Two New Sesquiterpenoids from the Soft Coral Paralemnalia thyrsoides

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TWO NEW SESQUITERPENOIDS FROM THE SOFT CORAL *PARALEMNALIA THYRSOIDES*

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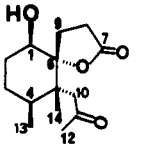
ABSTRACT.—Two new sesquiterpenoids, pathylactone A [**1**] and parathylone [**2**], were isolated from the soft coral *Paralemnalia thyrsoides*. Compound **1** is a rare norsesquiterpene with a γ-spirolactone moiety, and its absolute stereochemistry was assigned. Compound **2** is a nardosinane-type sesquiterpene with a unique C_8-C_9 unsaturated functionality. Three previously reported sesquiterpenoids were also isolated from this source.

Soft corals of the genus *Paralemnalia* (Alcyonaceae) are well known to be rich in sources of sesquiterpenoids and norsesquiterpenoids. The most common type of these components is the rearranged nardosinane class of sesquiterpenoids (1–5). In our continuing study on the components of soft corals we have obtained two new sesquiterpenoids, named pathylactone A [**1**] (6) and parathylone [**2**], along with three known sesquiterpenoids isolated from *Paralemnalia thyrsoides* Ehrenberg collected off the South China Sea. The known sesquiterpenoids were identified as 2-deoxy-12-oxolemnacarnol (1), 11,12-dihydroxyeremophila-6,10-diene (4), and a norsesquiterpenoid **3** (5).

Pathylactone A [**1**] analyzed for $C_{14}H_{22}O_4$ by ms, *m/z* 254 $[M]^+$, and ^{13}C nmr (DEPT) (Table 1). Ir absorption at 1780, 1719, and 1178 cm^{-1} together with ^{13}C-nmr signals at δ 207.6, 175.5, and 91.2 ppm indicated that **1** contains a ketone and a spiro γ-lactone moiety (7,8). On the basis of ir and ^{13}C nmr (δ 3.7, d), the presence of a secondary hydroxyl group was revealed. By means of ^1H-^1H COSY, ^1H-^{13}C COSY, and ^1H-^{13}C LRCOSY [C-5↦H-13, H-14, and H-10; C-6↦H-9 and H-14; C-7↦H-8], the presence of three isolated units of mutually coupled protons was established: i.e., those from C-1 through C-4 to the C-13 methyl group, those from C-10 to C-12, and a two-carbon unit C-8 and C-9. The connectivity of these units using ^1H-^{13}C LRCOSY led to the structure of **1** for pathylactone A.

H-1 was assigned as axial based upon a large coupling (10.9 Hz) with the axial proton at C-2. Thus the hydroxyl group at C-1 was assigned as equatorial. The relative stereochemistry of the molecule was determined by difference nOe spectra. NOe's were found between H-1 and H_a-3, H_2-10; H-13 methyl and H_a-2, H-4, H-8, H-9; H-14 and H_2-10, H-12. All



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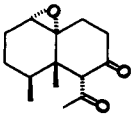

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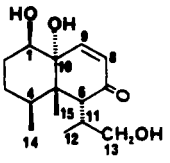

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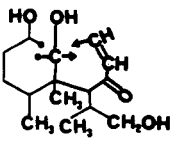

A

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

Position	Compound			
	1		**2**	
	^{13}C	^{1}H	^{13}C	^{1}H
1	63.7, d	4.33 (dd; 10.9, 3.9)	73.1, d	3.80 (t; 2.8)
2	28.6, t	1.90 (dddd; 14.1, 10.9, 10.2, 2.3)	29.4, t	1.23 (m)
		2.06 (dd; 14.1, 3.9)		2.16 (m)
3	26.7, t	1.44 (m)	24.1, t	1.37 (m)
		1.80 (m)		1.67 (m)
4	33.0, d	2.39 (m)	30.0, d	2.54 (ddq; 11.4, 4.4, 6.9)
5	45.9, s	—	41.0, s	—
6	91.8, s	—	56.9, d	2.24 (d; 4.6)
7	175.5, s	—	201.8, s	—
8	29.1, t	2.50 (dd; 20.3, 9.4)	133.9, d	6.41 (s)
		2.65 (dd; 20.3, 9.4)		
9	24.5, t	2.32 (t; 9.4)	143.6, d	6.40 (s)
10	46.6, t	2.69 (s)	74.9, s	—
11	207.6, s	—	26.4, d	2.54 (m)
12	32.6, q	2.10 (s)	15.2, q	0.69 (d; 6.5)
13	15.4, q	0.94 (d; 7.8)	64.7, t	3.19 (t; 12.2)
				3.74 (dd; 12.2, 6.5)
14	17.7, q	1.12 (s)	13.7, q	0.74 (d; 6.9)
15			17.6, q	1.05 (s)
OH		2.81 (1H, exchangeable)		1.87 (3H, exchangeable)

[a]Data were recorded in $CDCl_3$ at 100 for ^{13}C and 400 MHz for ^{1}H nmr. Values are in ppm for TMS, coupling constants (*J*) are in Hz.

these observations indicated that the C-13 and C-14 methyl groups were on the same face of the molecule, while H-1, H_2-10 were axial and situated on the opposite face; the C-13 methyl must be axial and C-14 methyl equatorial. In addition, the observation of an nOe between C-13 methyl and H-8, H-9 enabled the assignment of the orientation of the spirolactone ring as shown in structure 1.

In the cd spectrum of **1**, a positive Cotton effect [$\Delta\epsilon = +5.3$ (206 nm)] for the $n \rightarrow \pi^*$ transition of the γ-lactone was observed (9), indicating that the absolute stereochemistry of **1** may be assigned as 1*R*, 4*S*, 5*R*, 6*R*. A preliminary account of the structure elucidation of **1** has been published (6).

The co-occurrence of **1** and 2-deoxy-12-oxolemnacarnol is of interest from a biogenetic point of view. 2-Deoxy-12-oxolemnarcarnol appears to be a precursor of the rare spirolactone. We propose a biogenetic trans ring opening of the epoxide and the simultaneous cleavage of the C-6–C-7 bond followed by γ-lactone formation to construct the molecule of **1**. Pathylactone A is the first example of a γ-spirolactone norsesquiterpenoid from a marine organism.

Parathylone [**2**] crystallized as colorless needles. The molecular formula of parathylone was established as $C_{15}H_{24}O_4$ on the basis of eims, $[M]^+$ 268, along with ^{13}C-nmr DEPT data (Table 1). Its uv γ max 219 nm (ε 8150, EtOH) and ir spectra (1655, 3452–3418 cm^{-1}) showed absorbances characteristic of an α,β-unsaturated ketone moiety and OH groups. Its ^{13}C-nmr data [δ 73.05 (t), 64.65 (t), 74.94 (s)] together with the data of ^{1}H-nmr [1.87 (3×H exchangeable), 3.19, 3.74 (H_2-13), 3.80 (H-1)] clearly revealed the presence of a primary, a secondary,

and a tertiary hydroxyl group. Considering the unsaturation from the conjugated ketone, this molecular formula indicated that **2** was bicyclic.

^{1}H-^{1}H COSY and ^{1}H-^{13}C COSY permitted establishment of two proton systems: one at C-1 through C-4, and another at C-6 through C-13. Connection of the C-6 methine to the C=O group was suggested by H-6 resonating as a doublet at δ 2.24. The connectivity of these units was assigned on the basis of ^{1}H-^{13}C long range COSY spectra. Two- or three-bond coupling from the methyl protons at C-15 to C-4, C-6 and C-10, and from H-8 to C-7 enabled linking of the units as partial structure **A**. The important observations of the coupling from H-9 to C-10 and from H-1 to C-10 led to the molecular structure of parathylone as **2**. Comparison of the ^{13}C-nmr chemical shifts of parathylone with those reported for other sesquiterpenes of the nardosinane type supported the structure assignment (3–5).

The carbon-carbon double bond was assigned the *Z* geometry based upon the very small $J_{8,9}$(<0.1 Hz) value. The coupling constant ($J_{1,2}$=2.8 Hz) suggested the H-1 was equatorial; consequently, the OH group at C-1 was axial. H-4 was assigned as axial due to its coupling constant (11.4, 4.4). An unusual downfield shift of the methyl protons at C-15 was contributed by the deshielding of 8,9 double bond indicating clearly that the ring fusion must be trans and that the OH group at C-10 was axial as well. Since many nardosinane-type sesquiterpenoids in nature have a 1,10-epoxide on the opposite face of the methyl groups (C-14, C-15), these trans diaxial OH groups were evidently formed as the result of a biogenetic trans ring opening of the corresponding epoxide.

The stereochemistry of C-6 and C-11 was resolved by NOESY spectroscopy. An nOe correlation between H-6 and H-12, H-14, H-15 showed that they are on the same face of the molecule, indicating H-6 to be equatorial and the substituent axial. It is interesting to note that the primary alcohol and the ketone group may be engaged in H bonding. The ir spectrum of a dilute solution of **2** in CCl_4 gave a strong OH stretching broad band at 3457–3331 cm^{-1} ($\Delta\nu$ 126 cm^{-1}), which indicated the presence of an H bond (10). Further lowering the concentration by about 3 times resulted in reduction of intensity of the OH band. Therefore the OH group at C-11 was H-bonded to the ketone group and constrained the rotation about the C-6–C-11 bond. Combination of the observation of an nOe between H-12 and H-6, H-14, H-15 with the lack of such effect between H-11 and any other protons enabled the assignment of the configuration at C-11 as shown, which is in agreement with other sesquiterpenoids isolated from the same soft coral (2,3).

To our knowledge, most nardosinane-type sesquiterpenes have an olefinic bond situated at 1(10); **2** is the first nardosinane-type sesquiterpene with an 8,9 double bond.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Nmr spectra were recorded on a JNM-GX400 instrument operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. A VG analytical ZAB-HF-3F mass spectrometer was used. Ir spectra were recorded on a Nicolet 5DX FT-IR spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter.

ANIMAL MATERIAL.—The soft coral *P. thyrsoides* was collected from the Xisha Islands in the South China Sea. A voucher specimen is deposited in the Reseach Center of Organic Natural Products, Zhongshan University, Guangzhou, China.

EXTRACTION AND ISOLATION.—Chopped dry specimen (1.5 kg) was extracted three times with EtOH. The concentrated extract was partitioned between EtOAc and H_2O. The EtOAc-soluble fraction (80 g) was chromatographed on Si gel eluting with Me_2CO/petroleum ether mixtures of increasing polarity. The first fraction was further separated by preparative tlc [petroleum ether-EtOAc (1:3)]. Compound **1** (200 mg, 0.013%) was obtained. The second fraction was subjected to

a vacuum chromatography on Si gel H using a solvent system consisting of EtOAc-$CHCl_3$ (1:10) to give parathylone [**2**], 20 mg (0.0013%).

Pathylactone A [**1**].—Colorless needles: mp 44.5–47.0; $[\alpha]_D$ −7.8 (c=0.041, MeOH); ir (KBr) 3490, 2886, 1780, 1719, 1444, 1360, 1221, 1178, 1130, 1020, 930, 780 cm^{-1}; ^1H and ^{13}C nmr see Table 1; eims *m/z* (rel. int.) $[M]^+$ 254 (7), 237 (11), 215 (50), 193 (16), 179 (33), 167 (84), 152 (30), 125 (68), 119 (100), 111 (66), 91 (18), 69 (23), 55 (42).

Parathylone A [**2**].—Colorless needles: mp 108.5–109.5; $[\alpha]_D$ −16.0 (c=0.050, MeOH); ir (KBr) 3452, 3418, 3394, 2962, 2938, 2872, 1655, 1462, 1387, 1259, 1203, 1140, 1078, 1048, 967, 934, 871 cm^{-1}; ^1H and ^{13}C nmr see Table 1; eims *m/z* (rel. int.) $[M]^+$ 268 (1), $[M-H_2O]^+$ 250 (13), $[M-2H_2O]^+$ 232 (20), 221 (100), 205 (9), 191 (21), 177 (58), 159 (21), 149 (29), 136 (43), 119 (37), 109 (48), 95 (51), 81 (52), 69 (61), 55 (90).

2-Deoxy-12-oxolemnacarnol.—Colorless needles: mp 166.0–167.0; ir (KBr) 3500, 1760, 1670, 1462, 1265; ms $[M]^+$ 250 (100). Identified as 2-deoxy-12-oxolemnacarnol by comparison with literature data (1).

11,12-Dihydroxyeremophila-6,10-diene.—Colorless oil; eims $[M]^+$ 236, $[M-H_2O]^+$ 218, $[M-MeOH]^+$ 205. Identified as 11,12-dihydroxyeremophila-6,10-diene by comparison with literature data (4).

Compound **3**.—Colorless needles: mp 163.5–164.5; $[\alpha]_D$ −276 (c=0.1, $CHCl_3$); ir (KBr) 1706 cm^{-1}. The ^1H- and ^{13}C-nmr data were consistent with those of the compound reported previously (5).

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