Unusual terpenoid constituents of the soft coral *Sinularia dissecta*†

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Chemical examination of the soft coral *Sinularia dissecta* furnished six known terpenoids, along with a new sequiterpenoid seco-africanane (**1**) and a new norcembrane diterpene (**2**),

Marine organisms have been found to be storehouses of a variety of secondary metabolites, particularly terpenoids with unusual functionalization.[1] A literature survey revealed that the genus *Sinularia* is a rich source of variety of sesquiterpenes, cembrane derived diterpenes and polyhydroxylated steroids.[2] In continuation to our search for biologically active compounds from the genus *Sinularia*[3–10] we examined the soft coral *Sinularia dissecta* collected from the Mandapam coast during June 1996.

The 1:1 dichloromethane : methanol extract of the soft coral *Sinularia 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 : acetone mixtures to acetone afforded six known compounds $\Delta^{9(15)}$-africanene,[11] (+)β-elemene,[12], 2,3-seco-2,3-africananedione,[13] isomandapamate,[14] methyl 5,8-epoxy-18-nor-3,6,10-trioxocembra-12(Z),15-dien-20-oate,[15] 5,11-*diepi* sinuleptolide (**3**),[15] and two new compounds 4-acetoxy-3,15-dinor-2,3-seco-2-africanone (**1**) and 11-*epi* sinuleptolide (**2**).

Compound **1** was obtained as colourless oil, $[\alpha]^{25}_{D}$+ 45.1° (*c* 0.6, $CHC1_3$) and analysed for $C_{15}H_{24}O_3$ by HR EIMS and ^{13}NMR spectral data, requires four degrees of unsaturation. The IR absorptions at 1735, 1705 and 1020 cm^{-1} indicated the presence of a ketone and a acetyl groups. The ^{13}C NMR spectrum of compound **1** showed signals from 15 carbons, which includes an ester carbonyl at δ 170.2 (s) and a ketonic carbonyl at δ 204.5 (s) accounting for two degrees of unsaturation, hence compound **1** is bicyclic in nature.

The ^{1}H NMR spectrum of compound **1** contained signals for four methyls at δ 0.86 (3H, s), 0.96 (3H, s), 0.99 (3H, s), 2.12 (3H, s) and a trisubstituted cyclopropane signals at δ 0.3 (1H, dd), 0.66 (1H, m) and 0.74 (1H, dd) and the downfield spectrum showed signal at 4.78 (2H, m). The foregoing spectral data is similar to that of 2,3-seco-2,3-africananedione[8] except for the signal at δ 4.78, which could be attributed to acetoxy methylene protons, and was further confirmed by ^{13}C NMR spectrum signals at δ 74.6 (t) and 172.0 (s) instead of two ketonic carbonyls at δ 208.8 (s) and 209.3 (s) as noticed in 2,3-seco-2,3-africananedione. The above spectral data suggested that compound **1** might be selective Bayer-Villiger oxidation product of 2,3-seco-2,3-africananedione in the side chain and the structure was established as 4-acetoxy-3,15-dinor-2,3-seco-2-africanone (**1**).

Compound **2** was obtained as white solid, m.p.212-214 °C, $[\alpha]^{25}_{D}$ + 9.1° (*c* 0.66, $CHC1_3$). UV λ_{max}221 (ε 15336) nm and IR spectrum indicated the presence of hydroxyl (3520 cm^{-1}), α, β-unsaturated ester (1720 cm^{-1}) besides olefinic unsaturation (1640 and 900 cm^{-1}). From the study of ^{1}H and ^{13}C NMR spectra data compound **2** was recognized as highly oxygenated tricyclic norcembranolide.[15].

It was analysed for $C_{19}H_{24}O_6$ by HREIMS requires eight degrees of unsaturation. The ^{13}C NMR spectrum contained nineteen carbons, including four non-ketonic oxygen bearing carbons at δ 85.58 (d), 80.65 (s), 77.97 (d), 76.34 (d), two ketonic carbonyls at δ 209.49 (s), 214.69 (s), one lactone carbonyl at δ 171.29 (s) and four double bond carbons at δ 148.70 (s), 145.82 (d), 132.76 (s), 111.21 (t), accounted for five degrees of unsaturation, hence compound **2** is tricyclic in nature.

The ^{1}H NMR spectrum (Table 1) of compound **2** showed a α, β-unsaturated trisubstituted double bond proton at δ 6.53 (1H, dd, *J* = 6, 11 Hz, 13-H), an isopropenyl group at δ 4.86 (1H, s, 16-H_b), and 4.80 (1H, s, 16-H_a), 1.83 (3H, s, 17-H_3), three oxygen bearing methine protons at δ 4.65 (1H, d, *J* = 6.8 Hz, 10-H), 4.61 (1H, s, 11-H), 4.40 (1h, d, *J* = 10.0 Hz, 5-H) and a tertiary emthyl connected to an oxygenated carbon at δ 1.49 (3H, s, 18-H_3). The ^{1}H NMR spectrum of **2** is similar to that of **3** except for C-5 methine proton signal at δ 4.40 shifted downfield by 0.12 ppm as compared to 5,11-*diepi* sinuleptolide (**3**).[15]

The relative stereochemistry of compound **2** was established by ^{1}H-^{1}H COSY and NOESY spectra. In the ^{1}H-^{1}H COSY spectrum the signal at δ 6.53 (1H, dd, 13-H) showed correlations with δ 2.16 (1H, ddd, 14-H_a), 3.71 (1H, ddd, 14-H_b); the signal at δ 4.65 (1H, d, 10-H) showed correlation with δ 2.40 (1H, dd, 9-H_a) and the signal at δ 4.40 (1H, d,5-H) showed correlation with δ 2.56 (1H, dd, 4-H_a). The stereochemistries in compound **2** were established by NOESY spectral data. The NOESY correlations between the signals at δ 6.53 (1H, dd, 13-H) and 4.61 (1H, s, 11-H), suggested the *E* configuration of the double bond at C_{12}–C_{13}. The signal at δ 1.49 (3H, s, 18-H_3) showed correlations with δ 2.41 (1H, d, 7-H_a) and 2.40 (1H, dd, 9-H_a), suggested the chiral centre C-8 has S configuration The signals at δ 4.61 (1H, s, 11-H) showed correlation with δ 2.40 (1H, dd, 9-H_a) and did not show correlation with 5-H suggested the chiral centre C-10 has *R* configuration. The signal at δ 1.83 (3H, s, 17-H_3) showed correlation with δ 2.16 (ddd, 14-H_b), established the chiral centre C-1 has *S* configuration. The signal at δ 4.40 (1H, d, C-5) showed correlations with δ 2.56 (1H, dd, 4-H_a) and 2.62 (1H, d, 4-H_b) and did not show correlations with 11-H methine proton. The chiral centres at C-5 and C-11 have *S* and *R* configurations by comparing with sinuleptolide.[16]. From the foregoing spectral data the structure of the compound **2** was established as (1*S*,5*S*,8*S*,10*R*,11*R*)-5,8-epoxy-11-hydroxy-18-nor-3,6-dioxo-12,15-cembradien-20,10-olide. Hence, compound **2** is 11-*epi* sinuleptolide[16] or is a stereoisomer of 5,11-*diepi* sinuleptolide (**3**)[15] at C-5 position, isolated from the soft coral of the genus *Sinularia* sp. Previously, for 5,11-*diepi* sinuleptolide (**3**) ^{13}C NMR was not reported and the same is now reported. Furthermore, compound **2** is a stereoisomer of 5-*epi* sinuleptolide at C-5 and C-11 positions, isolated from the soft coral *Sinularia leptoclados*.[17]

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 200 MHZ and Varian Unity 400 MHz spectromoter using TMS as internal standard. Chemical shifts are reported in parts per million and

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

Table 1 ^1H* and ^{13}C NMR+ spectral data of compounds **2** and **3**

	δ		δ_H mult. (*J* = Hz)		COSY	NOESY
Position	**3**	**2**	**3**	**2**	**2**	**2**
1	41.02 d	41.74 d	2.81 dddd (3.4, 3.2, 8, 11)	2.80 dddd (3.4, 3.2, 8, 11)	14a-H, 2a-H, 2b-H	14a-H, 14b-H, 2a-H, 2b-H, 17-H
2a-H	46.18 t	47.09 t	2.54 dd (3.4, 14)	2.52 dd (3.4 14)	1-H, 2b-H	1-H, 2b-H
b-H			2.57 dd (11, 14)	2.56 dd (11, 14)	1-H, 2a-H	1-H, 2a-H
3	209.15 s	209.49 s				
4a-H	46.06 t	46.27 t	2.57 dd (9.5, 15)	2.56 dd (10.0, 15)	5-H, 4b-H	4b-H, 5-H
b-H			2.62 dd (3, 15)	2.62 d (15)	4a-H	4a-H, 5-H
5	77.65 d	77.97 d	4.28 dd (3.5, 10)	4.40 d (10.0)	4a-H	4a-H, 4b-H
6	214.51 s	214.69 s				
7a-H	52.05 t	52.52 t	2.41 d (17)	2.41 d (17)	7b-H	7b-H, 18-H
b-H			2.54 d (17)	2.54 d (17)	7a-H	7a-H
8	80.39 s	80.65 s				
9a-H	42.28 t	42.81 t	2.05 d (15)	2.05 d (15)	9b-H, 10-H	9b-H, 10-H, 11-H, 18-H
b-H			2.40 dd (7, 15)	2.40 dd (7, 15)	9a-H	9a-H, 10-H
10	85.32 d	85.58 d	4.65 d (7)	4.65 d (6.8)	9a-H	9a-H, 9b-H
11	76.09 d	76.34 d	4.61 s	4.61 s		9a-H, 13-H
12	132.50 s	132.76 s				
13	145.38 d	145.82 d	6.53 dd (6, 11)	6.53 dd (6, 11)	14a-H, 14b-H	11-H, 14a-H, 14b-H
14a-H	30.54 t	31.32 t	2.15 ddd (6, 8, 14)	2.16 ddd (6, 8, 14)	13-H, 14b-H	1-H, 14b-H, 17-H
b-H			3.71 ddd (3.4, 11, 14)	3.71 ddd (3.5, 11, 14)	13-H, 14a-H	1-H, 14a-H, 17-H
15	148.36 s	148.70 s				
16-Ha	110.83 t	111.21 t	4.80 s	4.80 s		16b-H
Hb			4.86 s	4.86 s		16a-H, 17-H
17	21.70 q	22.05 q	1.83 a	1.83 s		1H, 14a-H, 14b-H, 16b-H
19	30.36 q	31.00 q	1.49 s	1.49 s		7a-H, 9a-H
20	171.09 s	171.29 s				

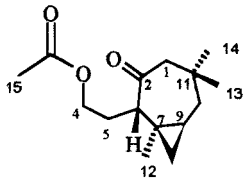
*$CDC1_3$, 400 MHz; +$CDC1_3$, 50 MHz

coupling constants (*J*) are expressed in Hertz. UV and IR spectra recorded on Shimadzu and Perkin-Elmer 240-C instruments. Elemental analysis was carried out on a Perkin-Elmer 240-C instrument. The mass spectra were recorded on VG Auto Spec-M-instruments.

Collection extraction and isolation procedure: The soft coral *Sinularia dissecta* (Tixier Durivault) was collected at Mandapam Coast in Gulf of Manner during June 1996 and a voucher specimen (IIC-233) is on deposit at National Institute of Oceanography Goa, India. The freshly collected specimen (1.5 kg dry weight after extraction) was extracted with CH_2C1_2 MEOH (1:1, 3 × 1.5 lit) at room temperature. The combined extract was filtered and the solvent was removed under reduced pressure to yield greenish gum (90 g). The crude extract was partitioned between water and ethyl acetate The organic layer was concentrated under vacuum and subjected for gel filtration (Sephadex LH-20) chromatography using 1:1 dichloromethane ; methanol followed by silica gel chromatography (100 – 200 mesh) using solvents of increasing polarity from hexane through ethyl acetate to acetone. Passing further, the selected fractions were purified overf a silica gel column or reverse phase HPLC column to yield eight pure compounds.

4-Acetoxy-3,15-dinor-2,3-seco-2-africanone (**1**): Colourless oil: 12 mg (0.0006% dry wt.); $[\alpha]^{25}_D$ + 45.1° (*c* 0.6, $CHC1_3$); IR (neat): ν_{max} 3050, 1735, 1705, 1405, 1365, 1165 and 1020 cm^{-1}, ^1H NMR (400 MHz, $CDC1_3$); δ 0.3 (1H, dd, *J* = 4.5, 4.5 Hz); 0.66 (1H, m), 0.74 (1H, dd, *J* = 4.5, 8.5 Hz), 0.86 (3H, s), 0.96 (3H, s), 0.99 (3H, s), 1.33 (1H, dd, *J* = 11, 15 Hz), 1.62-1.68 (1H, m), 1.78-1.84 (1H, m), 1.96 – 2.02 (1H, m), 2.12 (3H, s), 2.16-2.19 (1H, m), 2.24 (1H, dd, *J* = 1.8 15 Hz), 2.28–2.42 (1H, m) and 4.78 (2H, m); ^{13}C NMR (100 MHz, $CDC1_3$): δ 16.9 (s), 19.18 (q), 21.40 (t), 21.90 (d), 25.27 (q), 29.75 (q), 32.36 (q), 35.18 (s), 41.42 (t), 42.62 (t), 53.70 (d), 60.34 (t), 74.60 (t), 170.20 (s) and 209.50 (s); E1 MS : *m/z* 236 (M^+-CH_4), 179 (10), 163 (15), 149 (12), 135 (10), 125 (20), 112 (80), 97 (40), 79 (30), 67 (40), 55 (60) and 43 (100); HREIMS (*m/z*): 236. 1772 (M^+-O for $C_{15}H_{24}O_2$, for 236.1771).

11-Epi sinuleptolide (**2**): White solid; 50 mg (0.0025% dry wt), mpt 212–214 °C; $[\alpha]^{25}_D$ + 9.1° (*c* 0.66, $CHC1_3$); IR ($CHC1_3$): V_{max} 3520, 3020, 2935, 1720, 1640, 1380 and 900 cm^{-1}; ^1H NMR (400 MHz, $CDC1_3$): see Table 1, ^1H NMR (200 MHz,C_5D_5N): δ 1.62(3H, s, 17-H_3), 1.72(3H, s, 19-H_3), 2.24 (1H, ddd, *J* = 14.5, 4.5, 4.5 HZ, 14a-H), 2.18 (1H, d, *J* = 15.4 Hz, 9a-H), 2.32(1H, dd, *J* = 15.4, 8.2 Hz, 9b-H), 2.46(1H, d, *J* = 18.3 Hz, 7a-H), 2.48(1H, d 1H, *J* = 14.0 Hz, 2a-H), 2.62(1H, dd, *J* = 13.2, 9.5 Hz, 4a-H), 2.64(1H, d, *J* = 18.3 Hz, 7b-H), 2.92(2H, m, 2b-H, 4b-H), 2.98(1H, m, 1-H), 4.12(1H, ddd, *J* = 14.8, 11.0, 4.5 Hz, 14b-H), 4.70(1H, d, *J* = 9.5 Hz, 5-H), 4.82(1H, s, 16a-H), 4.83(1H, d, *J* = 1.5 Hz, 16b-H), 4.98(1H, s, 11-H), 5.0(1H, d, *J* = 8.0 Hz, 10-H) and 6.70(1H, dd, *J* = 11.0, 4.5 Hz, 13-H); ^{13}C NMR (50 MHz, $CDC1_3$): See Table 1; ^{13}C NMR (50 MHz, C_5D_5N): δ 21.69 (q, C-17), 29.64 (q, C-19), 29.73 (t, C-14), 40.26 (d, C-1), 41.76 (t,



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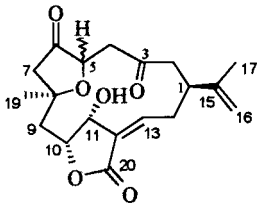

2. 5 *S*
3. 5 *R*

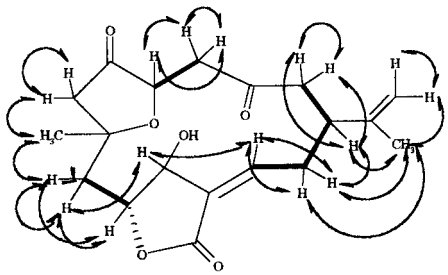

Fig. 1 The ^{1}H-^{1}H COSY (bold lines) and NOESY (arrows) correlations for Compound **2**.

C-9), 44.87 (t, C-4), 46.19 (t, C-2), 51.62 (t, C-7), 76.12 (d, C-11), 77.45 (d, C-5), 79.94 (s, C-8), 84.89 (d, C-10), 110.54 (t, C-16), 133.54 (s, C-12), 142.94 (d, C-13), 148.01 (s, C-15), 170.20 (s, C-20), 207.03 (s, C-3) and 214.12 (s, C-6); EIMS: *m/z* 348(M^+) (5) 330(3), 149(10), 123(8), 109(15), 97(25), 69(20), 55(60), 43(100) and 41(90); HREIMS (*m/z*): 348.15712 (M^+ for $C_{19}H_{24}O_6$, Calc. 348.15720).

5,11-Diepi sinuleptolide (**3**)[15]: White solid; 5 mg (0.00025% dry wt), mpt 196–7 °C; $[\alpha]^{25}_{D}$ + 3.8° (c 0.004, $CHC1_3$); IR ($CHC1_3$): V_{max} 3600, 3020, 2925, 1760, 1720, 1375, 1270, 1220, 1180 and 1090 cm^{-1}, ^{1}H NMR (200 MHz, $CDC1_3$): see Table 1, ^{1}H NMR (200 MHz, C_5D_5N): δ 1.45 (3H, s, 19-H3), 1.68(3H, s, 17-H3), 2.20(1H, d, *J* = 15.4 Hz, 9a-h), 2.22 (1H, ddd, *J* = 15.4, 3.7, 3.7 Hz, 14a-H), 2.42 (1H, dd, *J*=15.4, 8.0 Hz, 9b-H), 2.52(1H, dd, *J*=18.5, 14.0 Hz, 2a-H), 2.54(2H, d, *J*=15.4 Hz, 7a-H), 2.75 (1H, dd, *J* = 16.1, 9.5 Hz, 4a-H), 2.82 (1H, m, 2b-H), 2.88 (1H, dd, *J* = 16.2, 2.9 Hz, 4b-H), 3.05 (1H, m, 1-H), 4.21(1H, m, 14b-H), 4.60 (1H, dd, *J* = 9.5, 2.9 Hz, 5-H), 4.80(1H, br s, 16a-H), 4.81(1H, br s, 16b-H), 4.98(1H, d, *J* = 8.1 Hz, 10-H), 5.0 (1H, s, 11-H) and 6.64(1H, dd, *J* = 11, 3.5 Hz, 13-H); ^{13}C NMR (50 MHz, $CDCl_3$): see Table 1; ElMS: *m/z* 348 (M^+) (2), 149(20), 97(15), 69(25), 55(60) and 43(100).

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