Isolation and Structures of New Halogenated Prostanoids from the Okinawan Soft Coral *Clavularia viridis*

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Fifteen new halogenated prostanoids **9**−**23** were isolated as minor constituents from the Okinawan soft coral *Clavularia viridis*. Compounds **9**−**11** were new members of iodovulone, and compounds **12**−**18** were 12-*O*-acetyliodovulones, 12-*O*-acetylbromovulones, and 12-*O*-acetylchlorovulones. Compounds **19**−**23** were 10,11-epoxy congeners of iodovulone, bromovulone, and chlorovulone. The structures of these compounds were determined on the basis of spectroscopic analysis and chemical conversion.

The Okinawan soft coral *Clavularia viridis* Quoy and Gaimard (class Anthozoa, subclass Octocorallia, order Stolonifera) has been recognized as a rich source of marine prostanoids exemplified by clavulones.[1,2] These marine prostanoids have attracted much attention because of their unique structural features, biological activities,[1,3−5] and biosynthesis.[6,7] Among them, halogenated prostanoids such as chlorovulones[8,9] are especially of interest due to their stronger antiproliferative activity[8] against tumor cells than that of clavulones. The structures of halogenated prostanoids[8−12] found hitherto from *C. viridis* are shown in Figure 1 (**1**−**8**). Our further investigations on new prostanoids[13−16] from *C. viridis* have resulted in the isolation of 15 new halogenated prostanoids, **9**−**23**, as minor constituents. This paper describes the isolation and structures of these halogenated prostanoids.

Results and Discussion

The hexane extract (6.83 g out of 14.5 g) of the freeze-dried soft coral (470 g) was chromatographed on a silica gel column eluted with hexane, hexane−EtOAc (3:1 and 1:1), EtOAc, and MeOH, in turn, to obtain five fractions. The second fraction was again chromatographed on a silica gel column eluted with hexane−EtOAc (9:1, 8:2, and 7:3) to afford seven fractions (fractions A−G). Further separation and purification of fractions D (517 mg), E (384 mg), and F (636 mg) using HPLC and recycling HPLC gave as minor constituents compounds **12**−**18** from fraction D, compounds **9**−**11** and **19**−**23** from fraction E, and previously reported 7-acetoxy-7,8-dihydroiodovulone I (**8**) and its congeners[12] from fraction F.

Structures of New Iodovulones 9−**11.** The HREIMS and ^{13}C NMR data of compound **9** {$[\alpha]_D$ +23.7° ($CHCl_3$)} indicated this molecule to possess an iodine-containing molecular formula of $C_{21}H_{29}O_4I$ [*m*/*z* 454.1001 $[M - H_2O]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005)]. Two UV absorptions [241 (ϵ 16 000), 311 (ϵ 14 000) nm] indicated the presence of a cross-conjugated enone system like chlorovulones. The IR spectrum showed absorptions due to hydroxyl (3459 cm^{-1}) and two carbonyl (1738, 1704 cm^{-1}) groups. The ^{13}C NMR spectrum exhibited all 21 carbon signals for two methyls, eight methylenes, six methines, and five quaternary carbons (Table 1), whose chemical shift values indicated the presence of one ketonic carbonyl [189.8 (C, C-9)], one ester carbonyl [173.6 (C, C-1)], eight olefinic carbons [147.5 (CH, C-5), 125.9 (CH, C-6), 133.8 (CH, C-7), 132.8 (C, C-8), 106.2 (C, C-10), 165.1 (CH, C-11), 121.7 (CH, C-14), 135.1 (CH, C-15)], and one oxygen-bearing carbon [81.5 (C, C-12)]. Among these olefinic carbons, the highest field one [106.2 (C)] should bear an iodine atom by comparison with the corresponding ^{13}C value [102.8 (C)] of 2-iodo-2-cyclopentenone.[17] The ^1H NMR spectrum of **9** (Table 1) showed signals due to a carbomethoxy [3.67 (3H, s)], a terminal methyl [0.89 (3H, t, J = 7.1 Hz, H-20)], and six olefinic protons [6.28 (1H, td, J = 7.1, 15.0 Hz, H-5), 6.76 (1H, dd, J = 11.8, 15.0 Hz, H-6), 7.03 (1H, d, J = 11.8 Hz, H-7), 7.67 (1H, s, H-11), 5.21 (1H, td, J = 7.8, 10.9 Hz, H-14), 5.54 (1H, td, J = 7.4, 10.9 Hz, H-15)]. The spectral data of **9** were very similar to those of chlorovulone II (**2**) and iodovulone I (**6**).

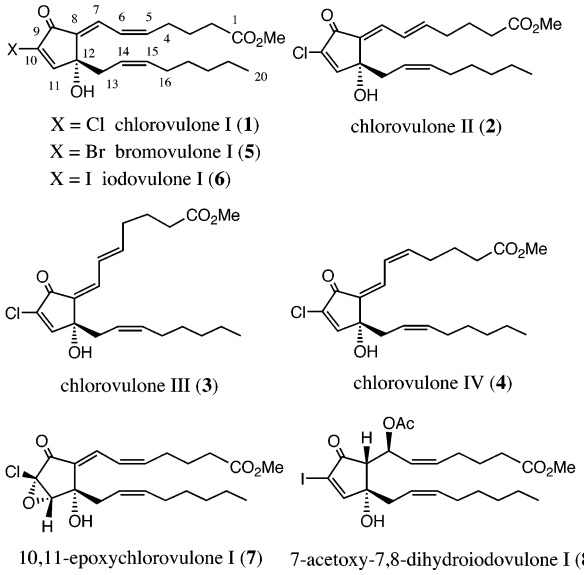

Figure 1. Structures of halogenated prostanoids previously isolated from *Clavularia viridis*.

After direct ^1H and ^{13}C correlations were established from the HMQC spectrum, the gross structure of **9** was elucidated on the basis of the analysis of $^1H-^1H$ COSY and HMBC spectra (Figure 3). The $^1H-^1H$ COSY spectrum revealed sequences of the correlations from H-2 [2.35 (2H, t, J = 7.4 Hz)] to H-7 [7.03 (1H, d, J = 11.8 Hz)], from H-13 [2.64 (1H, br dd, J = 7.8, 14.3 Hz), 2.78 (1H, br dd, J = 7.8, 14.3 Hz)] to H-17 [1.32 (2H, m)], and from H-19 [1.30 (2H, m)] to H-20 [0.89 (3H, t, J = 7.1 Hz)], as shown by the bold lines in Figure 3. The HMBC correlations from

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Table 1. NMR Data[a] for Compounds **9**, **10**, and **11**

	9		**10**	**11**
no.	δ_C	δ_H	δ_H	δ_H
1	173.6 (C)			
2	33.3 (CH_2)	2.35 (2H, t, 7.4)	2.34 (2H, t, 7.4)	2.35 (2H, t, 7.3)
3	23.8 (CH_2)	1.83 (2H, quint., 7.4)	1.80 (2H, quint., 7.4)	1.79 (2H, m)
4	32.8 (CH_2)	2.31 (2H, dt, 7.1, 7.4)	2.28 (2H, m)	2.39 (2H, m)
5	147.5 (CH)	6.28 (1H, td, 7.1, 15.0)	6.19 (1H, td, 7.0, 14.9)	6.07 (1H, td, 7.8, 10.8)
6	125.9 (CH)	6.76 (1H, dd, 11.8, 15.0)	7.58 (1H, dd, 11.4, 14.9)	7.52 (1H, dd, 10.8, 12.1)
7	133.8 (CH)	7.03 (1H, d, 11.8)	6.61 (1H, d, 11.4)	6.99 (1H, d, 12.1)
8	132.8 (C)			
9	189.8 (C)			
10	106.2 (C)			
11	165.1 (CH)	7.67 (1H, s)	7.64 (1H, s)	7.65 (1H, s)
12	81.5 (C)			
13	36.5 (CH_2)	2.64 (1H, br dd, 7.8, 14.3)	2.52 (1H, br dd, 7.8, 14.1)	2.55 (1H, br dd, 7.7, 14.6)
		2.78 (1H, br dd, 7.8, 14.3)	2.63 (1H, br dd, 7.4, 14.1)	2.64 (1H, br dd, 7.7, 14.6)
14	121.7 (CH)	5.21 (1H, td, 7.8, 10.9)	5.29 (1H, br ddd, 7.4,,7.8, 10.9)	5.31 (1H, td, 7.7, 10.9)
15	135.1 (CH)	5.54 (1H, td, 7.4, 10.9)	5.57 (1H, td, 7.3, 10.9)	5.57 (1H, td, 7.4, 10.9)
16	27.5 (CH_2)	1.98 (2H, m)	1.99 (2H, m)	1.98 (2H, m)
17	29.1 (CH_2)	1.32 (2H, m)	1.34 (2H, m)	1.32 (2H, m)
18	31.4 (CH_2)	1.26 (2H, m)	1.28 (2H, m)	1.27 (2H, m)
19	22.6 (CH_2)	1.30 (2H, m)	1.30 (2H, m)	1.31 (2H, m)
20	14.1 (CH_3)	0.89 (3H, t, 7.1)	0.89 (3H, t, 7.0)	0.88 (3H, t, 7.1)
OCH_3	51.6 (CH_3)	3.67 (3H, s)	3.68 (3H, s)	3.68 (3H, s)

[a] Assignments of the ^{13}C (125 MHz) and ^1H (500 MHz) signals were made on the basis of HMQC analysis. δ ppm in $CDCl_3$. J in Hz.

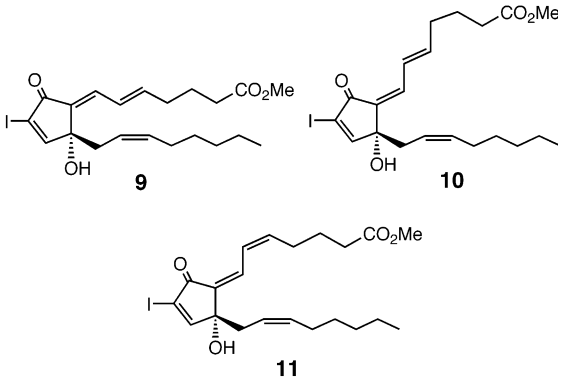


Figure 2. Structures of new iodovulones.

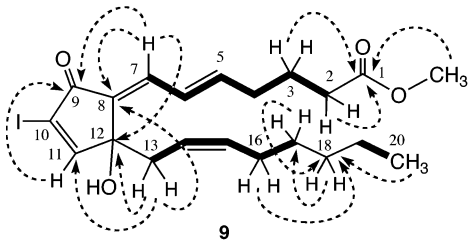


Figure 3. $^1H-^1H$ correlations (bold lines) and key HMBC correlations (broken arrows) of **9**.

H-7 [7.03 (1H, d)] to C-8 [132.8 (C)] and C-9 [189.8 (C)] disclosed that the cyclopentenone carbonyl group conjugated with the double bond between C-7 and -8 to form a cross-conjugated dienone system from C-5 to C-9. The correlation from H-11 [7.67 (1H, s)] to the carbonyl group at C-9 confirmed the presence of a 2-iodo-2-cyclopentenone system. The correlations from H-13 to C-8, -11, and -12 (bearing a tertiary hydroxyl group) indicated the connectivity between C-12 and -13. The connectivity of the carbomethoxy group to C-2 was indicated by the correlations from H-2 and -3 to the carbomethoxy carbonyl carbon. Finally, correlations from H-16 [1.98 (2H, m)], -17 [1.32 (2H, m)], -19 [1.30 (2H, m)], and -20 [0.89 (3H, t)] to C-18 [31.4 (CH_2)] demonstrated the presence of a terminal butyl group. Thus, the prostanoid structure for **9** was completed.

The 5*E* and 14*Z* configurations of two disubstituted double bonds were determined on the basis of the ^1H coupling constants between the olefinic protons: H-5 and H-6 (J = 15.0 Hz), and H-14 and H-15 (J = 10.9 Hz), respectively. The 7*E* configuration of the trisubstituted double bond was deduced by comparison of the chemical shift of H-6 [6.76 (1H, dd)] with those of clavulones. Clavulone II with 7*E* configuration showed the value of 6.75 (1H, dd) for H-6, while clavulone III with 7*Z* configuration showed the value of 7.74 (1H, dd) for H-6, which is strongly deshielded by the carbonyl group at C-9.

Table 2. CD Data[a] (nm ($\Delta\epsilon$)) for Compounds **9**, **10**, **11**, and Iodovulone I (**6**)

9	**10**	**11**	iodovulone I (**6**)
359 (+2.0)	368 (+3.8)	367 (+1.4)	365 (+2.7)
284 (−3.0)	291 (−4.6)	289 (−2.2)	295 (−5.0)
257 (−3.3)	260 (−4.6)	261 (−2.0)	260 (−5.3)
230 (+8.0)	235 (+15.6)	234 (+7.1)	235 (+11.4)

[a] CD spectra were measured in MeOH.

The absolute configuration at C-12 bearing the tertiary hydroxyl group was elucidated by comparing the CD spectrum of **9** (Table 2 and Supporting Information) with that of iodovulone I[10] (**6**), possessing 12*R* configuration. As summarized in Table 2, the CD data of **9** resemble those of **6**, indicating the 12*R* configuration in **9**. Compound **9** was named iodovulone II.

The molecular formula of compound **10** {$[\alpha]_D$ +25.0° ($CHCl_3$)} was indicated to be $C_{21}H_{29}O_4I$, the same as that of **9** from the HREIMS measurement. Although the ^{13}C NMR data could not be obtained owing to its small amount,[18] the ^1H NMR data of **10** (Table 1) were very similar to those of **9**, except for the chemical shifts of H-6 [7.58 (1H, dd, J = 11.4, 14.9 Hz)] and H-7 [6.61 (1H, d, J = 11.4 Hz)], which were analogous to those of chlorovulone III (**3**), possessing 5*E* and 7*Z* configurations. Compound **10** was thus assigned as a 7*E* isomer of **9**. The absolute configuration (12*R*) was determined on the basis of CD data (Table 2 and Supporting Information), which exhibited Cotton effects similar to those of iodovulones I (**6**) and II (**9**). Compound **10** was named iodovulone III.

The molecular formula of compound **11** was indicated to be $C_{21}H_{29}O_4I$, the same as that of **9** and **10** from the HREIMS measurement. The $[\alpha]_D$ and ^{13}C NMR data were

Table 3. NMR Data[a] for Compounds **12** and **13**

	12		**13**
no.	δ_C	δ_H	δ_H
1	173.9 (C)		
2	33.6 (CH_2)	2.34 (2H, t, 7.3)	2.34 (2H, t, 7.4)
3	24.1 (CH_2)	1.81 (2H, quint., 7.3)	1.83 (2H, quint., 7.4)
4	33.1 (CH_2)	2.30 (2H, br dt, 7.0, 7.3)	2.30 (2H, m)
5	148.2 (CH)	6.28 (1H, td, 7.0, 15.1)	6.17 (1H, td, 7.2, 15.2)
6	125.5 (CH)	6.52 (1H, dd, 11.8, 15.1)	7.60 (1H, dd, 11.4, 15.2)
7	133.3 (CH)	7.02 (1H, d, 11.8)	6.54 (1H, d, 11.4)
8	130.3 (C)		
9	189.1 (C)		
10	106.6 (C)		
11	162.9 (CH)	7.85 (1H, s)	7.90 (1H, s)
12	87.1 (C)		
13	35.7 (CH_2)	2.66 (1H, br dd, 8.6, 14.0)	2.62 (1H, br dd, 7.6, 14.1)
		2.96 (1H, br dd, 7.4, 14.0)	2.89 (1H, br dd, 6.6, 14.1)
14	121.1 (CH)	5.14 (1H, br ddd, 7.4, 8.6 10.6)	5.17 (1H, br ddd, 6.6,,7.6, 10.9)
15	135.8 (CH)	5.52 (1H, td, 7.4, 10.6)	5.51 (1H, td, 7.4, 10.9)
16	27.9 (CH_2)	1.94 (2H, m)	1.96 (2H, m)
17	29.5 (CH_2)	1.31 (2H, m)	1.34 (2H, m)
18	32.0 (CH_2)	1.26 (2H, m)	1.27 (2H, m)
19	23.0 (CH_2)	1.29 (2H, m)	1.30 (2H, m)
20	14.5 (CH_3)	0.89 (3H, t, 7.1)	0.88 (3H, t, 7.0)
OCH_3	52.0 (CH_3)	3.67 (3H, s)	3.67 (3H, s)
CH_3CO	169.5 (C)		
CH_3CO	21.7 (CH_3)	2.04 (3H, s)	2.03 (3H, s)

[a] Assignments of the ^{13}C (125 MHz) and ^1H (500 MHz) signals were made on the basis of HMQC analysis. δ ppm in $CDCl_3$. J in Hz.

not obtained owing to its small amount.[19] The ^1H NMR data (Table 1) were very similar to those of **10**, except for the coupling constant between H-5 and H-6 (J = 10.8 Hz) and chemical shifts of H-5 [6.07 (1H, td, J = 7.8, 10.8 Hz] and H-7 [6.99 (1H, d, J = 12.1 Hz)], which were analogous to those of chlorovulone IV (**4**) possessing 5*Z* and 7*Z* configurations. Compound **11** was thus assigned as a (5*Z*) isomer of **10**. The absolute configuration (12*R*) was determined on the basis of CD data (Table 2 and Supporting Information), which exhibited a pattern similar to those of iodovulones I (**6**), II (**9**), and III (**10**). Compound **11** was named iodovulone IV.

Structures of New Halogenated Prostanoid Acetates 12−18. The HREIMS and ^{13}C NMR data of compound **12** indicated this molecule to possess an iodine-containing molecular formula of $C_{23}H_{31}O_5I$ [*m/z* 454.1023 $[M - CH_3CO_2H]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005)]. UV absorptions at 238 (ϵ 14 000) and 307 (ϵ 13 000) nm were similar to those of iodovulones, indicating the presence of a cross-conjugated cyclopentenone system. The IR spectrum showed absorptions due to carbonyl groups (1738, 1707 cm^{-1}), but an absorption due to hydroxyl groups was not observed. The presence of an acetoxyl group in **12** was demonstrated by ^1H NMR [2.04 (3H, s)] and ^{13}C NMR [21.7 (CH_3), 169.5 (C)] spectra. The ^1H NMR and ^{13}C NMR data (Table 3) were very similar to those of iodovulone II (**9**), except for the presence of the signals due to the acetoxyl group and the lower chemical shift of C-12 [87.1 (C)] than that of **9** [81.5 (C)], indicating that **12** was the corresponding acetyl ester of the tertiary hydroxyl group in **9**. This structure was confirmed by the analysis of the HMQC, $^1H-^1H$ COSY, and HMBC spectra. The absolute configurations of compounds **12**−**18** were described later. Compound **12** was named 12-*O*-acetyliodovulone II. The ^1H NMR data (Table 3) of compound **13** ($C_{23}H_{31}O_5I$) were very similar to those of **12** except for the chemical shifts of H-6 [7.60 (1H, dd, J = 11.4, 15.2 Hz)] and H-7 [6.54 (1H, d, J = 11.4 Hz)], indicating that compound **13** was a (7*Z*) isomer of **12**. Compound **13** was named 12-*O*-acetyliodovulone III.

The ^1H NMR data (Table 4) of bromine-containing compound **14** ($C_{23}H_{31}O_5Br$) were quite similar to those of **12**, except for the upfield chemical shift of H-11 [7.60 (1H, s)]. Two MS peaks with a ratio of about 1:1 at *m/z* 406 $\{C_{21}H_{27}O_3{}^{79}Br\ [M - CH_3CO_2H]^+\}$ and 408 $\{C_{21}H_{27}O_3{}^{81}Br\ [M - CH_3CO_2H]^+\}$ indicated the presence of one bromine atom in the molecule of **14**. These findings disclosed that **14** was a bromine-substituted congener of **12** at C-10. Compound **14** was named 12-*O*-acetylbromovulone II. The ^1H NMR data (Table 4) of compound **15** ($C_{23}H_{31}O_5Br$) were very similar to those of **14**, except for the chemical shifts of H-6 [7.59 (1H, dd, J = 11.4, 15.2 Hz)] and H-7 [6.59 (1H, d, J = 11.4 Hz)], indicating that compound **15** was a 7*Z* isomer of **14**. Compound **15** was named 12-*O*-acetylbromovulone III.

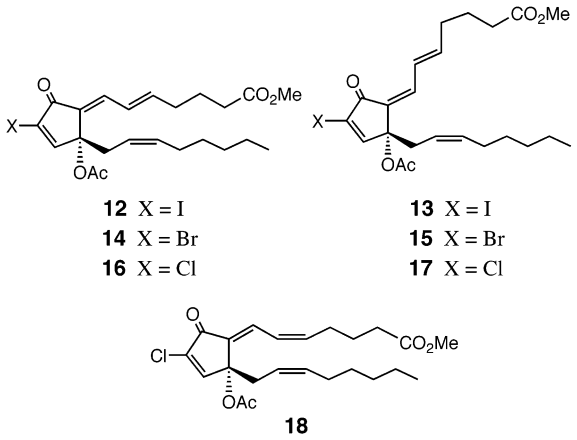


Figure 4. Structures of new halogenated prostanoid acetates.

The ^1H NMR data (Table 5) of chlorine-containing compound **16** ($C_{23}H_{31}O_5Cl$) were quite similar to those of **12** and **14**, except for the upfield chemical shift of H-11 [7.40 (1H, s)]. Two MS peaks with a ratio of about 3:1 at *m/z* 362 $\{C_{21}H_{27}O_3{}^{35}Cl\ [M - CH_3CO_2H]^+\}$ and 364 $\{C_{21}H_{27}O_3{}^{37}Cl\ [M - CH_3CO_2H]^+\}$ indicated the presence of one chlorine atom in the molecule of **16**. These findings disclosed that compound **16** was a chlorine-substituted congener of **12** or **14** at C-10. The structure of **16** was confirmed by chemical conversion. Chlorovulone II[8,9] (**2**) was treated with acetic anhydride in pyridine at 50 °C to

Table 4. ^{1}H NMR Data[a] for Compounds **14** and **15**

	14	**15**
no.	δ_H	δ_H
1		
2	2.34 (2H, t, 7.4)	2.35 (2H, t, 7.5)
3	1.82 (2H, quint., 7.4)	1.81 (2H, quint., 7.5)
4	2.31 (2H, br dt, 7.3, 7.4)	2.30 (2H, m)
5	6.28 (1H, td, 7.3, 15.0)	6.18 (1H, td, 7.2, 15.2)
6	6.53 (1H, dd, 11.9, 15.0)	7.59 (1H, dd, 11.4, 15.2)
7	7.02 (1H, d, 11.9)	6.59 (1H, d, 11.4)
8		
9		
10		
11	7.60 (1H, s)	7.64 (1H, s)
12		
13	2.70 (1H, br dd, 8.3, 14.2)	2.65 (1H, br dd, 7.3, 14.1)
	3.00 (1H, br dd, 7.0, 14.2)	2.93 (1H, br dd, 7.7, 14.1)
14	5.15 (1H, br ddd, 7.0, 8.3, 10.7)	5.18 (1H, br ddd, 7.3, 7.7, 10.9)
15	5.52 (1H, td, 7.4, 10.7)	5.53 (1H, td, 7.4, 10.9)
16	1.95 (2H, m)	1.97 (2H, m)
17	1.31 (2H, m)	1.34 (2H, m)
18	1.27 (2H, m)	1.27 (2H, m)
19	1.30 (2H, m)	1.30 (2H, m)
20	0.88 (3H, t, 7.1)	0.88 (3H, t, 7.1)
OCH_3	3.67 (3H, s)	3.67 (3H, s)
CH_3CO	2.04 (3H, s)	2.03 (3H, s)

[a] ^{1}H (500 MHz). δ ppm in $CDCl_3$. J in Hz.

give an acetate, whose ^{1}H NMR and CD data were identical with those of **16**. Compound **16** was named 12-*O*-acetylchlorovulone II.

The ^{1}H NMR data (Table 5) of compound **17** ($C_{23}H_{31}O_5Cl$) were quite similar to those of **13** and **15** except for the upfield chemical shift of H-11 [7.43 (1H, s)], indicating that compound **17** was a chlorine-substituted congener of **13** or **15** at C-10. Compound **17** was named 12-*O*-acetylchlorovulone III.

The ^{1}H NMR data (Table 5) of chlorine-containing compound **18** ($C_{23}H_{31}O_5Cl$) were very similar to those of **16** and **17**, except for the chemical shift and coupling constant of H-5, -6, and -7, indicating that compound **18** was a geometrical isomer of **16** with 5*E* and 7*E* configurations or **17** with 5*E* and 7*Z* configurations. The coupling constant (J = 10.8 Hz) between H-5 and H-6 in **18** indicated 5*Z* configuration. The higher field chemical shift of H-6 [6.53 (1H, dd, J = 10.8, 12.6 Hz)] in **18** than that [7.59 (1H, dd, J = 11.3, 15.4 Hz)] in **17** demonstrated 7*E* configuration. These findings indicated that compound **18** was the corresponding acetate of chlorovulone I (**1**). Compound **18** was named 12-*O*-acetylchlorovulone I.

The absolute configuration of the chiral center at C-12 in **12**−**18** was elucidated on the basis of CD data. As mentioned above, chlorovulone II (**2**) possessing 12*R* configuration was converted to the corresponding acetate, whose CD data were very similar to those of natural 12-*O*-acetylchlorovulone II (**16**) (Table 6), indicating the same 12*R* configuration in **16**. The CD data of compounds **12**−**15**, **17**, and **18** were also very similar to those of the acetate of chlorovulone II, indicating 12*R* configuration for these compounds.

Structures of New Halogenated Prostanoid Epoxides 19−**23.** The HREIMS and ^{13}C NMR data of compound **19** {$[\alpha]_D$ −20.3° ($CHCl_3$)} indicated this molecule to possess an iodine-containing molecular formula of $C_{21}H_{29}O_5I$ [*m*/*z* 488.1061 $[M]^+$ (calcd for $C_{21}H_{29}O_5I$, 488.1060)]. A UV absorption at 300 (ϵ 21 000) nm indicated the presence of a conjugated dienone system. The IR spectrum showed absorptions due to hydroxyl (3441 cm^{-1}) and carbonyl (1729 cm^{-1}) groups. The ^{1}H and ^{13}C data (Table 7) indicated the presence of one carbomethoxy group [δ_H 3.67 (3H, s), δ_C 173.5 (C, C-1)], one conjugated ketone [δ_C 188.6 (C, C-9)], three double bonds, two oxygen-bearing carbons [δ_C 77.0 (C, C-12), 67.0 (CH, C-11)], eight methylenes, one quaternary carbon [δ_C 29.7 (C, C-10)], and one methyl group [δ_H 0.88 (3H, t, J = 7.0 Hz, H-20), δ_C 14.0 (CH_3, C-20)]. The NMR data of **19** were similar to those of iodovulone II (**9**), except for the signals due to the C-10 and -11 positions: the olefinic ^{1}H and ^{13}C signals of the C-10 [δ_C 106.2 (C)] and C-11 [δ_H 7.67 (1H, s), δ_C 165.1 (CH)] positions present in **9** disappeared, and the signals [δ_H 3.88 (1H, s), δ_C 29.7 (C), 67.0 (CH)] newly appeared instead. This finding clearly indicated the presence of an epoxide between C-10 and -11 in **19**. The unusual high-field chemical shift [29.7 (C)] of

Table 5. NMR Data[a] for Compounds **16**, **17**, and **18**

	16	**17**	**18**	
no.	δ_H	δ_H	δ_C	δ_H
1			173.5 (C)	
2	2.35 (2H, t, 7.4)	2.35 (2H, t, 7.5)	33.3 (CH_2)	2.35 (2H, t, 7.4)
3	1.82 (2H, quint., 7.4)	1.81 (2H, quint., 7.5)	24.4 (CH_2)	1.79 (2H, quint., 7.4)
4	2.31 (2H, br dt, 7.1, 7.4)	2.31 (2H, m)	37.3 (CH_2)	2.42 (2H, br td, 7.4, 7.7)
5	6.29 (1H, td, 7.1, 15.0)	6.18 (1H, td, 6.9, 15.4)	135.5 (CH)	6.09 (1H, td, 7.7, 10.8)
6	6.53 (1H, dd, 11.9, 15.0)	7.59 (1H, dd, 11.3, 15.4)	123.0 (CH)	6.53 (1H, dd, 10.8, 12.6)
7	7.02 (1H, d, 11.9)	6.61 (1H, d, 11.3)	144.5 (CH)	7.32 (1H, d, 12.6)
8			133.4 (C)	
9			186.5 (C)	
10			138.7 (CH)	
11	7.40 (1H, s)	7.43 (1H, s)	150.3 (CH)	7.39 (1H, s)
12			83.3 (C)	
13	2.70 (1H, br dd, 8.2, 14.1)	2.67 (1H, br dd, 7.5, 14.2)	35.5 (CH_2)	2.71 (1H, br dd, 8.1, 14.1)
	3.01 (1H, br dd, 7.9, 14.1)	2.94 (1H, br dd, 7.5, 14.2)		3.02 (1H, br dd, 7.5, 14.1)
14	5.15 (1H, br ddd, 7.9, 8.2, 10.6)	5.18 (1H, td, 7.5, 10.9)	120.7 (CH)	5.14 (1H, br ddd, 7.5, 8.1, 10.9)
15	5.53 (1H, td, 7.4, 10.6)	5.53 (1H, td, 7.4, 10.9)	127.3 (CH)	5.52 (1H, td, 7.3, 10.9)
16	1.95 (2H, m)	1.97 (2H, br td, 7.4, 7.5)	27.5 (CH_2)	1.94 (2H, br td, 7.2, 7.3)
17	1.32 (2H, m)	1.32 (2H, m)	29.0 (CH_2)	1.31 (2H, m)
18	1.26 (2H, m)	1.26 (2H, m)	31.5 (CH_2)	1.28 (2H, m)
19	1.30 (2H, m)	1.30 (2H, m)	22.5 (CH_2)	1.29 (2H, m)
20	0.88 (3H, t, 7.1)	0.88 (3H, t, 7.0)	14.0 (CH_3)	0.88 (3H, t, 7.1)
OCH_3	3.68 (3H, s)	3.67 (3H, s)	51.7 (CH_3)	3.69 (3H, s)
CH_3CO			169.3 (C)	
CH_3CO	2.03 (3H, s)	2.03 (3H, s)	21.3 (CH_2)	2.03 (3H, s)

[a] Assignments of the ^{13}C (125 MHz) and ^{1}H (500 MHz) signals were made on the basis of HMQC analysis. δ ppm in $CDCl_3$. J in Hz.

Table 6. CD Data[a] (nm ($\Delta\epsilon$)) for Compounds **12**−**18** and 12-*O*-Acetylchlorovulone II

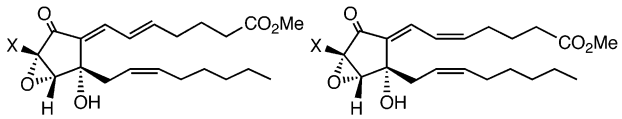
12	13	14	15	16	17	18	12-*O*-acetylchlorovulone II
355 (+1.6)	364 (+0.6)	354 (+1.1)	362 (+0.5)	358 (+1.2)	357 (+0.8)	358 (+1.5)	359 (+0.6)
326 (+1.6)	323 (+0.2,sh)	313 (+1.8)	322 (+0.6)	313 (+2.1)	322 (+1.0)	324 (+1.7)	313 (+0.8)
250 (−4.5)	253 (−1.1)	251 (−4.0)	254 (−1.4)	250 (−4.8)	250 (−2.5)	252 (−4.6)	249 (−2.0)
225 (+6.2)	227 (+2.9)	222 (+5.2)	221 (+3.5)	221 (+6.7)	220 (+4.8)	221 (+5.4)	220 (+3.2)

[a] CD spectra were measured in MeOH.

Table 7. NMR Data[a] for Compounds **19** and **20**

	19		**20**
no.	δ_C	δ_H	δ_H
1	173.5 (C)		
2	33.3 (CH_2)	2.34 (2H, t, 7.4)	2.37 (2H, t, 7.4)
3	23.8 (CH_2)	1.81 (2H, quint., 7.4)	1.79 (2H, quint., 7.4)
4	32.7 (CH_2)	2.30 (2H, dt, 7.1, 7.4)	2.39 (2H, m)
5	149.0 (CH)	6.23 (1H, td, 7.1, 15.1)	6.12 (1H, td, 8.5, 10.9)
6	125.8 (CH)	6.82 (1H, dd, 11.9, 15.1)	6.84 (1H, dd, 10.9, 12.6)
7	141.9 (CH)	7.20 (1H, d, 11.9)	7.53 (1H, d, 12.6)
8	130.4 (C)		
9	188.6 (C)		
10	29.7 (C)		
11	67.0 (CH)	3.88 (1H, s)	3.88 (1H, s)
12	77.0 (C)		
13	35.4 (CH_2)	2.69 (1H, br dd, 8.1, 14.1) 2.73 (1H, br dd, 7.6, 14.1)	2.72 (2H, d, 7.8)
14	120.5 (CH)	5.20 (1H, br ddd, 7.6, 8.1, 10.9)	5.21 (1H, td, 7.8, 10.9)
15	135.7 (CH)	5.60 (1H, br td, 7.4, 10.9)	5.60 (1H, td, 7.4, 10.9)
16	27.6 (CH_2)	2.00 (2H, m)	1.99 (2H, m)
17	29.0 (CH_2)	1.32 (2H, m)	1.35 (2H, m)
18	31.5 (CH_2)	1.26 (2H, m)	1.28 (2H, m)
19	22.5 (CH_2)	1.30 (2H, m)	1.32 (2H, m)
20	14.0 (CH_3)	0.88 (3H, t, 7.0)	0.89 (3H, t, 7.0)
OCH_3	51.6 (CH_3)	3.67 (3H, s)	3.68 (3H, s)

[a] Assignments of the ^{13}C (125 MHz) and ^1H (500 MHz) signals were made on the basis of HMQC analysis. δ ppm in $CDCl_3$. *J* in Hz.



19 X = I
21 X = Br
23 X = Cl

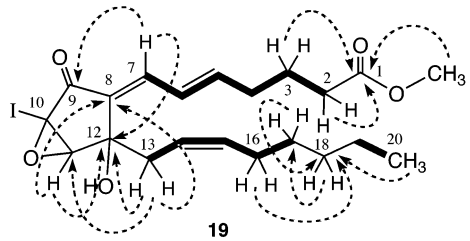
20 X = I
22 X = Br

Figure 5. Structures of new halogenated prostanoid epoxides.

the epoxidic quaternary carbon at C-10 is attributed to the iodine atom at this position.

The structure of **19** was confirmed by the analysis of 2D NMR spectra. Direct $^1H-^{13}C$ correlations were established from the HMQC spectrum, and then the $^1H-^1H$ COSY and HMBC spectra were measured. Sequences of the correlations from H-2 to H-7, from H-13 to H-17, and from H-19 to H-20 as shown by the bold lines in Figure 6 were elucidated on the basis of $^1H-^1H$ COSY analysis. HMBC correlations as shown by broken arrows in Figure 6 connected partial structures to give the gross structure for **19**.

The 5*E* and 14*Z* configurations of the two disubstituted double bonds were determined on the basis of the ^1H coupling constants between the olefinic protons: H-5 and -6 (J = 15.1 Hz), and H-14 and -15 (J = 10.9 Hz), respectively. The 7*E* configuration of the trisubstituted double bond was indicated by the chemical shift of H-6 [6.82 (1H, dd, J = 11.9, 15.1 Hz)] similar to that of **9** [6.76 (1H, dd, J = 11.8, 15.0 Hz)].



19

Figure 6. $^1H-^1H$ correlations (bold lines) and key HMBC correlations (broken arrows) of **19**.

Table 8. CD Data[a] (nm ($\Delta\epsilon$)) for Compounds **19**, **20**, **23**, and 10,11-Epoxychlorovulone I (**7**)

19	**20**	**23**	10,11-epoxychlorovulone I (**7**)
349 (−1.6)	353 (−0.9)	347 (−1.4)	349 (−0.9)
313 (+1.9)	297 (+1.3)	297 (+4.0)	298 (+1.8)
272 (+4.6)	283 (+1.8)	264 (+3.3)	261 (+1.8)
218 (−14.7)	219 (−5.6)	220 (−0.3)	216 (−2.3)

[a] CD spectra were measured in MeOH.

The relative configuration between the chlorine atom at C-10 and H-11 on the epoxide of the cyclopentanone ring should be *cis*. The NOE correlations between H-11 [3.88 (1H, s)] and H-13 [2.69 (1H, br dd, J = 8.1, 14,1 Hz*)*, 2.73 (1H, br dd, J = 7.6, 14,1 Hz)] observed in the NOESY spectrum demonstrated a *cis* relationship between H-11 and the ω side chain. The absolute stereochemistry was elucidated by comparing the CD data of **19** with those of 10,11-epoxychlorovulone I (**7**), whose absolute configurations (10*R*, 11*S*, 12*S*)[11] were previously established (Table 8). The CD data of **19** resembled those of 10,11-epoxychlorovulone I (**7**), indicating the same (10*R*, 11*S*, 12*S*) configurations in **19** as those of **7**. Compound **19** was named 10,11-epoxychlorovulone II.

The ^1H NMR data (Table 7) of compound **20** ($C_{21}H_{29}O_5I$) were quite similar to those of **19**, except for the signals due to H-5, -6, and -7, indicating that compound **20** was a geometrical isomer with 5*E* and 7*E* configurations. The absolute configuration, the same as that of **19**, was deduced from the CD data (Table 8), which exhibited a Cotton effect similar to that for **19**. Compound **20** was named 10,11-epoxyiodovulone I.

The ^1H NMR data (Table 9) of bromine-containing compound **21** ($C_{21}H_{29}O_5Br$) were quite similar to those of **19**, except for the slight downfield chemical shift of H-11, indicating that compound **21** was a bromine-substituted congener of **19** at C-10. Although the CD spectrum of **21** was not observed, the absolute configuration of **21** may be the same as that of the other halogenated prostanoids coexisting in *C. viridis*. Compound **21** was named 10,11-epoxybromovulone II.

The ^1H NMR data (Table 9) of compound **22** ($C_{21}H_{29}O_5Br$) were very similar to those of **21**, except for the signals due to H-5, -6, and -7, indicating that **22** was a geometrical isomer with 5*Z* and 7*E* configurations. Although the CD spectrum of **22** was not observed, the absolute configuration of **22** may be the same as that of the other halogenated prostanoids coexisting in *C. viridis*. Compound **22** was named 10,11-epoxybromovulone I.

Table 9. ^{1}H NMR Data[a] for Compounds **21**, **22**, and **23**

no.	**21** δ_H	**22** δ_H	**23** δ_H
1			
2	2.33 (2H, t, 7.4)	2.34 (2H, t, 7.4)	2.34 (2H, t, 7.4)
3	1.81 (2H, quint., 7.4)	1.79 (2H, quint., 7.4)	1.81 (2H, quint., 7.4)
4	2.30 (2H, dt, 6.9, 7.4)	2.40 (2H, m)	2.29 (2H, m)
5	6.27 (1H, td, 6.9, 15.1)	6.14 (1H, td, 7.4, 10.5)	6.28 (1H, td, 7.1, 15.1)
6	6.82 (1H, dd, 11.9, 15.1)	6.83 (1H, dd, 10.5, 12.6)	6.82 (1H, dd, 11.9, 15.1)
7	7.21 (1H, d, 11.9)	7.54 (1H, d, 12.6)	7.21 (1H, d, 11.9)
8			
9			
10			
11	3.93 (1H, s)	3.94 (1H, s)	3.95 (1H, s)
12			
13	2.71 (2H, d, 7.8)	2.72 (2H, d, 7.6)	2.71 (2H, d, 7.8)
14	5.23 (1H, td, 7.8, 10.9)	5.22 (1H, td, 7.6, 10.9)	5.24 (1H, td, 7.8, 11.0)
15	5.61 (1H, td, 7.3, 10.9)	5.61 (1H, td, 7.3, 10.9)	5.61 (1H, td, 7.4, 11.0)
16	1.99 (2H, m)	2.00 (2H, m)	2.00 (2H, m)
17	1.33 (2H, m)	1.33 (2H, m)	1.36 (2H, m)
18	1.27 (2H, m)	1.28 (2H, m)	1.28 (2H, m)
19	1.31 (2H, m)	1.32 (2H, m)	1.32 (2H, m)
20	0.88 (3H, t, 7.0)	0.89 (3H, t, 7.0)	0.88 (3H, t, 7.0)
OCH_3	3.67 (3H, s)	3.68 (3H, s)	3.67 (3H, s)

[a] δ ppm in $CDCl_3$. *J* in Hz.

The ^{1}H NMR data (Table 9) of chlorine-containing compound **23** {$[\alpha]_D$ −21.5° ($CHCl_3$), $C_{21}H_{29}O_5Cl$} were quite similar to those of **19** and **21**, indicating that compound **23** was a chlorine-substituted congener of **19** or **21** at C-10. The NOE correlations between H-11 [3.95 (1H, s)] and H-13 [2.71 (2H, d, J = 7.8 Hz)] observed in the NOESY spectrum demonstrated a *cis* relationship between H-11 and the ω side chain. The absolute configuration, the same as that of **19** and **21**, was deduced from the CD data (Table 8). Compound **23** was named 10,11-epoxychlorovulone II.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP-370 automatic polarimeter. UV spectra were recorded with a JASCO V-520 spectrophotometer. IR spectra were recorded with a Perkin-Elmer FT-IR 1600 spectrophotometer. MS spectra were taken with a Micromass Auto Spec spectrometer. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, with a Bruker DRX-500 using $CDCl_3$ as a solvent. Proton chemical shifts were referenced to the residual $CHCl_3$ signal at δ 7.26 ppm (s, singlet; d, doublet; t, triplet; q, quartet; quint., quintet; m, multiplet; br, broad). Carbon chemical shifts were referenced to the central peak of $CDCl_3$ at δ 77.0 ppm. Two-dimensional (2D) NMR spectra (^{1}H−^{1}H COSY, HMQC, HMBC, NOESY) spectra were measured by a Bruker DRX-500 using standard Bruker pulse sequences. Liquid column chromatography (LCC) was carried out on a Merck Si gel 60 (particle size; 0.063−0.200 mm). Medium-pressure liquid chromatography (MPLC) was carried out with a Kusano CIG prepack column CPS-HS-221-05 (Si gel). HPLC was conducted with a YMC-Pack SIL-06 column (silica gel, SH-043-5-06, normal-phase) and a YMC-Pack ODS-AM column (ODS silica gel, SH-343-5, reversed-phase). The HPLC system was equipped with a recycle loop, which was used depending on need.

Animal Material. The soft coral, *Clavularia viridis* Quoy and Gaimard (order Stolonifera, family Clavularidae), was collected from a coral reef off Ishigaki Island, Okinawa Prefecture, Japan, in March 1988, at a depth of 1−2 m. The freeze-dried specimens were kept at −50 °C. A voucher specimen is on deposit at Tokyo University of Pharmacy and Life Science, Tokyo, Japan.

Extraction and Isolation. Freeze-dried specimens (470 g) were extracted successively with hexane (2 L × 2), AcOEt (2 L × 2), and MeOH (2 L × 2). After filtration, each extract was concentrated under reduced pressure to give hexane (14.5 g), AcOEt (3.7 g), and MeOH (33.4 g) extracts. A part of the hexane extract (6.83 g) was chromatographed on a silica gel column eluted with hexane (1 L), hexane−EtOAc (3:1, 850 mL and 1:1, 700 mL), AcOEt (700 mL), and MeOH (700 mL), in turn, to give five fractions.

The third fraction [0.77 g, eluted with hexane−AcOEt (1:1)] containing mainly clavulones I, II, and III was separated by reversed-phase HPLC [eluted with CH_3CN-H_2O (8:2)] to give clavulone II (281 mg) and a mixture of clavulones I and III (325 mg).

The second fraction [4.54 g, eluted with hexane−AcOEt (3:1)] was separated by normal-phase LCC eluted with hexane−AcOEt (9:1, 8:2, and 7:3) to give seven fractions (fractions A−G). Fraction D (517 mg) was subjected to repeated normal-phase HPLC [hexane−ether (7:3), hexane−EtOAc (4:1)] and reversed-phase recycling HPLC [CH_3CN-H_2O (4:1)] to give compounds **12** (0.9 mg), **13** (0.6 mg), **14** (0.4 mg), **15** (0.2 mg), **16** (0.3 mg), **17** (0.4 mg), and **18** (0.3 mg). Similar separation and purification of fraction E (384 mg) using LCC [hexane−EtOAc (8:2)], normal-phase MPLC [hexane−EtOAc (4:1)], and repeated reversed-phase recycling HPLC [CH_3CN-H_2O (7:3)] gave compounds **9** (1.2 mg), **10** (0.3 mg), **11** (0.1 mg), **19** (0.8 mg), **20** (0.5 mg), **21** (0.1 mg), **22** (0.1 mg), and **23** (0.3 mg), along with chlorovulone I (**1**, 1.0 mg),[8,9] bromovulone I (**5**, 0.6 mg),[10] iodovulone I (**6**, 1.2 mg),[10] and 10,11-epoxychlorovulone I (**7**, 0.6 mg).[5] From fraction F (636 mg), 7-acetoxy-7,8-dihydroiodovulone I (**8**) and its congeners were isolated.[12]

Iodovulone II (9): colorless oil; $[\alpha]_D^{25}$ +23.7° (*c* 0.07, $CHCl_3$); CD, see Table 2; IR ν_{max} (cm^{-1}) 3459, 1738, 1704, 1633, 1435, 1377; UV (MeOH) λ_{max} nm (ϵ), 241 (16 000), 311 (14 000); ^{1}H and ^{13}C NMR, see Table 1; EIMS (*m*/*z*) $[M - H_2O]^+$ 454; HREIMS (*m*/*z*) 454.1001 $[M - H_2O]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005).

Iodovulone III (10): colorless oil; $[\alpha]_D^{25}$ +25.0° (*c* 0.02, $CHCl_3$); CD, see Table 2; IR ν_{max} (cm^{-1}) 3440, 1737, 1702, 1632, 1461, 1376; UV (MeOH) λ_{max} nm (ϵ) 239 (14 000), 317 (11 000); ^{1}H NMR, see Table 1; EIMS (*m*/*z*) $[M]^+$ 472; HREIMS (*m*/*z*) 454.1007 $[M - H_2O]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005).

Iodovulone IV (11): colorless oil; CD, see Table 2; IR ν_{max} (cm^{-1}) 3443, 1738, 1705, 1633, 1462, 1377; UV (MeOH) λ_{max} nm (ϵ) 237 (5400), 312 (6300); ^{1}H NMR, see Table 1; EIMS (*m*/*z*) $[M]^+$ 472; HREIMS (*m*/*z*) 454.1016 $[M - H_2O]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005).

12-*O*-Acetyliodovulone II (12): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1707, 1637, 1435, 1367, 1226, 1020; UV (MeOH) λ_{max} nm (ϵ), 238 (14 000), 307 (13 000); ^{1}H and ^{13}C NMR, see Table 3; EIMS (*m*/*z*) $[M - CH_3CO_2H]^+$ 454; HREIMS (*m*/*z*) 454.1023 $[M - CH_3CO_2H]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005).

12-*O*-Acetyliodovulone III (13): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1700, 1634, 1435, 1368, 1227, 1021; UV (MeOH) λ_{max} nm (ϵ) 225 (15 000), 245 (8600), 312 (6500); ^{1}H NMR, see Table 3; EIMS (*m*/*z*) $[M - CH_3CO_2H]^+$ 454; HREIMS (*m*/*z*) 454.1029 $[M - CH_3CO_2H]^+$ (calcd for $C_{21}H_{27}O_3I$, 454.1005).

12-*O*-Acetylbromovulone II (14): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1714, 1637, 1456, 1367, 1225, 1020; UV (MeOH) λ_{max} nm (ϵ) 230 (11 000), 308 (11 000); ^{1}H NMR, see Table 4; EIMS (*m*/*z*) $[M - CH_3CO_2H]^+$ 406, 408 (1:1); HREIMS (*m*/*z*) 406.1136 $[M - CH_3CO_2H]^+$ (calcd for $C_{21}H_{27}O_3{}^{79}Br$, 406.1144).

12-*O*-Acetylbromovulone III (15): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1716, 1634, 1455, 1368, 1227, 1020; UV (MeOH) λ_{max} nm (ϵ) 219 (8600), 237 (sh, 7400), 312 (6700); ^{1}H NMR, see Table 4; EIMS (*m*/*z*) $[M - CH_3CO_2H]^+$ 406, 408 (1:1); HREIMS (*m*/*z*) 406.1137 $[M - CH_3CO_2H]^+$ (calcd for $C_{21}H_{27}O_3{}^{79}Br$, 406.1144).

12-*O*-Acetylchlorovulone II (16): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1731, 1714, 1640, 1454, 1368,

1226, 1021; UV (MeOH) λ_{max} nm (ϵ) 233 (11 000), 307 (12 000); ^{1}H NMR, see Table 5; EIMS (*m*/*z*) [M − CH_3CO_2H]$^+$ 362, 364 (3:1); HREIMS (*m*/*z*) 362.1634 [M − CH_3CO_2H]$^+$ (calcd for $C_{21}H_{27}O_3{}^{35}Cl$, 362.1649).

12-*O*-Acetylchlorovulone III (17): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1737, 1731, 1713, 1633, 1437, 1368, 1216, 1019; UV (MeOH) λ_{max} nm (ϵ) 231 (9800), 309 (8500); ^{1}H NMR, see Table 5; EIMS (*m*/*z*) [M − CH_3CO_2H]$^+$ 362, 364 (3:1); HREIMS (*m*/*z*) 362.1634 [M − CH_3CO_2H]$^+$ (calcd for $C_{21}H_{27}O_3{}^{35}Cl$, 362.1649).

12-*O*-Acetylchlorovulone I (18): colorless oil; CD, see Table 6; IR ν_{max} (cm^{-1}) 1738, 1731, 1714, 1633, 1434, 1368, 1226, 1021; UV (MeOH) λ_{max} nm (ϵ) 236 (11 000), 309 (13 000); ^{1}H and ^{13}C NMR, see Table 5; EIMS (*m*/*z*) [M]$^+$ 422, 424 (3:1); HREIMS (*m*/*z*) 362.1666 [M − CH_3CO_2H]$^+$ (calcd for $C_{21}H_{27}O_3{}^{35}Cl$, 362.1649).

10,11-Epoxyiodovulone II (19): colorless oil; $[\alpha]_D{}^{25}$ −20.3° (*c* 0.05, $CHCl_3$); CD, see Table 8; IR ν_{max} (cm^{-1}) 3441, 1729, 1628, 1454, 1375, 1206; UV (MeOH) λ_{max} nm (ϵ) 300 (21 000); ^{1}H and ^{13}C NMR, see Table 7; EIMS (*m*/*z*) [M]$^+$ 488; HREIMS (*m*/*z*) 488.1061 [M]$^+$ (calcd for $C_{21}H_{29}O_5I$, 488.1060).

10,11-Epoxyiodovulone I (20): colorless oil; $[\alpha]_D{}^{25}$ −97.3° (*c* 0.04, $CHCl_3$); CD, see Table 8; IR ν_{max} (cm^{-1}) 3441, 1729, 1622, 1454, 1376, 1209; UV (MeOH) λ_{max} nm (ϵ) 300 (17 000); ^{1}H NMR, see Table 7; EIMS (*m*/*z*) [M]$^+$ 488.

10,11-Epoxybromovulone II (21): colorless oil; $[\alpha]_D{}^{25}$ −57.3° (*c* 0.01, $CHCl_3$); IR ν_{max} (cm^{-1}) 3440, 1731, 1631, 1462, 1377, 1237; UV (MeOH) λ_{max} nm (ϵ) 298 (12 000); ^{1}H NMR, see Table 9; EIMS (*m*/*z*) [M]$^+$ 440, 442 (1:1); HREIMS (*m*/*z*) 440.1195 [M]$^+$ (calcd for $C_{21}H_{29}O_5{}^{79}Br$, 440.1198).

10,11-Epoxybromovulone I (22): colorless oil; $[\alpha]_D{}^{25}$ −18.5° (*c* 0.01, $CHCl_3$); IR ν_{max} (cm^{-1}) 3440, 1731, 1632, 1462, 1378, 1215; UV (MeOH) λ_{max} nm (ϵ) 299 (9700); ^{1}H NMR see Table 9; EIMS (*m*/*z*) [M]$^+$ 440, 442 (1:1).

10,11-Epoxychlorovulone II (23): colorless oil; $[\alpha]_D{}^{25}$ −21.5° (*c* 0.02, $CHCl_3$); CD, see Table 8; IR ν_{max} (cm^{-1}) 3440, 1731, 1631, 1455, 1377, 1239; UV (MeOH) λ_{max} nm (ϵ) 298 (18 000); ^{1}H NMR, see Table 9; EIMS (*m*/*z*) [M]$^+$ 396, 398 (3:1); HREIMS (*m*/*z*) 396.1705 [M]$^+$ (calcd for $C_{21}H_{29}O_5{}^{35}Cl$, 396.1704).

Acetylation of Chlorovulone II (2). To a solution of chlorovulone II (**2**, 1.4 mg) in dry pyridine (0.8 mL) was added acetic anhydride (0.4 mL), and the mixuture was stirred at 50 °C for 4 h. The mixture was concentrated under reduced pressure to yield a residue, which was dissolved in EtOAc, and the solution was passed through a silica gel short column eluted with EtOAc. The crude product was purified by reversed-phase HPLC [eluent: CH_3CN-H_2O (4:1)] to give 12-*O*-acetylchlorovulone II (**16**, 0.2 mg), whose ^{1}H NMR and CD spectra were identical with those of natural **16**.

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Supporting Information Available: CD spectra of compounds **9**, **10**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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