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New Dolabellane-Type Diterpenoids from the Okinawan Soft Coral of the Genus *Clavularia*

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(Received August 23, 2001)

Two new diterpenoids, **2** and **4**, having a dolabellane skeleton were isolated from the Okinawan soft coral of the genus *Clavularia*. Their structures were determined based on spectroscopic analysis, chemical conversion and X-ray crystallographic analysis. One of these diterpenoids showed cytotoxic activity against tumor cells.

Soft corals belonging to the genus *Clavularia*, inhabiting abundantly in the Okinawan sea waters, have been recognized as rich sources for marine natural products, most of which possess unique structural features and remarkable biological activities. A series of prostanoids[1] and steroids[2] were found from *Clavularia viridis*. On the other hand a variety of terpenoids[3] were isolated from other species of *Clavularia*, such as *C. koellikeri*. During our continuing studies on the chemical constituents of Okinawan soft coral of the genus *Clavularia*, two new dolabellane-type diterpenoids were isolated as well as two known diterpenoids from the unknown species of *Clavularia*. This paper describes the isolation and structure determination of these compounds (Chart 1.).

The MeOH extract of soft coral, collected on the coral reef of Ishigaki Island (Okinawa prefecture, Japan) in 1998, was partitioned between EtOAc and H_2O. An aliquot (10 g) of the EtOAc-soluble portion (18.9 g) was chromatographed on a silica-gel column by elution with hexane, hexane–EtOAc (4:1), EtOAc, and MeOH in turn to give four fractions. Further repeated chromatographic separation and purification of the fraction 2 (3.4 g) gave compounds **1** (30 mg) and **2** (48 mg). Similar chromatographic separation and purification of the portion (1.0 g) of the fraction 3 (6.0 g) gave compounds **3** (78 mg) and **4** (95 mg). Compound **1** [colorless viscous oil, $[\alpha]_D^{25}$ +33.2° (*c* 1.14, $CHCl_3$)] was identified as dolabellatrienone,[4] isolated from the Caribbean gorgonian octocoral, *Eunicea calyculata*, by a comparison of their spectral data. The absolute stereochemistry of dolabellatrienone was established by the synthesis.[5] Compound **3** [colorless needles, $[\alpha]_D^{22}$ −51.9° (*c* 1.25, $CHCl_3$)] was identified as claenone,[3e] found from the Okinawan soft coral of the genus *Clavularia* during our previous study. The absolute stereochemistry of claenone was also confirmed by the synthesis.[6]

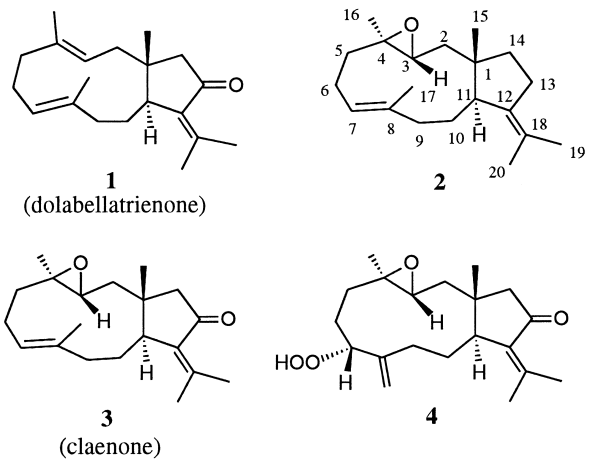

Chart 1. Structures of **1**, **2**, **3**, and **4**.

The molecular formula of $C_{20}H_{32}O$ for **2** [colorless cubics, $[\alpha]_D^{22}$ −214.0° (*c* 1.28, $CHCl_3$)] was determined by elemental analysis (found C 83.08%, H 10.89%; calcd C 83.27%, H 11.18%) and the ^{13}C NMR spectrum. All 20 carbons appeared in the ^{13}C NMR spectrum, and DEPT experiments indicated the presence of five methyls, seven sp^3 methylenes, two sp^3 methines, two sp^3 quaternary carbons, one sp^2 methine and three sp^2 quaternary carbons. The ^1H and ^{13}C NMR spectra (Table 1) showed the presence of a trisubstituted epoxide [δ_H 2.98 (1H, dd, J = 3.0, 11. 2 Hz), δ_C 61.7 (C), 64.8 (CH)], a trisubstituted double bond [δ_H 5.07 (1H, br d, J = 11.0 Hz), δ_C 127.5 (CH), 133.7 (C)], a tetrasubstituted double bond [δ_C 122.8 (C), 141.6 (C)], and three olefinic methyls [δ_H 1.55 (3H, s), 1.62 (3H, s), 1.72 (3H, br s)]. These spectral data, coupled with the degree of unsaturation (five), disclosed a tricyclic structure for **2**.

The proton correlations observed in ^1H–^1H COSY showed the presence of the partial structures **a**, **b**, **c** and **d** in **2**, as illustrated in Fig. 1. After assignments of all the direct ^{13}C–^1H correlations were made based on an HMQC analysis, the HMBC spectrum of **2** was measured and analyzed to obtain the gross structure of **2**, as shown in Fig. 2. The correlations from H-7 in the partial structure **a** to C-9 in **d**, from the methyl protons

Table 1. NMR Data ($CDCl_3$, δ ppm) for **2**[a)]

Position	^{13}C (125 MHz)	^{1}H (500 MHz)[b)]
1	44.4 (C)	
2	39.4 (CH_2)	1.24 (1H, dd, *J* 11.2, 13.3)
		1.57 (1H, dd, *J* 3.0, 13.3)
3	64.8 (CH)	2.98 (1H, dd, *J* 3.0, 11.2)
4	61.7 (C)	
5	38.8 (CH_2)	1.24 (1H, m)
		2.16 (1H, ddd, *J* 2.1, 4.8, 13.5)
6	24.5 (CH_2)	2.22 (1H, m)
		2.39 (1H, dddd, *J* 4.8, 11.0, 13.3, 15.4)
7	127.5 (CH)	5.07 (1H, br d, *J* 11.0)
8	133.7 (C)	
9	37.3 (CH_2)	2.06 (1H, m)
		2.32 (1H, ddd, *J* 8.7, 10.4, 12.8)
10	27.2 (CH_2)	1.49 (2H, m)
11	42.7 (CH)	2.52 (1H, br t, *J* 6.6)
12	141.6 (C)	
13	27.8 (CH_2)	2.11 (1H, m)
		2.21 (1H, m)
14	41.3 (CH_2)	1.44 (1H, br dd, *J* 3.1, 12.6)
		1.65 (1H, td, *J* 11.1, 12.6)
15	23.7 (CH_3)	1.29 (3H, s)
16	15.3 (CH_3)	1.13 (3H, s)
17	16.8 (CH_3)	1.72 (3H, br s)
18	122.8 (C)	
19	21.6 (CH_3)	1.55 (3H, s)
20	21.4 (CH_3)	1.62 (3H, s)

a) Assignments of the direct ^{13}C and ^{1}H signals were made based on the HMQC analysis.
b) *J* in Hz.

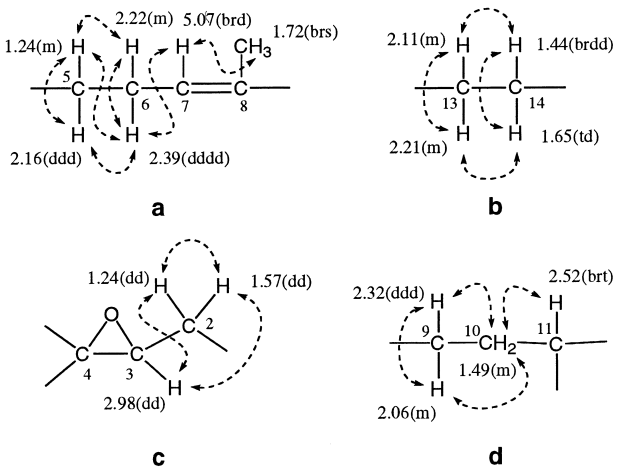

Fig. 1. Partial structures and ^{1}H–^{1}H correlations observed in the ^{1}H–^{1}H COSY of **2**.

(H-17) in **a** to C-9 in **d**, and from H-9 in **d** to C-8 in **a** connected the partial structures **a** and **d** between C-8 and C-9. The connection of the partial structures **a** and **c** between C-5 and C-4 was indicated based on the correlations from H-5 in **a** to C-4 in **c** and from H-3 to C-5. The presence of an isopropylidene group was demonstrated by the correlations from the two olefinic methyl protons [δ_H 1.55 (3H, s), 1.62 (3H, s)] to the olefinic carbons [δ_C 122.8 (C), 141.6 (C)] of the tetrasubstituted double bond. The connection of this isopropylidene group to both partial structures **b** and **d** was indicated by the correlations from H-14 in **b** to C-12 and from H-10 in **d** to C-12. The presence of the methyl group at C-4 was indicated by the correlation from this methyl proton [δ_H 1.13 (3H, s)] to C-4. Finally the connection of the quaternary carbon at C-1 [δ_C 44.4 (C)] to each partial structure **b**, **c** and **d** as well as to the methyl group [δ_H 1.29 (3H, s)] was exhibited by the correlations from H-14 in **b** to C-1, from H-2 in **c** to C-1 and H-10 in **d** to C-1, to give a bicarbocyclic gross structure for **2**.

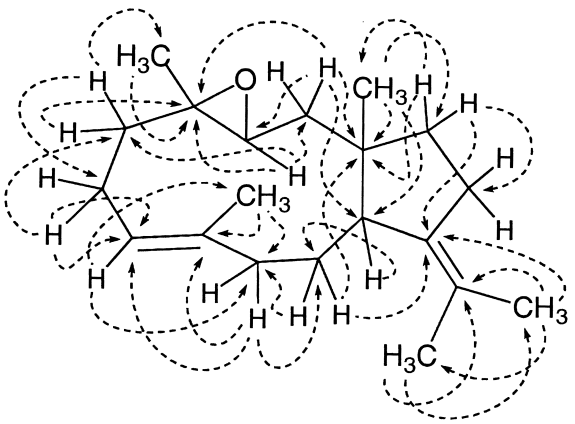

Fig. 2. ^{1}H–^{13}C long-range correlations observed in the HMBC spectrum of **2**.

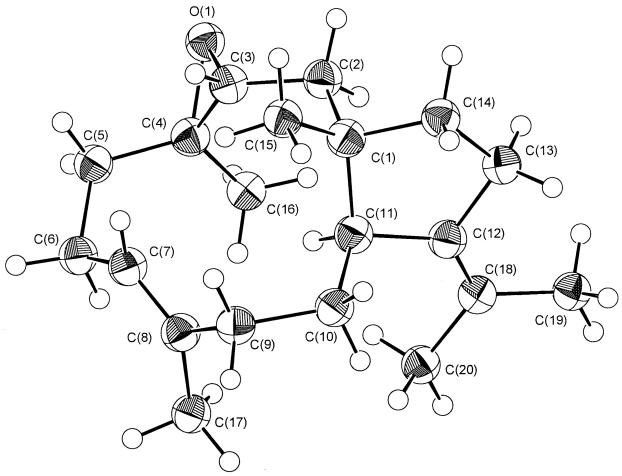

Fig. 3. Perspective view (ORTEP) of the molecule of **2**.

The relative stereochemistry of four chiral centers (C-1, -3, -4 and -11) as well as the stereochemistry of the trisubstituted double bond in **2** were determined by X-ray crystallographic analysis on a single crystal of **2**. The result of the X-ray analysis is shown in Fig. 3, disclosing the 1*S**, 3*R**, 4*R** and 11*S** relative configurations for the chiral centers as well as the *E* configuration for the double bond. Compound **2** was thus elucidated to have a structure corresponding to the 13-deoxy derivative of claenone (**3**). The absolute stereochemistry of **2** was suggested to be the same as that of **3**.

The molecular formular of $C_{20}H_{30}O_4$ for **4** [colorless cubics, $[\alpha]_D^{25}$ +111.8° (*c* 0.17, $CHCl_3$)] was determined by elemental analysis (found C 71.55%, H 9.02%; calcd C 71.82%, H 9.04%) and HREIMS [found *m/z* 334.2168 (M^+); calcd for $C_{20}H_{30}O_4$ 334.2144]. All 20 carbons appeared in the ^{13}C NMR

Table 2. NMR Data ($CDCl_3$, δ ppm) for **4**[a)]

Position	^{13}C (125 MHz)	^{1}H (500 MHz)[b)]
1	37.9 (C)	
2	39.4 (CH_2)	1.33 (1H, dd, *J* 11.4, 13.7)
		1.77 (1H, dd, *J* 2.1, 13.7)
3	61.3 (CH)	3.16 (1H, dd, *J* 2.1, 11.4)
4	61.0 (C)	
5	36.9 (CH_2)	1.39 (1H, br t, *J* 12.6)
		2.17 (1H, br dd, *J* 5.8, 12.6)
6	28.9 (CH_2)	1.97 (1H, m)
		2.23 (1H, m)
7	86.7 (CH)	4.62 (1H, d, *J* 7.0)
8	150.1 (C)	
9	35.9 (CH_2)	2.38 (1H, dt, *J* 4.5, 13.7)
		2.51 (1H, m)
10	33.7 (CH_2)	1.49 (1H, dt, *J* 5.6, 14.1)
		1.94 (1H, m)
11	42.9 (CH)	2.53 (1H, br d, *J* 11.6)
12	137.3 (C)	
13	205.4 (C)	
14	54.7 (CH_2)	2.11 (1H, dd, *J* 0.8, 17.8)
		2.45 (1H, d, *J* 17.8)
15	22.6 (CH_3)	1.45 (3H, s)
16	15.8 (CH_3)	1.12 (3H, s)
17	118.0 (CH_2)	5.33 (1H, br s)
		5.37 (1H, br s)
18	149.6 (C)	
19	21.1 (CH_3)	2.19 (3H, s)
20	24.4 (CH_3)	1.79 (3H, s)
OOH		7.77 (1H, s)

a) Assignments of the direct ^{13}C and ^{1}H signals were made based on the HMQC analysis.
b) *J* in Hz.

spectrum, and DEPT experiments indicated the presence of four methyls, six sp^3 methylenes, three sp^3 methines, two sp^3 quaternary carbons, one sp^2 methylene and four sp^2 quaternary carbons (Table 2). The presence of an α-isopropylidenecyclopentanone system **e** (Fig. 4), the same as that in claenone (**3**), was demonstrated by UV [254 nm (ε 7800)], IR (1703, 1620 cm^{-1}), ^{13}C NMR [δ_C 205.4 (C, C-13), 149.6 (C, C-18), 137.3 (C, C-12), 54.7 (CH_2, C-14), 37.9 (C, C-1)], and ^{1}H NMR [δ_H 1.45 (3H, s, H-15), 2.11 (1H, dd, J = 0.8, 17.8 Hz, H-14), 2.45 (1H, d, J = 17.8 Hz, H-14), 2.19 (3H, s, H-19), 1.79 (3H, s, H-20)] (Table 2) spectra. ^{1}H and ^{13}C NMR spectra also showed signals due to a trisubstituted epoxide [δ_H 3.16 (1H, dd, J = 2.1, 11.4 Hz, H-3); δ_C 61.3 (CH, C-3), 61.0 (C, C-4)], and due to a terminal olefin [δ_H 5.33 (1H, br s, H-17), 5.37 (1H, br s, H-17); δ_C 118.0 (CH_2, C-17), 150.1 (C, C-8)]. The presence of a secondary hydroperoxide group was demonstrated by the IR absorption (3319 cm^{-1}) and the low-field ^{1}H signal at δ 7.77 (1H, s) due to the hydroperoxy proton in addition to the ^{1}H and ^{13}C NMR data [δ_H 4.62 (1H, d, J = 7.0 Hz, H-7); δ_C 86.7 (CH, C-7)]. These spectroscopic findings coupled with ^{1}H–^{1}H correlations observed in the ^{1}H–^{1}H COSY gave partial structures **e**, **f** , **g** and **h**, as shown in Fig. 4.

After assignments of the direct ^{13}C–^{1}H correlations were made based on the HMQC analysis, the HMBC spectrum of **4** was measured and analyzed to obtain the gross structure of **4**. As shown in Fig. 5, the correlations from H-2 in the partial structure **f** to C-1 in **e** and from H-14 in **e** to C-2 in **f** connected

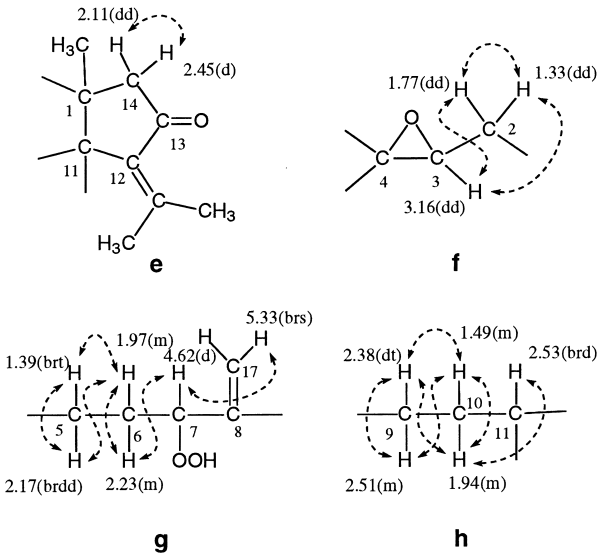

Fig. 4. Partial structures and ^{1}H–^{1}H correlations observed in the ^{1}H–^{1}H COSY of **4**.

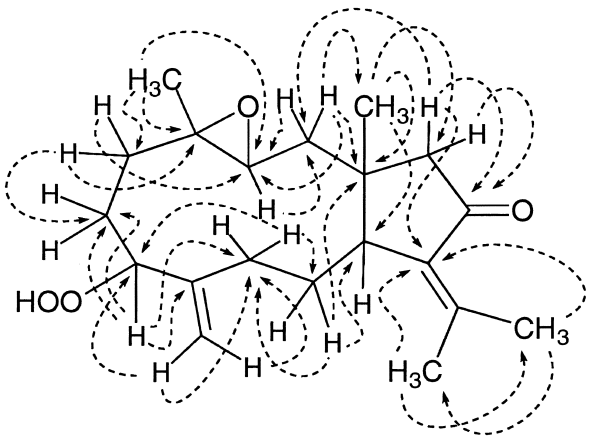

Fig. 5. ^{1}H–^{13}C long-range correlations observed in the HMBC spectrum of **4**.

the partial structures **e** and **h** between C-1 and C-2. The presence of the methyl group at C-4 was indicated by the correlations from this methyl proton (H-16) to both C-3 and C-4. The connection of the partial structures **f** and **g** between C-4 and C-5 was demonstrated by the correlations from H-5 to both C-3 and C-4, and from H-16 (CH_3 at C-4) to C-5. The correlations from H-17 (CH_2) to C-9 and from H-9 to C-7 connected **g** and **h**. Finally, the partial structure **h** was connected to **e** at C-11, to give a bicarbocyclic gross structure for **4**.

The relative stereochemistry of five chiral centers (C-1, -3, -4, -7 and -11) was determined by X-ray crystallographic analysis on a single crystal of **4**. The result of the X-ray analysis is shown in Fig. 6, demonstrating 1R^*, 3R^*, 4R^*, 7R^* and 11S^* relative configurations for the chiral centers. The absolute stereochemistry of **4** was disclosed by the chemical correlation between **4** and claenone (**3**). During the above-mentioned isolation process, claenone (**3**) in a solution was found to be gradually changed to **4** at room temperature. This change must be attributed to air-oxidation on the double bond at C-7 of **3**.

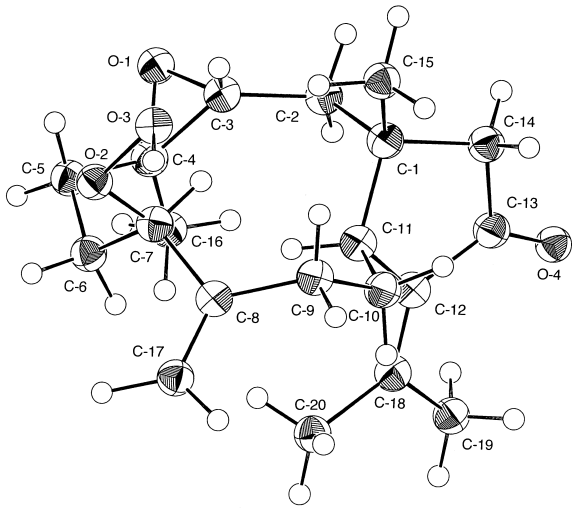

Fig. 6. Perspective view (ORTEP) of the molecule of **4**.

Thus, a solution of **3** in EtOAc was stirred at room temperature under an atmosphere of O_2 to find a 37% conversion of **3** to **4**, whose ^{1}H NMR data and the $[\alpha]_D$ value were identical to those of **4** obtained by the above-mentioned isolation. Since the absolute stereochemistry of **3** was previously established by synthesis,[6] the absolute stereochemistry of **4** was determined as 1*R*, 3*R*, 4*R*, 7*R* and 11*S* configurations. The chemical conversion of **3** to **4** suggested that **4** might be formed from **3** during the isolation process.

Compound **4** showed moderate cytotoxic activity against colon cancer (KM-12), lung cancer (DMS273), melanoma (LOX-IMVI), ovarian cancer (OVCAR-3 and OVCAR-4), and stomach cancer (MKN7 and MKN28) cells, evaluated in the Jpn. Fdn. for Cancer Res. 39 cell line assay;[7] the results are given in Table 3. The pattern of differential cytotoxicity of **4** was evaluated by Compare Program, and was revealed not to be correlated with that shown by any of the other compounds including currently used anticancer drugs; the correlation coefficient value was less than 0.5. This indicates that **4** may have a new mode of action.

Table 3. The GI_{50} Values for the Compound **4** against the 39 Cell Lines[a)]

Panel/Cell Line	GI_{50} (μM)	Panel/Cell Line	GI_{50} (μM)
Breast Cancer		Melanoma	
HBC-4	—[b)]	LOX-IMVI	2.4
BSY-1	—	Ovarian Cancer	
HBC-5	—	OVCAR-3	3.9
MCF-7	10	OVCAR-4	1.8
MDA-MB-231	—	OVCAR-5	14
CNS Cancer		OVCAR-8	—
U251	—	SK-OV-3	—
SF-268	—	Renal Cancer	
SF-295	9.6	RXF-631L	—
SF-539	—	ACHN	—
SNB-75	—	Stomach Cancer	
SNB-78	—	St-4	—
Colon Cancer		MKN1	—
HCC2998	—	MKN7	1.0
KM-12	4.4	MKN28	4.4
HT-29	—	MKN45	—
HCT-15	—	MKN74	5.5
HCT-116	—	Prostate Cancer	
Lung Cancer		DU-145	—
NCI-H23	—	PC-3	—
NCI-H226	—		
NCI-H522	13		
NCI-H460	—		
A549	—		
DMS273	4.8		
DMS114	—		

a) The GI_{50} value is the concentration that yielded 50% growth.
b) The value is more than 15 μM.

Experimental

General Method. Optical rotations were measured in a $CHCl_3$ solution with a JASCO DIP-370 automatic polarimeter. IR spectra were recorded with a Perkin-Elmer FTIR 1600 spectrophotometer and UV spectra with a JASCO V-520 spectrophotometer. NMR spectra were recorded with a Bruker DRX-500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometer. Two-dimensional (2D) NMR spectra (^{1}H–^{1}H COSY, HMQC and HMBC) were measured using standard Bruker pulse sequences. The chemical shifts are expressed on a δ ppm scale with $CHCl_3$ (^{1}H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). The multiplicities of the ^{13}C resonance were achieved by DEPT experiments, which were performed using polarization transfer pulses of 90° and 135°, first obtaining only signals for CH groups and then positive signals for CH and CH_3 and negative signals for CH_2 groups. Mass spectra (MS) and high-resolution electron impact MS (HREIMS) were taken with a Micromass Auto Spec spectrometer.

Column chromatography was carried out on Merck silica gel 60 (70–230 mesh). Flash column chromatography was performed on Merck silica gel 60 (230–400 mesh). High-performance liquid chromatography (HPLC) was conducted with a YMC-Pack SIL-06 column (silica gel, SH-043-5-06, for normal phase) and a YMC-Pack ODS-AM column (ODS silica gel, SH-343-5AM, for reversed phase).

Isolation and Purification. Soft coral of the genus *Clavularia* (order Stolonefera, family Clavularidae) was collected on the coral reef near Ishigaki Island, Okinawa Prefecture, Japan in October 1998 at a depth of 1–2 m. A voucher specimen (No. SC-98-11) is on deposit at Tokyo University of Pharmacy and Life Science, Tokyo, Japan.

Wet specimens (1.1 kg) were immersed in MeOH. The MeOH extract was partitioned between EtOAc and H_2O. The EtOAc layer was concentrated under reduced pressure to give an EtOAc-soluble portion (18.9 g). An aliquot (10 g) of the EtOAc-soluble portion was chromatographed on a silica-gel column. Stepwise elution with hexane, hexane–EtOAc (4:1), EtOAc, and MeOH gave four fractions. Fraction 2 (3.5 g) (eluted with hexane–EtOAc = 4:1) was chromatographed on a silica-gel column. Elution with hexane–EtOAc (10:1) gave seven fractions. Further purification of fraction 3 (142 mg) with reversed-phase HPLC (eluted with MeOH–H_2O = 9:1) gave compound **1** (30 mg). Purification of fraction 2 (340 mg) by flash chromatography (eluted with hexane–2-propanol = 20:1) and then normal phase HPLC (eluted with hexane–2-propanol = 30:1) gave compound **2** (48 mg).

An aliquot (1.0 g) of fraction 3 (6.0 g) obtained by the first chromatographic separation of the EtOAc soluble portion (10 g) was chromatographed on a silica-gel column. Elution with hexane–EtOAc (4:1) gave five fractions. Further repeated purifica-

Table 4. Crystallographic Data for **2** and **4**

	2	**4**
Crystal data		
Formula	$C_{20}H_{32}O$	$C_{20}H_{30}O_4$
Mol wt	288	334
Cryst. system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a/Å	14.935(5)	11.806(3)
b/Å	14.886(5)	27.509(7)
c/Å	8.399(2)	11.711(3)
V/Å	1799(1)	3803(2)
Z	4	8
Data collection		
Temperature/K	298	298
No. of reflns measd	2053	4210
No. of ind reflns	1898	3967
No. of obsd reflns	1621	3469
Refinement		
R	0.049	0.049
wR	0.062	0.062
S	1.022	1.300
(Δ/σ)	0.0007	0.0100
$(\Delta/\rho)_{max}$/eÅ^{-3}	0.29	0.24
$(\Delta/\rho)_{min}$/eÅ^{-3}	−0.13	−0.20

tion of fraction 1 (599 mg) with flash chromatography (hexane–EtOAc = 5:1) gave compounds **3** (273 mg) and **4** (96 mg).

Compound 1 (Dolabellatrienone). Colorless viscous oil. $[\alpha]_D^{25}$ +33.2° (*c* 1.14, $CHCl_3$). ^{1}H and ^{13}C NMR data were identical with those of dolabellatrienone.[4]

Compound 2. Colorless cubics. $[\alpha]_D^{22}$ −214.0° (*c* 1.28, $CHCl_3$). Anal. Found: C, 83.08; H, 10.89%. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18%. ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) are listed in Table 1.

Compound 3 (Claenone). Colorless needles. $[\alpha]_D^{22}$ −51.9° (*c* 1.25, $CHCl_3$). ^{1}H and ^{13}C NMR data were identical with those of claenone.[3e]

Compound 4. Colorless cubics. $[\alpha]_D^{25}$ +111.8° (*c* 0.17, $CHCl_3$). EIMS *m*/*z* 334 (M^+). HREIMS *m*/*z* 334.2168 (M^+, $C_{20}H_{30}O_4$ requires 334.2144). Anal. Found: C, 71.55; H, 9.02%. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04%. IR (dry film) ν_{max} 3319, 3075, 2934, 1703, 1620, 892, 861, 827 cm^{-1}. UV (EtOH) λ_{max} 254 (ε 7800) nm. ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) are listed in Table 2.

Conversion of Claenone (3) to 4. A solution of **3** (30 mg) in EtOAc (5 mL) was stirred at room temperature for 7 days under an atmosphere of O_2. The product mixture was chromatographed on a silica-gel column by elution with hexane–EtOAc (4:1) to give **4** (11.8 mg) and unchanged **3** (12.3 mg).

X-ray Crystallography of 2 and 4. A colorless cubic crystal of **2** was obtained by recrystallization from MeOH–H_2O. A single crystal having dimensions of 0.35 × 0.25 × 0.15 mm was used for X-ray diffraction studies on a Mac Science MXC18 diffractometer employing graphite-monochromated Cu $K\alpha$ radiation (λ 1.54178 Å). A summary of the crystallographic data is given in Table 4. The structure was solved by a direct method using SIR92[8] in the CRYSTAN GM program system and refined by a full-matrix least-squares method using 1621 reflections [$I > 3.00\sigma(I)$] for 223 parameters. The final R value is 0.049. The bond lengths and bond angles are listed in Tables 5 and 6, respectively.

Table 5. Bond Lengths for **2** and **4**

Compound **2**			
C(1)–C(2)	1.543(3)	C(1)–C(11)	1.553(3)
C(1)–C(14)	1.540(3)	C(1)–C(15)	1.525(3)
C(2)–C(3)	1.489(3)	C(3)–C(4)	1.474(3)
C(3)–O(1)	1.449(2)	C(4)–C(5)	1.518(3)
C(4)–C(16)	1.499(3)	C(4)–O(1)	1.453(2)
C(5)–C(6)	1.533(3)	C(6)–C(7)	1.509(3)
C(7)–C(8)	1.335(3)	C(8)–C(9)	1.507(3)
C(8)–C(17)	1.496(4)	C(9)–C(10)	1.544(3)
C(10)–C(11)	1.542(3)	C(11)–C(12)	1.532(4)
C(12)–C(13)	1.512(3)	C(12)–C(18)	1.318(3)
C(13)–C(14)	1.513(3)	C(18)–C(19)	1.517(3)
C(18)–C(20)	1.516(4)		
Compound **4**			
O(1)–C(3)	1.442(3)	O(1)–C(4)	1.452(3)
O(2)–O(3)	1.461(3)	O(2)–C(7)	1.444(3)
O(4)–C(13)	1.205(3)	O(5)–C(23)	1.440(4)
O(5)–C(24)	1.448(4)	O(6)–O(7)	1.450(3)
O(6)–C(27)	1.438(3)	O(8)–C(33)	1.240(4)
C(1)–C(2)	1.546(3)	C(1)–C(11)	1.553(4)
C(1)–C(14)	1.531(3)	C(1)–C(15)	1.544(3)
C(2)–C(3)	1.502(4)	C(3)–C(4)	1.458(3)
C(4)–C(5)	1.511(3)	C(4)–C(16)	1.496(4)
C(5)–C(6)	1.523(4)	C(6)–C(7)	1.532(4)
C(7)–C(8)	1.508(3)	C(8)–C(9)	1.499(3)
C(8)–C(17)	1.314(4)	C(9)–C(10)	1.538(4)
C(10)–C(11)	1.551(4)	C(11)–C(12)	1.522(4)
C(12)–C(13)	1.474(4)	C(12)–C(18)	1.345(4)
C(13)–C(14)	1.510(4)	C(18)–C(19)	1.514(4)
C(18)–C(20)	1.506(5)	C(21)–C(22)	1.544(4)
C(21)–C(31)	1.568(4)	C(21)–C(34)	1.549(3)
C(21)–C(35)	1.537(3)	C(22)–C(23)	1.488(4)
C(23)–C(24)	1.456(4)	C(24)–C(25)	1.502(3)
C(24)–C(36)	1.501(2)	C(25)–C(26)	1.529(3)
C(26)–C(27)	1.532(3)	C(27)–C(28)	1.508(3)
C(28)–C(29)	1.507(3)	C(28)–C(37)	1.313(4)
C(29)–C(30)	1.523(3)	C(30)–C(31)	1.534(4)
C(31)–C(32)	1.528(4)	C(32)–C(33)	1.476(4)
C(32)–C(38)	1.355(4)	C(33)–C(34)	1.502(4)
C(38)–C(39)	1.517(4)	C(38)–C(40)	1.489(5)

Table 6. Bond Angles for **2**

C(2)–C(1)–C(11)	108.4(2)	C(2)–C(1)–C(14)	110.0(2)
C(2)–C(1)–C(15)	109.1(2)	C(11)–C(1)–C(14)	102.2(2)
C(11)–C(1)–C(15)	118.4(2)	C(14)–C(1)–C(15)	108.4(2)
C(1)–C(2)–C(3)	115.0(2)	C(2)–C(3)–C(4)	128.3(2)
C(2)–C(3)–O(1)	117.9(2)	C(4)–C(3)–O(1)	59.6(2)
C(3)–C(4)–C(5)	119.1(2)	C(3)–C(4)–C(16)	122.5(2)
C(3)–C(4)–O(1)	59.4(2)	C(5)–C(4)–C(16)	114.7(2)
C(5)–C(4)–O(1)	114.5(2)	C(16)–C(4)–O(1)	113.5(2)
C(4)–C(5)–C(6)	113.9(2)	C(5)–C(6)–C(7)	111.3(2)
C(6)–C(7)–C(8)	127.5(2)	C(7)–C(8)–C(9)	119.7(2)
C(7)–C(8)–C(17)	123.1(2)	C(9)–C(8)–C(17)	117.2(2)
C(8)–C(9)–C(10)	112.8(2)	C(9)–C(10)–C(11)	115.5(2)
C(1)–C(11)–C(10)	117.2(2)	C(1)–C(11)–C(12)	103.6(2)
C(10)–C(11)–C(12)	112.3(2)	C(11)–C(12)–C(13)	109.2(2)
C(11)–C(12)–C(18)	127.3(2)	C(13)–C(12)–C(18)	123.4(3)
C(12)–C(13)–C(14)	105.0(2)	C(1)–C(14)–C(13)	106.6(2)
C(12)–C(18)–C(19)	121.8(2)	C(12)–C(18)–C(20)	123.5(3)
C(19)–C(18)–C(20)	114.6(2)	C(3)–O(1)–C(4)	61.0(2)

A colorless cubic crystal of **4** was obtained by recrystallization from hexane–AcOEt. A single crystal having dimensions of 0.5 × 0.4 × 0.2 mm was used for X-ray diffraction studies on a Mac Science MXC18 diffractometer employing graphite-monochromated Cu $K\alpha$ radiation. A summary of the crystallographic data is given in Table 4. The structure was solved by direct methods using SIR92 and refined by a full-matrix least-squares method using 3469 reflections [$I > 3.00\sigma(I)$] for 494 parameters. The final R value is 0.049. The bond lengths and bond angles are listed in Tables 5 and 7, respectively.

Table 7. Bond Angles for **4**

C(3)–O(1)–C(4)	60.5(2)	O(3)–O(2)–C(7)	106.7(2)
C(23)–O(5)–C(24)	60.5(2)	O(7)–O(6)–C(27)	106.9(2)
C(2)–C(1)–C(11)	109.3(2)	C(2)–C(1)–C(14)	108.1(2)
C(2)–C(1)–C(15)	110.1(2)	C(11)–C(1)–C(14)	102.9(2)
C(11)–C(1)–C(15)	116.5(2)	C(14)–C(1)–C(15)	109.4(2)
C(1)–C(2)–C(3)	113.2(2)	O(1)–C(3)–C(2)	118.5(2)
O(1)–C(3)–C(4)	60.1(2)	C(2)–C(3)–C(4)	126.4(2)
O(1)–C(4)–C(3)	59.4(2)	O(1)–C(4)–C(5)	116.2(2)
O(1)–C(4)–C(16)	111.2(2)	C(3)–C(4)–C(5)	117.9(2)
C(3)–C(4)–C(16)	122.1(2)	C(5)–C(4)–C(16)	116.1(2)
C(4)–C(5)–C(6)	112.8(2)	C(5)–C(6)–C(7)	113.5(2)
O(2)–C(7)–C(6)	103.9(2)	O(2)–C(7)–C(8)	112.6(2)
C(6)–C(7)–C(8)	116.0(2)	C(7)–C(8)–C(9)	117.6(2)
C(7)–C(8)–C(17)	120.1(2)	C(9)–C(8)–C(17)	122.2(2)
C(8)–C(9)–C(10)	116.6(2)	C(9)–C(10)–C(11)	118.4(3)
C(1)–C(11)–C(10)	117.1(3)	C(1)–C(11)–C(12)	103.9(3)
C(10)–C(11)–C(12)	109.0(3)	C(11)–C(12)–C(13)	108.2(3)
C(11)–C(12)–C(18)	126.4(3)	C(13)–C(12)–C(18)	125.4(3)
O(4)–C(13)–C(12)	129.1(3)	O(4)–C(13)–C(14)	123.0(2)
C(12)–C(13)–C(14)	107.8(2)	C(1)–C(14)–C(13)	105.6(2)
C(12)–C(18)–C(19)	122.8(3)	C(12)–C(18)–C(20)	122.7(3)
C(19)–C(18)–C(20)	114.4(3)	C(22)–C(21)–C(31)	109.8(2)
C(22)–C(21)–C(34)	107.7(2)	C(22)–C(21)–C(35)	110.4(2)
C(31)–C(21)–C(34)	102.4(2)	C(31)–C(21)–C(35)	116.2(3)
C(34)–C(21)–C(35)	109.8(2)	C(21)–C(22)–C(23)	113.4(2)
O(5)–C(23)–C(22)	118.7(2)	O(5)–C(23)–C(24)	60.0(2)
C(22)–C(23)–C(24)	126.4(2)	O(5)–C(24)–C(23)	59.5(2)
O(5)–C(24)–C(25)	116.0(2)	O(5)–C(24)–C(36)	112.6(2)
C(23)–C(24)–C(25)	118.4(2)	C(23)–C(24)–C(36)	121.3(2)
C(25)–C(24)–C(36)	115.9(2)	C(24)–C(25)–C(26)	113.1(2)
C(25)–C(26)–C(27)	113.6(2)	O(6)–C(27)–C(26)	104.2(2)
O(6)–C(27)–C(28)	112.1(2)	C(26)–C(27)–C(28)	115.7(2)
C(27)–C(28)–C(29)	117.1(2)	C(27)–C(28)–C(37)	120.3(2)
C(29)–C(28)–C(37)	122.6(2)	C(28)–C(29)–C(30)	115.0(2)
C(29)–C(30)–C(31)	117.9(3)	C(21)–C(31)–C(30)	117.3(3)
C(21)–C(31)–C(32)	104.6(2)	C(30)–C(31)–C(32)	109.8(2)
C(31)–C(32)–C(33)	106.9(2)	C(31)–C(32)–C(38)	125.1(3)
C(33)–C(32)–C(38)	127.9(3)	O(8)–C(33)–C(32)	125.3(3)
O(8)–C(33)–C(34)	124.9(3)	C(32)–C(33)–C(34)	109.8(2)
C(21)–C(34)–C(33)	105.3(2)	C(32)–C(38)–C(39)	121.7(3)
C(32)–C(38)–C(40)	123.9(3)	C(39)–C(38)–C(40)	114.4(3)

The authors express appreciation to Dr. Yasuo Shida and Mr. Haruhiko Fukaya, Tokyo University of Pharmacy and Life Science, for conducting HREIMS measurement and X-ray crystallographic analysis, respectively.

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