FOUR NEW PROSTANOIDS: CLAVIRIDENONE-A, -B, -C, AND -D FROM THE OKINAWAN SOFT CORAL <u>CLAVULARIA</u> VIRIDIS

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Summary: The structures of four new prostanoids named claviridenone-a, -b, -c, and -d, which were isolated from the Okinawan soft coral *Clavularia viridis*, were elucidated as 1, 2, 3, and 4, respectively.

During studies on marine natural products,¹⁾ we isolated four new prostanoids named claviridenone-a (1), -b (2), -c (3), and -d (4) (in the order of increasing polarity) from the Okinawan soft coral *Clavularia viridis* Quoy and Gaimard. This paper describes the chemical characterization of these new prostanoids from the physicochemical evidence.

The acetone extractive of the fresh soft coral, collected in July at Kohamajima, Okinawa Prefecture, was partitioned by an AcOEt-water solvent system. Purification of the AcOEt-soluble portion by repeated SiO₂ column chromatography and HPLC (µPORASIL) provided claviridenone-a (1), -b (2), -c (3), and -d (4) in 0.3, 3, 5, and 3% yield as slightly yellowish oil, respectively.

Claviridenone-b (2), $C_{25}H_{34}O_7$, $^{(\alpha)}_D$ [α]_D +26.7° (CHCl₃), showed the ester (1730, 1235 cm⁻¹) and the conjugated enone (1693, 1634 cm⁻¹) absorption bands but lacked the hydroxyl absorption band in its IR spectrum (CHCl₃). The UV spectrum (MeOH) of 2 exhibited presence of a cross-conjugated dienone chromophore (λ_{max} 230 nm, ϵ =13300; 296 nm, ϵ =13100) in its molecule, while the ¹³C NMR spectrum (50 MHz) demonstrated presence of one ketone function, two acetoxyl groups, one methoxy-carbonyl group, four olefinic moieties, seven methylene groups, and one methyl group (Table II). The ¹H NMR decoupling experiments (500 MHz) of 2 in detail suggested presence of following five partial structures in a monocarbocyclic acetogenin framework: i)C=CH-CH=CH-CH(OAc)-CH₂-COOCH₁3, ii -CO-CH=CH-CM

iii \square -CH₂-CH=CH-CH₂-(CH₂)_n-, iv -(CH₂)_m-CH₃, v -C-OAc (\square denoted a quaternary carbon, n + m = 3)

NaBH₄ reduction of 2 (at 0°C in MeOH-ether) furnished the tetrahydro derivative (5), $C_{25}H_{38}O_7$, IR (CHCl₃, cm⁻¹): 3470 (OH), 1725 (ester), UV (MeOH, λ_{max}): 247 nm, ϵ =22500 (diene). The ¹H NMR (200 MHz) of 5 indicated reduction of the ketone function in 2. It showed loss of signals due to the partial structure <u>ii</u>



but showed signals attributable to a newly formed secondary hydroxyl moiety (δ 4.12, br.d, J=9 Hz for 9-OH and δ 4.74, br.d.d, J=ca. 4.5, 9 Hz for 9-H). In the NOE experiments of 5, 20% increase of the 6-H signal (δ 6.65, d.d, J=15.6, 11.2 Hz) was observed upon irradiation at the 9-H signal, while 13% increase of the 9-H signal was observed upon irradiation at the 6-H signal. Thus, the partial structure <u>i</u> was shown to adjoin the ketone function in <u>ii</u>.³⁾ Based on these evidence, the prostanoid carbon skeleton of claviridenone-b was suggested.

Claviridenone-a (1), $C_{25}H_{34}O_7$, $[\alpha]_D - 82.2^{\circ}$ (CHCl₃); UV (MeOH, λ_{max} , nm): 230 (ϵ =12000), 294 (14000); IR (CHCl₃, cm⁻¹): 1732, 1690, 1632, 1220, claviridenone-c (3), $C_{25}H_{34}O_7$, $[\alpha]_D + 8.4^{\circ}$; UV: 230 (11700), 293 (15000); IR: 1735, 1700, 1637, 1230, and claviridenone-d (4), $C_{25}H_{34}O_7$, $[\alpha]_D - 24.9^{\circ}$; UV: 231 (10300), 294 (12700); IR: 1733, 1700, 1635, 1220, gave the ¹H NMR and ¹³C NMR signals as assigned in Table I and Table II.⁴

In the ¹H NMR and ¹³C NMR spectra of <u>1</u>, <u>2</u>, <u>3</u>, and <u>4</u>, obserbed signals due to the ω -chain and the five-membered ring almost agree, respectively. For example, in the case of <u>2</u>, signals assignable to 13-H₂ were observed at δ 2.68, 2.82 (AB in ABX, J_{AB}=14.4 Hz, J_{AX}=7.0 Hz, J_{BX}=7.5 Hz) and 14-H at δ 5.21 (X in ABX, d.tlike, J=11.0, *ca*. 7.3⁵) and 15-H at δ 5.52 (d.t, J=11.0, 7.5 Hz). Furthermore, comparison of those ¹³C NMR spectra with that of *cis*-2-octene demonstrated that 1, <u>2</u>, <u>3</u>, and <u>4</u> were prostanoids having an ω -chain of a *cis*-14-ene moiety.

When a benzene solution of either 1, 2, 3, or 4 was irradiated with fluorescent lamps (15 w x 2) for 40 hr, an identical mixture of 1, 2, 3, and 4 in *ca*. 1:6:12:2 ratio was provided. So that, these four prostanoids were considered to be geometric isomers of the double bonds in the α -chain. The 5,7-diene geometries of four compounds were determined by the ¹H NMR examinations in detail as shown in Table I. Thus, the 5-ene moieties in 1 and 4 were assigned Z while

	Ļ	2	z	4 ⁶⁾
2-H_	2.37(t,J=7.3)	2.39(t,J=7.8)	2.38(t,J=7.6)	2.38(t,J=7.4)
3-H2	ca.2.02(m)	2.03(m)	ca.2.03(m)	ca.1.95(m)
4 - ₩ [∠]	5.83(dt,J=8.5,7.5)	5.44(dt,J=6.1,5.5)	5.42(dt,J=7.0,7.0)	5.85(m)
5-H	5.76(dd,J=10.8,8.5)	6.02(dd,J=15.4,6.1)	6.02(dd,J=14.2,7.0)	5.85(m)
6-H	7.62(dd,J=10.8,12.2)	7.74(dd,J=15.4,11.2)	6.74(dd,J=14.2,11.7)	6.59(dd,J=10.0,12.7)
7-н	7.02(d,J=12.2)	6.51(d,J=11.2)	6.87(d,J=11.7)	7.27(d,J=12.7)
10-H	6.36(d,J=6.2)	6.36(d,J=6.4)	6.41(d,J=6.3)	6.43(d,J=6.4)
11-H	7.50(d,J=6.2)	7.51(d,J=6.4)	7.47(d,J=6.3)	7.48(d,J=6.4)
13-H ₂	2.64,2.84(AB in ABX,	2.68,2.82(AB in ABX,	2.66,2.89(AB in ABX,	2.66,2.96(AB in ABX,
-	J _{AB} =14.4,J _{AX} =7.4,	J _{AB} =14.4,J _{AX} =7.0,	J _{AB} =14.4,J _{AX} =8.3,	J _{AB} =14.4,J _{AX} =7.8,
	$J_{BX} = 7.3)$	J =7.5) BX	$J_{BX} = 6.8$	$J_{BX}^{T}=7.0$
14-H	5.27(X in ABX,dt-	5.21(X in ABX,dt-	5.20(X in ABX,dt-	5.20(X in ABX,dt-
	like)	like,J=11.0,ca.7.3)	like)	like)
15-н	5.54(m)	5.52(dt,J=11.0,7.5)	5.52(m)	5.52(m)
16-H ₂	ca.1.95(m)	1.96(dt,J=7.5,7.5)	1.96(m)	1.95(m)
17~Í9	1.23~1.32(6H,m)	1.23~1.32(6H,m)	1.23~1.32(6H,m)	1.23~1.32(6H,m)
20-H ₂	0.88(t,J=6.8)	0.88(t,J=6.8)	0.88(t,J=6.8)	0.88(t,J=6.8)
COOCH	3.68(s)	3.68(s)	3.68(s)	3.70(s)
0Ac J	2.03(s),2.07(s)	2.02(s),2.10(s)	2.06(s),2.07(s)	2.03,2.05(s)

Table I. ¹H NMR Data for 1, 2, 3, and 4^{a}

a) 2 was measured at 500 MHz in CDCl₃ and 1, 3, and 4 were at 200 MHz in CDCl₃.

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carbon	1	2	3	4~	5
1	172.9(s)	173.4(s)	173.2(s)	173.2(s)	173.7(s)
2	$29.1(t)^{d}$	$29.1(t)^{d}$	$29.1(t)^{d}$	$29.1(t)^{d}$	29.1(t)d
3	$29.6(t)^{d}$	$29.4(t)^{d}$	$29.3(t)^{d}$	$30.0(t)^{d}$	$29.4(t)^{d}$
4	68.2(d)	72.7(d)	73.0(d)	69.6(d)	73.2(d)
5	136.6(d) ^{e)}	141.3(d)	141.5(d)	139.0(d)	132.2(d)
6	127.9(d)	133.8(d)	129.6(d)	124.8(d)e	125.5(d)
7	136.5(d) ^{e)}	137.0(d)	137.3(d)	$135.4(d)^{f}$	129.1(d)
8	137.l(s)	136.0(s)	135.3(s)	137.9(s)	149.5(s)
9	194.2(s)	194.3(s)	193.6(s)	193.5(s)	70.9(d)
10	126.1(d)	126.8(d)	127.2(d)	124.6(d)e)	31.3(t)
11	156.7(d)	156.3(d)	158.3(d)	158.1(d)	37.8(t)
12	85.0(s)	85.5(s)	85.4(s)	85.4(s)	88.0(s)
13	36.1(t)	35.7(t)	36.1(t)	36.0(t)	32.8(t)
14	121.5(d)	121.7(d)	121.4(d)	121.4(d)	122.8(d)
15	134.7(d)	135.1(d)	135.3(d)	$135.3(d)^{\pm}$	133.6(d)
16	27.4(t)	27.5(t)	27.5(t)	27.5(t)	27.4(t)
17	29.8(t) ^{d)}	$29.9(t)^{d}$	29.7(t) ^{d)}	$30.0(t)^{d}$	$29.8(t)^{d}$
18	31.5(t)	31.6(t)	31.5(t)	31.5(t)	31.4(t)
19	22.5(t)	22.6(t)	22.6(t)	22.5(t)	22.5(t)
20	14.0(q)	14.0(q)	14.0(q)	14.0(q)	14.0(q)
COOCH 3	51.6(q)	51.8(q)	51.8(q)	51.8(q)	51.5(q)
<u>م</u> ا	170.1(s)	170.3(s)	170.2(s)	170.1(s)	171.0(s)
CH_C-	169.8(s)	169.9(s)	169.7(s)	169.4(s)	170.3(s)
³ [[,]	21.5(q)	21.7(q)	21.2(q)	21.2(q)	22.2(q)
0 × 2 (21.0(q)	21.0(q)	21.0(q)	20.9(q)	21.1(q)

¹³C NMR Data (50 MHz) for 1, 2, 3, 4, and 5^b, c) Table II.

b) Abbreviations given in parentheses denote the signal patterns observed in off-resonance experiments: d=doublet, q=quartet, s=singlet, t=triplet.
c) d~f The assignments for these signals within the same vertical column

may be interchanged.

those in 2 and 3 were assigned E, since the $J_{5,6}$ values for 1, 2, 3, and 4 were respectively 10.8, 15.4, 14.2, and 10.0 Hz. In addition, signals due to 6-H in 1 and 2 were observed at δ 7.62 (d.d, J=10.8, 12.2 Hz) and δ 7.74 (d.d, J=15.4, 11.2 Hz), while same signals in 3 and 4 were observed at δ 6.74 (d.d, J=14.2, 11.7 Hz) and δ 6.59 (d.d, J=10.0, 12.7 Hz). These findings indicated that 6-H in 1 and 2 was affected by anisotropic effect of the 9-CO moiety. Consequently, the 7-ene moieties in 1 and 2 were assigned Z while those in 3 and 4 were E.⁷⁾

Based on the accumulated evidence described above, the structures of claviridenone-a, -b, -c, and -d were formulated as 1, 2, 3, and 4, respectively. The absolute configurations at C-4 and C-12 of these prostanoids are under study.

Several types of prostanoids were hitherto shown to occur in various marine life such as gorgonian,^{8a)} red alga,^{8b)} and soft coral.^{8c)} The present prostanoids, claviridenone-a (1), -b (2), -c (3), and -d (4), are characteristic of possession of a cross-conjugated chromophore and their biogenesis and biological activity will be of interest.

References and Notes

- 1)For examples: a) M. Kobayashi, T. Yasuzawa, Y. Kyogoku, M. Kido, and I. Kitagawa, Chem. Pharm. Bull.(Tokyo), in the press; b) I. Kitagawa, M. Kobayashi, and Y. Kyogoku, Chem. Pharm. Bull. (Tokyo), <u>30</u>, 2045 (1982).
- 2) The molecular compositions of compounds with the chemical formulae were determined by high resolution mass spectrometry.
- 3) The tetrahydro derivative (6), $C_{25}H_{38}O_7$, UV (MeOH): 250 nm (ε =22900); IR (CHCl₃): 3490, 1725 (br) cm⁻¹, of claviridenone-c (3) was obtained by similar NaBH₄ reduction. In the NOE experiments of 6, 6% increase of the 7-H signal (δ 6.28, d, J=11.7 Hz) was observed upon irradiation at the 9-H signal (δ 4.37, br.s).
- 4) a) G. C. Levy, "Topics in Carbon-13 NMR Spectroscopy", Vol. 2, p. 82, New York (1976); b) G. Lukacs, F. Piriou, S. D. Gero, and D. A. Van Dorp, Tetrahedron Lett., 1973, 515; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 1973, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 1973, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and J. Fried, Proc. Nat. Acad. Sci. USA, 2015, 2015; c) G. F. Cooper and 2015; c) G. F. Cooper Acad. Sci. Proc. Proc 70, 1579 (1973).
- 70, 1579 (1973). 5) The resolution was yet inadequate for taking the J_{AX} and J_{BX} values from the X part signal, so that the X part was expressed as a doublet of t-like signal. 6) ¹H NMR data for 4 (200 MHz, in d₆-benzene, δ): 2.03 (t, J=7.3 Hz, 2-H₂), 1.73 (2H, m, 3-H₂), 5.77 (d.t-like, J=10.2, ca. 7 Hz, 4-H), 5.61 (d.d, J=10.2, 10.2 Hz, 5-H), 6.59 (d.d, J=10.2, 10.2 Hz, 6-H), 7.69 (d, J=10.2 Hz, 7-H), 6.22 (d, J=6.4 Hz, 10-H), 7.12 (d, J=6.4 Hz, 11-H), 2.60, 2.88 (AB in ABX, JAB=14.2, JAX=7.8, JBX=7.3 Hz, 13-H₂), 5.19 (X in ABX, d.t-like, J=10.2, ca. 7.5 Hz, 5) 14-H), 5.40 (m, 15-H), ca. 1.86 (m, 16-H₂), 1.21 (6H, br.s, 17~19-H₂), 0.88 (t, J=6.8 Hz, 20-H₃), 1.65, 1.66 (3H each, s, OAc x 2), 3.39 (3H, s, COOCH₃). 7) The signal due to 7-H in 2 was observed at δ 6.51 (d, J=11.2 Hz) while 7-H signals in 1, 3, and 4 were observed at δ 7.02 (d, J=12.2 Hz), δ 6.87 (d, J=11.7 Hz), and δ 7.27 (d, J=12.7 Hz). These facts suggested occurrence of anisotropic effect by the 9-CO group in 3 and 4 and presumably by the 4-OAc group in 1 and 4.
- group in 1 and 4. 8) a) W. P. Schneider, R. D. Hamilton, and L. E. Rhuland, J. Am. Chem. Soc., <u>96</u>, 2122 (1972); b) R. P. Gregson, J. F. Marwood, and R. J. Quinn, Tetrahedron Lett., <u>1979</u>, 4505; c) S. Carmely, Y. Kashman, Y. Loya, and Y. Benayahu, Tetrahedron Lett., <u>21</u>, 875 (1980).

(Received in Japan 31 August 1982)