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Pinnigorgiols A–C, 9,11-secosterols with a rare ring arrangement from a gorgonian coral *Pinnigorgia* sp.

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ABSTRACT

Pinnigorgiols A–C (**1**–**3**), three novel 9,11-secosterols with a rare carbon skeleton arrangement, were isolated from a gorgonian coral identified as *Pinnigorgia* sp. Compounds **1**–**3** possess novel carbon skeletons, which include a tricyclo[5,2,1,1]decane ring. The structures of **1**–**3** were established on the basis of spectroscopic methods. The novel compounds **1**–**3** were tested for in vitro cytotoxicity in hepatic stellate cells (HSCs) and displayed inhibitory effects on the generation of superoxide anions and the release of elastase by human neutrophils. Proliferation of HSCs plays a key role in the pathogenesis of liver fibrosis.

1. Introduction

Previous studies on the chemical constituents of marine invertebrates have led to the isolation of various 9,11-secosterols from soft corals,[1,2] gorgonian corals,[3–5] sponges,[6,7] and mollusks.[8] Compounds of this type have exhibited a diverse array of pharmacological activities, such as anticancer,[1,2,8] antimicrobial,[3] antiproliferative,[4,5] anti-inflammatory,[5] and antihistaminic activities.[6] Our chemical examination of the gorgonian coral *Pinnigorgia* sp. led to the isolation of pinnigorgiols A–C (**1**–**3**) (Fig. 1), which were found to possess an unprecedented carbon skeleton.

2. Results and discussion

Pinnigorgiol A (**1**) was obtained as a yellow oil and had the molecular formula $C_{28}H_{44}O_5$ as determined by HRESIMS at *m/z* 461.3231 (calcd for $C_{28}H_{44}O_5$+H, 461.3262), requiring seven degrees of unsaturation. The IR absorptions of **1** showed the presence of hydroxy (ν_{max} 3460 cm^{-1}), and ketonic carbonyl (ν_{max}

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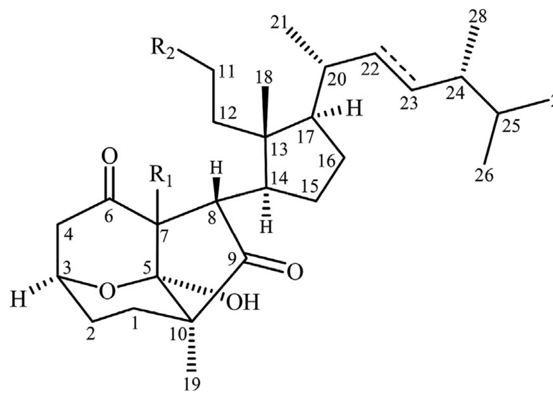

1: R_1=α-H, R_2=OH, Δ^{22}
2: R_1=α-H, R_2=OH
3: R_1=β-H, R_2=OAc, Δ^{22}

Fig. 1. The structures of pinnigorgiols A–C (**1**–**3**).

1699 cm^{-1}) groups. The ^{13}C NMR and DEPT data of **1** (Table 1) indicated the presence of 28 carbons, including six methyls, seven sp^3 methylenes (including one oxymethylene, δ_C 59.0), eight sp^3 methines (including one oxymethine, δ_C 70.3), one disubstituted double bond (δ_C 133.9 and 133.1), and five quaternary carbons (including one hemiketal carbon, δ_C 101.4 and two ketonic carbonyls, δ_C 216.6 and 208.0). The ^1H NMR spectrum (Table 1) exhibited six methyl signals at δ_H 1.11 (3H, s), 0.98 (3H, d, J=7.0 Hz), 0.91 (3H, d, J=7.5 Hz), 0.88 (3H, s), 0.83 (3H, d, J=6.5 Hz), and 0.81 (3H, d, J=6.5 Hz). The signal at δ_H 3.83 (2H, m) was assumed to be one oxymethylene group.

The ^1H–^1H COSY and HMBC correlations were further used to establish the molecular skeleton of **1** (Fig. 2). From the ^1H–^1H COSY spectrum of **1**, it was possible to establish the partial structure units from H_2-1/H_2-2/H-3/H_2-4, H-8/H-14/H_2-15/H_2-16/H-17/H-20/H-

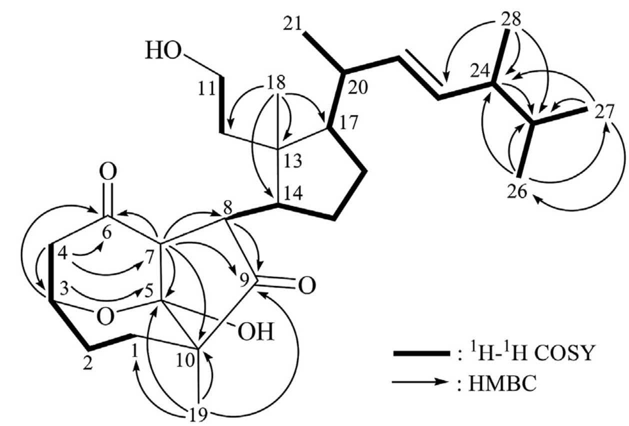

Fig. 2. ^1H–^1H COSY and selective key HMBC correlations of **1**.

Table 1
^1H and ^{13}C NMR data for secosterol **1**

C/H	δ_H[a]	δ_C[b]	δ_H[c]	δ_C[d]
1/1′	1.41 m; 1.26 m	26.5 (CH_2)[f]	1.41 m	27.9 (CH_2)
2/2′	2.01 tt (14.0, 5.0)[e]; 1.45 m	24.0 (CH_2)	1.92 m; 1.32 d (13.0)	25.1 (CH_2)
3	4.62 br s	70.3 (CH)	4.57 br s	71.2 (CH)
4/4′	2.91 dd (16.5, 7.0); 2.40 d (16.5)	43.9 (CH_2)	2.84 dd (16.0, 7.0); 2.41 d (16.0)	45.0 (CH_2)
5		101.4 (C)		102.8 (C)
6		208.0 (C)		209.3 (C)
7	3.22 s	59.6 (CH)	3.50 s	63.0 (CH)
8	3.21 d (9.6)	47.7 (CH)	3.65 d (8.0)	47.7 (CH)
9		216.6 (C)		218.1 (C)
10		50.0 (C)		51.5 (C)
11	3.83 m	59.0 (CH_2)	4.18 m; 4.09 m	58.6 (CH_2)
12/12′	1.89 dt (15.5, 5.5); 1.74 m	39.5 (CH_2)	2.24 m; 2.18 m	41.8 (CH_2)
13		46.6 (C)		47.7 (C)
14	2.19 m	47.2 (CH)	2.60 dt (10.5, 8.5)	50.1 (CH)
15	1.80 m	26.2 (CH_2)	2.18 m; 2.04 m	26.7 (CH_2)
16/16′	1.60 m; 1.45 m	24.1 (CH_2)	1.62 m; 1.53 m	25.7 (CH_2)
17	1.54 m	49.6 (CH)	1.74 m	50.4 (CH)
18	0.88 s	17.2 (CH_3)	1.19 s	18.4 (CH_3)
19	1.11 s	12.1 (CH_3)	1.44 s	14.0 (CH_3)
20	2.18 m	36.9 (CH)	2.33 q (7.0)	38.8 (CH)
21	0.98 d (7.0)	22.7 (CH_3)	1.08 d (6.5)	23.1 (CH_3)
22	5.27 dd (15.5, 8.0)	133.9 (CH)	5.35 dd (15.5, 8.5)	135.7 (CH)
23	5.19 dd (15.5, 8.0)	133.1 (CH)	5.24 dd (15.5, 8.5)	133.5 (CH)
24	1.86 m	43.1 (CH)	1.88 m	43.9 (CH)
25	1.45 m	33.1 (CH)	1.46 m	34.0 (CH)
26	0.83 d (6.5)	20.0 (CH_3)	0.86 d (6.5)	20.9 (CH_3)
27	0.81 d (6.5)	19.7 (CH_3)	0.85 d (6.5)	20.5 (CH_3)
28	0.91 d (7.5)	17.5 (CH_3)	0.95 d (7.0)	18.4 (CH_3)

[a] Spectrum recorded at 500 MHz in $CDCl_3$.
[b] Spectrum recorded at 125 MHz in $CDCl_3$.
[c] Spectrum recorded at 500 MHz in pyridine-d_5.
[d] Spectrum recorded at 125 MHz in pyridine-d_5.
[e] J values (in Hz) in parentheses.
[f] Multiplicity deduced from DEPT and HMQC spectra and indicated by the usual symbols.