Dendronpholides A−R, Cembranoid Diterpenes from the Chinese Soft Coral *Dendronephthya* sp.

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A systematic examination of the Chinese soft coral *Dendronephthya* sp. resulted in the isolation and characterization of 18 new cembranoid diterpenes, namely, dendronpholides A−R (**2−19**), along with 11-episinulariolide and an enantiomer of sandensolide. Their structures were determined through extensive spectroscopic (IR, MS, 2D NMR) data analyses and by comparison with those reported in literature. The cytotoxicity of several compounds against human tumor cell lines was also evaluated.

Soft corals of the genus *Dendronephthya* (Nephtheidae) are distributed throughout tropical coastal waters of the Indo-Pacific Ocean. This genus is highly prolific and is represented by about 248 species. However, only a few species of *Dendronephthya* have been chemically examined so far. Previous chemical examination of *Dendronephthya* soft corals resulted in the isolation of polyhydroxysteroids[1–4] as main metabolites, along with a few sesquiterpenoids,[2] oxylipin derivatives,[5] and numerous fatty acids.[6] Bioactivity tests revealed that the fatty acids and trigonelline possess antifouling activity.[7,8] However, no diterpenes have been reported from this genus. In the course of our investigation regarding the chemical diversity of soft corals growing in the South China Sea, an unidentified species of the genus *Dendronephthya* was collected in the coral reef of Sanya Bay, Hainan Province, China. The bioassay-guided fractionation led to the isolation of 18 new cembrane-type diterpenes, along with (−)-sandensolide and 11-episinulariolide. This paper reports on the structure elucidation of the new compounds as well as cytotoxicity data for some cembranes.

Results and Discussion

A cytotoxicity bioassay revealed that the EtOAc fraction of the EtOH extract from *Dendronephthya* sp. possessed inhibitory activities against the human tumor cell lines HL-60 (inhibitory rate 95.1% per 100 μg/mL), BGC-823 (inhibitory rate 92.7% per 100 μg/mL), Bel-7402 (inhibitory rate 74% per 100 μg/mL), and KB (inhibitory rate 70.5% per 100 μg/mL), while the water-soluble fraction showed no activity. An extensive chromatography of the EtOAc fraction resulted in the isolation of 20 cembranoid diterpenes.

Compound **1** had a molecular formula of $C_{20}H_{30}O_4$, as determined by HRFABMS data (*m/z* 357.2028 [M + Na]$^+$, calc 357.2026). A comparison of ^{1}H and ^{13}C NMR data and examination of 2D NMR spectroscopic data revealed that the structure of **1** is identical to sandensolide.[9–11] The 8*E*,11*E*-configurations were recognized from the chemical shifts of C-19 (δ_C 15.0) and C-20 (δ_C 10.0) and also by the NOESY cross-peaks between H-9 (δ_H 5.40, dd)/H-7 (δ_H 2.23, m) and H-11 (δ_H 5.35, brd)/H-13 (δ_H 3.97, dd). The protons H-1, H-5, and H-13 are oriented on the same face as in the case of sandensolide, which could be shown by the NOE relationships of H-5 (δ_H 3.60, dd)/H-1 (δ_H 1.90, m), H-13/H-11, H-5/H-9, H-9/H-10a (δ_H 2.34), and H-11/H-1a. However, the antipode rotation of **1** ($[\alpha]^{20}_D$ −45.0 (*c* 0.5, CHCl$_3$)] compared to that of (+)-

sandensolide ($[\alpha]^{20}_D$ +46.0 (0.84, CHCl$_3$),[9] suggested that compound **1** was an enantiomer of the latter.

Dendronpholide A (**2**) had a molecular formula of $C_{22}H_{32}O_5$ as established by HRFABMS (*m/z* 399.2140 [M + Na]$^+$, calc 399.2142), implying seven degrees of unsaturation. Its ^{1}H and ^{13}C NMR data (Table 1) were very similar to those of **1**, as characterized by the ^{1}H NMR resonances at δ_H 5.55 (1H, brs, H-17a) and 5.97 (1H, brs, H-17b) and the ^{13}C NMR resonances at δ_C 145.5 (C-15), 169.0 (C-16), and 124.6 (C-17) for an α-*exo*-methylene carbonyl group and the olefinic protons at δ_H 5.28 (1H, dd, *J* = 7.5, 7.5 Hz, H-9) and 5.53 (1H, dd, *J* = 8.5, 8.5 Hz, H-11) for two trisubstituted double bonds at C-8/C-9 and C-11/C-12. The remarkable downfield tertiary oxygenated carbon at δ_C 86.4 was assignable to C-4 of a seven-membered lactone ring.[9] Those assignments were further confirmed by COSY, HMQC, and HMBC data analysis. The structure of **2** was distinguished from **1** by the exhibition of an additional acetyl group [δ_H 2.04 (3H, s), δ_C 21.4, and 170.9], which was linked to C-5 (δ_C 71.3). This conclusion was confirmed by the HMBC interaction between H-5 (δ_H 5.25, d, *J* = 11.5 Hz) and the acetyl carbonyl carbon. The relative stereochemistry of **2** was the same as **1**, as evidenced from the similar NMR data and NOESY relationships (Figure 1).

Dendronpholide B (**3**) shared the same molecular formula as **2**, as determined by the HRFABMS and NMR data. Its ^{1}H and ^{13}C NMR data (Table 1) closely resembled those of **2**, with the exception that the C-13 resonance of **3** shifted upfield to δ_C 64.5, whereas the chemical shift of C-20 appeared at δ_C 17.5, in contrast to δ_C 10.0 ppm of **2**. This difference could be explained by the γ-gauche effect of the latter compound when OH-13 is β-oriented. In addition, H-13 (δ_H 4.46, d, *J* = 11.5 Hz) of **3**, representing one doublet spin rather than that with dd coupling of **2** (Table 1), suggested that **3** is an epimer of **2** at C-13. The NOE correlation between H-13 and the methylene proton H-10 (δ_H 3.17, ddd) instead of H-13/H-11, as observed in **2**, supported this assignment. The NOE connection of H-5 (δ_H 5.34, d)/H-1 (δ_H 2.23) deduced the α-orientation of H-1 and H-5.

The NMR spectroscopic data of dendronpholide C (**4**) (Table 1) were closely related to those of **1**. The difference was attributed to the chemical shift of C-4, which in **4** appeared at δ_C 74.6 (s) instead of δ_C 87.5 (s) in **1**, implying the lactone ring of the latter compound to be opened, and C-4 of **4** was connected to a hydroxy group. Moreover, the NMR spectra of **4** presented an additional methoxy group [δ_H 3.67 (3H, s), δ_C 52.1], whose protons correlated to a carbonyl carbon at δ_C 167.5 (C-16) in the HMBC. This finding led to the assignment of a methyl ester at C-16. The relative stereochemistry of **4** was the same as **1** as indicated by the similar NMR and NOE data observed.

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Table 1. ¹H and ¹³C NMR Data of Dendronepholides A−E (**2−6**) in DMSO-d_6

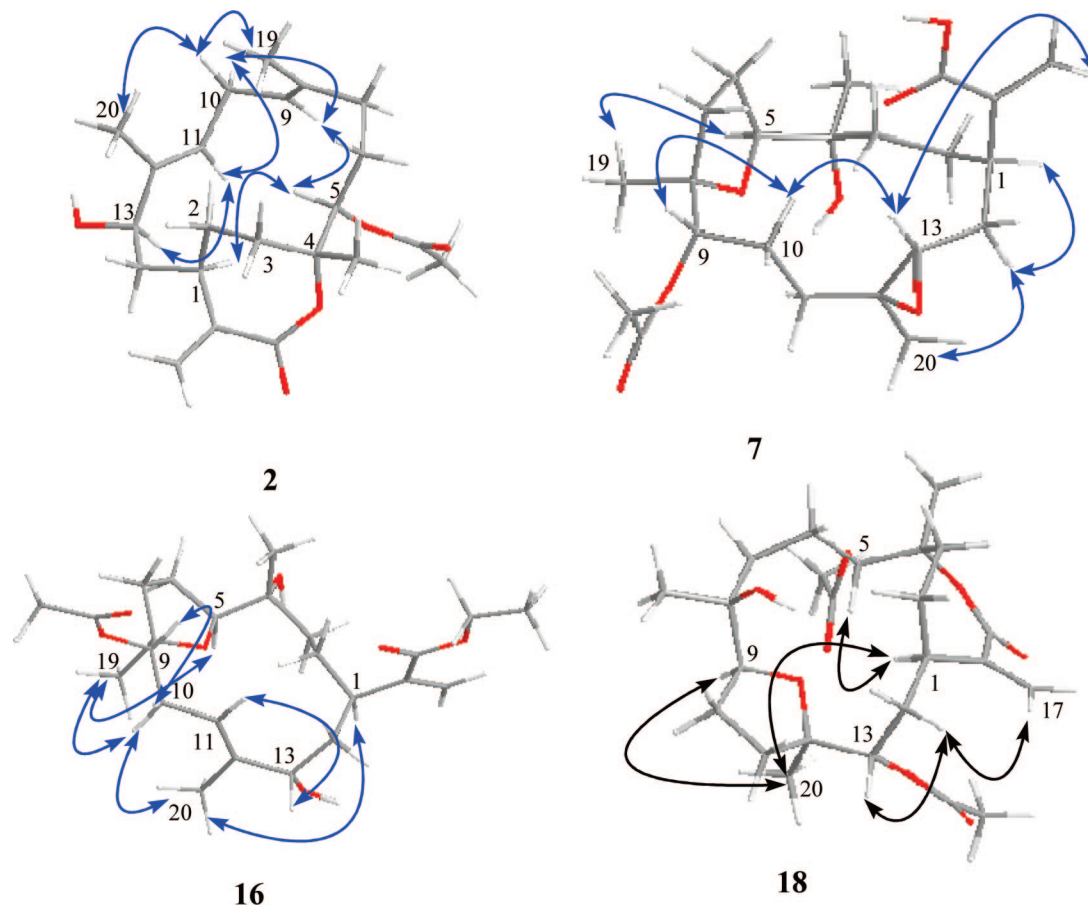| position	2		3		4		5		6	
1	2.46 m	31.9 CH	2.23 ddd (8.0,8.0,10.0)	32.0 CH	2.18 ddd (7.0,7.5,12.5)	38.1 CH	2.16 m	39.4 CH	2.23 ddd (4.0,10.5,10.5)	38.5 CH
2	1.08 ddd (3.5,11.0,11.0) 1.71 m	28.1 CH₂	1.10 mv 1.80 m	29.4 CH₂	1.28 m 1.28 m	26.2 CH₂	1.26 m 1.29 m	26.4 CH₂	1.18 m 1.20 m	25.3 CH₂
3	1.80 m 1.90 m	32.1 CH₂	1.78 m 2.00 m	32.6 CH₂	0.90 ddd (6.0,6.0,12.0) 1.20 m	38.1 CH₂	1.40 m 1.70 m	39.2 CH₂	1.10 ddd (2.0,2.0,12.0) 1.40 ddd (3.5,11.5,12.0)	39.5 CH₂
4		86.4 C		86.4 C		74.6 C		72.7 C		78.8 C
5	5.25 d (11.5)	71.3 CH	5.34 d (9.0)	71.8 CH	3.16 d (10.0)	70.1 CH	4.92 d (11.0)	74.8 CH		214.2 C
6	1.38 dd (13.5,13.5) 1.50 m	27.9 CH₂	1.50 m	27.3 CH₂	1.22 m 1.50 m	28.9 CH₂	1.20 m 1.48 m	29.2 CH₂	2.40 brdd (3.0,14.0) 3.20 ddd (2.0,11.0,14.0)	33.1 CH₂
7	1.78 m 1.90 m	34.1 CH₂	1.75 m 2.00 m	34.7 CH₂	1.97 brd (12.5) 2.09 dd (12.5,12.5)	34.9 CH₂	1.92 dd (5.5,13.0) 1.92 dd (5.5,13.0)	33.3 CH₂	2.00 dd (3.0, 15.0) 2.33 ddd (2.0, 11.0,15.0)	31.7 CH₂
8		133.8 C		130.1 C		135.4 C		134.9 C		133.4 C
9	5.28 dd (7.5,7.5)	125.2 CH	5.48 m	127.6 CH	5.25 (dd, 7.5,7.5)	124.0 CH₂	5.43 dd (6.0,6.0)	122.6 CH	5.03 m	122.7 CH
10	2.60 dd (6.5,8.0)	25.9 CH₂	2.41 brd (14.5) 3.17 ddd (11.0,11.5,14.5)	26.8 CH₂	2.40 ddd (7.0,7.5,12.0) 2.94 ddd (7.5,10.0,12.0)	26.6 CH₂	2.50 ddd (6.0,7.5,12.0) 2.70 ddd (6.0,8.0,12.0)	26.2 CH₂	2.46 2.71 ddd (7.5,7.5,13.5)	26.5 CH₂
11	5.53 brd (8.5,8.5)	126.3 CH	5.07 brd (10.0)	127.8 CH	5.17 brd (10.0)	126.6 CH	5.37 dd (7.5,8.0)	123.9 CH	5.02 m	125.0 CH
12		134.7 C		135.7 C		133.3 C		138.8 C		135.3 C
13	3.94 dd (6.0, 12.0)	75.5 CH	4.46 d (11.5)	64.5 CH	3.95 dd (7.0,10.0)	75.4 CH	3.69 dd (6.5,10.0)	73.9 CH	3.79 dd (4.5, 10.0)	74.4 CH
14	1.54 m 1.80 m	38.5 CH₂	1.60 m 1.80 m	39.5 CH₂	1.45 m 1.50 m	41.4 CH₂	1.69 m 1.69 m	38.1 CH₂	1.50 m 1.60 m	40.0 CH₂
15		145.5 C		146.2 C		144.3 C		140.5 C		143.5 C
16		169.0 C		168.6 C		167.5 C		167.7 C		167.2 C
17	5.55 brs 5.97 brs	124.6 CH₂	5.47 brs 5.94 brs	123.9 CH₂	5.57 brs 6.12 brs	124.9 CH₂	5.30 brs 6.27 brs	124.1 CH₂	5.49 brs 6.17 brs	125.2 CH₂
18	1.19 s	24.9 CH₃	1.20 s	23.9 CH₃	0.98 s	24.4 CH₃	0.95 s	23.7 CH₃	1.03 s	24.5 CH₃
19	1.67 s	16.8 CH₃	1.65 s	16.2 CH₃	1.54 s	16.1 CH₃	1.65 s	17.9 CH₃	1.56 s	16.4 CH₂
20	1.56 s	10.0 CH₃	1.53 s	17.5 CH₃	1.60 s	10.0 CH₃	1.57 s	10.7 CH₃	1.52 s	10.7 CH₃
Ac	2.04 s	21.4 CH₃ 170.9 C	2.05 s	21.2 CH₃ 170.3 C			2.00 s	21.6 CH₃ 170.9 C		
OMe OEt			3.67 s	52.1 CH₃			3.69 s	52.3 CH₃	4.15 q (7.0) 1.23 t (7.0)	60.8 CH₂ 14.5 CH₃

Figure 1. Key NOE correlations of compounds **2**, **7**, **16**, and **18**.

The NMR spectroscopic data of dendronpholide D (**5**) were very compatible with those of **4**, except for the presence of an additional acetyl group, as indicated by a ^{1}H NMR resonance at δ_H 2.00 (3H, s) and its corresponding ^{13}C NMR resonance at δ_C 21.6, as well as a carbonyl signal at δ_C 170.9. This assignment was confirmed by the molecular formula of **5** being 42 amu higher than **4**, as determined by HRFABMS data (m/z 431.2398 [M + Na]$^+$, calc 431.2403). The acetoxy group was deduced to be connected to position C-5 on the basis of the HMBC correlation from H-5 (δ_H 4.92, d, J = 11.0 Hz) to the acetyl carbonyl carbon. The similar NOE connectivity of **5** in comparison with **4** and **2**, as observed between H-5/H-1 (δ_H 2.16), H-5/H-9 (δ_H 5.43), and H-13 (δ_H 3.69)/H-11 (δ_H 5.37), allowed the assignment of H-1α, H-5α, and H-13α.

Dendronpholide E (**6**) had a molecular formula of $C_{22}H_{34}O_5$, as established by the HRFABMS data (m/z 401.2293 [M + Na]$^+$, calc 401.2298). A comparison of ^{1}H and ^{13}C NMR data (Table 1) indicated that **6** possessed a cembra-8,11-diene backbone, closely related to **5**. However, the ^{13}C NMR spectrum presented a ketone signal at δ_C 214.2, which was determined to be positioned at C-5 on the basis of the HMBC relationship from H$_3$-18 (δ_H 1.03, s) to C-5, C-4 (δ_C 78.8) and C-3 (δ_C 39.5). Moreover, an ethoxy group [δ_H 1.23 (3H, t, J = 7.0 Hz), 4.15 (2H, q, J = 7.0 Hz)] was observed in the ^{1}H NMR spectrum, which was shown to form an ethyl ester at C-16 through HMBC correlation between δ_H 4.15 (2H, q) and the carbonyl carbon δ_C 167.2 (C-16). The NOE relationships between H-13 (δ_H 3.79)/H-2a (δ_H 1.20), H-13/H-11 (δ_H 5.02), and H-1 (δ_H 2.23)/H-2a revealed that **6** shared the same relative stereochemistry as **5**.

The molecular formula of dendronpholide F (**7**) was determined as $C_{22}H_{34}O_7$ from HRFABMS (m/z 409.2230 [M − 1]$^-$, calc 409.2231) and NMR data. The ^{1}H and ^{13}C NMR data of **7** (Tables 2 and 3) resembled those of 9-acetoxy-5,8-tetrahydrofuran-12,13-epoxycembr-15(17)-en-16,4-olide,[10,11] which was featured by the

presence of an acetyl group [δ_H 2.04 (3H, s), δ_C 21.3 and 171.8], oxygenated carbons at δ_C 88.3 (C-5) and 83.3 (C-8) for a 5,8-tetrahydrofuran ring, and the carbon resonances at δ_C 61.3 (C-12) and 59.0 (C-13) for an 12,13-epoxide. The protons at δ_H 5.60 (1H, brs, H-17a) and 6.15 (1H, brs, H-17b) in association with the carbon resonances at δ_C 146.0 (C-15), 169.0 (C-16), and 124.0 (C-17) were attributed to an α-*exo*-methylene acetyl group, which was positioned at C-1 (δ_C 38.2, d) according to the HMBC interaction between H$_2$-17 and C-1. The chemical shift of C-4 (δ_C 72.8) was indicative of a hydroxy group linking to C-4. Thus, the terminal group at C-16 was determined to be a carboxylic acid. The molecular weight of **7**, being 18 amu higher than the ε-lactone analogue,[10,11] supported this structural assignment. The presence of a NOESY correlation between H-5 (δ_H 3.87, dd, J = 5.5, 10.0 Hz)/H$_3$-19 (δ_H 1.14, s) revealed *cis*-geometry for the 5,8-tetrahydrofuran ring, while the absence of NOEs between H$_3$-20 (δ_H 1.30, s)/H-13 (δ_H 2.83, brd, J = 7.5 Hz) and H-9 (δ_H 4.87, d, J = 11.0 Hz)/H$_3$-19, but the observation of NOEs between H-13/H-10a (δ_H 1.60, m) and H-9/H-10a (Figure 1) implied a *trans*-configuration of the 12,13-epoxide and the β-orientation of H-9 and H-13. The NOE of H-13/H-17a (δ_H 5.60) assigned H-1 to an α-orientation.

The HRFABMS and NMR data gave the molecular formula of dendronpholide G (**8**) as $C_{23}H_{36}O_7$, which was 14 amu higher than that of **7**. A comparison of the NMR and IR data revealed that **8** differed from **7** solely due to the substitution at C-16, where a methyl ester of **8** replaced a carboxylic acid of the latter. This assignment was supported by the presence of a methoxy group (δ_H 3.70, s; δ_C 53.2) and the HMBC correlation of its protons with the carbonyl carbon C-16. The relative stereochemistry of **8** was the same as in the case of **7**, as evidenced by the similar NMR data and NOE relationship.

The structure of dendronpholide H (**9**) was closely related to **8** due to the close similarity of the NMR data. The distinction was

Table 2. ¹H NMR Data of Dendronepholides F–P (**7–17**)

	7[a]	8[a]	9[b]	10[a]	11[a]	12[a]	13[a]	14[a]	15[a]	16[a]	17[a]
1	2.67 m	2.68 m	2.85 m	2.65 m	2.60 m	2.68 m	3.10 m	3.15 m	2.98 m	2.63 ddd (3.0,10.5,10.5)	2.65 m
2	1.55 m 1.71 m	1.67 m 1.74 m	1.65 m 1.77 m	1.55 m 1.55 m	1.36 m 1.88 m	1.50 m 1.55 m	1.62 m 1.98 m	1.33 m 1.70 m	1.25 m 1.65 m	1.30 m 1.73 m	1.29 m 1.73 m
3	1.36 dd (12.0,12.0) 1.62 m	1.36 dd (11.0,11.0) 1.57 m	1.63 m 1.65 m	1.30 dd (5.5,11.0) 2.10 ddd (2.0,11.0,11.0)	1.19 m 1.46 m	1.25 dd (5.5,12.5) 2.00 dd (11.0,12.5)	0.84 m 1.34 m	0.86 m 1.35 m	0.90 m 1.40 m	1.16 m 1.46 m	1.17 m 1.47 m
5	3.87 dd (5.5,10.0)	3.88 dd (6.0,10.5)	4.02 dd (6.0,11.0)	3.78 dd (5.0,11.5)	3.85 dd (4.5,11.0)	3.77 dd (5.0,11.5)	3.82 dd (5.0,10.5)	3.81 dd (6.5,11.0)	3.83 dd (6.0,11.0)	3.59 dd (7.0,7.0)	3.58 dd (7.0,7.0)
6	1.56 m 1.80 m	1.65 m 1.80 m	1.68 m 1.77 m	1.55 m 1.70 m	1.55 m 1.80 m	1.56 m 1.58 m	1.50 m 1.71 m	1.48 m 1.70 m	1.45 m 1.71 m	1.72 m 1.76 m	1.72 m 1.75 m
7	1.56 m 1.76 dd (5.5,12.0,13.5)	1.60 m 1.75 m	1.70 m 1.92 m	1.52 m 1.80 m	1.69 m 2.21 dd (7.5,12.0)	1.52 m 1.79 m	1.60 m 1.76 m	1.60 m 1.77 m	1.55 m 1.74 m	1.41 m 1.58 m	1.42 m 1.56 m
9	4.87 d (11.0)	4.86 d (11.0)	5.04 d (10.5)	4.81 dd (4.0,9.5)	4.14 d (11.5)	4.78 brd (10.0)	4.73 d (10.5)	4.74 d (10.5)	4.70 d (10.0)	4.65 d (11.0)	4.64 d (11.5)
10	1.60 m 1.90 dd (10.5,13.0)	1.62 m 1.90 dd (9.0,14.0)	1.72 m 1.85 m	1.52 m 1.80 m	1.63 m 2.30 brd (14.5)	1.55 m 1.70 m	1.50 m 1.93 m	1.48 m 1.95 m	1.50 m 1.92 m	2.15 brd (13.5) 2.48 ddd (11.0,10.5,13.5)	2.15 brd (13.5) 2.45 m
11	0.72 dd (10.5,13.5) 1.98 dd (8.5,13.5)	0.73 dd (11.0,13.5) 1.99 dd (9.0,13.5)	0.90 dd (11.0,14.0) 2.08 m	1.40 m 1.50 m	1.42 m 1.74 m	1.50 m	1.59 m 1.61 m	1.48 m 1.72 m	1.45 m 1.75 m	5.26 d (10.5)	5.25 d (10.0)
13	2.83 dd (2.5,10.0)	2.83 dd (3.5,10.0)	3.03 dd (2.5,10.0)	4.37 d (11.0)	4.58 brd (10.5)	4.55 d (12.0)	4.38 d (12.0)	4.38 d (11.5)	3.34 d (10.5)	3.99 brd (10.0)	3.98 dd (3.5,10.5)
14	1.50 m 1.77 m	1.52 m 1.73 m	1.62 m 1.92 m	1.60 dd (11.0,14.5) 1.98 brd (14.5)	1.80 m 1.98 brd (14.5)	1.52 m 1.99 brd (14.5)	1.45 m 1.95 m	1.60 m 2.05 m	1.40 m 1.45 m	1.40 m 1.54 m	1.42 m 1.57 m
17	5.60 brs 6.15 brs	5.77 brs 6.25 brs	5.82 brs 6.43 brs	5.72 brs 6.22 brs	5.83 brs 6.37 brs	5.68 brs 6.18 brs	5.43 brs 6.11 brs	5.45 brs 6.14 brs	5.42 brs 6.08 brs	5.46 brs 6.09 brs	5.49 brs 6.11 brs
18	0.95 s	0.95 s	1.10 s	1.05 s	0.92 s	1.05 s	0.81 s	0.82 s	0.84 s	0.93 s	0.92 s
19	1.14 s	1.15 s	1.24 s	1.09 s	1.16 s	1.10 s	1.15 s	1.16 s	1.13 s	1.10 s	1.11 s
20	1.30 s	1.31 s	1.38 s	1.12 s	1.04 s	1.10 s	1.23 s	1.21 s	1.16 s	1.54 s	1.54 s
Ac	2.04 s	2.05 s	2.08 s	2.05 s	2.04 s	2.04 s	2.05 s	2.05 s	2.04 s	2.04 s	2.01 s
		3.70 s				3.09 s		3.71 s	3.43 s		3.66 s
CH₃ CH₂			1.32 t (7.0) 4.24 q (7.0)				1.31 t (7.0) 4.18 q (7.0)		1.23 t (7.0) 4.16 q (7.0)	1.20 t (7.0) 4.13 q (7.0)	

[a] Measured in DMSO-d_6. [b] Measured in CDCl$_3$.

Table 3. ^{13}C NMR Data of Dendronepholides F–P (**7–17**)

position	7[a]	8[a]	9[b]	10[a]	11[a]	12[a]	13[a]	14[a]	15[a]	16[a]	17[a]
1	38.2 CH	39.2 CH	37.8 CH	36.1 CH	36.0 CH	35.9 CH	33.8 CH	33.8 CH	33.6 CH	37.7 CH	37.4 CH
2	26.8 CH$_2$	27.4 CH$_2$	26.7 CH$_2$	30.9 CH$_2$	29.3 CH$_2$	30.0 CH$_2$	31.8 CH$_2$	31.8 CH$_2$	31.0 CH$_2$	25.6 CH$_2$	25.5 CH$_2$
3	36.43 CH$_2$	37.0 CH$_2$	36.0 CH$_2$	34.5 CH$_2$	32.2 CH$_2$	34.4 CH$_2$	25.3 CH$_2$	25.3 CH$_2$	26.4 CH$_2$	42.5 CH$_2$	42.2 CH$_2$
4	72.8 C	73.6 C	73.8 C	72.8 C	72.4 C	72.4 C	71.8 C	71.8 C	71.8 C	72.6 C	72.4 C
5	88.3 CH	89.1 CH	87.9 CH	87.5 CH	88.5 CH	87.5 CH	89.1 CH	89.0 CH	89.0 CH	86.4 CH	85.9 CH
6	27.8 CH$_2$	28.6 CH$_2$	27.4 CH$_2$	29.4 CH$_2$	28.0 CH$_2$	29.2 CH$_2$	26.7 CH$_2$	26.2 CH$_2$	26.8 CH$_2$	26.1 CH$_2$	25.8 CH$_2$
7	35.9 CH$_2$	36.7 CH$_2$	36.3 CH$_2$	35.8 CH$_2$	36.2 CH$_2$	35.6 CH$_2$	36.4 CH$_2$	36.4 CH$_2$	36.4 CH$_2$	36.7 CH$_2$	36.5 CH$_2$
8	83.3 C	84.1 C	83.8 C	83.5 C	82.4 C	83.4 C	82.9 C	82.9 C	83.0 C	84.4 C	84.2 C
9	76.1 CH	76.8 CH	75.9 CH	77.5 CH	77.1 CH	77.1 CH	77.9 CH	77.9 CH	78.4 CH	78.3 CH	78.1 CH
10	24.5 CH$_2$	25.3 CH$_2$	24.5 CH$_2$	23.1 CH$_2$	24.1 CH$_2$	22.3 CH$_2$	22.1 CH$_2$	22.0 CH$_2$	23.4 CH$_2$	30.1 CH$_2$	29.9 CH$_2$
11	34.9 CH$_2$	35.6 CH$_2$	34.9 CH$_2$	35.5 CH$_2$	36.9 CH$_2$	30.0 CH$_2$	38.0 CH$_2$	38.0 CH$_2$	38.2 CH$_2$	122.5 CH	122.2 CH
12	61.3 C	62.1 C	61.3 C	71.8 C	73.0 C	77.0 C	74.2 C	74.2 C	75.1 C	135.7 C	135.5 C
13	59.0 CH	59.6 CH	59.8 CH	78.0 CH	80.1 CH	77.2 CH	68.3 CH	68.2 CH	81.2 CH	75.0 CH	74.7 CH
14	32.2 CH$_2$	33.2 CH$_2$	32.4 CH$_2$	24.9 CH$_2$	23.0 CH$_2$	24.5 CH$_2$	21.9 CH$_2$	22.2 CH$_2$	30.1 CH$_2$	42.4 CH$_2$	42.2 CH$_2$
15	146.0 C	144.6 C	143.2 C	141.0 C	140.4 C	140.9 C	144.5 C	144.5 C	145.8 C	145.8 C	145.3 C
16	169.0 C	168.4 C	167.3 C	166.4 C	166.3 C	165.3 C	167.7 C	167.7 C	167.5 C	167.5 C	167.8 C
17	124.0 CH$_2$	125.4 CH$_2$	124.2 CH$_2$	128.3 CH$_2$	131.1 CH$_2$	127.3 CH$_2$	123.6 CH$_2$	123.6 CH$_2$	122.8 CH$_2$	124.9 CH$_2$	124.8 CH$_2$
18	25.4 CH$_3$	26.2 CH$_3$	25.4 CH$_3$	25.2 CH$_3$	27.9 CH$_3$	25.0 CH$_3$	23.9 CH$_3$	23.9 CH$_3$	24.2 CH$_3$	19.8 CH$_3$	19.6 CH$_3$
19	21.2 CH$_3$	22.1 CH$_3$	21.1 CH$_3$	23.6 CH$_3$	21.2 CH$_3$	22.5 CH$_3$	21.3 CH$_3$	21.3 CH$_3$	21.2 CH$_3$	19.6 CH$_3$	19.3 CH$_3$
20	17.7 CH$_3$	18.3 CH$_3$	17.3 CH$_3$	24.1 CH$_3$	25.6 CH$_3$	17.3 CH$_3$	26.7 CH$_3$	26.7 CH$_3$	24.7 CH$_3$	10.7 CH$_3$	10.4 CH$_3$
Ac	21.3 CH$_3$ 171.8 C	21.9 CH$_3$ 171.7 C	20.9 CH$_3$ 171.4 C	21.5 CH$_3$ 171.2 C	21.6 CH$_3$ 170.9 C	21.3 CH$_3$ 170.9 C	21.3 CH$_3$ 171.3 C	22.1 CH$_3$ 171.3 C	21.3 CH$_3$ 171.2 C	21.7 CH$_3$ 170.5 C	21.4 CH$_3$ 170.2 C
CH$_3$O		53.2 CH$_3$				49.3 CH$_3$		52.4 CH$_3$	60.2 CH$_3$		52.1 CH$_3$
CH$_3$CH$_2$O			14.2 CH$_3$ 60.9 CH$_2$				14.6 CH$_3$ 60.9 CH$_2$		14.6 CH$_3$ 60.8 CH$_2$	14.8 CH$_3$ 60.9 CH$_2$	

^{a} Measured in DMSO-d_6. ^{b} Measured in CDCl$_3$.

ascribed to the presence of an ethyl ester at C-16 of **9** instead of a methyl ester of **8**, as indicated by the ^{1}H NMR resonances at δ_H 1.32 (3H, J = 7. Hz) and 4.24 (2H, J = 7.0 Hz) and their corresponding carbons at δ_C 14.2 and 60.9. This assignment was confirmed by the HMBC correlation between the oxymethylene protons and the carbonyl carbon at C-16.

Dendronpholide I (**10**) had a molecular formula of C$_{22}$H$_{36}$O$_8$, as determined by HRFABMS (m/z 451.2313 [M + Na]$^+$, calc 451.2308) and NMR data, implying five degrees of unsaturation. The IR and NMR data (Tables 2 and 3) were compatible with those of **7**, indicating an analogue of 9-acetoxy-5,8-tetrahydrofurancembr-15(17)-en-4-ol-16-oic acid. The ^{13}C NMR resonances at δ_C 87.5 (C-5) and 83.5 (C-8) were attributed to a 5,8-tetrahydrofuran ring, while the signals at δ_H 2.05 (3H, s) and δ_C 21.5 and 171.2 were attributed to an acetoxy group. The linkage of the acetoxy group at C-9 was assigned by the HMBC correlations from H-9 (δ_H 4.81, dd, J = 4.0, 9.5 Hz) to the acetyl carbonyl carbon, C-8, C-11, and C-19 (δ_C 23.6). The hydroxy group at C-4 of **7** was also recognized in **10**, which was evident from the ^{13}C NMR resonance at δ_C 72.8 (C-4), along with the HMBC correlation. However, compound **10** lacked an epoxide group but presented two additional hydroxylated carbons at δ_C 71.8 (C-12) and 78.0 (C-13). The HMBC relationship from H$_3$-20 (δ_H 1.12, s) to C-11 (δ_C 35.5), C-12, and C-13 confirmed the linkage of the hydroxy groups at C-12 and C-13. Consequently, C-16 bore a carboxylic acid, as in the case of **7**, which could be accounted for by the FABMS data and the degrees of unsaturation in the molecule. The NOEs of H-5 (δ_H 3.78, dd, J = 5.0, 11.0 Hz)/Me-19 (δ_H 1.09, s) determined a *cis*-geometry of the 5,8-tetrahydrofuran ring, while the NOEs between H-13 (δ_H 4.37, d, J = 11.0 Hz)/H-9 and H-13/H-17a (δ_H 5.72) revealed the β-orientations of H-9 and H-13 and the α-face of H-1.

Dendronpholide J (**11**) had the same molecular formula as **10**, and the NMR spectroscopic data of both compounds were very similar. The difference could be distinguished by regarding the chemical shift of H-9 of **11**, which was shifted upfield to δ_H 4.14 (1H, d, J = 11.5 Hz), whereas H-13 shifted downfield to δ_H 4.58 (1H, brd, J = 10.5 Hz), and the corresponding carbon C-13 (δ_C 80.1) of **11** was about 2 ppm more downfield than that of **10**. These findings suggested that the acetoxy group is positioned at C-13 of **11**. The HMBC correlation from H-13 to the acetyl carbonyl carbon at δ_C 170.9 confirmed the acetyl location. Thus, the structure of **11** was a 9-hydroxy-13-acetyl analogue of **10**.

The IR and 1D and 2D NMR spectroscopic data analysis revealed that the structure of dendronpholide K (**12**) is closely related to **10**, except for the presence of an additional methoxy group (δ_H 3.09, s). The more downfield-shifted C-12 (δ_C 77.0) compared to that of **10**, in association with the HMBC relationship from methoxy protons and H$_3$-20 to C-12, led to the assignment of the methoxy group at C-12. The NOE relationships of H-1/H-5, H-5/H$_3$-19, and H-9/H-13 suggested that **12** shared partial relative configurations of **10**. The NOE interaction between the methoxy protons and H-13 determined OMe-12β.

Dendronpholide L (**13**) had a molecular formula of C$_{24}$H$_{40}$O$_8$, as determined by HRFABMS (m/z 457.2794 [M + 1]$^+$, calc 457.2798) and NMR data. Analysis of the IR and NMR spectroscopic data (Tables 2 and 3) indicated that **13** possesses a 9-aceoxy-5,8-tetrahydrofurancembra-4,12,13-triol pattern, closely related to **10**. An ethoxy group was observed from the ^{1}H NMR data at δ_H 1.31 (3H, t, J = 7.0 Hz) and 4.18 (2H, q, J = 7.0 Hz) and their corresponding carbons at δ_C 14.6 and 60.9. This group was deduced to form an ethyl ester at C-16 (δ_C 167.7), according to HMBC correlation between the oxymethylene protons and C-16. However, an examination of the ^{13}C NMR data (Table 3) revealed that the chemical shifts surrounded the 14-membered ring somehow differed from those of **10**, implying that the geometry of the backbone was varied. The NOESY cross-peaks from H-9 (δ_H 4.73) and H-5 (δ_H 3.82, dd) to H-7b (δ_H 1.59, m) and from H-5 to H$_3$-18, but the

absence of a H-5/H$_3$-19 correlation, suggested a *trans*-geometry of the 5,8-tetrahydrofuran ring, and H-5, H-9, and H$_3$-18 are positioned in the same orientation. Since H-1 was biogenetically assumed to be α, the NOEs of H-13 (δ_H 4.38, d, $J = 12$ Hz)/H-14a (δ_H 1.95), H-1 (δ_H 3.10, m)/H-14a, and H-13/H$_3$-20 (δ_H 1.23, s) allowed the assignment of OH-13β. In addition, the NOEs of H-17a (δ_H 5.43)/H-2b (δ_H 1.98, m) and H$_3$-18/H-2b revealed the β-orientation of H$_3$-18, H-5, and H-9.

Dendronpholide M (**14**) differed from **13** solely by the substitution at C-16, where a methyl ester of **14** replaced the ethyl ester of the latter. This assignment was proved by the HMBC correlation between the methoxy protons (δ_H 3.71, s) and a carbonyl carbon at δ_C 167.7 (C-16), in association with the molecular weight of **14** being 14 amu less than **13**. The close similarity of NMR and NOE data suggested that both compounds share the same relative stereochemistry.

The molecular formula of dendronpholide N (**15**) was established as $C_{25}H_{42}O_8$ through HRFABMS (*m/z* 493.2769 [M + Na]$^+$, calc 493.2771) and NMR data analysis. The ^{1}H and ^{13}C NMR data of **15** were comparable with those of **13**, except for the presence of an additional methoxy group (δ_H 3.43, s; δ_C 60.2) and the chemical shift of C-13 appearing rather downfield at δ_C 81.2. These findings suggested that the methoxy group was linked to C-13. This assignment was confirmed by the HMBC relationship between the methoxy protons and C-13 and, in turn, from H-13 (δ_H 3.34, d, $J = 10.5$ Hz) to the carbons at δ_C 60.2 (MeO), 24.7 (C-20), 75.1 (C-12), and 30.1 (C-14). Accordingly, the structure of **15** was a 13-methoxy derivative of **13**. The relative stereochemistry of **15** is the same as **13** due to the comparable NMR and NOE data.

The NMR spectroscopic data of dendronpholide O (**16**) (Tables 2 and 3) were closely related to those of **10**, indicating the presence of a 9-acetoxy-5,8-tetrahydrofuran-4-hydroxycembrane nucleus. The difference was evidenced by the presence of an additional double bond, whose NMR data presented at δ_H 5.26 (1H, d, $J = 10.5$ Hz) and the corresponding carbons at δ_C 122.5 and 135.7. This vinyl group was deduced to be located at C-11/C-12 through the HMBC correlations from Me-20 (δ_H 1.54, s) to both vinyl carbons and C-13 (δ_C 75.0). The HMBC data also confirmed a hydroxy group to be positioned at C-13. In addition, an ethoxy group was observed from the ^{1}H NMR resonances at δ_H 1.20 (3H, t, $J = 7.0$ Hz) and 4.13 (2H, q, $J = 7.0$ Hz). It was positioned at C-16 to form an ethyl ester, based on the HMBC correlation between the oxymethylene protons (δ_H 4.13) and the carbonyl carbon C-16 (δ_C 167.5). The NOE interactions between H-13 (δ_H 3.99)/H-11 (δ_H 5.26), H$_3$-20/H-1, H$_3$-20/H-10a (δ_H 2.48), H$_3$-19 (δ_H 1.10, s)/H-10a, and H-5 (δ_H 3.59)/H$_3$-19 (Figure 1) were assignable to H-13β, H-9β, H-5α, H-1α, and 11*E*, while the 5,8-tetrahydrofuran ring required a *cis*-fusion. The remaining relative configurations of **16** were the same as **10**, as shown bt the similar NOE relationships.

By comparison of the NMR and MS data, and on the basis of a methoxy proton of **17** (δ_H 3.66, s) showing HMBC correlation to C-16 (δ_C 167.8), the structure of dendronpholide P (**17**) was thus determined as a methyl ester of **16**.

The molecular formula of dendronpholide Q (**18**) was established as $C_{24}H_{36}O_8$ by HRFABMS (*m/z* 453.2484 [M + 1]$^+$, calc 453.2483) and NMR data, implying seven degrees of unsaturation. An examination of 1D and 2D NMR (COSY, HMQC, and HMBC) disclosed the gross structure of **18** to be closely related to sinulariolone.[13] The quaternary carbon signal at δ_C 88.3 was assigned to the lactone oxygenated carbon at C-4, while the carbon resonances at δ_C 84.9 (C-9) and 85.6 (C-12) were ascribed to a 9,12-tetrahydrofuran ring. However, a ketone at C-5 of sinulariolone was absent in **18**, replaced by an oxymethine at δ_C 74.5 (C-5). The ^{1}H and ^{13}C NMR spectra of **18** exhibited two acetyl groups, as observed from the methyl singlets at δ_H 2.05 (3H, s) and 2.06 (3H, s), and their corresponding carbons at δ_C 21.4 (2 × C), in association with the HMBC correlation. The locations of the acetoxy

groups were determined by the HMBC spectrum, in which an oxymethine proton at δ_H 6.23 (1H, brd, $J = 10.5$ Hz, H-5) correlated to an acetyl carbonyl carbon (δ_C 170.7), while the other oxymethine proton at δ_H 4.92 (1H, dd, $J = 4.0, 11.5$ Hz, H-13) interacted with the second acetyl carbonyl carbon. Thus, the quaternary carbon C-8 (δ_C 72.9) was substituted by a hydroxy group. The NOE correlations between H-1 (δ_H 3.19)/H-5, and H-1/H-20 (δ_H 1.14, s) suggested α-orientation of H-1, H-5, and H-20, while H-13 and H-17a (δ_H 5.52) interacted with H-2 (δ_H 2.40, m) (Figure 1), leading to the assignment of H-13β. Furthermore, the NOE interaction between H-9 (δ_H 3.84, dd) and H$_3$-20 revealed a *cis*-fusion of the 9,12-tetrahydrofuran ring. These assignments agreed with the structure of sinulariolone that was determined through X-ray diffraction.[13]

A comparison of NMR and IR spectroscopic data indicated that dendronpholide R (**19**) had the same backbone as **18**. However, the methyl group Me-19 of **18** was absent in **19**, replaced by an *exo*-methylene group, which was identified by the NMR data at δ_H 4.94 (1H, brs) and 5.02 (1H, brs), and their corresponding carbon (δ_C 116.9). Compound **19** only presented one acetyl group (δ_H 2.03, s; δ_C 21.3, 170.7) instead of two as in **18**. The HMBC relationship between H-5 (δ_H 4.66, dd, $J = 3.5, 9.0$ Hz) and the acetyl carbonyl carbon led to the conclusion that the acetoxy group was positioned at C-5. The chemical shift of C-4 (δ_C 72.6) required the substitution of a hydroxy group. Thus, the degrees of unsaturation in the molecule were accounted for by a carboxylic group at C-16. The presence of NOE interactions between H-9 (δ_H 4.45, dd, $J = 6.0, 10.0$ Hz)/H$_3$-20, H-13/H-2, H-13/H-17a (δ_H 5.84), and H-1/H-5 suggested that the relative stereochemistry of **19** was the same as **18**.

(−)-Sandensolide and dendronpholides A−C, G, I−K, and O−R represent differently substituted derivatives of cembranoides, whose bioactivities regarding cell growth inhibition were tested by applying on human tumor cell lines HCT-8, Bel-7402, BGC-823, A549, and A2780. Dendronpholides C (**4**), G (**8**), and J (**11**) showed a selective and significant inhibition against BGC-823 (IC$_{50}$ = 0.05, 0.02, 0.20 μg/mL, respectively), whereas the other compounds showed no bioactivity (IC$_{50}$ > 10 μg/mL). A comparison of the cytotoxicity data between sandensolide and **4** revealed that the methyl ester functionality plays a crucial role in the inhibition of BGC-823 compared to the seven-membered lactone, while the 12,13-epoxide of **8** is an important functionality.

This is the first report of cembranolides from the soft coral genus *Dendronephthya* that provided new chemotaxonomic markers of this genus. This finding implied that the genus *Dendronephthya* is phylogenetically related to *Sinularia*. The ethyl ester analogues may be artifacts derived during extraction.

Experimental Section

General Experimental Procedures. Optional rotations were measured on a Perkin-Elmer 243B polarimeter. IR spectra were determined on Thermo Nicolet Nexus 470 FT-IR spectrometer. ^{1}H, ^{13}C, and 2D NMR spectra were recorded on Bruker Avance-500 and Varian INOVA-500 NMR spectrometers using TMS as an internal standard. The chemical shifts were given in δ (ppm) and coupling constants in Hz. HRFABMS were obtained from GCT-MS instruments. 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) and Kromasil semipreparative columns (10 μm, ODS, 10 mm × 250 mm).

Animal Material. The soft coral *Dendronephthya* sp. was collected from the inner coral reef at a depth of 10 m in Sanya Bay, Hainan Island of China, in May 2003. The fresh samples were frozen immediately. The specimen was identified by Leen van Ofwegen (National Museum of Natural History Naturalis). The coral (HSE-5) was deposited at the State Key Laboratory of Natural and Biomimetic Drugs, Peking University, China, and also deposited at the National Museum of Natural History Naturalis, The Netherlands.

Table 4. ¹H NMR, ¹³C NMR, HMBC, and NOESY Data of Dendronepholides Q and R (**18**, **19**) in DMSO-d_6

position	18				19			
	δ_H	δ_C	HMBC (H→C)	NOE	δ_H	δ_C	HMBC (H→C)	NOE
1	3.19 ddd (6.5,0,10.0,0,10.0)	32.4 CH	C-15, C-16, C-17, C-13	H-5, H-20	2.64 ddd (3.5,3.5,3.5,11.5)	35.5 CH	C-15, C-3, C-4, C14	H-17 (5.84), H-5
2	1.04 m 2.36 (6.5,11.0,14.0)	29.0 CH₂	C-4, C-1, C-14, C-15		1.60 dd (12.0,12.0) 1.75 m	29.6 CH₂		
3	1.81 m 2.00 m	33.1 CH₂		H-17a, H-13	1.80 m 2.30 dd dd (6.5,12.0)	36.3 CH₂	C-1, C-4, C-18	
4		88.3 C				72.6 C		
5	6.23 brd (10.5)	74.5 CH	C-18, Ac (170.7), C-7, C-5	H-9, H-1, H-3 (2.00)	4.66 dd (3.5, 9.0)	79.0 CH	C-18, C-5, C-7	H-1
6	1.50 m 1.70 m	25.8 CH₂			1.75 m 1.95 m	28.8 CH₂		
7	1.40 m 1.61 m	39.5 CH₂			1.87 m 1.98 m	27.8 CH₂		
8		72.9 C				147.3 C		
9	3.84 dd (4.5,8.5)	84.9 CH	C-19, C-8, C-7	H-20	4.45 dd (6.0, 10.0)	84.9 CH	C-19, C-10, C-8	H-20
10	1.78 m 1.85 m	25.2 CH₂			1.85 m 1.90 m	28.4 CH₂		
11	1.28 m 1.62 m	36.8 CH₂			1.38 m 1.65 m	36.3 CH₂		
12		85.6 C				82.4 C		
13	4.92 dd (4.0, 11.5)	76.2 CH	Ac, C-20, C-11, C-12, C-14	H-20, H-2 (2.36),H-11(1.28)	4.21 d (11.5)	77.2 CH	C-20, C-1, C-12	H-3 (2.30), H-14 (2.15)
14	1.65 m 1.85 m	33.9 CH₂			1.65 2.15 brd (15.5)	24.0 CH₂	C-15, C-2, C-12	
15		144.6 C				140.1 C		
16		168.2 C				166.0 C		
17	5.52 brs 6.03 brs	124.1 CH₂	C-1, C-15, C-16		5.84 brs 6.37 brs	130.7 CH₂	C-1, C-15, C-16	
18	1.24 s	24.2 CH₃	C-3, C-4, C-5		1.05 s	25.0 CH₃	C-3, C-4, C-5	
19	1.00 s	19.0 CH₃	C-7, C-8, C-9		4.94 s 5.02 s	116.9 CH₂	C-7, C-8, C-9	
20	1.14 s	16.0 CH₃	C-11, C-12, C-13	H-1, H-9	1.16 s	20.8 CH₃	C-11, C-12, C-13	
Ac	2.05 s	21.4 CH₃ 170.7 C	C=O		2.03 s	21.3 CH₃₊ 170.7 C	C=O	
Ac	2.06 s	21.4 CH₃ 170.0 C	C=O					

Chart 1
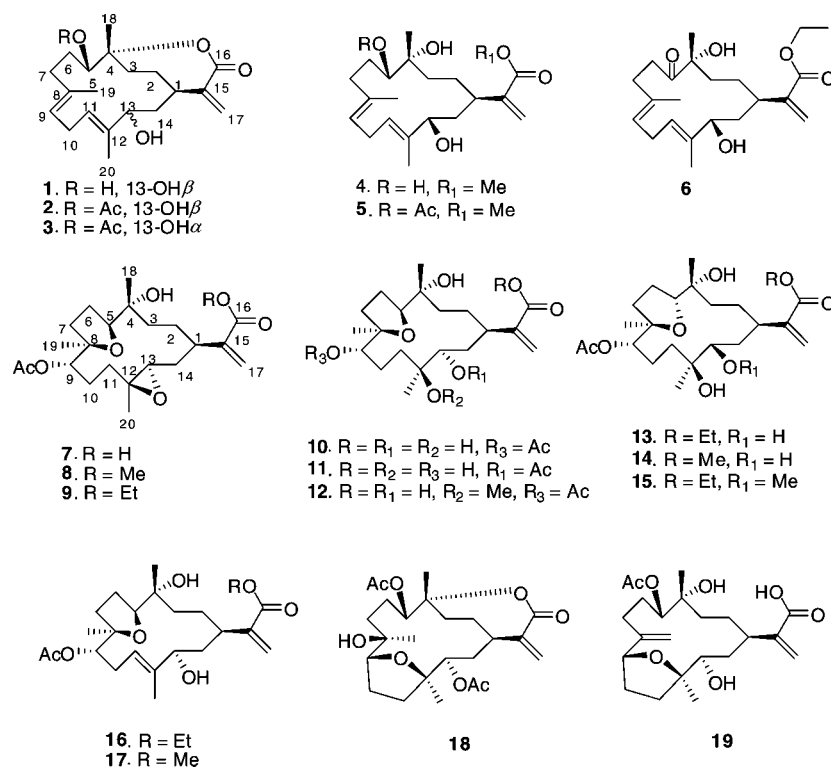
Extraction and Isolation. The frozen soft coral *Dendronephthya* sp. was homogenized and then extracted with EtOH. The concentrated extract was desalted by dissolving in MeOH to yield a residue (102.7 g). This residue was partitioned between H₂O and EtOAc, and then *n*-butanol. The bioactive EtOAc fraction (10.0 g) was subjected to Si gel column chromatography, eluting with a gradient (petroleum ether–acetone, 20:1, 10:1, 5:1, 2:1) to obtain 15 fractions (F1–F15). F1–F4 (2.8 g) mainly contained lipids as detected by ¹H NMR. F11 (577.5 mg) was subsequently subjected to Si gel column (200–300 mesh) chromatography by eluting with acetone–petroleum ether (2:1) to yield three portions (F11-PA, F11-PB, and F11-PC). F11-PA (123.0 mg) was separated on an ODS HPLC column with MeOH–H₂O (3:1) as a mobile phase to afford **18** (2.8 mg), **3** (4.0 mg), **16** (6.8 mg), and **2** (10.0 mg), while F11-PB (50 mg) and F11-PC (30.0 mg) were processed in the same way as F11-PA on an ODS column eluting with MeOH–H₂O (4:1) to yield (−)-sandensolide (30.0 mg) and **4** (16.7 mg). F10 (877.2 mg) was subjected to flash chromatography on a Si gel column (200–300 mesh) eluting with acetone–petroleum ether (4:1) to obtain three portions, F10-PA, F10-PB, and F10-PC. F10-PA (20 mg) was chromatographed on an ODS column by using MeOH–H₂O (4:1) as an eluant to yield episinulariolide (2.7 mg) and **9** (6.0 mg). Following the same protocol as for F10-FA, F10-PB (100 mg) was separated on an ODS column with MeOH–H₂O (3:2) as eluant to obtain **19** (2.2 mg), **6** (2.5 mg), **14** (4.5 mg), and **15** (2.0 mg). Compounds **5** (2.4 mg) and **13** (3.0 mg) were isolated from F10-PC (43 mg). Fraction F8 (303 mg) was subjected to flash chromatography on a Si gel column eluting with acetone–petroleum ether (3:1) to obtain fractions F8-PA, F8-PB, and F8-PC. F8-PA (81 mg) was separated by semipreparative HPLC (ODS) using MeOH–H₂O (3:2) as the mobile phase to yield **11** (13 mg), **10** (7.0 mg), **7** (7.0 mg), and **17** (2.7 mg). Following the same protocol, **12** (2.5 mg), **8** (4.6 mg), and **7** (3.5 mg) were purified from fraction F8-PB (21 mg) by semipreparative HPLC with MeOH–H₂O (5:1) as the mobile phase.

(−)-Sandensolide (1): colorless oil; $[\alpha]^{20}_D$ −45.0 (*c* 0.5, CHCl₃); IR (KBr) ν_{max} 34276, 2935, 2859, 1691, 1451, 1407, 1238, 1147, 1026 cm⁻¹; ¹H NMR (DMSO-d_6) δ 1.90 (1H, m, H-1), 0.99 (1H, ddd, *J* = 4.0, 11.0, 11.5 Hz, H-2a), 2.14 (1H, m, H-2b), 1.55 (1H, m, H-3a), 2.00 (1H, m, H-3b), 3.60 (1H, dd, *J* = 6.5, 10.0 Hz, H-5), 4.78 (1H, d, *J* = 6.5 Hz, OH-5), 1.26 (1H, ddd, *J* = 3.0, 10.5, 10.5 Hz, H-6a), 1.70 (1H, ddd, *J* = 3.0, 10.5, 10.5 Hz, H-6b), 2.00 (1H, m, H-7a), 2.23 (1H, ddd, *J* = 2.5, 11.5, 11.5 Hz, H-7b), 5.40 (1H, dd, *J* = 6.0, 10.0 Hz, H-9), 2.34 (1H, m, H-10a), 3.07 (ddd, *J* = 10.0, 10.0, 12.0 Hz, H-10b), 5.35 (1H, brd, *J* = 10.0 Hz, H-11), 3.97 (1H, ddd, *J* =

3.0, 4.0, 12.0 Hz, H-13), 4.72 (1H, d, *J* = 3.0 Hz, OH-13), 1.58 (2H, m, H₂-14), 5.48 (1H, brs, H-17a), 6.02 (1H, brs, H-17b), 1.12 (3H, s, H-18), 1.45 (3H, s, H-19), 1.51 (3H, s, H-20); ¹³C NMR NMR (DMSO-d_6) δ 33.8 (C-1), 29.1 (C-2), 32.1 (C-3), 87.5 (C-4), 65.7 (C-5), 26.3 (C-6), 35.0 (C-7), 133.4 (C-8), 125.6 (C-9), 26.9 (C-10), 126.2 (C-11), 133.6 (C-12), 75.0 (C-13), 38.9 (C-14), 145.9 (C-15), 169.3 (C-16), 123.8 (C-17), 23.3 (C-18), 15.0 (C-19), 10.0 (C-20); HRFABMS *m/z* 357.2028 (calc for C₂₀H₃₀O₄Na, 357.2036).

Dendronpholide A (2): colorless oil; $[\alpha]^{20}_D$ −137.0 (*c* 0.18, CHCl₃); IR (KBr) ν_{max} 3402, 2932, 2862, 1740, 1711, 1624, 1454, 1374, 1285, 1238, 1144, 1025 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; HRFABMS *m/z* 399.2140 [M + Na]⁺ (calc for C₂₂H₃₂O₅Na, 399.2143).

Dendronpholide B (3): colorless oil; $[\alpha]^{20}_D$ −51.4 (*c* 0.20, CHCl₃); IR (KBr) ν_{max} 3402, 2928, 2859, 1743, 1712, 1625, 1453, 1375, 1284, 1239, 1146, 1095, 1025 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; HRFABMS *m/z* 377.2322 [M + 1]⁺ (calc for C₂₂H₃₃O₅, 377.2322).

Dendronpholide C (4): colorless oil; $[\alpha]^{20}_D$ −70.0 (*c* 0.20, CHCl₃); IR (KBr) ν_{max} 3384, 2950, 2856, 1716, 1625, 1440, 1276, 1236, 1199, 1149, 1048, 1025, 1006 cm⁻¹; ¹H and ¹³C NMR data, see Tables 1; HRFABMS *m/z* 389.2293 [M + Na]⁺ (calc for C₂₁H₃₄O₅Na, 389.2298).

Dendronpholide D (5): colorless oil; $[\alpha]^{20}_D$ −16.2 (*c* 0.25, CHCl₃); IR (KBr) ν_{max} 3419, 2936, 1717, 1632, 1439, 1244, 1045 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; HRFABMS *m/z* 431.2398 [M + Na]⁺ (calc for C₂₃H₃₆O₆Na, 431.2403).

Dendronpholide E (6): colorless oil; $[\alpha]^{20}_D$ −40.0 (*c* 0.10, CHCl₃); IR (KBr) ν_{max} 3432, 2929, 2856, 1713, 1626, 1449, 1384, 1149, 1126, 1097, 1029 cm⁻¹; ¹H and ¹³C NMR data, see Table 1; HRFABMS *m/z* 401.2292 [M + Na]⁺ (calc for C₂₂H₃₄O₅Na, 401.2298).

Dendronpholide F (7): colorless oil; $[\alpha]^{20}_D$ +5.36 (*c* 0.19, CHCl₃); IR (KBr) ν_{max} 3432,, 29278, 1728, 1626, 1553, 1443, 1376, 1237, 1149, 1105, 1040 cm⁻¹; ¹H and ¹³C NMR data, see Tables 2 and 3; HRFABMS *m/z* 409.2230 [M − 1]⁻ (calc for C₂₂H₃₃O₇, 409.2231).

Dendronpholide G (8): colorless oil; $[\alpha]^{20}_D$ +10 (*c* 0.10, CHCl₃); IR (KBr) ν_{max} 3467, 2971, 2872, 1721, 1627, 1440, 1374, 1238, 1154, 1108, 1039 cm⁻¹; ¹H and ¹³C NMR data, see Tables 2 and 3; HRFABMS *m/z* 447.2351 [M + Na]⁺ (calc for C₂₃H₃₆O₇Na, 447.2353).

Dendronpholide H (9): colorless oil; $[\alpha]^{20}_D$ +20.0 (*c* 0.10, CHCl₃); IR (KBr) ν_{max} 3513, 2927, 2856, 1714, 1627, 1463, 1374, 1238, 1150, 1107, 1037 cm⁻¹; ¹H and¹³C NMR data, see Tables 2 and 3; HRFABMS *m/z* 461.2513 [M + Na]⁺ (calc for C₂₄H₃₈O₇Na, 461.2510).

Dendronpholide I (10): colorless oil; $[\alpha]^{20}_D$ −33.3 (*c* 0.23, CHCl₃); IR (KBr) ν_{max} 3408, 2971, 2935, 2877, 1723, 1620, 1458, 1375, 1298,

1244, 1151, 1029 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 451.2313 [M + Na]$^+$ (calc for C$_{22}$H$_{36}$O$_8$Na, 451.2308).

Dendronpholide J (11): colorless oil; [α]$^{20}_D$ −27.2 (*c* 0.18, CHCl$_3$); IR (KBr) ν_{max} 3431, 2928, 2858, 1726, 1619, 1454, 1377, 1240, 1122, 1089 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 451.2310 [M + Na]$^+$ (calc for C$_{22}$H$_{36}$O$_8$Na, 451.2308).

Dendronpholide K (12): colorless oil; [α]$^{20}_D$ −84.9 (*c* 0.11, CHCl$_3$); IR (KBr) ν_{max} 3468, 2935, 2869, 1727, 1621, 1462, 1375, 1300, 1243, 1154, 1054, 1026 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 441.2535 [M − H]$^-$ (calc for C$_{23}$H$_{37}$O$_8$, 441.2537).

Dendronpholide L (13): colorless oil; [α]$^{20}_D$ −26.5 (*c* 0.20, CHCl$_3$); IR (KBr) ν_{max} 3445, 2974, 2935, 2876, 1717, 1626, 1451, 1378, 1235, 1152, 1118, 1034 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 457.2794 [M + 1]$^+$ (calc for C$_{24}$H$_{41}$O$_8$, 457.2798).

Dendronpholide M (14): colorless oil; [α]$^{20}_D$ −35.5 (*c* 0.13, CHCl$_3$); IR (KBr) ν_{max} 3451, 2971, 2925, 2855, 1720, 1629, 1443, 1379, 1251, 1153, 1119, 1035 cm^{-1}; ^{1}H and^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 443.2467 [M + 1]$^+$ (calc for C$_{23}$H$_{38}$O$_8$, 443.2645).

Dendronpholide N (15): colorless oil; [α]$^{20}_D$ −16.7 (*c* 0.12, CHCl$_3$); IR (KBr) ν_{max} 3438, 2975, 2935, 1717, 1627, 1460, 1382, 1236, 1151, 1118, 1034 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 493.2769 [M + Na]$^+$ (calc for C$_{25}$H$_{42}$O$_8$Na, 493.2771).

Dendronpholide O (16): colorless oil; [α]$^{20}_D$ −10.8 (*c* 0.18, CHCl$_3$); IR (KBr) ν_{max} 3376, 2981, 2931, 2875, 1715, 1624, 1447, 1375, 1244, 1152, 1027 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 461.2506 [M + Na]$^+$ (calc for C$_{24}$H$_{38}$O$_7$Na, 461.2509).

Dendronpholide P (17): colorless oil; [α]$^{20}_D$ −9.1 (*c* 0.18, CHCl$_3$); IR (KBr) ν_{max} 3413, 2976, 2950, 2873, 1735, 1719, 1625, 1439, 1376, 1243, 1148, 1027 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 3; HRFABMS *m/z* 447.2344 [M + Na]$^+$ (calc for C$_{23}$H$_{36}$O$_7$Na, 447.2353).

Dendronpholide Q (18): colorless oil; [α]$^{20}_D$ +65.0 (*c* 0.20, CHCl$_3$); IR (KBr) ν_{max} 3406, 2926, 2859, 1739, 1710, 1627, 1459, 1375, 1238, 1146, 1072, 1027 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 4; HRFABMS *m/z* 453.2484 [M + 1]$^+$ (calc for C$_{24}$H$_{37}$O$_8$, 453.2483).

Dendronpholide R (19): colorless oil; [α]$^{20}_D$ −16.7 (*c* 0.18, CHCl$_3$); IR (KBr) ν_{max} 3432, 2967, 2933, 1726, 1619, 1454, 1376, 1237, 1169, 1043 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 4; HRFABMS *m/z* 409.2229 [M − 1]$^-$ (calc for C$_{22}$H$_{33}$O$_7$, 409.2231).

Cytotoxicity Assays. The cytotoxic properties of the crude extract were tested in vitro using human cancer cell lines including HL-60 (leukemia), BGC-823 (gastric), BeL-7402 (hepatoma), and KB (nasopharyngeal). The crude extract had inhibitory activity against the BGC-823 cell line. The cytotoxic properties of the isolated compounds were tested in vitro using human cancer cell lines including HCT-8 (colon), BGC-823, BeL-7402, A-549 (lung adenocarcinoma), and A2780 (ovary). The bioassays used the MTT method as described in the literature.[14]

Supporting Information Available: IR, MS, and ID and 2D NMR spectra for dendronpholides A–R (**2–19**). This material is available free of charge via the Internet at http://pubs.acs.org.

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