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Rhabdastrellins A−F, Isomalabaricane Triterpenes from the Marine Sponge *Rhabdastrella* aff. *distincta*

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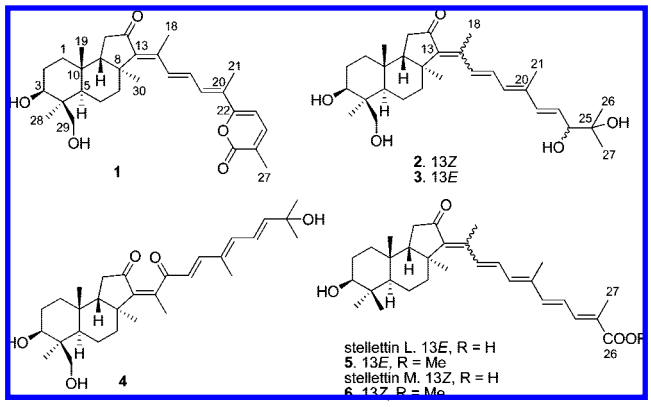
Chemical examination of the marine sponge *Rhabdastrella* aff. *distincta* resulted in the isolation of six new isomalabaricane triterpenes, rhabdastrellins A−F (**1**−**6**), which were present as minor components, along with stellettins L and M. Their structures were elucidated on the basis of extensive spectroscopic data analyses and comparison with spectroscopic data of known analogues. The cytotoxicity of compounds **1**−**6** against a small panel of human tumor cell lines was also evaluated.

Sponges of the genus *Rhabdastrella* (Ancorinidae) are widely distributed in tropical oceans, with about 19 species being documented.[1] Previous chemical investigations mainly focused on *R. globostellata*, from which about 30 isomalabaricane triterpenoids were isolated.[2−8] Isomalabaricane is a trivial name representing a group of compounds possessing a *trans-syn-trans* tricyclic nucleus conjugated to a polyene side chain. This rare class of triterpenoids is mostly found in marine sponges from the genera *Stelletta*, *Jaspis*, *Geodia*, and *Rhabdastrella*, all of which belong to the order Astrophorida.[9−14] Isomalabaricanes were previously reported to significantly inhibit the growth of tumor cells. In the South China Sea, two species of these yellow sponges (*Rhabdastrella globostellata* and *R.* aff. *distincta*) were previously examined chemically, from which 12 isomalabaricane analogues were isolated.[7,8] The present work reports on the isolation and structural elucidation of six new isomalabaricane triterpenoids (**1**−**6**) that were isolated as minor components.



Results and Discussion

Bioassay-guided fractionation of a MeOH extract of *R.* aff. *distincta* revealed that the $CHCl_3$-soluble fraction exhibited inhibitory activity against human tumor cell lines HL-60, BGC-823, and MDA-MB-423. This cytotoxic fraction was then subjected to repeated chromatographic separation followed by semipreparative HPLC purification to obtain rhabdastrellins A−F (**1**−**6**), together with stellettins L and M. The latter compounds were recently reported from the sponge *Stelletta tenuis*.[11]

The molecular formula $C_{30}H_{40}O_5$ of rhabdastrellin A (**1**) was determined through HREIMS (*m*/*z* 487.3408 $[M + 1]^+$, calcd 487.3418) and NMR data, implying 11 degrees of unsaturation. The UV absorption maxima at 312 and 395 nm in MeOH suggested the presence of a highly conjugated polyene chromophore, while the IR absorptions at 3265 and 1688 cm^{-1} implied the presence of carbonyl and hydroxyl functionalities. The ^{13}C NMR spectrum exhibited 30 carbon resonances, including 10 olefinic carbons, six methyl groups, a ketone (δ_C 206.2, qC, C-12), and an ester-type carbonyl carbon (δ_C 161.8, qC), which was attributed to an unsaturated δ-lactone as indicated in stellettins A−C.[15] The ^1H NMR spectrum of **1** showed three tertiary methyl resonances at δ_H 0.75 (3H, s, H-19), 1.46 (3H, s, H-28), and 1.19 (3H, s, H-30) and three olefinic methyl resonances at δ_H 2.68 (3H, s, H-18), 1.71 (3H, s, H-21), and 1.98 (3H, s, H-27). In addition, five olefinic protons represented an ABX spin system at δ_H 6.99 (1H, d, J = 15.2 Hz, H-15), 7.06 (1H, dd, J = 10.4, 15.2 Hz, H-16), and 7.58 (1H, d, J = 10.4 Hz, H-17) and an AB spin system at δ_H 5.62 (1H, d, J = 6.8 Hz, H-23) and 6.40 (1H, d, J = 6.8 Hz, H-24). These NMR spectroscopic features were characteristic of an isomalabaricane triterpene and were very similar to those of jaspolide B.[14] The only difference was that a methyl group at C-4 of the latter was replaced by a hydroxymethylene unit (δ_H 3.22, 4.32, δ_C 63.9) in **1**, which was confirmed from the HMBC correlations of the hydroxymethylene protons to C-3 (δ_C 80.4, CH), C-4 (δ_C 43.6, qC), and C-5 (δ_C 47.1, CH) and a long-range *W*-coupling to C-28 (δ_C 23.8, CH_3). Complete assignments of protons and carbons of **1** (Tables 1 and 2) were established through 2D NMR experiments ($^1H-^1H$ COSY, HMQC, and HMBC). The geometry of the tricycle core was determined as *trans-syn-trans* based on NOE interactions between H_3-19/H-9 (δ_H 1.52, dd) and H_3-30/H-5 (δ_H 1.62, d) and the comparable NMR data between **1** and jaspolide B.[14] The double doublet of H-3 (δ_H 3.24, dd, J = 5.7, 12.1 Hz) indicated an axial orientation of H-3 and consequently a 3β-hydroxy group, in contrast to a broad singlet for H-3β of the known analogues.[4] The β-orientation of the hydroxymethylene group at C-4 was evident from the NOESY correlations between H_3-19/H-29a (δ_H 4.32, d) and H-3/H_3-28. The significant downfield shift of H_3-18 (δ_H 2.68, s) due to its location in the deshielding zone of the ketone group at

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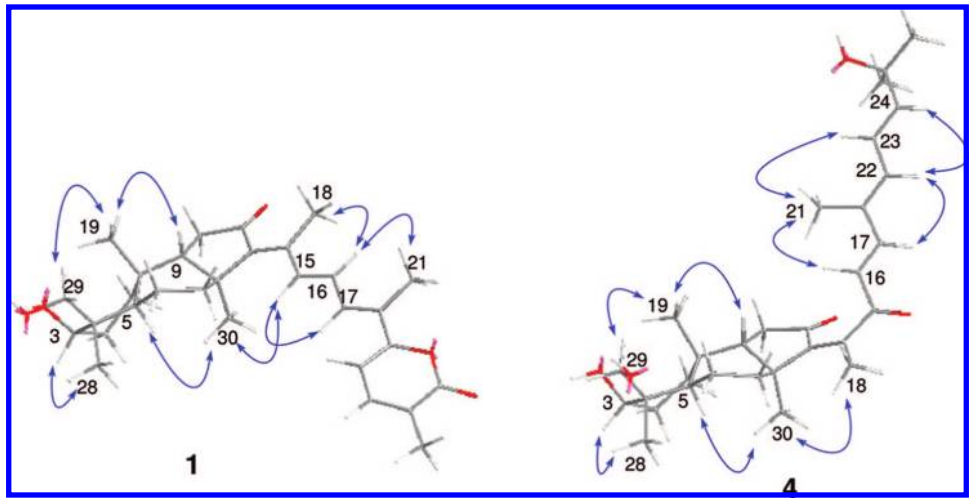

Figure 1. NOESY interactions observed for compounds **1** and **4**.

Table 1. ^{1}H NMR Data for Rhabdastrellins A−F (**1**−**6**)

no.	**1**[a]	**2**[b]	**3**[a]	**4**[c]	**5**[a]	**6**[a]
1	1.04 m; 1.24 m	1.38 m; 1.59 m	1.04 m; 1.25 m	1.44 m; 1.65 m	1.00 m; 1.12 m	1.03 m; 1.21 m
2	1.23 m; 1.42 m	1.84 m	1.49 m	1.82 m	1.02 m; 1.47 m	1.02 m; 1.60 m
3	3.24 dd (5.7, 12.1)	3.47 dd (5.5, 11.0)	3.17 dd (6.5, 11.0)	3.46 dd (5.5, 11.5)	3.05 dd (5.0, 11.0)	3.10 dd (5.5, 11.0)
5	1.62 d (10.8)	1.81 m	1.64 m	1.86 m	1.49 m	1.44 m
6	1.58 ; 1.44 m	1.82 m; 1.54 m	1.68 m	1.92 m; 1.69 m	1.15 m; 1.51 m	1.31 m; 1.58 m
7	1.56 m; 1.96 m	2.10 m	2.11 m	2.24 m; 2.11 m	2.06 m	1.02 m; 1.81 m
9	1.52 dd (8.1, 15.7)	1.79 m	1.52 m	1.99 m	1.50 m	1.56 m
11	2.10 m; 1.92 m	2.11 m	2.16 m	2.16 m; 2.26 m	2.08 m	2.19 m
15	6.99 d (15.2)	8.12 d (15.5)	6.83 d (15.0)		6.77 d (15.0)	9.00 d (15.0)
16	7.06 dd (10.4, 15.2)	7.10 dd (11.5, 15.5)	7.14 dd (11.5, 15.0)	6.15 d (15.5)	6.98 dd (11.5, 15.0)	7.10 dd (11.5, 15.0)
17	7.58 d (10.4)	6.25 d (11.5)	6.42 d (11.5)	7.05 d (16.0)	6.50 d (11.5)	6.51 d (11.5)
18	2.68 s	2.07 s	2.76 s	1.98 m	2.60 s	1.91 s
19	0.75 s	1.04 s	0.70 s	1.12 s	0.68 s	0.81 s
21	1.71 s	1.95 s	1.84 s	1.95 s	1.72 s	2.13 s
22		6.45 d (15.5)	6.59 brd (15.5)	6.49 d (11.5)	6.50 d (15.0)	6.46 d (15.0)
23	5.62 d (6.8)	5.97 dd (6.5, 15.5)	5.92 dd (7.5, 15.0)	6.72 dd (11.5, 15.0)	6.57 dd (11.0, 15.0)	6.61 dd (11.5, 15.0)
24	6.40 d (6.8)	3.97 d (6.5)	3.94 d (7.0)	6.14 d (15.0)	7.61 d (11.0)	7.69 d (11.5)
26		1.14 s	1.20 s	1.35 s		
27	1.98 s	1.14 s	1.22 s	1.35 s	2.03 s	1.86 s
28	1.46 s	1.23 s	1.38 s	1.27 s	0.76 s	0.88 s
29	4.32 d (11.5)	3.41 d (11.0)	4.16 d (11.0)	3.65 d (11.5)	1.03 s	1.13 s
	3.22 d (11.5)	4.06 d (11.0)	3.35 d (11.0)	3.98 d (11.5)		
30	1.19 s	1.39 s	1.28 s	1.48 s	1.20 s	1.18 s
OCH_3					3.48 s	3.59 s

[a] In C_6D_6. [b] In acetone-d_6. [c] In CD_3OD.

C-12, along with the upfield shift of H-15 (δ_H 6.99, d), was in agreement with 13*E*. The coupling constant ($J_{H\text{-}15/H\text{-}16}$ = 15.2 Hz) in conjunction with NOE interactions between H_3-18/H-16 (δ_H 7.06, dd) and H-16/H_3-21 (δ_H 1.71, s) defined 15*E* and 17*E* geometries in the side chain.

Rhabdastrellin B (**2**) had a molecular formula of $C_{30}H_{46}O_5$ as established through HRFABMS (*m*/*z* 487.3408 $[M + H]^+$, calcd for 487.3418) and NMR data. A comparison of the NMR data (Tables 1 and 2) revealed that **2** possessed the same tricyclic nucleus substructure as that of **1**. The hydroxyl substitution at C-3 and C-29 was evident from the proton resonances at δ_H 3.41 (1H, d, J = 11.0 Hz, H-29a) and 4.06 (1H, d, J = 11.0 Hz, H-29b) for CH_2OH-29, and δ_H 3.47 (1H, dd, J = 5.5, 11.0 Hz, H-3), in association with the DQFCOSY and HMBC correlations. The ^{1}H NMR spectrum for the side chain in **2** presented five conjugated olefinic protons, which were ascribed to an ABX spin system at δ_H 8.12 (1H, d, J = 15.5 Hz, H-15), 7.10 (1H, dd, J = 11.5, 15.5 Hz, H-16), and 6.25 (1H, d, J = 11.5 Hz, H-17) and an AB spin system at δ_H 6.45 (1H, d, J = 15.5 Hz, H-22) and 5.97 (1H, dd, J = 6.5, 15.5 Hz, H-23). In addition, the side chain contained four methyl groups resonating at δ_H 2.07 (3H, s, H-18), 1.95 (3H, s, H-21), and 1.14 (6H, s, H-26, H-27) and a hydroxymethine proton at δ_H 3.97 (d, J = 6.5 Hz, H-24). The complete proton and carbon assignments were obtained from the ^{1}H−^{1}H COSY, HMQC, and HMBC spectra (Tables 1 and 2). 2D NMR data analysis indicated that the side chain of **2** was identical to that of globostellatic acid I[4] with the substitution of hydroxyl groups at C-24 and C-25, respectively. The similar NOESY correlations and NMR data of **2** compared to those of the tricyclic skeleton in **1** confirmed a *trans-syn-trans* ring junction, while OH-3 and CH_2OH-29 were β-oriented. The values of coupling constants $J_{H\text{-}15/H\text{-}16}$ = 15.5 Hz and $J_{H\text{-}22/H\text{-}23}$ = 15.5 Hz, along with the NOESY correlations of H_3-21/H-16 and H_3-21/H-23, indicated 15*E*, 17*E*, and 22*E*, whereas 13*Z* was assigned by a NOESY cross-peak between H_3-18/H_3-30. The chemical shift of H-15 at δ_H 8.12 (d) implied its location in the deshielding environment of the ketone group, which also supported the assignment of 13*Z*. The configuration of the chiral center at C-24 was undefined.

The molecular formula of rhabdastrellin C (**3**) as established by HRFABMS is identical to that of **2**. A comparison of the NMR data (Tables 1 and 2) confirmed that **3** was a stereoisomer of **2** at C-13. This was evident from the downfield shift of H_3-18 at δ_H 2.76 (3H, s) and upfield shift of H-15 at δ_H 6.83 (1H, d, J = 15.0 Hz) being similar to those of **1** and indicating a 13*E*-configuration

Table 2. ^{13}C NMR Data for Rhabdastrellins A−F (**1**−**6**)

no.	**1**[a]	**2**[b]	**3**[a]	**4**[c]	**5**[a]	**6**[a]
1	32.9 CH_2	33.7 CH_2	32.9 CH_2	34.2 CH_2	33.4 CH_2	33.1 CH_2
2	25.8 CH_2	29.5 CH_2	29.2 CH_2	29.8 CH_2	29.4 CH_2	29.2 CH_2
3	80.4 CH	80.3 CH	80.4 CH	80.8 CH	79.0 CH	78.7 CH
4	43.6 qC	44.1 qC	43.5 qC	44.7 qC	39.2 qC	38.8 qC
5	47.1 CH	47.8 CH	47.2 CH	48.3 CH	46.8 CH	46.5 CH
6	18.7 CH_2	19.7 CH_2	18.8 CH_2	20.1 CH_2	18.7 CH_2	18.3 CH_2
7	39.5 CH_2	39.3 CH_2	39.8 CH_2	38.0 CH_2	40.0 CH_2	38.2 CH_2
8	44.7 qC	45.3 qC	44.5 qC	44.3 qC	45.0 qC	44.5 qC
9	49.7 CH	51.0 CH	49.7 CH	52.5 CH	49.9 CH	49.8 CH
10	35.1 qC	37.2 qC	35.0 qC	36.7 qC	35.6 qC	35.4 qC
11	36.4 CH_2	36.0 CH_2	36.4 CH_2	35.6 CH_2	36.6 CH_2	36.7 CH_2
12	206.2 qC	206.6 qC	206.6 qC	206.2 qC	206.1 qC	204.9 qC
13	148.9 qC	147.1 qC	147.2 qC	148.3 qC	148.1 qC	147.4 qC
14	139.2 qC	142.7 qC	140.0 qC	144.0 qC	138.3 qC	140.6 qC
15	137.0 CH	133.5 CH	133.4 CH	203.8 qC	135.4 CH	135.4 CH
16	128.1 CH	131.3 CH	131.5 CH	125.2 CH	131.4 CH	129.8 CH
17	130.0 CH	132.3 CH	132.2 CH	150.3 CH	143.4 CH	136.3 CH
18	14.4 CH_3	16.1 CH_3	14.4 CH_3	17.8 CH_3	14.5 CH_3	15.5 CH_3
19	22.4 CH_3	22.7 CH_3	22.2 CH_3	22.6 CH_3	22.2 CH_3	22.0 CH_3
20	130.4 qC	138.8 qC	137.7 qC	134.5 qC	140.0 qC	138.2 qC
21	12.3 CH_3	13.1 CH_3	12.8 CH_3	12.4 CH_3	12.8 CH_3	12.4 CH_3
22	158.6 qC	136.3 CH	136.3 CH	141.0 CH	143.4 CH	143.9 CH
23	102.5 CH	131.1 CH	129.5 CH	123.6 CH	125.0 CH	123.9 CH
24	138.5 CH	79.8 CH	79.5 CH	148.9 CH	138.7 CH	138.8 CH
25	124.5 qC	73.0 qC	72.5 qC	71.5 qC	128.2 qC	128.0 qC
26	161.8 qC	25.2 CH_3	23.8 CH_3	29.8 CH_3	168.3 qC	168.0 qC
27	16.6 CH_3	25.9 CH_3	26.3 CH_3	29.8 CH_3	13.1 CH_3	12.8 CH_3
28	23.8 CH_3	24.1 CH_3	23.6 CH_3	24.2 CH_3	16.1 CH_3	15.9 CH_3
29	63.9 CH_2	64.2 CH_2	63.7 CH_2	65.2 CH_2	29.2 CH_3	29.0 CH_3
30	25.8 CH_3	24.9 CH_3	25.8 CH_3	25.2 CH_3	26.1 CH_3	24.6 CH_3
OCH_3					51.5 CH_3	51.2 CH_3

[a] In C_6D_6. [b] In acetone-d_6. [c] In CD_3OD.

of **3**. This assignment was also supported from the NOESY correlation between H-15/H_3-30. The coupling constants ($J_{H\text{-}15/H\text{-}16}$ = 15.0 Hz, $J_{H\text{-}22/H\text{-}23}$ = 15.5 Hz) and the NOESY correlations between H-16/H_3-21 and H-17/H-22 were consistent with *E*-geometries of Δ^{15}, Δ^{17}, and Δ^{22}.

The molecular formula of rhabdastrellin D (**4**) was established as $C_{30}H_{44}O_5$ by HRFABMS and NMR data, implying nine degrees of unsaturation. The ^1H and ^{13}C NMR data of **4** (Tables 1 and 2) were assigned through 2D NMR (^1H−^1H COSY, HMQC, HMBC) data analyses. Apart from the NMR data for the tricyclic core of an isomalabaricane skeleton, which showed close similarity with those of **1**−**3**, the NMR spectroscopic data for the side chain were nearly identical to those of globostellatic acid A,[16] as observed by a conjugated ketone group at δ_C 203.8 (qC, C-15), a hydroxylated carbon at δ_C 71.5 (qC, C-25), eight olefinic carbons (three for quaternary carbons and five for methines), and four methyl groups. The composition of the side chain was unambiguously established by 2D NMR. The similar NOESY correlations and NMR data of **4** compared to those of **1**−**3** suggested that **4** possessed the same configurations of the tricyclic skeleton and its substituents as assigned for the latter compounds. The geometries of 13*Z*, 16*E*, 20*E*, and 23*E* were evident from the *J* values of H-16 and H-22 and the NOESY cross-peaks between H_3-18/H_3-30, H-16/H_3-21, and H-17/H-22.

The molecular formula of rhabdastrellin E (**5**) was determined as $C_{31}H_{44}O_4$ by HREIMS (*m*/*z* 480.3235 $[M]^+$, calcd 480.3240) and was 14 amu higher than that of stellettin L.[11] The ^1H and ^{13}C NMR data of **5** were almost superimposable to those of stellettin M except for the presence of an additional methoxy group (δ_H 3.48, s; δ_C 51.5, CH_3). The HMBC cross-peak between the methoxy protons and the carbonyl carbon at δ_C 168.3 (qC, C-26) confirmed that **5** is a methyl ester of stellettin L at the terminal carboxylic acid C-26. The stereochemistry of **5** was identical to stellettin L on the basis of the similarities of NMR and NOE data.

The NMR data of rhabdastrellin F (**6**) indicated that the congener **6** is a 13*Z* isomer of **5** and closely resembled stellettin M.[11] The 13*Z*-configuration was evident from the chemical shifts of H-15 (δ_H 9.00, d, J = 15.0 Hz) and H_3-18 (δ_H 1.91, s) in association with the NOESY correlation between H_3-18/H_3-30. The methyl ester group at the terminus of the side chain was recognized by the ^1H and ^{13}C NMR resonances of a methoxy group (δ_H 3.59, s; δ_C 51.2, CH_3) and its protons showing HMBC correlation to the carbonyl carbon at δ_C 168.0 (qC, C-26).

The methylation of stellettin L was achieved with the help of ethereal diazomethane to yield compound **5**, while stellettin M was completely converted to **6** using the same method. These facts further supported the structural assignments of compounds **5** and **6**.

Rhabdastrellins A−E (**1**−**6**) were tested against a small panel of human tumor cell lines including HL-60, BGC-823, and MDA-MB-435. Compound **1** possessed moderate inhibitory activity toward HL-60 (IC_{50} = 4.2 μg/ml), while the rest were inactive (IC_{50} > 10 μg/mL).

Isomalabaricane triterpenoids are a group of unstable natural products, which are easily isomerized at C-13 or autoxidated in the polyene side chain upon exposure to light or storage at room temperature. The ^1H NMR spectrum of the crude extract obtained from the fresh sponge indicated that it mostly contains isomalabaricanes with 13*E*-configuration (H-15 of most isomalabaricanes appeared around 7.0 ppm). Thus, the 13*Z* isomers are suggested to be the artifacts produced during isolation.

Experimental Section

General Experimental Procedures. Optional rotations were measured with a WZZ-1S digital automatic polarimeter. UV spectra were recorded on a Shimadzu UV-210A spectrophotometer. IR spectra were determined on a Thermo Nicolet Nexus 470 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded on an AVANCE-500 FT 500 MHz NMR spectrometer using TMS as an internal standard. EIMS were performed with a Bruker APEX-II mass spectrometer, while HREIMS and HRFABMS were obtained on GCT-MS instruments (Micromass UK). Column chromatography was carried out on Si gel (160−200 and 200−300 mesh), and GF_{254} Si gel for TLC was provided by Qingdao Marine Chemistry Co. Ltd. HPLC chromatography was performed on an Alltech instrument (426-HPLC pump, Alltech UV−vis-200 detector) with a Kromasil semipreparative column (10 μm, ODS, 10 mm × 250 mm).

Animal Material. The marine sponge *Rhabdastrella* aff. *distincta* Thiele, 1900 (Demospongiae; Astrophorida: Ancorinidae) was collected from the coral reef of Hainan, the South China Sea, in June 2002. The species was identified by one of the authors (N.J.V.). A voucher specimen is deposited at the State Key Laboratory of Natural and Biomimetic Drugs, Peking University (HS-14), and the Zoological Museum of Amsterdam (ZMA POR. 16728).

Extraction and Isolation. The freeze-dried sponge sample (4.2 kg, wt) was homogenized and extracted with MeOH. The concentrated extract was partitioned between H_2O and CH_2Cl_2 to obtain a CH_2Cl_2 extract (5.0 g), which was subjected to Si gel column chromatography using a gradient of petroleum ether (PE)−acetone (5:1, 2:1, 1:1) as eluant to obtain six fractions (FA−FF). The polar fraction FF (30 mg) was separated on a Si gel column with the eluant of PE−acetone (3:1) to afford **1** (4.0 mg) and stellettins M (6.8 mg) and L (3.4 mg). Fraction FE (90 mg) was subjected to a Sephadex LH-20 column with PE−$CHCl_3$−MeOH (5:5:1) as eluant to get a mixture of isomalabaricane triterpenes (35 mg), and this mixture was subsequently purified on a Si gel column eluting with PE−acetone (5:1) to yield **2** (3.0 mg), **3** (1.5 mg), and **4** (4.0 mg). Fraction FD (30 mg) was separated on a semipreparative HPLC with MeOH−H_2O (85:15) as a mobile phase to obtain **5** (2.7 mg) and **6** (4.2 mg).

Methylation of Stellettins L and M. To a flask with stellettin L (3.8 mg) was added ethereal diazomethane reagent. The flask was left at room temperature under stirring overnight. The reacted product was concentrated and subjected to a silica gel column eluting with PE−acetone (4:1) to yield **5** (4.0 mg). Stellettin M (3.5 mg) was reacted in the same manner as described for stellettin L to yield **6** (2.3 mg).

Rhabdastrellin A (1): yellow oil; $[\alpha]_D$ −17.2 (*c* 0.25, acetone); UV (λ_{max}) 312, 395 nm^{-1}; IR (KBr) ν_{max} 3265, 2956, 2872, 1688, 1432

cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS *m/z* 480 $[M]^+$; HREIMS *m/z* 480.2872 $[M]^+$ (calcd for $C_{30}H_{40}O_5$, 480.2876).

Rhabdastrellin B (2): yellow oil; $[\alpha]_D$ +56.2 (*c* 0.23, acetone); UV (λ_{max}) 259, 369 nm^{-1}; IR (KBr) ν_{max} 3390, 2930, 2873, 1686, 1450, 1171, 1027 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m/z* 487 $[M+1]^+$; HRFABMS *m/z* 487.3408 $[M+1]^+$ (calcd for $C_{30}H_{47}O_5$, 487.3418).

Rhabdastrellin C (3): yellow oil; $[\alpha]_D$ −231.1 (*c* 0.12, acetone); UV (λ_{max}) 257, 368 nm^{-1}; IR (KBr) ν_{max} 3356, 2978, 2857, 1673, 1452, 1170, 1028 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m/z* 487 $[M+1]^+$; HRFABMS *m/z* 487.3423 $[M+1]^+$ (calcd for $C_{30}H_{47}O_5$, 487.3418).

Rhabdastrellin D (4): yellow oil; $[\alpha]_D$ +140.3 (*c* 0.31, acetone); UV (λ_{max}) 225, 324 nm^{-1}; IR (KBr) ν_{max} 3404, 2930, 2872, 1715, 1631, 1598, 1377, 1025 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m/z* 485 $[M+1]^+$; HRFABMS *m/z* 485.3255 $[M+1]^+$ (calcd for $C_{30}H_{45}O_5$, 485.3261).

Rhabdastrellin E (5): yellow oil; $[\alpha]_D$ −37.8 (*c* 0.15, acetone); UV (λ_{max}) 296, 393 nm^{-1}; IR (KBr) ν_{max} 3284, 2927, 2857, 1704, 1437, 1167 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS *m/z* 480 $[M]^+$; HREIMS *m/z* 480.3235 $[M]^+$ (calcd for $C_{31}H_{44}O_4$, 480.3240).

Rhabdastrellin F (6): yellow oil; $[\alpha]_D$ −27.3 (*c* 0.12, acetone); UV (λ_{max}) 298, 371, 392 nm^{-1}; IR (KBr) ν_{max} 3325, 2929, 2870, 1704, 1438, 1169 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS *m/z* 480 $[M]^+$; HREIMS *m/z* 480.3221 $[M]^+$ (calcd for $C_{31}H_{44}O_4$, 480.3240).

Cytotoxic Assays. The cytotoxic activity of compounds **1**−**6** was tested against human tumor cell lines (HL-60, BGC-823, MDA-MB-423). The bioassays were performed in the same manner as described previously.[8]

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