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New 8-hydroxybriarane diterpenoids from the gorgonians *Junceella juncea* and *Junceella fragilis* (Ellisellidae)

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Abstract

Four new 8-hydroxybriarane diterpenoids, including junceols A–C (**1**–**3**) and fragilide D (**4**), have been isolated from the gorgonian corals *Junceella juncea* and *Junceella fragilis*, respectively. The structures of briaranes **1**–**4** were elucidated by the interpretations of spectral data analysis. Briaranes **1**–**3** have displayed inhibitory effects on superoxide anion generation by human neutrophils.

Keywords: *Junceella*; Junceol; Fragilide; Briarane; Superoxide anion

1. Introduction

We recently reported a series of novel terpenoid derivatives from the Formosan octocorals, including the briarane diterpenoids from *Briareum* sp.,[1] *Briareum excavatum*,[2–4] *Ellisella robusta*,[5–8] *Junceella fragilis*,[4,9–15] *Junceella juncea*;[11,16] and the caryophyllane sesquiterpenoids from *Rumphella antipathies*.[17–22] In continuation of our search for bioactive natural substances from the invertebrates collected off Taiwanese waters, we have further isolated four new 8-hydroxybriarane diterpenoids, junceols A–C (**1**–**3**) and fragilide D (**4**), from the gorgonians *J. juncea* and *J. fragilis* (Ellisellidae), respectively. Briarane-type natural products are suggested to be originally synthesized by host corals,[11,23] and the compounds of this type were proven to possess various biological activity.[24,25] In this paper, we described the isolation, structure determination, and biological activity of above new metabolites. The structures, including the relative configurations of briaranes **1**–**4**, were elucidated by spectroscopic methods. Briaranes **1**–**3** showed inhibitory effects on superoxide anion generation by human neutrophils.

2. Results and discussion

2.1. Isolation and structure determination of junceols from *J. juncea*

Previous chemical investigations of the gorgonian coral *J. juncea* have yielded a series of interesting new natural products including 37 briaranes, juncins A–Z,[16,26–30] (+)-gemmacolides A and B,[27] juncin ZI,[30] and juncenolides A–G;[31–35] five

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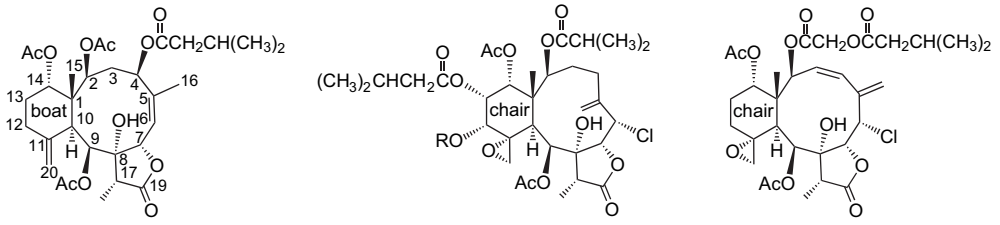

1 **2**:R= Ac , **3**:R=C(O)$CH_2CH(CH_3)_2$ **4**

steroid derivatives, junceellosides A–D[36] and 4′-*O*-acetyl-3-*O*-[β-D-arabinopyranosyloxy]-cholest-5-ene-3β,19-diol;[37] a glycerol derivative, 1,2-*O*-[2′-hydroxyoctadecyl]-glycerol;[37] and a sphingolipid, (2*S*,3*R*,4*E*)-1,3-dihydroxy-2-[(nonadecanoyl)-amino]-octadec-4-ene.[38]

Junceol A (**1**) was obtained as a white powder. The HRESIMS data recorded at 615.2780 established the molecular formula of **1** as $C_{31}H_{44}O_{11}$ (calcd for $C_{31}H_{44}O_{11}$+Na, 615.2781). The IR absorptions of **1** showed the presence of 3470, 1786, and 1733 cm^{-1}, consistent with the presence of hydroxy, γ-lactone, and ester groups. From the ^{13}C NMR data of **1** (Table 1), the presence of a trisubstituted olefin and an exocyclic carbon–carbon double bond were deduced from the signals of four carbons resonating at δ 151.1 (s, C-11), 144.5 (s, C-5), 123.8 (d, CH-6), and 113.0 (t, CH_2-20), and further supported by three olefin proton signals at δ 5.79 (1H, dd, *J*=10.4, 1.2 Hz, H-6), 5.03 (1H, s, H-20a), and 4.88 (1H, s, H-20b) in the ^1H NMR spectrum of **1** (Table 2). Furthermore, in the ^{13}C NMR spectrum, five carbonyl resonances appeared at δ 175.9 (s, C-19), 172.2 (s, ester carbonyl), 170.5 (s, ester carbonyl), 170.3 (s, ester carbonyl), and 169.3 (s, ester carbonyl), confirming the presence of a γ-lactone and four esters in **1**. In the ^1H NMR spectrum, three acetate methyls (δ 1.90, 3H, s; 2.00, 3H, s; 2.22, 3H, s) and an isovaleroxy group (δ 0.95, 2×3H, d, *J*=6.8 Hz; 2.12, 1H, m; 2.17, 2H, d, *J*=7.6 Hz) were observed. The ^1H NMR spectrum of **1** also showed the presence of a vinyl methyl (δ 2.23, 3H, d, *J*=1.2 Hz, H_3-16), a methyl doublet (δ 1.12, 3H, d, *J*=7.2 Hz, H_3-18), a methyl singlet (δ 1.10, 3H, s, H_3-15), two aliphatic methine protons (δ 3.31, 1H, d, *J*=5.6 Hz, H-10; 2.47, 1H, q, *J*=7.2 Hz, H-17), five oxymethine protons (δ 5.59, 1H, d, *J*=10.4 Hz, H-7; 5.26, 1H, d, *J*=5.6 Hz, H-9; 5.22, 1H, dd, *J*=13.6, 5.2 Hz, H-4; 4.77, 1H, d, *J*=4.0 Hz, H-2; 4.70, 1H, d, *J*=4.0 Hz, H-14), and three pairs of aliphatic methylene protons (δ 2.75, 1H, dd, *J*=13.6, 13.6 Hz; 1.95, 1H, m, H_2-3; 2.27, 1H, m; 2.09, 1H, br t, *J*=6.8 Hz, H_2-12; 2.04, 1H, m; 1.77, 1H, m, H_2-13) were observed in the ^1H NMR spectrum of **1**.

From the ^1H–^1H COSY spectrum of **1** (Fig. 1), it was possible to establish the separate spin systems from H-2/3/4; H-6/7; and H-9/10. These data, together with the HMBC correlations between H-2/C-1, -3, -4, -10; H_2-3/C-1, -2, -4, -5; H-4/C-3, -5, -6; H-6/C-4, -7; H-7/C-5, -6, -8; H-9/C-7, -8, -10; and H-10/C-1, -2, -8, -9 (Fig. 1 and Table 3), established the connectivity from C-1 to C-10 within the 10-membered ring. A vinyl methyl attached at C-5 was confirmed by the allylic coupling between H_3-16 and H-6 and by the HMBC correlations between H-4/C-16; H-6/C-16; and H_3-16/C-4, -5, -6. The methylenecyclohexane ring, which is fused to the 10-membered ring at C-1 and C-10, was established by the ^1H–^1H COSY correlations between H_2-12/H_2-13 and H_2-13/H-14; and by the HMBC correlations between H-2/C-14; H-9/C-11; H-10/C-11, -12, -14, -20; H_2-12/C-10, -11, -13, -20; H_2-13/C-1, -12, -14; and H-14/C-1, -10, -12. The exocyclic carbon–carbon bond, which is attached to the six-membered

Table 1
^{13}C NMR data for diterpenoids **1**–**3**[a]

Position	1	2	3
1	47.4 (s)[b]	47.3 (s)	47.3 (s)
2	72.0 (d)	72.4 (d)	72.2 (d)
3	38.0 (t)	28.3 (t)	28.4 (t)
4	72.4 (d)	33.9 (t)	34.1 (t)
5	144.5 (s)	146.7 (s)	146.5 (s)
6	123.8 (d)	53.9 (d)	54.1 (d)
7	77.2 (d)	81.2 (d)	80.9 (d)
8	82.9 (s)	81.3 (s)	81.2 (s)
9	71.2 (d)	72.2 (d)	71.6 (d)
10	42.3 (d)	35.3 (d)	35.6 (d)
11	151.1 (s)	56.9 (s)	56.7 (s)[c]
12	25.7 (t)	73.6 (d)	73.1 (d)
13	27.6 (t)	66.5 (d)	66.5 (d)
14	73.7 (d)	73.0 (d)	72.9 (d)
15	15.1 (q)	14.3 (q)	14.3 (q)
16	26.1 (q)	121.2 (t)	121.1 (t)
17	42.5 (d)	51.4 (d)	51.4 (d)
18	6.4 (q)	5.9 (q)	5.7 (q)
19	175.9 (s)	174.3 (s)	174.3 (s)
20	113.0 (t)	50.4 (t)	50.6 (t)
Acetates	169.3 (s)	169.9 (s)	169.9 (s)
	21.8 (q)	20.8 (q)	20.9 (q)
	170.5 (s)	169.3 (s)	169.3 (s)
	20.9 (q)	21.2 (q)	21.2(q)
	170.3 (s)	169.2 (s)	
	21.2 (q)	20.6 (q)	
Isovalerates	172.2 (s)	171.8 (s)	172.1 (s)
	43.3 (t)	42.6 (t)	171.8 (s)
	25.9 (d)	24.9 (d)	43.5 (t)
	22.5 (q)	22.3 (q)	42.6 (t)
	22.3 (q)	22.3 (q)	25.6 (d)
			25.0 (d)
			22.3 (4×q)
Isobutyrates		177.1 (s)	177.4 (s)
		34.0 (d)	34.1 (d)
		19.1 (q)	19.1 (q)
		17.9 (q)	17.9 (q)

[a] Spectra measured at 100 MHz in $CDCl_3$ at 25 °C.
[b] Multiplicity deduced by DEPT and HMQC spectra and indicated by usual symbols.
[c] Due to the broad signal, the ^{13}C NMR chemical shift for C-11 in **3** was assigned by the assistances of HMBC correlations.