (5:1) as eluent to yield the methyl ester of stellettin E (**11**, 52 mg) and the methyl ester of rhabdastrellic acid A (**13**, 45 mg). Fraction E (0.7 g) was separated by semipreparative HPLC (ODS, C_{18} , $\text{MeOH-H}_2\text{O}$, 90%) to afford compounds **1** (11.5 mg), **2** (5.8 mg), **3** (10.3 mg), and **4** (4.2 mg).

Isogoeditin A (1): yellow oil; $[\alpha]_{\text{D}}^{25} +68.7^\circ$ (*c* 0.34, MeOH); IR (KBr) ν_{max} 2957, 2925, 1698, 1647, 1601, 1556, 1381, 1171 cm^{-1} ; ^1H and ^{13}C NMR data, see Table 1; EIMS m/z 450 $[\text{M}]^+$ (15), 404 (13), 339 (10), 209 (14), 198 (19), 91 (20); HREIMS m/z 450.2780 (calcd for $\text{C}_{29}\text{H}_{38}\text{O}_4$, 450.2770).

13(E)-Isogoeditin A (2): yellow oil; $[\alpha]_{\text{D}}^{25} -5.9^\circ$ (*c* 0.15, acetone); IR (KBr) ν_{max} 2958, 2926, 1698, 1647, 1598, 1285, 1172 cm^{-1} ; ^1H and ^{13}C NMR data, see Table 1 and Table 2; EIMS m/z 450 $[\text{M}]^+$ (100), 407 (91), 393 (20), 368 (21), 353 (35), 326 (11); HREIMS m/z 450.2767 (calcd for $\text{C}_{29}\text{H}_{38}\text{O}_4$, 450.2770).

Isogoeditin B (3): yellow oil; $[\alpha]_{\text{D}}^{25} -74.6^\circ$ (*c* 0.05 acetone); IR (KBr) ν_{max} 2926, 2857, 1731, 1697, 1647, 1605, 1376, 1247, 1164 cm^{-1} ; ^1H and ^{13}C NMR data, see Table 3; EIMS m/z 494 $[\text{M}]^+$ (10), 440 (9), 360 (16), 315 (60), 314 (55), 141 (52), 108 (17); HREIMS m/z 494.3011 (calcd for $\text{C}_{31}\text{H}_{42}\text{O}_5$, 494.3032).

22,23-Dihydrostellentin B (4): yellow oil; $[\alpha]_{\text{D}}^{25} +19^\circ$ (*c* 0.2, acetone); IR (KBr) ν_{max} 2920, 2852, 1715, 1679, 1652, 1233, 1011 cm^{-1} ; CD (MeOH) $\Delta\epsilon$ (nm) -10.4 (247); ^1H and ^{13}C NMR data, see Table 2; EIMS m/z 464 $[\text{M}]^+$ (27), 384 (34), 365 (40), 313 (50), 285 (15), 241 (14), 185 (17), 159 (28), 149 (35); HREIMS m/z 464.2942 (calcd for $\text{C}_{30}\text{H}_{40}\text{O}_4$, 464.2927).

Methyl ester of rhabdastrellic acid A (13): yellow oil; $[\alpha]_{\text{D}}^{25} -6.2^\circ$ (*c* 0.18, acetone); ^1H NMR (500 MHz, C_6D_6) 7.70 (1H, dd, $J = 11.0, 1.2$ Hz, H-24), 7.13 (1H, dd, $J = 11.0, 15.0$ Hz, H-16), 6.87 (1H, d, $J = 15.0$ Hz, H-15), 6.70 (1H, dd, $J = 11.0, 15.0$ Hz, H-23), 6.64 (1H, d, $J = 15.0$ Hz, H-22), 6.46 (1H, d, $J = 11.0$ Hz, H-17), 3.60 (3H, s, OCH_3), 2.69 (3H, s, H₃-18), 2.43 (1H, m, H-2b), 2.30 (1H, m, H-2a), 2.14 (1H, m, H-11b), 2.11 (3H, s, H₃-27), 2.11 (1H, m, H-5), 2.08 (1H, m, H-7b), 2.04 (1H, m, H-11a), 1.84 (3H, s, H₃-21), 1.67 (1H, m, H-7a), 1.47 (1H, m, H-1b), 1.42 (1H, m, H-9), 1.41 (1H, m, H-6b), 1.24 (3H, s, H₃-30), 1.17 (3H, s, H₃-28), 1.05 (1H, m, H-6a), 1.06 (3H, s, H₃-29), 1.01 (1H, m, H-1a), 0.63 (3H, s, H₃-19); ^{13}C NMR (125 MHz, C_6D_6) 216.4 (s, C-3), 205.9 (s, C-12), 168.5 (s, C-26), 147.0 (s, C-13), 143.5 (d, C-22), 140.7 (s, C-14), 138.8 (d, C-24), 138.8

(s, C-20), 135.4 (s, C-17), 135.0 (d, C-15), 131.9 (d, C-16), 128.0 (s, C-25), 125.4 (d, C-23), 51.7 (s, OCH_3), 47.8 (d, C-5), 46.8 (s, C-4), 45.7 (d, C-9), 45.2 (s, C-8), 38.9 (s, C-2), 36.8 (t, C-7), 34.9 (s, C-10), 33.6 (t, C-1), 32.5 (t, C-11), 31.4 (t, C-6), 30.3 (q, C-30), 26.1 (q, C-28), 23.4 (q, C-19), 19.8 (q, C-29), 14.7 (q, C-18), 13.3 (q, C-21), 13.0 (q, C-27); EIMS m/z 478 $[\text{M}]^+$.

Cytotoxicity Assays. The cytotoxic activity of compounds **1–13** was investigated using a small panel of human cancer cell lines, comprised of HL-60, PC-3MIE8, BGC-823, MDA-MB-423, Bel₇₄₀₂, and HeLa. The bioassays were performed in the same manner as described previously.¹⁶

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References and Notes

- Rao, Z.; Deng, S.; Wu, H.; Jiang, S. *J. Nat. Prod.* **1997**, *60*, 1163–1164.
- Tasdemir, D.; Mangalindan, G. C.; Concepcion, G. P.; Verbitski, S. M.; Rabindran, S.; Miranda, M.; Greenstein, M.; Hooper, J. N. A.; Harper, M. K.; Ireland, C. M. *J. Nat. Prod.* **2002**, *65*, 210–214.
- Rao, Z. G.; Deng, S. Z.; Wu, H. M.; Jiang, S. K. *Gaodeng Xuebao Huaxue Xuebao* **1998**, *19*, 406–407.
- Bourguet-Kondracki, M. L.; Longeon, A.; Debitus, C.; Guyot, M. *Tetrahedron Lett.* **2000**, *41*, 3087–3090.
- Zhang, W. H.; Che, C. T. *J. Nat. Prod.* **2001**, *64*, 1489–1492.
- Su, J. Y.; Meng, Y. H.; Zeng, L. M.; Fu, X.; Schmitz, F. *J. Nat. Prod.* **1994**, *57*, 1450–1451.
- McCormick, J. L.; McKee, T. C.; Cardellina, J. H., II; Leid, M.; Boyd, M. R. *J. Nat. Prod.* **1996**, *59*, 1047–1050.
- McKee, T. C.; Bokesch, H. R.; McCormick, J. L.; Rashid, M. A.; Spielvogel, D.; Gustafson, K. R.; Alavanja, M. M.; Cardellina, J. H., II; Boyd, M. R. *J. Nat. Prod.* **1997**, *60*, 431–438.
- McCabe, T.; Clardy, J.; Minale, L.; Pizza, C.; Zollo, F.; Riccio, R. *Tetrahedron Lett.* **1982**, *23*, 3307–3310.
- Kobayashi, J.; Yuasa, K.; Kobayashi, T.; Sasaki, T.; Tsuda, M. *Tetrahedron Lett.* **1996**, *52*, 5745–5750.
- Tabudravu, J. N.; Jaspars, M. *J. Nat. Prod.* **2001**, *64*, 813–815.
- Ravi, B. N.; Wells, R. *J. Aust. J. Chem.* **1982**, *35*, 39–50.
- Ravi, B. N.; Wells, R. *J. Org. Chem.* **1981**, *46*, 1998–2001.
- Lan, Y. H.; Chang, F. R.; Yu, J. H.; Yang, Y. L.; Chang, Y. L.; Lee, S. J.; Wu, C. *J. Nat. Prod.* **2003**, *66*, 487–490.
- Cavalheiro, A. J.; Yoshida, M. *Phytochemistry* **2000**, *53*, 811–819.
- Xu, M.; Deng, Z.; Li, J.; Fu, H.; Proksch, P.; Lin, W. *J. Nat. Prod.* **2004**, *67*, 762–766.

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