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A NOVEL NORDITERPENOID FROM THE OKINAWAN SOFT CORAL *SINULARIA* SP.

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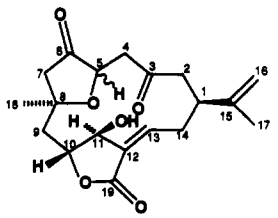
ABSTRACT.—A novel norditerpenoid, sinuleptolide [(1*S*,5*S*,8*S*,10*R*,11*S*)-11-hydroxy-1-isopropenyl-8-methyl-3,6-dioxo-5,8-epoxycyclotetradec-12-ene-10,12-carbolactone] [**1**], was isolated from the Okinawan soft coral *Sinularia* sp. The structure of **1** was established mainly on the basis of nmr spectroscopic data.

Soft corals have been recognized as a rich source of diterpenoids with the cembrane skeleton (1), but only two papers have been published on norcembranolides, lacking the methyl group at C-4 (2,3). In 1978 Bowden *et al.* (2) reported the structure of norcembrenolide [**2**] for the first time. Furthermore, in 1985 Sato *et al.* (3) reported the structures of four related compounds of **2**. In continuation of our survey of marine organisms for pharmacologically active substances, we have isolated a novel norditerpenoid from *Sinularia* sp. collected from Okinawa Island. We now report the isolation and structure elucidation of this new compound, designated sinuleptolide [**1**].

The MeOH-CH_2Cl_2 (1:1) extract of the soft coral was partitioned between EtOAc and H_2O. The EtOAc-soluble portion was repeatedly subjected to Si gel medium-pressure cc, followed by Sephadex LH-20 cc and reversed-phase hplc, to yield sinuleptolide [**1**] together with norcembrenolide [**2**].

The molecular formula $C_{19}H_{24}O_6$ of **1** determined by hreims was the same as that of **2**. The ^{1}H- and ^{13}C-nmr spectral data of **1** were very similar to those of **2** (Table 1), suggesting that **1** might be a stereoisomer of **2**. This assumption was confirmed as follows. The ^{1}H-^{1}H COSY and ^{13}C-^{1}H COSY experiments established the subunits a to c [C-2–C-13 (a), C-4–C-5 (b), and C-9–C-11 (c)] (Figure 1, bold lines). These subunits could be connected on the basis of the HMBC correlations (Figure 1, arrows), leading to a planar structure **1** for sinuleptolide.

The relative stereochemistry of sinuleptolide [**1**] was established by difference nOe experiments (Figure 2). The *E* configuration of the double bond was assigned on the basis of an nOe between H-13 and H-11. The nOe's between H-17/H-13 and H-17/H-14β established the C-1 *S* configuration. An nOe was detected between H-11/H-5, confirming the C-5 *S* and C-11 *S* configuration. Furthermore, nOe's were observed between H-18/H-7α and H-18/H-9α, indicating the C-8 *S* configuration. The remaining chiral center C-10 must have the *R* configuration judging from nOe's between H-11/H-5 and H-11/H-9β, and examination of Dreiding models. Thus, **1** was the C-5 epimer of **2**, assigned as (1*S*,5*S*,8*S*,10*R*,11*S*)-11-hydroxy-1-



1 (5*S*)
2 (5*R*)

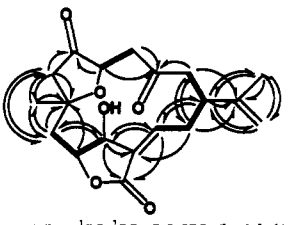


FIGURE 1. The ^{1}H-^{1}H COSY (bold lines) and HMBC (arrows) correlations for sinuleptolide [**1**].

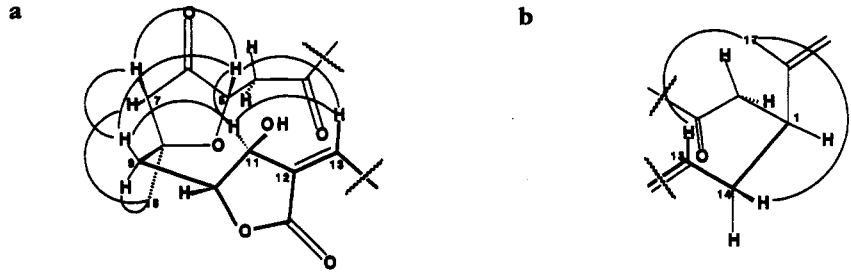


FIGURE 2. The nOe correlations for **1**.

isopropenyl-8-methyl-3,6-dioxo-5,8-epoxycyclotetradec-12-ene-10,12-carbolactone. The pharmacological study of **1** and **2** is in progress.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The following instruments were used: Yanagimoto micro melting point apparatus, JASCO FT/IR-5300 (ir), JASCO DIP-360 polarimeter (optical rotation), JEOL JMS-HX-100 mass spectrometer (hrms), JEOL JNM-GX-400FT NMR spectrometer (^{1}H and ^{13}C nmr).

CORAL TAXONOMY.—The soft coral *Sinularia* sp. (2.2 kg, wet wt) was collected at a depth of 2–3 m in Okinawa Island in June 1990 and immediately frozen (−20°). The voucher specimen of the *Sinularia* colony from which the norditerpenoid compound was extracted has been accessioned in the Museum's collection as NTM C11701. Unfortunately, the material from the basal surface of the

TABLE 1. ^{1}H- and ^{13}C-nmr Data for Compounds **1** and **2**.[a]

Position	Compound			
	1		**2**	
	^{1}H	^{13}C	^{1}H	^{13}C
1	3.00 (m)	40.2 (t)	3.07 (m)	39.6 (d)
2	2.45 (d, 13.9) 2.89–2.94 (m)	46.2 (t)	2.50 (dd, 18.3, 13.9) 2.82 (m)	45.8 (t)
3		207.0 (s)		205.8 (s)
4	2.60 (dd, 13.2, 11.7) 2.89–2.95 (m)	44.8 (t)	2.73 (dd, 16.1, 9.5) 2.87 (dd, 16.1, 2.9)	44.0 (t)
5	4.70 (d, 11.0)	77.5 (d)	4.58 (dd, 9.5, 2.9)	75.8 (d)
6		214.2 (s)		215.2 (s)
7	2.44 (d, 18.3) 2.61 (d, 18.3)	51.6 (t)	2.52 (2H, d, 15.4)	51.7 (t)
8		80.0 (s)		79.5 (s)
9	2.17 (d, 15.4) 2.31 (dd, 15.4, 8.1)	41.8 (t)	2.22 (d, 15.4) 2.47 (dd, 15.4, 8.1)	43.0 (t)
10	5.00 (d, 8.1)	84.9 (d)	4.98 (d, 8.1)	84.4 (d)
11	4.95 (s)	76.2 (d)	4.99 (s)	75.8 (d)
12		133.6 (s)		134.3 (s)
13	6.67 (dd, 11.0, 4.4)	142.9 (d)	6.65 (dd, 11.0, 3.7)	142.9 (d)
14	2.22 (ddd, 14.7, 4.4, 4.4) 4.15 (ddd, 14.7, 11.0, 4.4)	29.7 (t)	2.25 (ddd, 15.4, 3.7, 3.7) 4.21 (ddd, 15.4, 11.0, 6.6)	28.1 (t)
15		148.0 (s)		147.8 (s)
16	4.79 (s) 4.82 (d, 1.5)	110.6 (t)	4.81 (s) 4.82 (s)	110.5 (t)
17	1.61 (3H, s)	21.9 (q)	1.69 (3H, s)	21.9 (q)
18	1.71 (3H, s)	29.7 (q)	1.45 (3H, s)	26.1 (q)
19		170.0 (s)		169.6 (s)

[a]Chemical shifts (ppm) obtained in C_5D_5N (multiplicity, J in Hz).

colony below the polyp region is not present, and so it is unlikely that the specimen will ever be further identified with any certainty. The general morphology of the fragment is like that of *Sinularia conferta* (Dana) sensu Whitelegge, as illustrated by Verseveldt (4) (plate 7 and Figure 1). There is also similarity between the skeletal elements (the sclerites) in the surface of the lobes and those of Whitelegge's specimen. The interior sclerites, however, are distinctly different in both general shape and tuberculation. The sclerites from the surface of the lobes are also similar to those of *Sinularia fungoides* Thompson & Henderson, a species with completely different morphology, and *Sinularia manaarensis* Verseveldt, a species with ill-defined morphology, having been described from a juvenile specimen. It is unlikely that the specimen is conspecific with *S. manaarensis*, known only from Sri Lanka, as the interior sclerites are quite different. Comparison between basal sclerites is not possible because the voucher specimen, which may represent a new species, is incomplete.

EXTRACTION AND ISOLATION PROCEDURES.—The frozen sample (2.2 kg) was lyophilized and exhaustively extracted with MeOH-CH_2Cl_2 (1:1) (2 liters×4) at room temperature for 1 day. The extract was concentrated, and the resulting residue was extracted with EtOAc (500 ml×3). The EtOAc-soluble portion (19 g) was repeatedly subjected to Si gel flash cc (using increasing concentrations of MeOH in $CHCl_3$ as eluent), followed by Sephadex LH-20 cc [$CHCl_3$-MeOH (1:1)] and reversed-phase hplc (50% MeOH) to give **1** (120 mg, 0.06% wet wt) and **2** (600 mg, 0.027%).

Sinuleptolide [**1**].—Colorless prisms: mp 206–208° (from MeOH); $[\alpha]^{25}D$ +57.5° (c=0.27, MeOH); ν max (film) 3450–3550, 1755, 1732, 1707, 1678 cm^{-1}; ^1H nmr (C_5D_5N) see Table 1; ^{13}C nmr (C_5D_5N) see Table 1; hreims m/z $[M]^+$ 348.1549 (calcd for $C_{19}H_{24}O_6$, 348.1570); eims $[M]^+$ 348 (83), 330 (36), 165 (45), 109 (45), 97 (100).

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