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A NEW DITERPENE FROM A SOFT CORAL, *SINULARIA DISSECTA*¹M. VENKATA RAMI REDDY, S. LAKSHMAN, A.V. RAMA RAO, Y. VENKATESWARLU,*
and J. VENKATESWARA RAOOrganic Chemistry Division I, Toxicology Unit,
Indian Institute of Chemical Technology, Hyderabad 500007, IndiaABSTRACT.—A highly oxygenated cembranoid **1** has been isolated as a minor constituent from a soft coral, *Sinularia dissecta*.

Following the isolation of the novel furanocembranoid diterpene pukalide [**3**] (1) from a soft coral, *Sinularia abrupta*, several related compounds, 11 β ,12 β -epoxypukalide (2), 13 α -acetoxy-11 β ,12 β -epoxypukalide (3), 13 α -acetoxy-pukalide (3), and the bipinnatins (4), have been reported. As part of our search for biologically active compounds from marine sources, we investigated a soft coral, *Sinularia dissecta* (Tixier Durivault). The CH₂Cl₂-MeOH (1:1) extract of this soft coral afforded 9(15)-africanene (5,6), pukalide, (+)- β -elemene (7), and a new diterpene **1** structurally related to pukalide [**3**].

Compound **1**, [α]²⁵D -8.7 (CH₂Cl₂, c =0.12), analyzed for C₂₂H₂₈O₈ by microanalysis. Its mass spectrum exhibited only [M-H₂O]⁺ peak at m/z 402 under a variety of conditions. The ir absorptions at 3460 and 1705 cm⁻¹ indicated the presence of hydroxy and carbonyl groups, respectively. Compound **1** readily formed a monoacetate, thus confirming the presence

of a primary or secondary hydroxyl group.

The ¹H- and ¹³C-nmr spectra (Table 1) of compound **1** suggested the presence of an α,α' -dialkyl substituted β -carboxymethylfuran function, an isopropenyl group, and a methyl group on a carbon bearing an hydroxyl; these corresponded to the C-1 to C-6 functionality of pukalide. Further, the ¹H- and ¹³C-nmr spectra of compound **1** indicated the presence of a carbonyl carbon (¹³C δ 209.7 s), a trisubstituted double bond having a carbomethoxy group [¹H δ 7.0 (1H, t, J =6.4 Hz), 3.75 (3H, s); ¹³C δ 167.2 s, 143.6 d, 125.4 s, 52.1 q], and a methine carbon [¹H δ 4.63 (1H, s); ¹³C δ 73.5 d] bearing an hydroxyl group. The methine proton shifted upon acetylation to δ 5.8 (1H, s) in the ¹H-nmr spectrum of the acetate **2**. The foregoing spectral data revealed that compound **1** was a diester, with no evidence for the γ -lactone functionality present in pukalide [**3**]. In the ¹H-nmr spectrum of **1**, large geminal couplings were observed in the

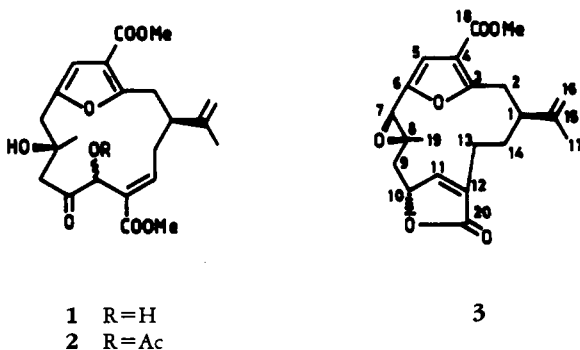


TABLE 1. ^1H - and ^{13}C -nmr Data of Compound **1** and ^1H Nmr of Its Acetate **2**
[chemical shift δ (ppm), multiplicity, J values in Hz] in CDCl_3 .

Position	Compound		
	1		2
	^1H	^{13}C	^1H
1	2.55 m (merged in one of the C-7 proton)	43.3 d	2.53 m
2	3.32 dd ($J=15, 2$) 2.85 dd ($J=15, 11$)	30.7 t	3.16 dd ($J=15, 2.7$) 2.92 dd ($J=15, 10.7$)
3	—	160.1 s	—
4	—	114.8 s	—
5	6.6 s	108.8 d	6.6 s
6	—	151.2 s	—
7	3.16 d ($J=18$) 2.55 d ($J=18$)	30.6 t	3.05 d ($J=18$) 2.61 d ($J=18$)
8	—	74.2 s	—
9	3.5 d ($J=17.5$) 3.4 d ($J=17.5$)	46.4 t	3.54, d ($J=17$) 3.42 d ($J=17$)
10	—	209.7 s	—
11	4.6 s	73.5 d	5.8 s
12	—	125.4 s	—
13	7.0 t ($J=7$)	143.6 d	6.97 dd ($J=5.7, 9.1$)
14	2.36 m	42.2 t	2.28 m
15	—	145.5 s	—
16	4.97 s 4.89 s	111.9 t	4.92 s 4.86 s
17	1.83 s	20.9 q	1.81 s
18	—	163.9 s	—
19	1.24 s	24.4 q	1.24 s
20	—	167.2 s	—
21	3.8 s	51.4 q	3.78 s
22	3.75 s	52.1 q	3.74 s

region between δ 2.3 and 3.6. The assigned values for the C-7 methylene protons were consistent with those observed in hexahydropukalide (1). In the ^1H -nmr spectrum of **1**, the signals for the C-1 methine and one of the C-7 methylene protons were overlapping. However, in the ^1H -nmr spectrum, when measured in CDCl_3 , containing few drops of C_6D_6 , H-1 shifted to δ 2.6 (1H, m).

The COLOC (2J) experiment revealed the disposition of carbonyl carbon, trisubstituted double bond, and the methine carbon bearing an hydroxyl group of **1**. A methyl proton signal at δ 1.24 was correlated with two methylene signals at δ 30.6 t, 46.4 t and with a quarternary carbon at δ 74.2 s. Isolated methylene

proton signals at δ 3.5 (d, 1H, $J=17.5$ Hz) and 3.4 (d, 1H, $J=17.5$ Hz) were coupled to a methyl signal at δ 24.4 q, to a quarternary carbon at δ 74.2 s, to a carbonyl carbon at δ 209.7 s, and to a methine carbon at δ 73.5 d, bearing an hydroxyl. Further, a multiplet signal at δ 2.36 was coupled to a olefinic signal at δ 125.4 s. In an nOe experiment, irradiation of the methyl signal at δ 1.24 caused enhancement of the signal at δ 4.6. The low field signal at δ 7.0 in the ^1H -nmr spectrum of **1** corresponding to the α, β -unsaturated trisubstituted double bond proton suggested that the C-12–C-13 double bond stereochemistry is *E* (8). The results discussed above were consistent with the structure proposed for **1**.

The in vitro I_{50} for **1** was 6.3×10^{-5} M, against rat (Wistar strain) brain AcChE.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected. Optical rotations were measured with a Jasco Dip 370 polarimeter. ^1H -nmr (400 MHz) and ^{13}C -nmr (50 MHz) spectra were recorded on a Varian Unity 400 MHz and a Varian Gemini spectrometer, respectively, using TMS as internal standard. Chemical shifts were reported in δ (ppm) values and coupling constants (J) in Hz. Elemental analysis was carried out on a Perkin-Elmer 240C. Uv and ir were recorded on a Shimadzu spectrophotometer. Mass spectra were recorded on a Finnigan Mat 1020.

COLLECTION, EXTRACTION, AND ISOLATION.—

The soft coral *S. dissecta* was collected by hand on intertidal rocks at Mandapam coast (N 17°, E 83°) in India during September 1991. A voucher specimen (IIC-91-A-030) is on deposit at the National Institute of Oceanography museum, Goa, India. A freshly collected specimen (3 kg) was extracted with CH_2Cl_2 -MeOH (1:1) (2 liters) at room temperature three times. The combined extract was filtered, and the solvent was removed under reduced pressure. The crude extract (3 g) was subjected to gel filtration chromatography (Sephadex LH-20) using CH_2Cl_2 -MeOH (1:1) as eluent. Repeated cc on Si gel using hexane/EtOAc gradients yielded pure compound **1** (60 mg) as shining needles: mp 170–172° (MeOH). Elemental analysis: found C 62.9%, H 6.76%; required for $\text{C}_{22}\text{H}_{28}\text{O}_8$, C 62.8%, H 6.72%. Uv λ max (MeOH) nm (ϵ) 216 (6676), 245 (3788); ir ν max (KBr) cm^{-1} 3460, 1705, 1641, 1606, 1559, 1435, 1209, 1085; ^1H and ^{13}C nmr see Table 1; eims m/z (%)

$[\text{M}-\text{H}_2\text{O}]^+$ 402 (10), 370 (15), 253 (20), 205 (50), 168 (100).

ACETYLTATION OF **1**.—A solution of **1** (10 mg) in Ac_2O /pyridine (0.5 ml) was allowed to stand at room temperature for one day. The crude product was chromatographed on Si gel to give the monoacetate **2** (10 mg): uv λ max (MeOH) nm (ϵ) 220 (10000), 245 (5666); ir ν max (neat) cm^{-1} 3430, 1736, 1704, 1634, 1605, 1559, 1430, 1223, 1076; ^1H nmr see Table 1; eims m/z (%) $[\text{M}]^+$ 462 (5), 402 (8), 370 (10), 253 (18), 205 (50), 168 (100).

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