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

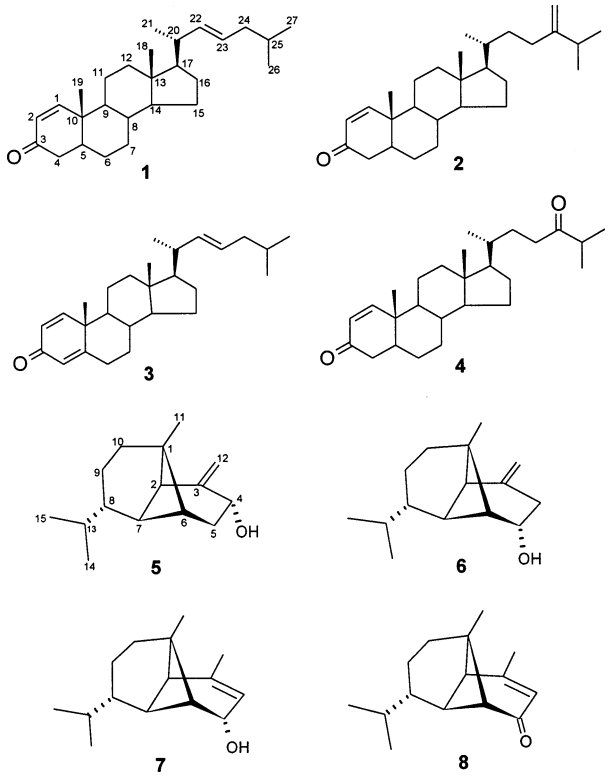
Chang-Yih Duh,*[,†] Ali A. H. El-Gamal,[†,‡] Pei-Ying Song,[†] Shang-Kwei Wang,[§] and Chang-Feng Dai[⊥]

Department of Marine Resources, National Sun Yat-sen University, Kaohsiung, Taiwan, Department of Microbiology, Kaohsiung Medical University, Kaohsiung, Taiwan, and Institute of Oceanography, National Taiwan University, Taipei, Taiwan, Republic of China

Received December 31, 2003

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

* To whom correspondence should be addressed. Tel: 886-7-525-2000, ext. 5036. Fax: 886-7-525-5020. E-mail: yihduh@mail.nsysu.edu.tw.
† National Sun Yat-sen University.
‡ On leave from Faculty of Pharmacy, Mansoura University, Egypt.
§ Kaohsiung Medical University.
⊥ National Taiwan University.

10.1021/np030550l CCC: $27.50
Published on Web 08/31/2004

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).

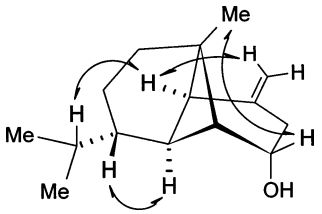


Figure 1. Key NOESY correlations of **6**.

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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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]

Acknowledgment. We thank J. M. Pezzuto, Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, for providing the P-388 cell lines. This work was supported by grants from the National Science Council of Taiwan awarded to C.-Y.D.

Supporting Information Available: ^{1}H−^{1}H 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.

NP030550L