Two New Sesterterpenes from the Marine Sponge, *Coscinoderma mathewsi*

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(Received September 21, 1998; CL-980727)

The sponge *Coscinoderma mathewsi* from Pohnpei, Micronesia contains two new sesterterpenes having a scalarane-type skeleton possessing cis **B/C** ring juncture. The structures of the new compounds were elucidated by interpretation of spectral data.

Many terpenoids of marine origin have unique structures and display cytotoxic activity.[1] Among the terpenoid structures, tetracyclic sesterterpenes with a scalarane skeleton have been extensively studied.[2-4] It is well known that many of these compounds occur in sponges of the order Dictyoceratida, family Spongiidae,[5,6] and tetracyclic rings (rings **A**, **B**, **C**, and **D**) are all *trans*-junctures having hydroxy group in ring **C**.[7] During our studies on biologically active secondary metabolites from marine sponges,[8] we have isolated two novel sesterterpenes, named coscinalactone (**1**) and coscinafuran (**2**), from the sponge *C. mathewsi*. The structures of these compounds were assigned based on the spectral data and found to have the different stereochemistry in the skeletal structure of known scalarane-type sesterterpenes. We describe here the isolation and structure elucidation of **1** and **2**.

The freeze-dried sponge was soaked in MeOH for 2 days; the MeOH extract was partitioned between $CHCl_3$ and H_2O; and the $CHCl_3$ layer was subjected to silica gel flash chromatography using a stepwise gradient of hexane/ethyl acetate. By NMR measurement, terpene derivatives were found in the $CHCl_3$ layer, and the derivatives having a characteristic aldehyde signal were contained in the 40% ethyl acetate fraction. Therefore, the compounds having an aldehyde signal were separated by repetitive HPLC (RI detector) on silica gel with 20% ethyl acetate in hexane, which yielded two new sesterterpenes having an aldehyde group and a unique scalarane-type skeleton.

The molecular formula, $C_{25}H_{36}O_3$, of compound **1** (0.013%, dry weight)[9] was determined by HREIMS ([M$^+$], *m/z* 384.2688, Δ 2.4 mmu). The presence of an aldehyde function was indicated by a MS fragment ion at *m/z* 355 [M$^+$ - CHO] and by an IR band at 1707 cm^{-1}. Analysis of 1D and 2D NMR data (400 MHz ; COSY, HMQC, HMBC, and NOESY) delineated a scalarane-type skeleton having four methyl groups (singlet at 1.09, 0.86, 0.85, and 0.76 ppm) and an aldehyde group (singlet at 9.71 ppm). From the ^{13}C chemical shifts at 172.7 (s), 168.7 (s), 113.9 (d), and 88.6 (d) ppm and IR absorptions at 1786, 1763, and 1649 cm^{-1}, it was clear that an α,β-unsaturated-γ-lactone was also present. On the basis of the chemical shift (α-methine proton, H-18, 4.52 ppm) and its HMBC correlations to C-13 (53.3 ppm), C-17 (168.7 ppm), and C-25 (203.3 ppm), it seemed to be attached to ring **D**.

The most significant difference between **1** and known scalarane compounds was observed in the CH_3-8 carbon signal. The downfield shift of the CH_3-8 resonance in **1** at 28.9 ppm as compared with that of known scalarane derivatives (16-17 ppm)[6,10] must be due to the different stereochemistry. The relative stereochemistry of **1** was determined by observation of a NOESY correlation between CH_3-8 and CHO-13. Also, correlations between H-14 and H-18, and between H-14 and CH_3-10 were observed, but no correlation between CH_3-8 and CH_3-10 could be detected. From these results, CH_3-8 and CH_3-10 must be on the opposite side and CH_3-8 and CHO-13 on the same side (Figure 1). This interpretation was supported by the coupling constants and a Dreiding model. The H-9 signal at 1.00 ppm [an apparent triplet, (dd), J = 5.3 Hz] indicates that the **B/C** ring juncture is *cis*-fused because vicinal couplings for H-11 are almost equal. On the other hand, the signals at 0.92 (H-5, dd, J = 3.6 and 10.9 Hz) and 2.10 ppm (H-14, dd, J = 2.9 and 12.8 Hz) coupled to the corresponding vicinal methylene protons (H-6 and H-15), support typical *ax-eq* and *ax-ax* coupling constants. Consequently, the stereochemistry of the remaining **A/B** and **C/D** ring junctures has been assigned *trans* stereochemistry.

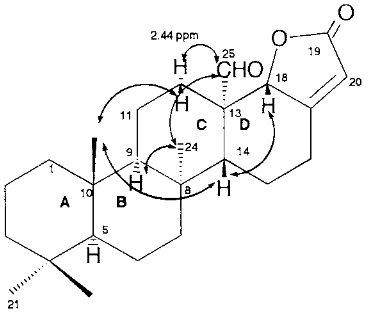

Figure 1. NOESY correlation of **1** (coscinalactone).

The molecular formula, $C_{25}H_{36}O_2$ of compound **2** (0.018%)[11] was determined by HREIMS ([M$^+$], *m/z* 368.2691, Δ -2.4 mmu), and its structure could be elucidated by comparison with the spectral data of **1** .

Thus, **2** bears an aldehyde group (270 MHz, ^{13}C; 197.8 ppm, ^1H; 9.77 ppm) and the same scalarane-type skeleton. The difference between the NMR spectra of **1** and **2** is based on two double bonds [^{13}C; 148.0 (s), 143.9 (d), 121.1 (s), and 111.0 (d) ppm, and ^1H ; doublets at 7.26 and 6.21 (J = 1.8 Hz)] and no ester group in **2**. These signals indicated a furan ring having α- and β-hydrogens, and a furan ring attached to ring **D** of the skeleton on the basis of HMBC correlations (Figure 2).

Compounds **1** and **2** are new. They possess an angular aldehyde group and have *cis*-fused **B/C** rings. The biogenesis of the novel compounds might be postulated as follows. Suvanine obtained from *Coscinoderma* sp. has a cis-fused **B/C** ring juncture and bears a furylethyl group at ring **C**.[8,12] The α-carbon of the furyl group reacts with ring **C** expelling a sulfonate, and generalizing an aldehyde. The α-position of **2** was oxidized to form a lactone (Figure 3).

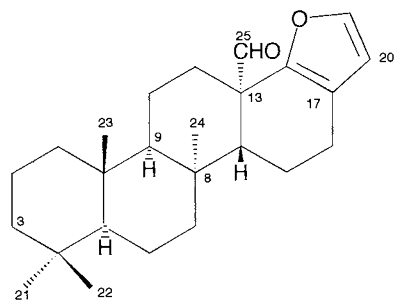

Figure 2. Structure of **2** (coscinafuran).

Table 1. NMR data for compounds **1** and **2** (in $CDCl_3$)

	Compound 1[a]			Compound 2[a]		
	^{13}C	^{1}H	HMBC (C:)	^{13}C	^{1}H	HMBC(C:)
1	41.9	1.87, 0.85		42.5	1.89, 1.38	
2	18.7	1.52, 1.41		18.9	1.38	
3	41.7	1.40, 1.12	2, 4	42.3	1.38, 1.12	
4	33.3			33.7		
5	54.6	0.92	4, 7, 10, 22	56.4	0.90[b]	
6	18.4	1.52, 1.24		19.3	1.15	
7	38.0	1.95, 1.18	6	39.8	2.17, 1.15	5, 8, 9, 14
8	37.1			37.8		
9	55.6	1.00	1, 8, 10, 11 12, 14, 23, 24	55.7	1.00[c]	
10	39.2			40.2		
11	17.3	1.77	8, 9, 10, 12 13	17.9	1.73	
12	29.2	2.44, 2.00	11, 13, 18	25.2	2.71, 1.75	9, 13, 14, 25
13	53.3			51.3		
14	45.3	2.10	8, 13, 25	45.9	2.34[d]	8, 13, 15, 24, 25
15	21.1	2.00, 1.87	8, 16	18.6	2.05, 1.52	
16	27.3	3.03, 2.44	20	23.0	2.68, 2.55	15, 17,18
17	168.7			121.1		
18	88.6	4.52	13, 17, 25	148.0		
19	172.7			143.9	7.26[e]	17, 18, 20
20	113.9	5.78	17, 18, 19	111.0	6.21	17, 18, 19
21	33.7	0.86	3, 4, 5, 22	34.5	0.85	3, 4, 5, 22
22	22.0	0.85	3, 4, 5, 21	22.8	0.82	3, 4, 21
23	19.2	1.09	1, 5, 9, 10	19.7	1.03	1, 5, 9
24	28.9	0.76	7, 8, 9, 14	28.3	0.90	7, 8, 9, 14
25	203.3	9.71	12, 13	197.8	9.77	13

[a] Compound **1** was measured at 400 MHz and **2** at 270 MHz.
[b] The coupling constant could not be measured because the signal was overlapped with other signals. [c] $J_{9\text{-}11a,11b} = 4.0$ Hz. [d] $J_{14\text{-}15a,15b} = 2.9, 12.0$ Hz.
[e] $J_{19\text{-}20} = 1.8$ Hz.

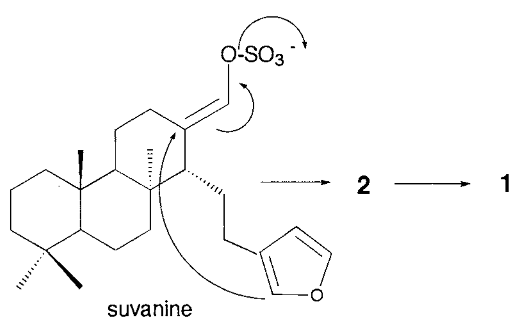

Figure 3. Biogenesis of **1** and **2**.

Investigation of the activities of these compounds and of the sponge are now in progress.

The authors wish to thank Professor P.J. Scheuer of the University of Hawaii for valuable advice and editorial comments. We are also grateful to Mr. N. Esumi of JEOL for 400 MHz-NMR measurements.

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