

Seco-Sethukarailin, a Novel Diterpenoid from the Soft Coral *Sinularia dissecta*[†]

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Seco-sethukarailin (**1**), a novel diterpenoid, has been isolated along with known sesquiterpenes $\Delta^{9(15)}$ -africanene, β -elemene, african-1-ene, 6*R*,7*R*-6,7-epoxycaryophyll-3(15)-ene, and known diterpenoids sethukarailin and isomandapamate, from the soft coral *Sinularia dissecta* collected from Mandapam Coast, South India. The structure of the novel diterpenoid *seco-sethukarailin* (**1**) was characterized by interpretation of spectral data.

Marine organisms have been found to be storehouses of a variety of secondary metabolites.¹ In particular, soft corals are a rich source of biologically active terpenoids with diverse structures.^{2,3} The soft corals of the genus *Sinularia* produce unusual cembrane diterpenoids, sesquiterpenes, and polyhydroxylated steroids.⁴ In continuation of our search for biologically active compounds from the genus *Sinularia*,^{5–10} we have reexamined the soft coral *Sinularia dissecta* (Alcyoniidae) collected from the Mandapam Coast during October 1997.

The 1:1 dichloromethane–methanol extract of the soft coral *S. dissecta* was subjected to gel filtration chromatography on Sephadex LH-20 (1:1 dichloromethane–methanol) followed by silica gel chromatography eluting with hexane through hexane–ethyl acetate mixtures to ethyl acetate to afford known compounds $\Delta^{9(15)}$ -africanene,^{11,12} β -elemene,¹³ african-1-ene,¹⁴ 6*R*,7*R*-6,7-epoxycaryophyll-3(15)-ene,^{15,16} isomandapamate,¹⁷ sethukarailin,¹⁸ and the new diterpene *seco-sethukarailin* (**1**).

Compound **1**, obtained as a viscous liquid (yield 0.003% on dry weight basis), analyzed for C₂₃H₃₀O₈ by elemental analysis and HREIMS, which required nine degrees of unsaturation. Its IR spectrum shows strong absorption bands at 1740 and 1670 cm⁻¹, indicative of α,β -unsaturated and saturated carbonyl functionalities, and the UV spectrum shows absorptions at λ_{\max} (log ϵ) 217 (3.79) and 313 (3.53) nm, indicating the presence of an enone and a dienone system.

The ¹H NMR spectrum of compound **1** indicated the presence of three olefinic protons [δ 7.05 (s, 1H), 6.85 (t, J = 8 Hz, 1H) and 5.16 (s, 1H)]; an isopropenyl group [δ 4.58 (br s, 1H), 4.74 (br s, 1H), and 1.60 (s, 3H)]; and an isolated methylene group [δ 3.41 (s, 2H)]. Further, its ¹H NMR spectrum revealed the presence of two ester methyls [δ 3.75 (s, 3H), 3.80 (s, 3H)]; a methoxy group [δ 3.20 (s, 3H)]; two ketonic methyls [δ 2.42 (s, 3H) and 2.20 (s, 3H)]; and a multiplet corresponding to five protons [δ 2.2–2.35].

The ¹³C and DEPT NMR spectra indicated the presence of nine quaternary carbons, six methyls, four methylene carbons, and four methine carbons. Furthermore, the ¹³C NMR spectrum of compound **1** indicated the presence of four double-bond carbons between δ 160 and 113, in addition to two ester carbonyls at δ 162.5 and 167.1 and two ketonic carbonyls at δ 204.8 and 197.1. The ¹³C NMR spectrum of compound **1** (Table 1) was typical of a furanocembranoid^{6,7,9,18} and is similar to that of sethukarailin

Table 1. Spectral Data for Compound **1**^a

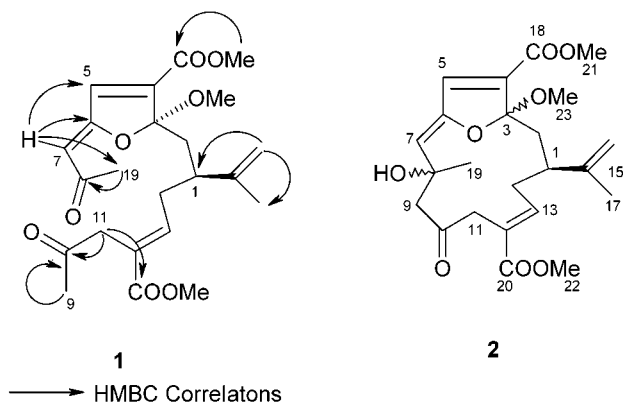
position	δ_{H}	δ_{C}^b	HMBC
1	2.32 (m, 1H)	41.2 d	C-15
2	2.22 (m, 2H)	33.7 t	
3		117.6 s	
4		139.8 s	
5	7.08 (s, 1H)	137.8 d	C-4
6		160.9 s	
7	5.32 (s, 1H)	105.8 d	C-19, C-5, C-6
8		197.1 s	
9	2.42 (s, 3H)	30.7 q	C-10
10		204.2 s	
11	3.41 (s, 2H)	41.5 t	C-10, C-20
12		126.6 s	
13	6.85 (t, J = 8 Hz, 1H)	143.5 d	
14	2.28 (m, 2H)	37.0 t	
15		145.7 s	
16	4.58 (s, 1H)	113.3 t	C-1, C-17
	4.73 (s, 1H)		
17	1.60 (s, 3H)	18.9 q	C-1, C-15
18		167.3 s	
19	2.20 (s, 3H)	29.6 q	C-8
20		162.4 s	
21	3.75 (s, 3H)	52.2 q	C-18
22	3.80 (s, 3H)	52.8 q	C-20
23	3.20 (s, 3H)	50.6 q	

^a ¹H NMR (500 MHz) and ¹³C NMR (125 MHz); δ in ppm, J in Hz. Spectra were recorded in CDCl₃ with TMS as internal standard. ^b Assignment of carbon types (s = C, d = CH, t = CH₂, q = CH₃) was made by DEPT.

(**2**)¹⁸ except for the presence of an additional ketonic carbonyl at δ 197.1 (s) and an extra methyl at δ 30.7 (q), which replace a quaternary carbon-bearing hydroxyl functionality at δ 70.7 (s) and a methylene group at δ 51.4 (t), respectively.¹⁸ A careful study of the spectral data (HMQC, HMBC, and NOESY) and comparison to those reported for sethukarailin (**2**) suggest that compound **1** is 8,9-*seco*-sethukarailin. This assignment is in full agreement with the HMQC, HMBC, and NOESY spectral data. In the HMBC spectrum of **1**, the C-7 vinylic proton showed correlations with C-19, C-5, and C-6. The C-11 methylene protons observed at δ 3.41 showed correlations with C-10 and C-20. The relative stereochemistry of the methoxyl group and geometry of the C6–C7 double bond were established by interpretation of the NOESY spectrum, in which the C-7 olefinic proton observed at δ 5.32 showed a correlation with the H-5, thus indicating the *Z* configuration of the C6–C7 double bond. The H-23 methoxyl resonance observed at δ 3.2 showed correlation with the H-1 methine resonance observed at δ 2.32, indicating both

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are on the same face of the molecule. Compound **1** may be an artifact resulting from methanol addition during extraction.¹⁸

The known sesquiterpene african-1-ene was recently isolated from the essential oil of *Lippia integrifolia*,¹⁴ and 6*R*,7*R*-6,7-epoxycaryophyll-3(15)-ene was earlier isolated from the heartwood of *Juniperus chinensis*.^{15,16} This is the first report of the isolation of these compounds from marine sources.

Experimental Section

General Experimental Procedures. The optical rotations were measured on a JASCO DIP-370 polarimeter. UV and IR spectra were recorded on Shimadzu-240 and Perkin-Elmer 240-C instruments, respectively. The ¹H NMR (500 MHz) and ¹³C NMR (125 MHz) spectra were recorded on a Varian Gemini 500 MHz spectrometer, using CDCl₃ as a solvent and TMS as internal standard. Chemical shifts are reported in parts per million, and coupling constants (*J*) are expressed in hertz. The MS were recorded on a VG Auto Spec-M instrument.

Animal Material. The soft coral *Sinularia dissecta* was collected on the Mandapam Coast in the Gulf of Mannar, Tamilnadu, India, during October 1997, and a voucher specimen (IIC-284) is on deposit at the National Institute of Oceanography, Goa, India.

Extraction and Isolation. The freshly collected specimens were soaked in MeOH at the site of collection until workup. The soft coral *S. dissecta* was freeze-dried (1.5 kg) and extracted with 1:1 CH₂Cl₂-MeOH (3 × 3 L) at room temperature. The combined extract, including initial methanol extract, was filtered, and the solvent was removed under reduced pressure to give a dark brown gummy mass (40 g). This crude extract (40 g) was subjected to gel filtration chromatography (Sephadex LH-20, 1:1 CH₂Cl₂-MeOH, 47 mm × 820 mm, 25

mL each fraction of 40 total continuous fractions) followed by silica gel chromatography using a step gradient of hexane, through hexane-EtOAc mixtures, finally to EtOAc, to yield Δ⁹⁽¹⁵⁾africanene (400 mg), β-elemene (160 mg), african-1-ene (25 mg), 6*R*,7*R*-6,7-epoxycaryophyll-3(15)-ene (50 mg), and the known diterpenoids sethukarailin (50 mg), isomandapamate (300 mg), and compound **1** (45 mg).

Compound 1: pale yellow, viscous liquid; [α]_D²⁵ -27.3 (*c* 0.25, CHCl₃); UV(MeOH) λ_{max} (log ε) 217(3.79), 313(3.53) nm; IR (CHCl₃) ν_{max} 1740, 1670, 1430, 1330, 1200, 900 cm⁻¹; ¹H NMR(CDCl₃, 500 MHz), see Table 1; ¹³C NMR (CDCl₃, 125 MHz), see Table 1; EIMS (70 eV) *m/z* 434 [M⁺]; HRFABMS *m/z* observed 435. 2029 [M + H⁺] (calcd for C₂₃H₃₁O₈ 435.2019 Δ +1 mmu), *R*_f 0.50 (40% EtOAc in hexane).

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