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BRIAEXCAVATOLIDE W, A NEW DITERPENOID FROM *BRIAREUM EXCAVATUM*

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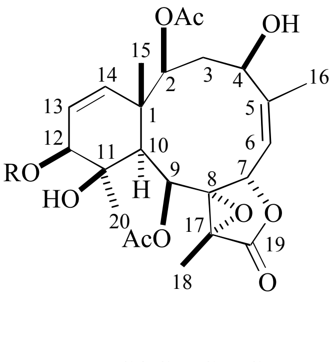
Abstract – A new briarane-type diterpenoid, briaexcavatolide W (**1**), has been isolated from the gorgonian coral *Briareum excavatum*. The structure was elucidated by spectroscopic methods.

In the previous studies by our research group, a series of new briarane-type diterpenoids, including excavatolides A–M,[1,2] U–Z,[3] and briaexcavatolides A–V,[4–7] have been isolated from the gorgonian coral *Briareum excavatum* (Nutting) (Anthozoa, Octocorallia, Gorgonacea, Briareidae).[8] Compounds of this type continue to intrigue investigators because of the structural novelty, complexity and various biological activities.[9] In this paper, we report here a minor new polyoxygenated diterpenoid, briaexcavatolide W (**1**), from the gorgonian *B. excavatum*.

Briaexcavatolide W (**1**) was obtained as a white powder. The HRFABMS of **1** provided a pseudomolecular ion $[M + H]^+$ at *m/z* 551.2484, indicating the molecular formula $C_{28}H_{38}O_{11}$ and ten degrees of unsaturation for this metabolite. The IR spectrum revealed absorption bands for hydroxyl (3463 cm^{-1}), and ester carbonyl (1734 cm^{-1}) moieties. The FABMS of **1** exhibited peaks at *m/z* 551 $(M + H)^+$, 533 $(M + H – H_2O)^+$, 491 $(M + H – HOAc)^+$, 473 $(M + H – HOAC – H_2O)^+$, 463 $(M + H – C_3H_7CO_2H)^+$, 455 $(M + H – HOAC – 2H_2O)^+$, 445 $(M + H – C_3H_7CO_2H – H_2O)^+$, 395 $(M + H – 2HOAC – 2H_2O)^+$, 385 $(M + H – C_3H_7CO_2H – HOAC – H_2O)^+$, 325 $(M + H – C_3H_7CO_2H – 2HOAC – H_2O),^+$ and 307 $(M + H – C_3H_7CO_2H – 2HOAC – 2H_2O)^+$, suggesting the presence of a butyryloxy, two acetoxy, and two hydroxyl groups in **1**. From the ^{13}C NMR spectral data (Table 1), a trisubstituted and a disubstituted double bonds were deduced from the signals of four carbons resonating at δ 147.7 (s), 141.8 (d), 122.1 (d) and 120.4 (d). An epoxyl group was confirmed from the signals of two quaternary oxygen-bearing carbons at δ 70.1 (s) and 62.4 (s), and from the chemical shift of the tertiary methyl protons, H_3-18 (δ 1.61, 3H, s). In the ^{13}C spectrum of **1**, four carbonyl resonances appeared at δ 172.2 (s), 171.1 (s), 170.2 (s), and 169.3 (s), and supported the presence of a γ-lactone and three additional esters in **1**. Two of the esters were identified as acetates by the presence of methyl resonances in the ^1H NMR spectrum at δ 2.23 (3H, s) and 2.10 (3H, s). The other ester was found to be an *n*-butyryloxy group based on NMR studies, including an ^1H–^1H COSY spectrum (Figure 1), which revealed seven contiguous protons (δ 2.28, 2H, t, *J* = 7.5 Hz; 1.65, 2H, m; 0.96, 3H, t, *J* = 7.5 Hz). The carbon signal at δ 172.2 (s) revealed correlation with the signals of the methylene protons resonating at δ 2.28 and 1.65 in the HMBC spectrum and was consequently assigned as the carbonyl carbon of the *n*-butyrate (Figure 1). From the ^1H–^1H COSY spectrum of **1**, it was possible to establish the proton sequences of H-2/H_2-3 and H_2-3/H-4; H_3-16/H-6; H-6/H-7; H-9/H-10; and H-12/H-13 and H-13/H-14. Furthermore, the methyl groups attached at C-5 and C-11 were confirmed by the HMBC correlations between H_3-16/C-4, C-5, C-6; and H_3-20/C-10, C-11, C-12. The ring-junctured C-15 methyl group was positioned at C-1 from the HMBC correlations between H_3-15/C-1, C-2, C-10, C-14. The *n*-butyryloxy group positioned at C-12 was confirmed from the connectivity between H-12 (δ 4.79) and carbonyl carbon (δ 172.2) of the *n*-butyryloxy group. In addition, the HMBC correlations also revealed that two acetates should attach at C-2 and C-9, respectively. On the basis of above analyses, two hydroxyl groups have to be positioned at C-4 and C-11, respectively. These data, together with the HMBC correlations between H_3-18/C-8, C-17, C-19, unambiguously established the molecular framework of **1**.



1: R = $COCH_2CH_2CH_3$

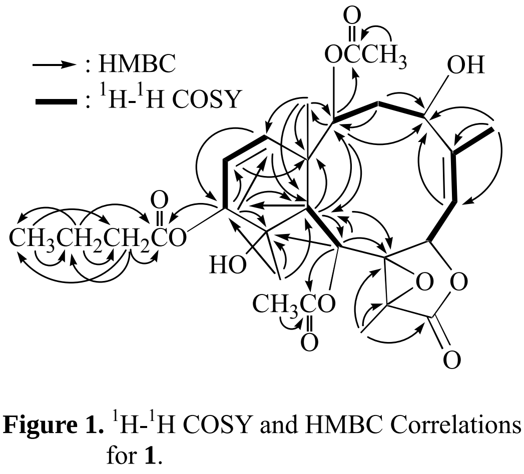


Figure 1. ^1H-^1H COSY and HMBC Correlations for **1**.

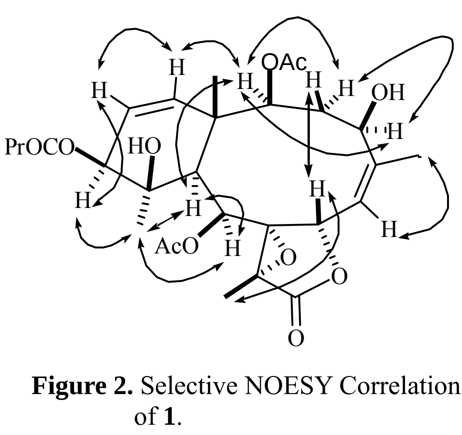


Figure 2. Selective NOESY Correlations of **1**.

The relative stereochemistry of **1** was elucidated from the vicinal ^1H–^1H coupling constants and by an NOESY experiment (Figure 2). The *cis* geometry of the C-13/C-14 double bond was indicated by a 10.5 Hz coupling constant between H-13 (δ 5.82, dd, *J* = 10.5, 5.5 Hz) and H-14 (δ 5.67, d, *J* = 10.5 Hz).

Moreover, strong NOE correlations were observed between H-10 and H-2, H-9, and H_3-20; while H_3-15 did not show NOE interactions with the above protons. Assuming the β-orientation of H_3-15, all of the protons of H-2, H-9, and H_3-20 should be positioned on the α face. One proton attaching at C-3 and resonating at δ 2.12 (m) was found to exhibit NOE correlations with H-2, and was assigned as H-3α. H-4 exhibited NOE interactions with both H-2 and H-3α, and was positioned on the α face. H-7 showed NOE correlations with H-3β and H_3-18, confirming the β-orientations for both of H-7 and H_3-18. The *n*-butyryloxyl group attaching at C-12 was placed on the β face by the observed NOE correlations between H-12 and H_3-20. On the basis of the above results, the structure of **1**, including the relative configuration, was elucidated unambiguously.

Table 1. ^{1}H and ^{13}C NMR Spectral Data for Briaexcavatolide W (**1**)

Position	^{1}H	^{13}C
1		45.5 (s)
2	4.49 (1H, d, *J* = 6.0 Hz)	77.8 (d)
3α/β	2.12 (1H, m); 2.82 (1H, dd, *J* = 15.0, 12.0 Hz)	41.7 (t)
4	4.31 (1H, dd, *J* = 12.0, 5.0 Hz)	71.1 (d)
5		147.7 (s)
6	5.51 (1H, d, *J* = 10.0 Hz)	122.1 (d)
7	6.18 (1H, d, *J* = 10.0 Hz)	73.3 (d)
8		70.1 (s)
9	5.77 (1H, d, *J* = 4.5 Hz)	66.8 (d)
10	2.58 (1H, d, *J* = 4.5 Hz)	44.2 (d)
11		73.5 (s)
12	4.79 (1H, d, *J* = 5.5 Hz)	73.1 (d)
13	5.82 (1H, dd, *J* = 10.5, 5.5 Hz)	120.4 (d)
14	5.67 (1H, d, *J* = 10.5 Hz)	141.8 (d)
15	1.27 (3H, s)	18.1 (q)
16	2.07 (3H, s)	25.7 (q)
17		62.4 (s)
18	1.61 (3H, s)	9.7 (q)
19		171.1 (s)
20	1.34 (3H, s)	28.0 (q)
acetate methyls	2.23 (3H, s)	21.7 (q)
	2.10 (3H, s)	21.1 (q)
acetate carbonyls		170.2 (s)
		169.3 (s)
n-butyrate		172.2 (s)
	2.28 (2H, t, *J* = 7.5 Hz)	36.5 (t)
	1.65 (2H, m)	18.4 (t)
	0.96 (3H, t, *J* = 7.5 Hz)	13.7 (q)

EXPERIMENTAL

General Experimental Procedures. Melting point was determined using a Fisher-Johns melting point apparatus and were uncorrected. Optical rotation values were measured on a JASCO DIP-370 digital polarimeter. IR spectra were recorded on a JASCO FT/IR-5300 infrared spectrophotometer. FABMS were obtained on a VG QUATTRO GC/MS spectrometer. HRFABMS were recorded on a JEOL JMS SX/SX 102A mass spectrometer. NMR spectra were recorded with a VARIAN UNITY INOVA 500 FT-NMR at 500 MHz for ^{1}H and 125 MHz for ^{13}C, in $CDCl_3$, using TMS as an internal standard. Silica gel (Merck, 230–400 mesh) was used during column chromatography. Precoated silica gel plates (Merck, Kieselgel 60 F_{254}) were used for analytical TLC. All solvents used were analytical grade.

Animal Material. The gorgonian *B. excavatum* was collected by hand using scuba in July 1995, off the Southern Taiwan coast at depths of 4–5 m, and was stored in a freezer until extraction. This organism was identified by comparison with descriptions.[9] A voucher specimen was deposited in the Department of Marine Resources, National Sun Yat-Sen Universtiy (specimen no. KTSC-103).

Extraction and Isolation. The extraction scheme followed the standard procedures of our previous reports.[1,2] The EtOAc extract of *B. excavatum* was separated by silica gel column chromatography using hexanes and hexanes–EtOAc mixtures of increasing polarity. Briaexcavatolide W (**1**) was eluted with hexanes–EtOAc (3:2).

Briaexcavatolide W (1): White powder (1.2 mg); mp 97.5–98.9 °C (from EtOAc); $[\alpha]_D^{27}$ -129° (c = 0.24, $CHCl_3$); IR (neat, $CHCl_3$): ν_{max} 3463, 1734 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; FABMS *m/z* (rel. int.) 551 [1, $(M + H)^+$], 533, 491, 473, 463, 455, 445, 395, 385, 325, 307; HRFABMS *m/z* 551.2484 (calcd for $C_{28}H_{38}O_{11}$ + H, 551.2493).

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