Steroids and Sesquiterpenoids from the Soft Corals *Dendronephthya gigantea* and *Lemnalia cervicorni*

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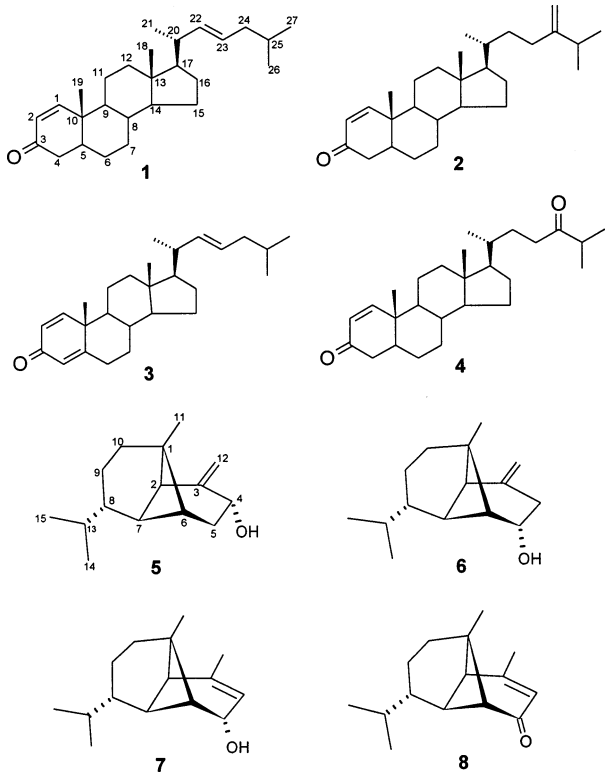
One new cytotoxic steroid, dendronesterone A (**1**), two new steroids, dendronesterones B and C (**2** and **3**), and a known steroid (**4**) were isolated from the methylene chloride solubles of the Formosan soft coral *Dendronephthya gigantea*. Two cytotoxic ylangene-type sesquiterpenoids, lemnalol (**5**) and the new compound cervicol (**6**), as well as two ylangene-type sesquiterpenoids, isolemnalol (**7**) (a new compound) and 4-oxo-α-ylangene (**8**), were isolated from the methylene chloride solubles of the Formosan soft coral *Lemnalia cervicorni*. Their structures were elucidated by 1D and 2D NMR spectral analysis, and their cytotoxicity against selected cancer cells was measured in vitro.

The genera *Lemnalia* and *Dendronephthya* have afforded bioactive sesquiterpenes[1−3] and steroids.[4−6] As part of our search for bioactive substances from marine organisms, the Formosan soft corals *Lemnalia cervicorni* May (Nephtheidae) and *Dendronephthya gigantea* Verrill (Nephtheidae) were studied because the CH_2Cl_2 extracts showed significant cytotoxicity to A549 (human lung adenocarcinoma), HT-29 (human colon adenocarcinoma), and P-388 (mouse lymphocytic leukemia) cell cultures as determined by standard procedures.[7,8] Bioassay-guided fractionation of CH_2Cl_2 extracts of *D. gigantea* resulted in the isolation of one new cytotoxic steroid, dendronesterone A (**1**), two new steroids, dendronesterones B and C (**2** and **3**), and a known steroid (**4**). Bioassay-guided fractionation of CH_2Cl_2 extracts of *L. cervicorni* resulted in the isolation of two cytotoxic ylangene-type sesquiterpenoids, lemnalol (**5**) and a new compound, cervicol (**6**), as well as two ylangene-type sesquiterpenoids, isolemnalol (**7**) (a new compound) and 4-oxo-α-ylangene (**8**).



Results and Discussion

Compound **1** had a molecular formula of $C_{27}H_{42}O$ as established by HREIMS. The ^{1}H NMR spectrum revealed the presence of two tertiary methyls (δ_H 0.71 and 1.01), three secondary methyls (δ_H 0.86, 0.87, and 1.01), and two olefinic protons (δ_H 5.20 and 5.27). The presence of an α,β-unsaturated carbonyl group was straightforward from NMR signals (Tables 1 and 2) at δ_H 5.85/δ_C 127.4, 7.15/158.7, and 200.4 (qC), as well as from an IR absorption at 1680 cm^{-1}. The 1D NMR data could account for 3 of the 7 degrees of unsaturation, suggesting the tetracyclic nature of **1**. Twenty-seven carbons including five methyls suggested that **1** was an analogue of cholesterol. COSY correlation between H-22/H-23 and HMBC correlations between Me-21/C-17, C-20, C-22, as well as the $J_{22,23}$ of 15.3 Hz, inferred an *E* double bond between C-22 and C-23. Rings A and B were elucidated on the basis of HMBC cross-peaks between Me-19/C-1, C-5, C-9, C-10 and H-4/C-3, whereas rings C and D were completed on the basis of HMBC correlations between Me-18/C-12, C-13, C-14, C-17. Comparison of ^{13}C NMR chemical shift values of **1** with those of five cholesta-1-en-3-ones reported from the octocoral *Alcyonium gracillimum*[9] inferred normal stereochemistry of the ring junctures of **1**. The NOESY correlations observed between H-11β and H-8, H-11β and H_3-18, H-11β and H_3-19, H-9 and H-14, H_3-18 and H-8, H_3-19 and H-8, H_3-18 and H-20, and H-9 and H-12α in **1** confirmed the relative configurations for each ring junction and chiral center. The stereochemistry of C-20 was determined by comparison of ^{1}H and ^{13}C NMR data with those of 5α,8α-epidioxycholesta-6,22-dien-3β-ol[10] and confirmed by NOESY correlation between H_3-21 and H-12β.

Compound **2** had a molecular formula of $C_{28}H_{44}O$ as determined by HREIMS. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) resembled those of **1** except for NMR

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Table 1. ^{1}H NMR Data for Metabolites **1**−**4** in $CDCl_3$

H	**1**[b]	**2**[a]	**3**[b]	**4**[a]
1	7.15 d (9.9)	7.15 d (10.0)	7.06 d (10.2)	7.14 d (10.0)
2	5.85 d (9.9)	5.85 d (10.0)	6.23 dd (10.2, 1.8)	5.86 dd (10.0, 0.5)
3				
4α	2.21 dd (18.0, 4.5)	2.23 dd (17.5, 6.5)	6.07 s	2.22 ddd (17.5, 3.5, 0.5)
4*β*	2.37 dd (18.0, 14.0)	2.37 dd (17.5, 14.8)		2.37 dd (17.5, 14.0)
5	1.96 m	1.90 m		1.92 m
6α	1.29 m	1.84 m	2.37 tt (12.9, 2.4)	1.42 m
6*β*	1.72 m		2.46 tdd (12.9, 3.9, 1.5)	
7	1.76 m	1.71 m	1.14 m	0.95 m, 1.72 m
8	1.50 m	1.42 m	1.28 m	1.43 m
9	1.01 m	0.98 m	1.14 m	1.22 m
11α	1.79 m	1.71 m	1.12 m	1.75 m
11*β*	1.52 m	2.28 m	1.74 m	1.45 m
12α	1.18 m	1.17 m	1.18 m	1.31 m
12*β*	2.05 m	2.04 m	2.05 m	1.99 dt (12.5, 3.0)
14	1.18 m	1.07 m	1.01 m	1.10 m
15	1.60 m	1.08 m, 1.58 m	1.61 m	1.12 m, 1.59 m
16	1.46 m	1.40 m	1.72 m	1.12 m, 1.65 m
17	1.22 m	1.14 m	1.15 m	1.63 m
18	0.71 s	0.70 s	0.75 s	0.73 s
19	1.01 s	1.00 s	1.23 s	1.01 s
20	2.07 m	1.43 m	2.00 m	2.53 dq (8.5, 7.0)
21	1.01 d (6.6)	0.95 d (6.5)	1.00 d (6.6)	1.03 d (7.0)
22	5.20 dd (15.3, 7.5)	1.42 m	5.19 dd (15.3, 7.8)	
23	5.27 dt (15.3, 8.4)	0.95 m	5.27 dt (15.3, 8.4)	2.36 m, 2.45 m
24	1.85 m		1.86 m	1.43 m
25	1.56 m	2.17 m	1.28 m	1.52 m
26	0.86 d (6.6)	1.03 (7.0)	0.85 d (6.6)	0.90 d (6.9)
27	0.87 d (6.6)	1.03 (7.0)	0.86 d (6.6)	0.90 d (6.9)
28		4.66 s, 4.72 s		

[a] Recorded at 500 MHz. [b] Recorded at 300 MHz.

Table 2. ^{13}C NMR Data (*δ*) for Metabolites **1**−**4** in $CDCl_3$

	1[b]	**2**[a]	**3**[b]	**4**[a]
1	158.7	158.7	156.1	158.4
2	127.4	127.3	127.5	127.4
3	200.4	202.4	186.5	200.2
4	41.1	41.0	123.8	41.0
5	44.4	44.3	169.5	44.2
6	28.7	28.2	33.0	27.6
7	31.4	30.9	33.7	31.2
8	35.7	35.7	35.6	35.6
9	50.1	49.9	52.5	49.9
10	39.1	39.5	43.7	38.9
11	21.3	21.2	22.9	21.2
12	39.7	39.8	39.6	39.6
13	42.7	42.7	42.6	42.9
14	56.5	56.3	55.6	55.7
15	24.2	24.1	24.4	24.3
16	27.7	27.1	28.6	27.5
17	56.0	56.0	55.9	52.1
18	12.4	12.2	12.3	12.4
19	13.0	13.0	18.8	13.0
20	40.2	35.7	40.1	49.4
21	20.9	18.6	20.8	16.5
22	138.0	34.6	137.8	214.9
23	126.5	31.3	126.6	39.7
24	42.0	156.6	42.0	32.4
25	28.6	31.3	28.6	27.7
26	22.4	21.8	22.3	22.4
27	22.3	22.0	22.4	22.4
28		106.0		

[a] Recorded at 125 MHz (assigned by DEPT, COSY, HSQC, and HMBC experiments). [b] Recorded at 75 MHz (assigned by DEPT, COSY, HSQC, and HMBC experiments).

signals due to the side chain. The stereochemistry of the side chain was determined by comparison of ^{13}C NMR data with those of stoloniferone G[11] and confirmed by NOESY correlations between H_3-21 and H-12*β*, H_3-18 and H-20, H_3-18 and H-11*β*, and H_3-18 and H-8.

Compound **3** had a molecular formula of $C_{27}H_{40}O$ as determined by HREIMS. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) resembled those of **1** except the double bond at C-4. The presence of an α,*β*-α′,*β*′-unsaturated carbonyl group was straightforward from NMR signals at δ_H 6.23/δ_C 127.5, 7.06/156.1, 6.07/123.8, 169.5 (qC), and 186.5 (qC), an IR absorption at 1676 cm^{-1}, and a UV maximum at 245 nm. HMBC correlations from H-1 to C-3/C-5, from H-2 to C-4/C-10, and from H-4 to C-2/C-10 confirmed the α,*β*-α′,*β*′-unsaturated carbonyl group at ring A. Comparisons of ^{13}C NMR chemical shift values of **3** with those of cholesta-1,4-dien-3-ones reported from a soft coral *Minabea* sp.[12] disclosed the expected all-*trans* stereochemistry at the ring junctures of **3**. Stereochemistry at C-20 was determined by comparison of ^{13}C NMR data with those of **1** and confirmed by NOESY correlation between H_3-21 and H-12*β*. Thus, **3** is a methyl 3-oxocholesta-1,4,22-triene.

Compound **4** had a molecular formula of $C_{27}H_{42}O_2$ as determined by HREIMS. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) were identical with those of cholest-1-ene-3,22-dione isolated from the octocoral *Alcyonium gracillimum*.[9] However, according to our detailed analysis of the 2D NMR spectra of **4**, the ^{1}H and ^{13}C NMR chemical shifts at C-23 and C-24 should be exchanged.

The methylene chloride extract (37.1 g) of *L. cervicorni* was chromatographed on a silica gel column using *n*-hexane−CH_2Cl_2 (1:3) as eluent to give compound **5** as colorless crystals (170 mg), which was identified by comparison of physical and spectral data with those of lemnalol.[3] The ^{1}H and ^{13}C NMR chemical shifts, which were not completely assigned previously,[3] were assigned by 1D and 2D NMR (COSY, NOESY, HSQC, HMBC, and 2D INADEQUATE) methods.

Compound **6** was analyzed for $C_{15}H_{24}O$ by HRFABMS and NMR spectral data. The presence of a secondary alcohol was indicated by IR (3572 cm^{-1}), ^{1}H NMR (*δ* 4.20 dt), and ^{13}C NMR (*δ* 68.1 CH). The presence of an *exo*-methylene functionality was indicated by ^{1}H NMR (*δ* 4.66 s, 4.72 s) and ^{13}C NMR (*δ* 107.2 CH_2, 147.8 qC).

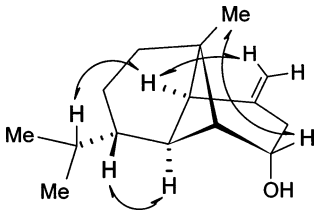

Figure 1. Key NOESY correlations of **6**.

The ^{13}C NMR also showed signals of three methyl carbons (δ 19.7, 20.1, 21.6), three sp^3 methylene carbons (δ 36.4, 24.2, 36.8), five sp^3 methine carbons (δ 48.5, 55.6, 37.4, 44.0, 32.5), and one sp^3 quaternary carbon (δ 43.0). The ^{1}H NMR spectrum of **6** showed signals due to a tertiary methyl at δ 0.68 (3H, s) and an isopropyl group at δ 0.89 (6H, d, J = 6.6 Hz) and 1.55 (1H, m) in addition to the signals at δ 2.82 (1H, dd, J = 16, 8 Hz), 2.57 (1H, d, J = 5.4 Hz), 2.38 (1H, ddt, J = 16, 8, 3 Hz), and 2.24 (1H, s). These NMR features were analogous to those of compound **5** with the exception that the resonances for the hydroxymethine at C-4 (δ_H 4.42 d; δ_C 66.5 CH) were replaced by the hydroxymethine at C-5 (δ_H 4.20 dt; δ_C 68.1 CH). Cross-peaks in the ^{1}H−^{1}H COSY spectrum of **6** showed couplings between the hydroxymethine proton at δ 4.20 (m, H-5) and the methine proton at δ 1.73 (m, H-6). HMBC correlations of **6** from H-5 to C-3, C-6, and C-7 and from H-7 to C-1, C-2, C-3, C-5, C-6, and C-13 comfirmed the location of a secondary hydroxyl at C-5 in **6** instead of C-4 in **5**. The relative stereochemistry of **6** was established by NOESY experiment (Figure 1). NOESY correlations from H-5 to H$_3$-11 and H-6 showed that these protons occurred on the same side of the molecule. NOESY correlations from H-2 to H-13 showed that these protons occurred on the other side of the molecule. In the ^{1}H NMR data of **6**, a large long-range coupling (J = 5.4 Hz) observed between H-2 (δ 2.57 d) and H-6 indicated the presence of a bridged cyclobutane system. In addition, no coupling was observed between H-7 (δ 2.24 s) and the adjacent protons (H-2, H-6, and H-8), suggesting a dihedral angle of approximately 90° between these protons.[3]

Compound **7** has the molecular formula $C_{15}H_{24}O$, as determined by HRFABMS and NMR spectral data. The NMR spectra resembled those of **6**. However, a methyl-bearing *Z*-trisubstituted olefin (δ_H 1.74 br s, 5.42 br s; δ_C 23.0 CH$_3$, 119.9 CH, 147.6 qC) in **7** replaced the *exo*-methylene in **6**. COSY cross-peaks from H-4 to H-12 and H-5 as well as HMBC correlations between H-12 and C-3, C-4, and C-2 comfirmed the position of the methyl-bearing *Z*-trisubstituted olefin. In the NOESY experiment, NOEs from H-5 to H$_3$-11 and H-6 showed that these protons occurred on the same side of the molecule. NOESY correlations from H-2 to H-13 showed that these protons occurred on the other side of the molecule. Significant differences of ^{13}C NMR chemical shifts (C-2, C-4, C-6, and C-9) from those of the β-isopropyl stereoisomer[13] as well as NOESY correlation between H-2 and H-13 of **7** confirmed the α-configuration of the isopropyl group.

The molecular formula $C_{15}H_{22}O$ of compound **8** was revealed by HRFABMS and NMR spectral data. The NMR features of compound **8** were analogous to those of **7** with the exception that the resonance for the 5-hydroxyl methine was replaced by a ketone (δ_C 203.3). HMBC correlations between H-12 and C-2, C-3, and C-4; H-6 and C-5 and C-8; and H-7 and C-2, C-3, C-5, C-6, C-9, and C-13 confirmed the ketone at C-5. The ^{13}C NMR data of **8** were identical with those of oxo-α-ylangene,[14] which was assigned as a β-isopropyl stereoisomer of **8**. However, NOESY correlation between H-2 and H-13 of **8** indicated the α-configuration of the isopropyl group. HMBC data led to a revision in the ^{13}C NMR assignments of C-8, C-9, C-10, C-11, and C-12 of oxo-α-ylangene assigned by Uchio.[14,15]

Table 3. ^{1}H NMR Data (δ) for Metabolites **5**−**8** in CDCl$_3$

	5[a]	**6**[b]	**7**[b]	**8**[b]
2	2.61 d (6.0)	2.57 d (5.4)	2.09 d (5.4)	2.47 d (6.6)
4	4.42 d (7.5)	2.38 ddt (16.0, 8.0, 3.0) 2.82 dd (8.0, 16.0)	5.42 br s	5.80 br s
5	2.23 ddd (2.0, 8.0, 14.0) 1.85 ddd (1.5, 4.0, 14.0)	4.20 dt (8.0, 3.0)	4.27 br s	
6	1.65 m	1.73 m	1.77 m	2.27 d (6.6)
7	2.23 s	2.24 s	1.85 s	2.66 s
8	1.55 m	1.62 m	1.59 m	1.69 m
9	1.64 m	1.68 m	1.68 m	1.84 m
10	1.67 m	1.69 m	1.73 m	1.88 m
11	0.63 s	0.68 s	0.82 s	0.97 s
12	4.86 s 5.04 s	4.66 s 4.72 s	1.74 br s	2.02 br s
13	1.51 m	1.55 m	1.63 m	1.66 m
14	0.87 d (7.0)	0.89 d (6.6)	0.88 d (6.6)	0.85 d (6.6)
15	0.87 d (7.0)	0.89 d (6.6)	0.89 d (6.6)	0.89 d (6.6)

[a] Recorded at 500 MHz. [b] Recorded at 300 MHz.

Table 4. ^{13}C NMR Data (δ) for Metabolites **5**−**8** in CDCl$_3$

	5[a]	**6**[b]	**7**[b]	**8**[b]
1	42.3	43.0	48.8	56.9
2	47.2	48.5	44.7	46.7
3	154.8	147.8	147.6	169.6
4	66.5	36.4	119.9	122.3
5	34.0	68.1	70.6	203.3
6	47.6	55.6	54.5	64.3
7	42.0	37.4	42.0	56.4
8	44.3	44.0	44.9	44.9
9	21.4	24.2	22.7	22.1
10	36.5	36.8	36.9	36.7
11	20.2	19.7	18.9	20.4
12	111.4	107.2	23.0	24.0
13	32.3	32.5	32.5	32.0
14	20.0	21.6	19.9	19.7
15	19.4	20.1	19.4	19.5

[a] Recorded at 125 MHz (assigned by DEPT, 2D INADEQUATE, COSY, HSQC, and HMBC experiments). [b] Recorded at 75 MHz (assigned by DEPT, COSY, HSQC, and HMBC experiments).

Table 5. Cytotoxicity of Compounds **1**−**8**

	cell lines ED$_{50}$ (μM)	
compound	P-388	HT-29
1	9.84	>100
2	>100	>100
3	>100	>100
4	8.93	9.03
5	16.3	10.5
6	>50	>50
7	>50	>50
8	>50	>50
mithramycin[a]	0.15	0.21

[a] Mithramicin was used as positive control.

Cytotoxicity of the isolates is shown in Table 5. Compounds **1**, **4**, and **5** exhibited cytotoxicity against P-388 with ED$_{50}$ values of 9.45, 8.93, and 16.3 μM, respectively. Compounds **4** and **5** exhibited cytotoxicity against HT-29 with ED$_{50}$ values of 9.03 and 10.5 μM, respectively.

Experimental Section

General Experimental Procedures. Melting points were determined using a Yanagimoto micromelting point apparatus

and are reported uncorrected. Optical rotations were determined on a JASCO DIP-181 polarimeter. UV spectra were obtained on a Shimadzu UV-160A spectrophotometer, and IR spectra were recorded on a Hitachi 26-30 spectrophotometer. The NMR spectra were recorded on a Varian Anova 500 or a Bruker Avance 300 spectrometer. The chemical shifts were given in δ (ppm) and coupling constants in Hz. EIMS spectra were obtained with a JEOL JMS-SX/SX 102A mass spectrometer at 70 eV. Si gel 60 (Merck, 230−400 mesh) was used for column chromatography; precoated Si gel plates (Merck, Kieselgel 60 F_{254}, 0.25 mm) were used for TLC analysis.

Animal Material. The soft coral *D. gigantea* was collected at Green Island, off Taiwan, in September 2001, at a depth of 3−4 m and was stored for 4 weeks in a freezer until extraction. A voucher specimen, NSUGN-048, was deposited in the Department of Marine Resources, National Sun Yat-sen University, Taiwan.

The soft coral *L. cervicorni* was collected at Green Island, off Taiwan, in December 2000, at a depth of 3−4 m and was stored for 1 week in a freezer until extraction. A voucher specimen, NSUGN-040, was deposited in the Department of Marine Resources, National Sun Yat-sen University, Taiwan.

Extraction and Isolation. The soft coral *D. gigantea* was freeze-dried to give 1.88 kg of solid, which was extracted with CH_2Cl_2 (4.0 L × 3). After removal of solvent in vacuo, the residue (14.2 g) was chromatographed over Si gel 60 using *n*-hexane and *n*-hexane−EtOAc mixtures of increasing polarity. Elution by *n*-hexane−EtOAc (90:10) afforded fractions containing compounds **1** and **2**. Elution by *n*-hexane−EtOAc (83:17) afforded fractions containing compounds **3** and **4**. Compounds **1**−**4** were further purified by RP-18 HPLC column by eluting with MeOH−H_2O (93:7).

The soft coral *L. cervicorni* was freeze-dried to give 0.42 kg of solid, which was extracted with CH_2Cl_2 (3.0 L × 3). After removal of solvent in vacuo, the residue (37.1 g) was chromatographed over Si gel 60 using *n*-hexane and *n*-hexane−CH_2Cl_2 mixtures of increasing polarity. Elution by *n*-hexane−CH_2Cl_2 (1:3) afforded fractions containing compound **7**. Elution by CH_2Cl_2 afforded fractions containing compounds **7** and **8**. Elution by CH_2Cl_2−EtOAc (1:1) afforded fractions containing compound **6**. Compound **7** was further purified by Si gel column chromatography, by eluting with *n*-hexane−CH_2Cl_2 (49:1). Compounds **7** and **8** were further purified by Si gel column chromatography by eluting with *n*-hexane−acetone (99:1). Compound **6** was further purified by Si gel column chromatography, by eluting with *n*-hexane−EtOAc (47:3).

Dendronesterone A (1): white solid; $[\alpha]^{25}_D$ +16° (*c* 0.3, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 226 (3.60) nm; IR (KBr) ν_{max} 1680 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m/z* 382 $[M]^+$ (12), 367 (5), 298 (36), 107 (100); HREIMS, *m/z* $[M]^+$ 382.3216 (calcd for $C_{27}H_{42}O$, 382.3225).

Dendronesterone B (2): white solid; $[\alpha]^{25}_D$ +18° (*c* 0.1, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 222 (3.56) nm; IR (KBr) ν_{max} 1690 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m/z* 396 $[M]^+$ (6), 382 (16), 312 (39), 269 (43), 122 (100); HREIMS, *m/z* $[M]^+$ 396.3392 (calcd for $C_{28}H_{44}O$, 396.3381).

Dendronesterone C (3): white solid; $[\alpha]^{25}_D$ +26° (*c* 0.6, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 245 (4.10) nm; IR (KBr) ν_{max} 1676 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m/z* 380 $[M]^+$ (8), 365 (2), 270 (20), 122 (100); HREIMS, *m/z* $[M]^+$ 380.3066 (calcd for $C_{27}H_{40}O$, 380.3069).

Lemnalol (5): colorless needles; mp 47−48°C; $[\alpha]^{25}_D$ −7.89° (*c* 0.60, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 214 (3.50) nm; IR (KBr) ν_{max} 3558, 1634 cm^{-1}; ^1H NMR, see Table 3; ^{13}C NMR, see Table 4; EIMS *m/z* 220 $[M]^+$ (1), 202 (12), 159 (86), 145 (25); HRFABMS, *m/z* $[M + H]^+$ 221.1904 (calcd for $C_{15}H_{25}O$, 221.1906).

Isolemnalol (6): oil; $[\alpha]^{25}_D$ +3.33° (*c* 0.66, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 212 (3.56) nm; IR (KBr) ν_{max} 3572, 1630 cm^{-1}; ^1H NMR, see Table 3; ^{13}C NMR, see Table 4; EIMS *m/z* 220 $[M]^+$ (3), 202 (6), 187 (9), 159 (3), 136 (41), 105 (63); HRFABMS, *m/z* $[M + H]^+$ 221.1909 (calcd for $C_{15}H_{25}O$, 221.1906).

Cervicol (7): oil; $[\alpha]^{25}_D$ −70.8° (*c* 0.80, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 212 (3.88) nm; IR (KBr) ν_{max} 3582, 1632 cm^{-1}; ^1H NMR, see Table 3; ^{13}C NMR, see Table 4; EIMS *m/z* 202 $[M - H_2O]^+$ (7), 154 (14), 137 (16), 119 (40); HRFABMS, *m/z* $[M + H]^+$ 221.1899 (calcd for $C_{15}H_{25}O$, 221.1906).

4-Oxo-α-ylangene (8): oil; $[\alpha]^{25}_D$ +8.7° (*c* 0.62, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 225 (4.39) nm; IR (KBr) ν_{max} 1710, 1638 cm^{-1}; ^1H NMR, see Table 3; ^{13}C NMR, see Table 4; EIMS *m/z* 218 $[M]^+$ (1), 203 (3), 152 (32); HRFABMS, *m/z* $[M + H]^+$ 219.1746 (calcd for $C_{15}H_{23}O$, 219.1750).

Cytotoxicity Testing. P-388 cells were supplied by J. M. Pezzuto, Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago; A549 and HT-29 were purchased from the American Type Culture Collection. Cytotoxicity assays were carried out according to the procedure described previously.[8]

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Supporting Information Available: $^1H-^1H$ COSY and HMBC correlations of **1** and $^{13}C-^{13}C$ homonuclear shift correlation 2D spectrum (INADEQUATE) of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Jurek, J.; Scheuer, P. J. *J. Nat. Prod.* **1993**, *56*, 508−513.
(2) Kikuchi, H.; Manda, T.; Kobayashi, H.; Yamada, Y.; Iguchi, K. *Chem. Pharm. Bull.* **1983**, *31*, 1086−1088.
(3) Kikuchi, H.; Tsukitani, Y.; Yamada, Y.; Iguchi, K.; Drexler, S. A.; Clardy, J. *Tetrahedron Lett.* **1982**, *23*, 1063−1066.
(4) Tomono, Y.; Hirota, H.; Fusetani, N. *J. Org. Chem.* **1999**, *64*, 2272−2275.
(5) Tomono, Y.; Hirota, H.; Imahara, Y.; Fusetani, N. *J. Nat. Prod.* **1999**, *62*, 1538−1541.
(6) Yoshikawa, K.; Kanekuni, S.; Hnahusa, M.; Arihara, S.; Ohta, Y. *J. Nat. Prod.* **2000**, *63*, 670−672.
(7) Geran, R. I.; Greenberg, N. H.; MacDonald, M. M.; Schumacher, A. M.; Abbott, B. J. *Cancer Chemother. Rep.* **1972**, *3*, 1−91.
(8) Hou, R.-S.; Duh, C.-Y.; Chiang, M. Y.; Lin, C.-N. *J. Nat. Prod.* **1995**, *58*, 1126−1130.
(9) Seo, Y.; Jung, J. H.; Rho, J. R.; Shin, J.; Shon, J. *Tetrahedron* **1995**, *51*, 2497−2506.
(10) Gauvin, A.; Smadja, J.; Aknin, M.; Faure, R.; Gaydou, E.-M. *Can. J. Chem.* **2000**, *78*, 986−992.
(11) Duh, C.-Y.; El-Gamal, A. A. H.; Chu, C.-J.; Wang, S.-K.; Dai, C.-F. *J. Nat. Prod.* **2002**, *65*, 1535−1539.
(12) Ksebati, M.; Schmitz, F. J. *J. Org. Chem.* **1988**, *53*, 3926−3929.
(13) Daniewski, W.; Anczewski, W.; Gumulka, M.; Danikiewicz, W.; Jacobsson, U. Norin, T. *Phytochemistry* **1996**, *43*, 811−814.
(14) Uchio, Y. *Tetrahedron* **1978**, *34*, 2893−2899.
(15) Uchio, Y.; Matsuo, A.; Eguchi, S.; Nakayama, M.; Hayashi, S. *Tetrahedron Lett.* **1977**, 1191−1194.

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