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Cytotoxic Triterpenes from a Marine Sponge, *Stelletta* sp.[1]

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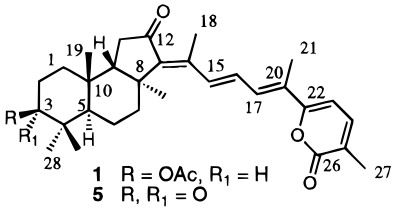
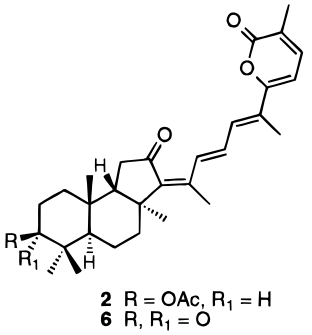
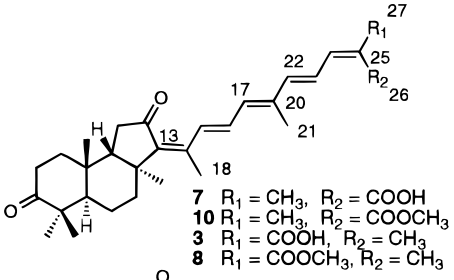
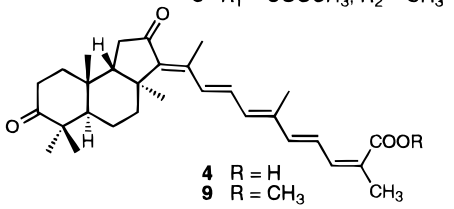
Bioassay-guided fractionation of an extract of a marine sponge, *Stelletta* sp., has led to the isolation and characterization of four new cytotoxic isomalabaricane triterpenes, named stellettins C (**1**), D (**2**), E (**3**), and F (**4**). Three known triterpenes (**5**−**7**) were also isolated from the same extract. The most sensitive of the tested cell lines (e.g., leukemia, central nervous system, renal) generally responded with GI_{50} concentrations in the low-to-mid nanomolar range.

Fractionation of the crude extract of a marine sponge, *Stelletta* sp., guided by the National Cancer Institute's (NCI) 60 human tumor cell line in vitro assay,[2−4] has led to the isolation and characterization of four new cytotoxic isomalabaricane triterpenes, named stellettins[5] C (**1**), D (**2**), E (**3**), F (**4**), and three known triterpenes, stellettins A and B (**5**[10] and **6**[7]), and **7**,[7] which we propose to call stellettin G. Natural products possessing the isomalabaricane skeleton are relatively rare, and only a handful of these compounds have been identified from marine organisms.[6−13] There have been several reports of secondary metabolites from the genus *Stelletta*, including triterpenes,[8,11,14] steroids,[14] and alkaloids.[15−16]









Results and Discussion

The organic extract of a *Stelletta* sp. collected in northern Australia was subjected to solvent−solvent partitioning to yield a cytotoxic CCl_4 fraction. After vacuum−liquid chromatography on Si gel, HPLC of the less polar, cytotoxic fractions gave stellettins A (**5**), B (**6**), C (**1**), and D (**2**). Purification of the more polar fraction by C_{18} HPLC gave a mixture of **3**, **4**, and **7**, which was separated after methylation to afford **8**−**10**. Stellettins C and D (**1** and **2**) and all the other pairs of geometric isomers could be separated and purified by HPLC, but each compound rapidly equilibrated to a mixture of geometric isomers upon exposure to light.

HRFABMS of **1** established a molecular formula of $C_{32}H_{42}O_5$, and UV absorptions at 417 and 395 nm suggested the presence of a highly conjugated system. The ^{13}C-NMR spectrum indicated the presence of a ketone (δ 206.2), an ester (δ 170.0), and four double bonds (eight resonances between δ 120 and 150). The ^{1}H-NMR spectrum of **1** contained signals for eight methyl groups and five olefinic protons. A prominent ^{1}H-NMR resonance at δ 4.71 correlated with a ^{13}C-NMR signal at δ 80.7 (HMQC) and clearly indicated an oxygen-bearing methine. HMBC correlations between a methyl singlet (δ 1.76) and the ester carbonyl (δ 170.0) and between δ 4.71 and the same carbonyl (δ 170.0) implied an acetate ester. A COSY experiment established the connectivity of three olefinic protons (δ 6.87, 6.92, 7.48), and their coupling constants allowed the assignment of the double bond geometries to give fragment **A**. The remaining two olefinic protons (δ 6.23, 5.46) were coupled to each other, and the proton at δ 6.23 had a long-range coupling (J = 1.2 Hz) to the methyl group at δ 1.89. The long-range heteronuclear correlations (HMBC) between pairs δ 5.46 (H23) and δ 158.7 (C22), δ 6.23 (H24) and δ 158.7 (C22), δ 6.23 (H24) and δ 161.8 (C26), combined with analyses of the carbon chemical shifts, strongly suggested the α-pyrone partial structure **B**. Fragments **A** and **B** were connected at quaternary carbons C20 and C22 by HMBC correlations to H17 and H23. Because all the sp^2 carbons were now accounted for, the remaining part of the structure had

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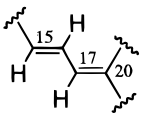
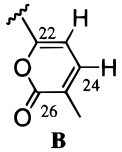
Table 1. Stellettin C (**1**) NMR Assignments in C_6D_6

position	^{13}C (ppm)	^{1}H (ppm)	HMBC to C #	NOE
1	33.0	1.17 0.90	2, 10, 19	
2	25.5	1.82 1.56		
3	80.7	4.71	4, 28, 29, $OCOCH_3$	2, 5, 28
4	38.3			
5	46.7	1.52	3, 4, 6, 7, 19, 29	3, 28, 30
6	18.5	1.33 1.07	5, 8, 10	
7	39.3	1.90 1.77	5, 6, 8, 13, 30	
8	44.9			
9	49.9	1.43	1, 5, 10, 11, 19, 30	19
10	35.4			
11	36.6	2.03 1.97	8, 12, 13 8, 9, 12	
12	206.2			
13	149.0			
14	139.3			
15	137.2	6.87	13, 16, 18	17, 30
16	130.6	6.92	14	18, 21
17	130.2	7.48	15, 21, 22	15
18	14.6	2.59	13, 14, 15	16
19	22.2	0.66	1, 5, 9, 10	9, 29
20	128.8			
21	12.5	1.57	17, 20, 22	23
22	158.7			
23	102.7	5.46	22, 25	
24	138.4	6.24	22, 26, 27	27
25	124.8			
26	161.8			
27	16.8	1.84	24, 25, 26	
28	29.3	0.92	3, 4, 5, 29	1, 3, 5, 6
29	17.2	0.86	3, 4, 5, 28	
30	26.1	1.07	7, 8, 9, 13	1, 5, 15
$OCOCH_3$	20.8	1.76	$OCOCH_3$	
$OCOCH_3$	170.0			

to be tricyclic. A series of NMR experiments, including COSY, HMQC, HMBC, and 1D proton decoupling, was used to define the tricyclic structure and its attachment to fragment **A** at C14, thus completing the gross structure of stellettin C (**1**).



A



B

The relative stereochemistry of **1** was determined by difference NOE experiments (Table 1). NOE enhancements observed for the pairs H18/H16, H16/H21, H30/H15, and H15/H17 firmly established the all-*E* configuration of the 13,15,17-triene system. As for the ring junctions of the tricyclic fragment, key NOE effects observed between H19/H29, H5/H28, H19/H9, and H5/H30 suggested a *trans-syn-trans* stereochemistry, consistent with an isomalabaricane skeleton. Irradiation of H3 led to NOE enhancements of H28 and H5, indicating that H3 was *cis* to H5.

The structures of compounds **2**−**10** were determined mainly from comparison of the ^{1}H- and ^{13}C-NMR data with those of **1** (Tables 2 and 3); relative stereochemistry was defined by NOE experiments for all compounds. Compound **2** has a molecular formula of $C_{32}H_{42}O_5$ and was, therefore, an isomer of **1**. Both the ^{1}H- and ^{13}C-NMR spectra of **2** shared many of the same characteristics with the spectra of **1**. The most striking difference was the presence of a proton resonance at δ 8.86 in **2** (in C_6D_6) in place of the proton at δ 6.87 (H15) in **1**. This large downfield shift suggested that this proton lay in the deshielding zone of the C12 carbonyl group. This would be possible if the C13−C14 double bond were to adopt the (*Z*)-orientation in **2**. This hypothesis was further supported by a change in the H18 chemical shift from δ 2.59 in **1** to δ 1.77 in **2**. An observed NOE between H18 and H30 and the absence of an NOE between H15 and H30 confirmed this assignment. Assignment of the relative stereochemistry of **2** was confirmed by NOE difference experiments.

HRFABMS revealed that **5** and **6** have the same molecular formula ($C_{30}H_{38}O_4$). Examination of the H18 and H15 resonances suggested that the two compounds were geometric isomers of the Δ^{13} olefin. The mass difference of 44 Daltons (C_2H_4O) between **5** and **1** suggested replacement of the acetate by a ketone. This was supported by the disappearance of NMR signals at δ 4.7 (1H) and δ 80.7, δ 170.0 and δ 20.8 (^{13}C) in the spectra of **5**, stellettin A. The appearance of a new carbon resonance at δ 216.5 in **5** signaled a new ketone carbonyl at C3. The tricyclic ring junction was confirmed, as before, by difference NOE experiments. Stellettin B (**6**) was determined to be the 13(*Z*)-isomer of **5** and was previously known, having been characterized primarily by X-ray diffraction.[7] Shortly after this work was completed, a paper describing the isolation of stellettin A (**5**) was published.[10] However, we report here the first full spectral assignments for both compounds.

Compounds **3**, **4**, and **7** proved difficult to separate. The IR spectrum of the mixture showed strong absorptions at 1700 and 1683 cm^{-1}, along with a broad band at 3000−3500 cm^{-1}, indicating the presence of a carboxylic acid group. Final purification of **7** was accomplished via preparative TLC. Treatment of the mixture with diazomethane allowed purification of the methyl esters **8**−**10**, derived from **3**, **4**, and **7**, respectively. All three esters have the same molecular formula, $C_{31}H_{42}O_4$ (HREIMS). All possessed six olefinic protons, eight methyl groups, and three carbonyl groups. It was apparent from the spectral data that the α-pyrone ring was not present in these compounds. A COSY experiment with compound **10** in $CDCl_3$ established the connectivity of the olefinic protons; the proton at δ 6.97 (dd, J = 15.1, 11.4) was coupled to δ 8.10 and δ 6.39 (d, J = 11.4), and the proton at δ 7.45 (dd, J = 15.1, 11.4) was similarly coupled to δ 6.46 and δ 6.52. HMQC and HMBC experiments allowed the full structural assignment of **10**. Scalar coupling constants and difference NOE experiments allowed the assignment of the (*E*)-configuration at C15, C17, and C22 and the (*Z*)-configuration at C13 and C24. The downfield shift of H23 to δ 7.45 indicated that this proton lay in the deshielding region of the ester carbonyl group, consistent with the 24(*Z*) assignment. The stereochemistry of the tricyclic core was found to be the same as in **1** and **2** by NOE experiments.

It appears that **10** was previously derived from extracts of the sponge *Jaspis stellifera*, although the originally proposed structure had the malabaricane (*trans-anti-trans*) skeleton.[7] Based on the X-ray structure determination of stellettin B[5] (**6**) and NMR spectral comparisons, McCabe *et al.*[8] suggested that the compounds reported by Ravi *et al.*[7] all had the isomalabaricane (*trans-syn-trans*) stereochemistry in the tricyclic skeleton.

Table 2. ^{1}H-NMR Data in C_6D_6 (**1**, **2**, **5**, **6**) or in $CDCl_3$ (**9**, **10**)

	compound [δ ppm (mult, *J* Hz)]					
position	1	2	5	6	9	10
1	1.17 (td, 13.8, 4.3)	1.19 (dt, 3.9, 13.2)	1.51 (ddd, 12.4, 12,1, 0.98)	1.52 (m)	2.15 (m)	2.16 (m)
	0.90 (m)	0.91 (m)	0.89 (m)	0.91 (m)	1.49 (m)	1.49 (m)
2	1.56 (m)	1.58 (m)	2.16 (ddd, 1.57, 9.8, 5.9)	2.17 (ddd, 16.1, 9.8, 3.4)	2.71 (ddd, 16.1, 12.2, 5.9)	2.36 (m)
	1.82 (m)	1.84 (m)	2.28 (ddd, 15.7, 11.8, 5.9)	2.28 (ddd, 16.1, 11.7, 5.9)	2.38 (m)	2.70 (ddd, 16.1, 12,2, 6.0)
3	4.71 (dd, 11.7, 4.9)	4.73 (dd, 11.7, 4.9)				
5	1.52 (br d, 12.5)	1.52 (br d, 11.7)	1.95 (dd, 13.2, 2.4)	1.95 (dd, 14.2, 2.4)	2.39 (dd, 13.2, 2.4)	2.36 (d, 12.7)
6	1.07 (m)	1.14 (m)	1.04 (m)	1.15 (m)	1.50 (m)	1.50 (m)
	1.33 (dd, 12.5, 8.8)	1.41 (m)	1.34 (m)	1.34 (m)	1.58 (m)	1.58 (m)
7	1.77 (m)	1.76 (m)	1.65 (t, 8.8)	1.54 (m)	2.16 (m)	2.05 (m)
	1.90 (m)	1.82 (m)	1.85 (br t, 6.6)	1.72 (m)		
9	1.43 (dd, 15.0, 7.6)	1.41 (dd, 15.6, 7.3)	1.32 (dd, 15.1, 7.0)	1.32 (dd, 15.1, 6.9)	1.85 (t, 10.6)	1.85 (t, 11.2)
11	1.97 (m)	1.96 (m)	1.90 (m)	1.88 (m)	2.20 (br d, 10.6)	2.21 (d, 11.2)
	2.03 (dd, 16.6, 7.6)	2.02 (dd, 16.6, 7.3)	1.98 (dd, 16.6, 7.0)	1.97 (dd, 16.6, 6.9)		
15	6.87 (d, 14.6)	8.86 (d, 15.1)	6.87 (d, 15.0)	8.87 (d, 15.6)	6.67 (d, 15.1)	8.10 (d, 15.1)
16	6.92 (dd, 14.6, 10.5)	6.91 (dd, 15.1, 11.0)	6.94 (dd, 15.0, 11.0)	6.89 (dd, 15.6, 11.4)	7.03 (dd, 15.1, 11.6)	6.97 (dd, 15.1, 11.4)
17	7.48 (d, 10.5)	7.32 (d, 10.7)	7.52 (d, 11.0)	7.34 (d, 11.4)	6.34 (d, 11.6)	6.39 (d, 11.4)
18	2.59 (s)	1.77 (s)	2.59 (s)	1.79 (s)	2.32 (s)	2.06 (s)
19	0.66 (s)	0.68 (s)	0.47 (s)	0.50 (s)	0.84 (s)	0.83 (s)
21	1.57 (d, 1.0)	1.71 (d, 1.0)	1.58 (d, 1.0)	1.71 (d, 1.0)	2.00 (s)	1.98 (br s)
22					6.43 (d, 15.1)	6.46 (d, 15.1)
23	5.46 (d, 6.8)	5.45 (d, 6.8)	5.47 (d, 6.8)	5.45 (d, 6.8)	7.50 (dd, 15.1, 11.2)	7.45 (dd, 15.1, 11.4)
24	6.23 (dd, 6.8, 1.0)	6.26 (dd, 6.8, 1.0)	6.24, dd, 6.8, 1.0)	6.26 (dd, 6.8, 1.0)	6.51 (d, 11.2)	6.52 (d, 11.7)
27	1.84 (d, 1.0)	1.89 (d, 1.0)	1.85 (d, 1.0)	1.89 (d, 1.0)	2.02 (s)	1.98 (br s)
28	0.92 (s)	0.93 (s)	0.95 (s)	0.93 (s)	1.10 (s)	1.09 (s)
29	0.86 (s)	0.88 (s)	1.04 (s)	1.06 (s)	1.03 (s)	1.03 (s)
30	1.07 (s)	0.98 (s)	0.98 (s)	0.96 (s)	1.41 (s)	1.38 (s)
OMe					3.77 (s)	3.78 (s)
OAc	1.76 (s)	1.77 (s)				

Table 3. ^{13}C-NMR Data in C_6D_6 (**1**, **2**, **5**, **6**) or in $CDCl_3$ (**9**, **10**)

carbon	**1**	**2**	**5**	**6**	**9**	**10**
1	33.0	33.0	31.2	31.2	31.3	31.3
2	25.5	24.7	33.3	33.3	33.5	33.5
3	80.7	80.6	216.5	216.7	219.2	219.2
4	38.3	38.1	46.6	46.6	46.8	46.9
5	46.7	46.7	45.4	45.4	45.4	45.4
6	18.5	18.4	19.7	19.6	19.8	19.7
7	39.3	38.3	38.2	37.1	38.5	37.2
8	44.9	44.6	45.0	44.7	45.0	44.9
9	49.7	49.9	47.5	47.5	47.8	47.9
10	35.4	35.5	34.6	34.6	34.8	34.8
11	36.6	36.7	36.7	36.7	36.7	36.9
12	206.2	204.7	206.0	204.5	207.0	206.1
13	149.0	148.0	148.2	147.1	146.2	145.7
14	139.3	140.3	139.8	140.7	142.0	142.9
15	137.2	137.2	137.0	137.0	133.7	133.9
16	130.6	130.9	130.7	130.8	132.2	130.9
17	130.2	129.2	130.1	129.4	134.1	135.0
18	14.6	15.7	14.5	15.7	14.5	16.0
19	22.2	22.2	23.3	23.2	23.5	23.5
20	128.8	128.3	128.9	128.9	139.4	138.8
21	12.5	12.6	12.5	12.6	13.2	13.1
22	158.7	159.6	158.6	159.6	142.6	143.3
23	102.6	101.7	102.8	101.8	127.2	126.5
24	138.4	138.5	138.6	138.4	141.0	141.5
25	124.7	124.1	124.9	124.2	126.2	125.6
26	161.8	161.9	161.8	161.9	167.9	168.0
27	16.8	16.9	16.9	16.9	21.0	21.0
28	29.3	29.2	29.2	29.0	29.2	29.2
29	17.2	17.2	19.6	19.6	19.4	19.4
30	26.1	25.5	25.9	24.5	25.9	24.7
$OCOCH_3$	170.0	170.0				
$OCOCH_3$	20.8	20.8				
OCH_3					51.5	51.4

Compound **8** was similar to **10**, except for chemical shift differences at H23 (δ 6.55) and H24 (δ 7.27). Difference NOE experiments suggested that **8** was the C24 24(*E*) isomer of **10**. Similarly, **9** differed from **10** at H15 (δ 6.67) and H18 (δ 2.32), a phenomenon previously observed between **1** and **2**, **5**, and **6**. Therefore, **9** was the 13(*E*) isomer of **10**.

Due to the rapid equilibration between **1** and **2**, **5,** and **6**, and **4** and **7**, mixtures of each pair of interconverting compounds was tested in the NCI's 60 human tumor cell line in vitro assay.[2−4] The more sensitive cell lines (e.g., leukemia, CNS, and renal lines) generally responded with GI_{50} concentrations in the low-to-mid nanomolar range (data not shown).

The stellettins are similar to the retinoic acid family in that both are highly conjugated isoprenoid carboxylic acid pigments. COMPARE analyses,[4] however, showed no tangible similarity between the NCI 60 human tumor cell line panel responses to the stellettins and retinoic acid. Moreover, **5** and **7**, each tested at a concentration of 1 μM, neither induced conformational changes in human retinoic acid (RARα) or mouse retinoid x (RXRα) receptors nor antagonized the ability of 9-*cis*-retinoic acid to do so, as detected by the differential proteolytic sensitivity assay.[17]

Experimental Section

Sponge Material and Extraction. The yellow sponge *Stelletta* sp. (Demospongiae, Choristida, Stellettidae; 1 kg, wet wt) was collected as part of an NCI collection contract by Dr. P. Murphy (AIMS) in the northern territory of Australia off the shore north of Cape Wilberforce at depth of 15 m in November 1990. The sponge (spherical, brown-purple exterior, brown-yellow interior) was identified by Dr. S. Pomponi, and a voucher specimen (Q66C4702) was deposited at the Smithsonian Institution.

Isolation. The crude organic extract (5.0 g) was partitioned between 90% aqueous MeOH and hexane (1.55 g). The MeOH solution was adjusted to 80% MeOH and extracted with CCl_4 (2.20 g). The aqueous

MeOH phase was adjusted to 70% MeOH and further extracted with $CHCl_3$ (0.50 g). The bulk of the activity was concentrated in the CCl_4 fraction, which was subjected to vacuum liquid chromatography on Si gel using EtOAc−CH_2Cl_2 (0−100% EtOAc) to yield two active fractions (1.025 g and 0.345 g, respectively). HPLC purification of the less polar fraction (80 mg) on a silica column (2.1 × 25 cm, 12 mL/min, EtOAc−CH_2Cl_2, 1:9) afforded compounds **1** (5.1 mg), **2** (12.0 mg), **5** (11.9 mg), and **6** (41.0 mg). HPLC purification of the more polar fraction (55 mg) on a C_{18} column (2.1 × 25 cm, 10 mL/min, MeOH−H_2O, 23:2) yielded a mixture (24.2 mg) of **3**, **4,** and **7**, part of which (5.0 mg) was treated with excess CH_2N_2 and purified by HPLC (silica, 1 × 25 cm, EtOAc−CH_2Cl_2, 2:23) to afford **8** (0.5 mg), **9** (2.2 mg), and **10** (1.6 mg).

Stellettin C (1): a yellow solid; $[\alpha]_D$ −250° (*c* 0.51, $CHCl_3$); UV (EtOH) λ max 418 nm (log ϵ 4.39), 395 (4.48), 313 (4.24); IR (film) ν max 3015, 2957, 1710, 1699, 1544, 1246 cm^{-1}; HREIMS *m/z* 506.3022; calcd for $C_{32}H_{42}O_5$, 506.3032; EIMS *m/z* 506 (95), 491 (20), 446 (10), 257 (100), 256 (60), 241 (35); for ^{1}H-NMR and ^{13}C-NMR in C_6D_6, see Tables 1−3.

Stellettin D (2): a yellow solid; $[\alpha]_D$ −19.4° (*c* 1.0, $CHCl_3$); UV (EtOH) λ max 418 nm (log ϵ 4.45), 400 (4.54), 313 (4.23); IR (film) ν max 3015, 2957, 1710, 1699, 1544, 1246 cm^{-1}; EIMS *m/z* 506 (100), 494 (40), 451 (30), 397 (40), 257 (100), 256 (50), 241 (20); HREIMS *m/z* 506.3002; calcd for $C_{32}H_{42}O_5$, 506.3032; for ^{1}H-NMR and ^{13}C-NMR in C_6D_6 , see Tables 2 and 3.

Stellettin A (5): a yellow solid; $[\alpha]_D$ +36.6° (*c* 1.23, $CHCl_3$); UV (EtOH) λ max 417 nm (log ϵ 4.24), 396 (4.35), 312 (4.03); IR (film) ν max 3068, 2958, 1704, 1700, 1544 cm^{-1}; HRFABMS *m/z* 462.2772; calcd for $C_{30}H_{38}O_4$, 462.2770; EIMS *m/z* 462 (100), 447 (30), 429 (10), 313 (100), 257 (80), 256 (70), 241 (40); ^{1}H-NMR and ^{13}C-NMR in C_6D_6, see Table 2 and 3; ^{1}H-NMR ($CDCl_3$) δ 7.26 (d, *J* = 11 Hz, H-17), 7.15 (dd, *J* = 7, 1, H-24), 6.99 (dd, *J* = 15, 11, H-16), 6.92 (d, *J* = 15, H-15), 6.23 (d, *J* = 7, H-23), 2.74 (ddd, *J* = 15.5, 11.8, 5.9, H-2), 2.43 (dd, *J* = 13.2, 2, H-5), 2.36 (ddd, *J* = 15.5, 10, 2, H-2), 2.33 (m, 1H), 2.33 (s, 3H, H-18), 2.22 (br d, *J* = 11, 2H, H-11), 2.17 (m, 2H), 2.12 (d, *J* = 1, 3H), 2.03 (d, *J* = 1, 3H), 1.86 (t, 11, H-9), 1.65 (br dd, *J* = 15, 11, 1H), 1.50 (m, 2H), 1.44 (s, 3H, H-30), 1.13 (s, 3H, H-28), 1.05 (s, 3H, H-29), 0.84 (s, 3H, H-19).

Stellettin B (6): a yellow solid; $[\alpha]_D$ +49.3° (*c* 0.28, $CHCl_3$); UV (EtOH) λ max 417 nm (log ϵ 4.24), 395 (4.34), 313 (4.03); IR (film) ν max 3068, 2958, 1704, 1700, 1544 cm^{-1}; HREIMS *m/z* 462.2780; calcd for $C_{30}H_{38}O_4$, 462.2770; EIMS *m/z* 462 (100), 450 (40), 447 (30), 407 (30), 353 (40), 313 (20), 257 (65), 256 (60), 241 (30); ^{1}H-NMR and ^{13}C-NMR in C_6D_6 see Table 2 and 3; ^{1}H-NMR ($CDCl_3$) δ 8.24 (d, *J* = 15 Hz, H-15), 7.23 (d, *J* = 11.5, H-17), 7.12 (dd, *J* = 6.8, 1, H-24), 6.92 (dd, *J* = 15, 11.5, H-16), 6.20 (d, *J* = 6.8, H-23), 2.7 (ddd, *J* = 16.1, 11.7, 5.8, 1H, H-2), 2.36 (m, 2H, H-5, H-2), 2.24 (dd, *J* = 11, 8.5, 1H), 2.22 (d, *J* = 16, H-11), 2.16 (m, 1H), 2.10 (d, *J* = 1, 3H), 2.07 (m, 2H), 2.05 (s, 3H, H-18), 2.01 (d, *J* = 1, 3H), 1.86 (dd, *J* = 14, 8.5, H-9), 1.59 (m, 1H), 1.51 (m, 2H), 1.38 (s, 3H, H-30), 1.09 (s, 3H, H-28), 1.04 (s, 3H, H-29), 0.84 (s, 3H, H-19).

Methyl ester of stellettin E (8): a yellow solid; $[\alpha]_D$ +36.0° (*c* 0.05, $CHCl_3$); UV (EtOH) λ max 410 nm (log ϵ 4.52), 395 (4.56), 294 (4.08); IR (film) ν max 3068, 2953, 1704, 1700, 1579 cm^{-1}; EIMS *m/z* 478 (22), 463 (5), 365 (100), 313 (15), 273 (14), 241 (18); HREIMS *m/z* 478.3088; calcd for $C_{31}H_{42}O_4$, 478.3083; ^{1}H-NMR ($CDCl_3$) δ 8.13 (d, *J* = 15.2, H-15), 7.27 (dd, *J* = 11, 1.5, H-24), 6.96 (dd, *J* = 15.2, 11.6, H-16), 6.62 (d, *J* = 15.1, H-22), 6.55 (dd, *J* = 15.1, 11, H-23), 6.43 (d, *J* = 11.6, H-17), 3.78 (s, 3H, OMe), 2.69 (ddd, *J* = 16.1, 12.1, 5.9, 1H, H-2), 2.05 (s, 3H, H-18), 1.98 (br s, 6 H, H-21, H-26), 1.38 (s, 3H, H-30), 1.10 (s, 3H, H-28), 1.04 (s, 3H, H-29), 0.84 (s, 3H, H-19); partial ^{13}C-NMR ($CDCl_3$, from HMQC) δ 143.7 (C-22), 138.7 (C-24), 135.8 (C-17), 134.5 (C-15), 130.4 (C-16), 124.0 (C-23), 51.7 (OCH_3), 45.2 (C-5), 36.8 (C-11), 31.2 (C-1), 29.2 (C-28), 24.5 (C-30), 23.3 (C-19), 19.3 (C-29), 15.8 (C-18), 12.9 (C-21, C-26).

Methyl ester of stellettin F (9): a yellow solid; $[\alpha]_D$ −54.4° (*c* 0.16, $CHCl_3$); UV (EtOH) λ max 410 nm (log ϵ 4.63), 395 (4.66), 292 (3.66); IR (film) ν max 3068, 2953, 1704, 1700, 1579 cm^{-1}; EIMS *m/z* 478 (30), 463 (7), 431 (8), 365 (100), 313 (15); HREIMS *m/z* 478.3082; calcd for $C_{31}H_{42}O_4$, 478.3083; for ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$, see Tables 2 and 3.

Methyl ester of stellettin G (10): a yellow solid; $[\alpha]_D$ +63.6° (*c* 0.22, $CHCl_3$); UV (EtOH) λ max 415 nm (log ϵ 4.53), 395 (4.55), 294 (3.81); IR (film) ν max 3068, 2953, 1704, 1700, 1579 cm^{-1}; EIMS *m/z* 478 (23), 365 (100), 313 (10), 159 (10); HREIMS *m/z* 478.3088; calcd for $C_{31}H_{42}O_4$, 478.3083; for ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$, see Tables 2 and 3.

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References and Notes

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