Briaexcavatolides S−V, Four New Briaranes from a Formosan Gorgonian *Briareum excavatum*

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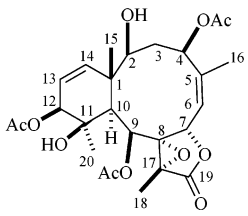
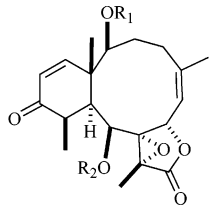
Four new briarane-type diterpenoids, briaexcavatolides S−V (**1**−**4**), have been isolated from a Formosan gorgonian *Briareum excavatum*. The structures, including the relative stereochemistry of these new metabolites, were established by extensive 1D and 2D NMR spectroscopic methods and by comparison of the related spectral data with those of known analogues.

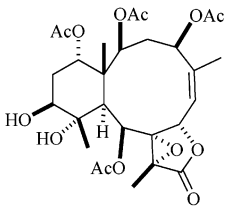
Previous investigations on the secondary metabolites of the Indo-Pacific gorgonian *Briareum excavatum* (Nutting) (phylum Cnidaria, class Anthozoa, subclass Octocorallia, order Gorgonacea, family Briareidae) have resulted in the isolation of a series of diterpenoids with a briarane carbon skeleton. These metabolites include excavatolides A−Z,[1−4] briaexcavatolides A−R,[5−7] and briantheins A−C.[8] In addition, over 300 briarane-type diterpenoids have been isolated from various marine organisms, and some of these metabolites were proven to possess interesting biological activities (e.g., cytotoxicity, antiinflammatory, antiviral, insecticidal, antifouling, immunomodulatory effect, antibacterial, and biotoxin).[9] Recently, several new briaranes have been discovered by different research groups.[10−14] Our continuing study on the chemical constituents of the Formosan gorgonian coral *Briareum excavatum* also has further yielded four new briaranes, briaexcavatolides S−V (**1**−**4**). The structures of these four minor components were elucidated by spectroscopic methods, including extensive 2D NMR spectral data analyses.



1



2: R_1 = Ac, R_2 = H
5: R_1 = $COCH_2CH_2CH_3$, R_2 = Ac



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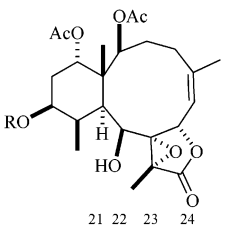

4: R = $COCH_2CH_2CH_3$
6: R = Ac

Briaexcavatolide S (**1**) was obtained as a white powder. The HRFABMS of **1** provided a pseudomolecular ion $[M + H]^+$ at *m/z* 523.2177, indicating the molecular formula $C_{26}H_{34}O_{11}$ and 10 degrees of unsaturation for this metabolite. The IR absorptions of **1** showed the presence of hydroxy (3449 cm^{-1}), γ-lactone (1780 cm^{-1}), and ester carbonyl (1732 cm^{-1}) groups in **1**. The FABMS of **1** exhibited peaks at *m/z* 523 $[M + H]^+$, 463 $[M + H - HOAc]^+$, 445 $[M + H - HOAc - H_2O]^+$, 403 $[M + H - 2HOAc]^+$, 385 $[M + H - 2HOAc - H_2O]^+$, 367 $[M + H - 2HOAc - 2H_2O]^+$, 343 $[M + H - 3HOAc]^+$, and 325 $[M + H - 3HOAc - 2H_2O]^+$, also suggesting the presence of three acetoxy and two hydroxy groups in the molecule of **1**. In the ^{13}C NMR data of **1** (Table 2), a trisubstituted olefin was identified by the signals of two carbons at δ 145.7 (s) and 123.4 (d), and a disubstituted olefin was found from the signals of carbons at δ 145.2 (d) and 118.8 (d). A tetrasubstituted epoxide containing a methyl substituent was confirmed from the signals of two quaternary oxygenated carbons at δ 71.4 (s) and 63.7 (s) and from the proton signal of a methyl (δ 1.59, 3H, s) (Table 1). From the ^{13}C NMR spectrum of **1**, four carbonyl resonances appeared at δ 172.1 (s), 170.7 (s), 170.2 (s), and 169.4 (s) and further confirmed the presence of a γ-lactone and three other ester groups. The esters were identified as acetates by the presence of methyl resonances in the ^1H NMR spectrum at δ 2.16 (3H, s), 2.02 (3H, s), and 1.99 (3H, s). From the above data, metabolite **1** was found to be a tetracyclic compound. The structure and all of the ^1H and ^{13}C chemical shifts of **1** were determined by the assistance of 2D NMR studies, including $^1H-^1H$ COSY and HMBC experiments (Figure 1). From the $^1H-^1H$ COSY spectrum of **1**, it was possible to establish the proton sequences from H-2 to H-4; H_3-16 to H-6; H-6 to H-7; H-9 to H-10; and H-12 to H-14. These data, together with the $^1H-^{13}C$ long-range correlations observed in the HMBC experiment, established the connectivity from C-1 to C-14 (Figure 1 and Table 3). A vinyl methyl group attached at the C-5 position was confirmed by the HMBC correlations between H_3-16 and C-4, C-5, and C-6. The cyclohexene ring, which is fused to the 10-membered ring at C-1 and C-10, was elucidated by the key HMBC correlations between H-9 and C-11; H-10 and C-11; OH-11 and C-10; H-12 and C-10; H-13 and C-1; and H-14 and C-1, C-10. The ring-junctured C-15 methyl group was positioned at C-1 from the key HMBC correlations between H_3-15 and C-1, C-2, and C-14. Furthermore, the HMBC correlations also revealed that three acetoxy groups should attach to C-4, C-9, and C-12, and the hydroxy

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Table 1. ^{1}H NMR Data for Diterpenoids **1**−**4**

position	**1**[a]	**2**[b]	**3**[c]	**4**[c]
2	3.29 dd (7.0, 6.0)[d]	5.00 d (8.5)	5.01 d (8.4)	5.01 d (7.6)
3α	2.00 m;	1.56 m;	1.98 m;	1.50 m
3β	3.11 dd (13.5, 12.0)	2.34 m	2.91 dd (15.2, 12.8)	2.78 m
4α	5.13 dd (12.0, 5.0)	1.96 br t (13.0);	5.03 m	1.86 m;
4β		2.58 dd (14.5, 7.0)		2.45 br d (12.4)
6	5.40 d (10.0)	5.40 d (8.5)	5.35 d (8.8)	5.25 d (8.4)
7	6.00 d (10.0)	5.58 d (8.5)	5.56 d (8.8)	5.49 d (8.4)
9	5.91 d (4.5)	3.82 dd (9.5, 6.0)	5.79 d (1.2)	3.81 br s
10	2.37 d (4.5)	3.57 dd (9.5, 4.5)	2.14 d (1.2)	2.26 m
11		2.75 m		2.08 m
12	4.75 d (6.0)		3.72 dd (12.8, 4.4)	5.07 m
13α	5.64 dd (11.0, 6.0)	6.02 d (10.5)	1.96 m;	1.85 m;
13β			1.59 m	1.70 m
14	6.12 d (11.0)	6.32 d (10.5)	4.81 dd (3.6, 2.0)	4.80 br s
15	1.26 s	1.38 s	1.23 s	1.29 s
16	2.04 s	1.68 s	2.15 s	1.98 s
18	1.59 s	1.61 s	1.78 s	1.55 s
20	1.31 s	1.17 d (8.0)	1.17 s	1.16 d (4.4)
2-OH	4.33 d (6.0)			
9-OH		4.96 d (6.0)		
11-OH	3.70 s			
acetate	2.16 s	2.27 s	2.24 s	2.04 s
methyls	2.02 s		2.13 s	1.98 s
	1.99 s		2.02 s	
			2.01 s	
n-butyrate				2.23 t (7.2)
				1.62 m
				0.93 t (7.2)

[a] Spectra recorded at 500 MHz in acetone-d_6 at 25 °C. [b] Spectra recorded at 500 MHz in $CDCl_3$ at 25 °C. [c] Spectra recorded at 400 MHz in $CDCl_3$ at 25 °C. [d] J values (in Hz) in parentheses. The values are in ppm downfield from TMS.

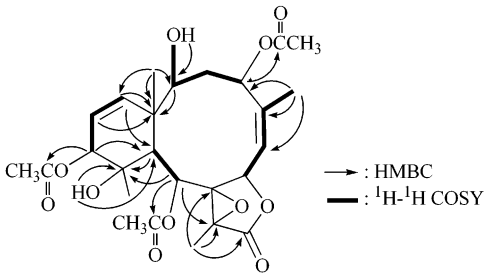

Figure 1. Selected ^{1}H−^{1}H COSY and HMBC correlations of **1**.

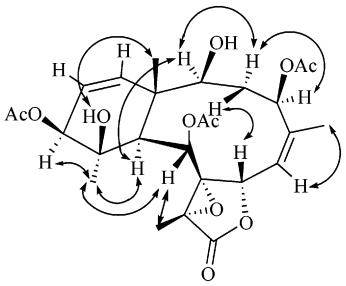

Figure 2. Selected NOE correlations of **1**.

group should be positioned at C-2 and C-11, respectively. These data, together with the HMBC correlations between H-9 and C-17 and between H_3-18 and C-8, C-17, and C-19, unambiguously established the molecular framework of **1**.

The relative stereochemistry of **1** was elucidated from the vicinal ^{1}H−^{1}H coupling constants and by a NOESY experiment (Figure 2 and Table 4). The *cis* geometry of the C-13/C-14 double bond was indicated by an 11.0 Hz coupling constant between H-13 (δ 5.64, dd, J = 11.0, 6.0 Hz) and H-14 (δ 6.12, d, J = 11.0 Hz). Moreover, in the NOESY experiment of **1**, H-10 gives NOE correlations to H-2 and H_3-20, but not to H_3-15, and OH-11 was found to show an NOE response with H_3-15, indicating that H-2, H-10, and H_3-20 are situated on the same face of the molecule and were assigned as the α-protons, since the C-15 methyl and the 11-hydroxy group are the β-substituents at C-1 and C-11, respectively. Also, H-9 showed NOE responses with H_3-18 and H_3-20. From consideration of molecular models, H-9 was found to be reasonably close to H_3-18 and H_3-20, when H-9 was α-oriented and H_3-18 was placed on the β-face. H-2 showed an NOE interaction with H-3α (δ 3.11), which further exhibited correlation with H-4α (δ 5.13), suggesting that the acetoxy group attached at the C-4 position was β-oriented. Furthermore, the NOE correlation between H_3-20 and H-12 indicated that the 12-acetoxy group was at the β-face and is *trans* to the C-20 methyl. In addition, H-7 (δ 6.00) was found to show a strong correlation with H-3β (δ 2.00), but not with H-4, suggesting the β-orientation of H-7. On the basis of the above observations, the structure of **1**, including the relative stereochemistry, was established.

The new diterpenoid briaexcavatolide T (**2**) had the molecular formula $C_{22}H_{28}O_7$ as determined by HRFABMS. Its IR spectrum exhibited a broad OH stretch at 3495 cm^{-1}, a γ-lactone carbonyl at 1780 cm^{-1}, an ester carbonyl at 1730 cm^{-1}, and an α,β-unsaturated ketone group at 1688 cm^{-1}. The latter structural moiety was confirmed by a strong UV absorption at 221 nm,[15] the presence of signals at δ 201.5 (s), 127.1 (d), and 153.3 (d) in the ^{13}C NMR spectrum (Table 2), and a mutually coupled pair of doublet signals (J = 10.5 Hz) in the ^{1}H NMR spectrum of **2** at δ 6.02 (H-13) and 6.32 (H-14), corresponding to the α- and β-olefinic protons, respectively. The FABMS of **2** showed peaks at 405 [M + H]$^+$, 345 [M + H − HOAc]$^+$, and 327 [M + H − HOAc − H_2O]$^+$, indicating the presence of an acetoxy and a hydroxy group in **2**. In the ^{1}H NMR spectrum of **2** (Table 1), an acetate methyl was observed at δ 2.27 (3H, s). Carbonyl resonances in the ^{13}C NMR spectrum of **2** at δ 172.3 (s) and 167.8 (s) suggested the presence of a γ-lactone and an acetoxy group. By the above observations, the structure of metabolite **2** could be seen to be very similar to those of a known compound, briareolide I (**5**).[16] Also, it was found that the acyloxy groups attaching at the C-2 and C-9 positions in **5** were replaced by an acetoxy and a hydroxy group, respectively, by comparing the related ^{1}H and ^{13}C NMR data of **2** with those of **5**. The locations of these two

Table 2. ^{13}C NMR Data for Diterpenoids **1**−**4**

position	**1**[a]	**2**[b]	**3**[c]	**4**[c]
1	48.0 (s)[d]	44.3 (s)	47.9 (s)	46.0 (s)
2	76.9 (d)	81.4 (d)	73.3 (d)	75.3 (d)
3	41.9 (t)	24.1 (t)	37.7 (t)	28.5 (t)
4	74.3 (d)	24.8 (t)	72.3 (d)	26.0 (t)
5	145.7 (s)	142.8 (s)	143.5 (s)	145.6 (s)
6	123.4 (d)	122.1 (d)	123.2 (d)	117.8 (d)
7	74.5 (d)	73.1 (d)	73.7 (d)	75.7 (d)
8	71.4 (s)	70.1 (s)	70.5 (s)	71.9 (s)
9	67.3 (d)	67.7 (d)	67.2 (d)	75.1 (d)
10	45.7 (d)	38.8 (d)	48.9 (d)	41.4 (d)
11	73.9 (s)	40.6 (d)	78.2 (s)	29.7 (d)
12	75.3 (d)	201.5 (s)	73.1 (d)	69.8 (d)
13	118.8 (d)	127.1 (d)	30.2 (t)	31.7 (t)
14	145.2 (d)	153.3 (d)	74.8 (d)	75.7 (d)
15	17.6 (q)	18.8 (q)	14.4 (q)	15.4 (q)
16	26.6 (q)	22.8 (q)	25.4 (q)	27.1 (q)
17	63.7 (s)	58.7 (s)	66.3 (s)	63.5 (s)
18	10.3 (q)	9.4 (q)	10.3 (q)	10.3 (q)
19	172.1 (s)	172.3 (s)	170.2 (s)	172.3 (s)
20	28.8 (q)	14.1 (q)	17.1 (q)	10.3 (q)
acetate	21.9 (q)	20.8 (q)	21.4 (q)	21.3 (q)
methyls	21.1 (q)		21.3 (q)	21.5 (q)
	21.0 (q)		21.1 (q)	
			21.1 (q)	
acetate	170.7 (s)	167.8 (s)	170.2 (s)	170.4 (s)
carbonyls	170.2 (s)		170.1 (s)	170.9 (s)
	169.4 (s)		170.0 (s)	
			168.0 (s)	
n-butyrate				172.8 (s)
				36.4 (t)
				18.4 (t)
				13.7 (q)

[a] Spectra recorded at 125 MHz in acetone-d_6 at 25 °C. [b] Spectra recorded at 125 MHz in $CDCl_3$ at 25 °C. [c] Spectra recorded at 100 MHz in $CDCl_3$ at 25 °C. [d] Multiplicity deduced by DEPT and indicated by usual symbols. The values are in ppm downfield from TMS.

functional groups in the structure of **2** were further confirmed by the ^{1}H−^{13}C long-range correlations between H-2 (δ_H 5.00) and the acetate carbonyl (δ_C 167.8); and OH-9 (δ_H 4.96) and C-9 (δ_C 67.7) (Table 3). On the basis of the above finding, and by the NOE correlations observed in the NOESY spectrum of **2** (Table 4), briaexcavatolide T (**2**) was found to be the 2-*O*-debutyryl-2-*O*-acetyl-9-*O*-deacetyl derivative of briareolide I (**5**).

Diterpenoid **3** (briaexcavatolide U), an amorphous white powder, was assigned as the molecular formula $C_{28}H_{38}O_{13}$ from its HRFABMS data. Thus, 10 degrees of unsaturation were determined for the molecule of **3**. The IR spectrum showed bands at 3588, 1782, and 1738 cm^{-1}, consistent with the presence of hydroxy, γ-lactone, and ester carbonyl functionalities in the structure of **3**. The FABMS of **3** exhibited peaks at *m/z* 583 $[M + H]^+$, 565 $[M + H - H_2O]^+$, 523 $[M + H - HOAc]^+$, 463 $[M + H - 2HOAc]^+$, 445 $[M + H - 2HOAc - H_2O]^+$, 403 $[M + H - 3HOAc]^+$, 385 $[M + H - 3HOAc - H_2O]^+$, 343 $[M + H - 4HOAc]^+$, 325 $[M + H - 4HOAc - H_2O]^+$, and 307 $[M + H - 4HOAc - 2H_2O]^+$, suggesting the presence of four acetoxy and two hydroxy groups in **3**. From the ^{13}C spectral data of **3** (Table 2), a trisubstituted olefin was deduced from the signals of two carbons resonating at δ 143.5 (s) and 123.2 (d). An 8,17-epoxide was confirmed from the signals of two quaternary oxygenated carbons at δ 70.5 (s) and 66.3 (s) and from the chemical shift of H_3-18 (δ 1.78, 3H, s). Furthermore, in the ^{13}C NMR spectrum of **3**, five carbonyl resonances appeared at δ 170.2 (s), 170.2 (s), 170.1 (s), 170.0 (s), and 168.0 (s), further confirming the presence of a γ-lactone and four ester groups in **3**. In the ^{1}H NMR spectrum of **3** (Table 1), four aceate methyls (δ 2.24, 3H, s; 2.13, 3H, s; 2.02, 3H, s; 2.01, 3H, s) were observed. The structure and all of the ^{1}H and ^{13}C chemical shifts of **3** were determined by the assistance of 2D NMR (^{1}H−^{1}H COSY, HMQC, and HMBC). From the results of the ^{1}H−^{1}H COSY and HMBC experiments of **3** (Figure 3 and Table 3), it was possible to establish the molecular framework of **3**. The relative configuration of **3** was also deduced by a NOESY experiment (Figure 4 and Table 4). H-10 was found to exhibit NOE correlations to H-2 and H-12, but not to H_3-15, indicating that H-2, H-10, and H-12 are all situated on the same face and were assigned as the α-protons since the C-15 methyl is β-oriented. H-14 was found to exhibit an NOE response with H_3-15, but not with H-10, revealing the β-orientation of this proton. H-2 showed NOE interactions with H-3α and H-4, suggesting the acetoxy group attaching at C-4 was β-oriented. Also, the hydroxy group attaching at C-11 was found to be in the α-face by the NOE correlations of H_3-20 with H_3-15 and H-13β. On the basis of the above observations and by careful analyses of other NOE correlations, the relative structure of **3** was established.

Table 3. HMBC Correlations for Diterpenoids **1**−**4**

carbon	**1**	**2**	**3**	**4**
1	H-3β, H-10, H-13, H-14, H_3-15	H-2, H-10, H-13, H-14, H_3-15	H-2, H-10, H_3-15	H-2, H-3, H-10, H_3-15
2	OH-2, H_2-3, H_3-15	H-10, H-14, H_3-15	H_2−3, H-10, H_3-15	H-3β, H-4α
3	OH-2, H-4	H-2	H-4	H-2, H-4α
4	H-2, H_2−3, H_3-16	H-2, H_3-16	H-2, H-6, H-3β	H-6
5	H-3β, H-4, H-7, H_3-16	H-7, H_3-16	H-3α, H-4, H-7, H_3-16	H-7, H_3-16
6	H-4, H-7, H_3-16	H-7, H_3-16	H-4, H-7, H_3-16	H-7, H_3-16
7	H-9	H-9	H-9	H-9
8	H-9, H-10, H_3-18	H-9, OH-9, H-10, H_3-18	H-9, H_3-18	H_3-18
9	H-10	OH-9	H-10	H_3-18
10	H-9, OH-11, H-12, H-14, H_3-15, H_3-20	H-2, H-9, OH-9, H-11, H-14, H_3-15, H_3-20	H-2, H-9, H_3-15, H_3-20	H-14, H_3-15, H_3-20
11	OH-11, H-9, H-10, H-12, H-13, H_3-20	H-10, H-13, H_3-20	H-9, H-10, H-12, H_3-20	H_3-20
12	OH-11, H-13, H-14, H_3-20	H-10, H-14, H_3-20	H-10, H-13β, H-14, H_3-20	H-13α, H_3-20
13	H-12	H-11, H-14, H_3-15		
14	H-12, H_3-15	H-2, H-13, H_3-15	H_3-15	H-13α, H_3-15
15	H-10, H-14	H-2, H-10, H-13, H-14	H-2, H-10	H-2
16		H_2-3, H_2-4	H-6	H-4α, H_3-16
17	H-9, H_3-18	H-9, H_3-18	H-9, H_3-18,	H_3-18
19	H_3-18	H-7, H_3-18	H-7, H_3-18	H_3-18
20	OH-11, H-12	H-10, H-11	H-10	H-10
2-O*C*OMe		H-2	H-2	H-2
4-O*C*OMe	H-4		H-4	
9-O*C*OMe	H-9		H-9	
12-O*C*OMe	H-12			
12-O*C*OPr				H_2-22, H_2-23

Table 4. NOESY Correlations for Diterpenoids **1**−**4**

	1	2	3	4
H-2	H-3α, H-10	H-3*β*, H-14, H_3-15	H-3α, H-4, H-10, H-14	H-3α, H-4α, H-10
H-3α	H-2, H-3*β*, H-4α	H-3*β*	H-2, H-4α, H-3*β*	H-2
H-3*β*	H-3α, H-7, H_3-15	H-2, H-3α, H-4α	H-3α, H-7	
H-4α	H-3α, H_3-16	H-3*β*, H-4*β*	H-2, H-3α, H_3-16	H-2
H-4*β*		H-4α, H-7, OH-9		H-4α
H-6	H-7, H_3-16	H-7, H_3-16	H-7, H_3-16	H_3-16
H-7	H-3*β*, H-6	H-4*β*, H-6, OH-9	H-3*β*, H-6	H-6
H-9	H-10, H_3-18, H_3-20	OH-9, H-10, H-11, H_3-15, H_3-18, H_3-20	H-10, H_3-18, H_3-20	H-11
H-10	H-2, H-9, H_3-20	H-9, H-11	H-2, H-9, H-12	H-2
H-11		H-9, H-10, H_3-20		H-9, H-12
H-12	H-13, H_3-20		H-10, H-13α	H-11, H-13α, H_2-22
H-13	H-12, H-14	H-14		
H-13α			H-12, H-13*β*	H-12
H-13*β*			H-13α, H_3-15, H_3-20	H-14
H-14	OH-2, H-13, H_3-15	H-2, H-13, H_3-15	H-2, H_3-15	H-13*β*, H_3-15
H_3-15	H-3*β*, OH-11, H-14	H-2, OH-9, H-14, H_3-20	H-13*β*, H-14, H_3-20	H-14
H_3-16	H-4α, H-6	H-6	H-4α, H-6	H-6
H_3-18	H-9, H_3-20	H-9, OH-9	H-9	H_3-24
H_3-20	H-9, H-10, H-12, H_3-18	H-9, H-11, H_3-15	H-9, H-13*β*, H_3-15	H_3-24
H_2-22				H-12, H_2-23
H_2-23				H_2-22
H_3-24				H_3-18, H_3-20
OH-2	H-14			
OH-9		H-7, H-9, H_3-15, H_3-18		
OH-11	H_3-15			

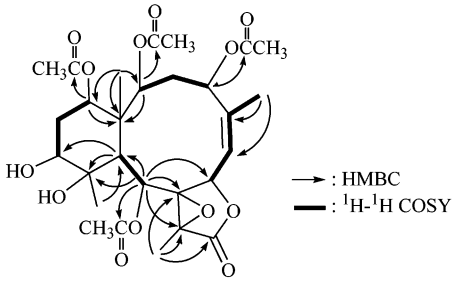

Figure 3. Selected ^{1}H−^{1}H COSY and HMBC correlations of **3**.

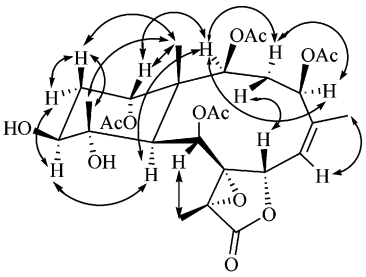

Figure 4. Selected NOE correlations of **3**.

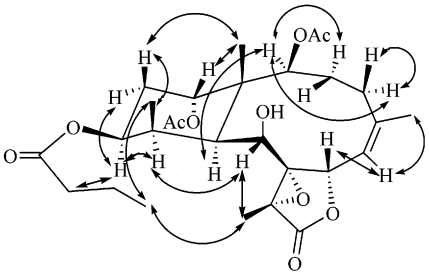

Figure 5. Selected NOE correlations of **4**.

Briaexcavatolide V (**4**) was isolated as a white powder and had the molecular formula $C_{28}H_{40}O_{10}$, as established by HRFABMS. Its IR spectrum exhibited a broad OH stretch at 3395 cm^{-1}, a *γ*-lactone carbonyl at 1774 cm^{-1}, and ester carbonyls at 1728 cm^{-1}. The FABMS of **4** exhibited peaks at *m*/*z* 537 $[M + H]^+$, 477 $[M + H - HOAc]^+$, 417 $[M + H - 2HOAc]^+$, 389 $[M + H - HOAc - C_3H_7COOH]^+$, 371 $[M + H - HOAc - C_3H_7COOH - H_2O]^+$, 329 $[M + H - 2HOAc - C_3H_7COOH]^+$, and 311 $[M + H - 2HOAc - C_3H_7COOH - H_2O]^+$, also suggesting the presence of a hydroxy, a butyryloxy, and two acetoxy groups in **4**. Carbonyl resonances in the ^{13}C NMR spectrum of **4** at *δ* 172.8 (s), 172.3 (s), 170.9 (s), and 170.4 (s) further confirmed the presence of a *γ*-lactone and three other esters (Table 2). In the ^{1}H NMR spectrum of **4** (Table 1), two acetate methyls were observed at 2.04 (3H, s) and 1.98 (3H, s). One acetoxyl positioned at C-2 was confirmed from the HMBC correlation between H-2 (δ_H 5.01) and the carbonyl carbon (*δ* 170.4) of the acetoxy group. The additional ester group was found to be an *n*-butyryloxy group on the basis of ^{1}H NMR studies, including an ^{1}H−^{1}H COSY spectrum, which revealed seven contiguous protons [*δ* 2.23 (2H, t, *J* = 7.2 Hz), 1.62 (2H, m), 0.93 (3H, t, *J* = 7.2 Hz)]. The carbon signal at δ_C 172.8 (s) was correlated with the signal of the methylene protons at *δ* 2.23 in the HMBC spectrum and was consequently assigned as the carbon atom of the *n*-butyrate carbonyl. As both H-12 and H-14 did not show HMBC correlations with carbons of the corresponding ester carbonyls, the main problem still remaining is the position of the *n*-butyryloxy group, which may be located at either C-12 or C-14. Further careful examination of the NOESY spectrum of **4** revealed that significant NOE interactions of α-H_2 (*δ* 2.23) and *γ*-H_3 (*δ* 0.93) of the *n*-butyryloxy group, with H-12 and H_3-20, respectively (selective NOE correlations of **4**, see Figure 5), were observed and established the C-12 position of the *n*-butyryloxy group and confirmed the C-14 position of the second acetoxy group. On the basis of the above information, it was revealed that diterpenoid **4** should be the 12-*O*-deacetyl-12-*O*-*n*-butyryl derivative of **6**.[1]

Experimental Section

General Experimental Procedures. Melting points were determined using a Fisher-Johns melting point apparatus and were uncorrected. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. The UV spectrum of **2** was taken in MeOH on a Perkin-Elmer UV/vis Lambda EZ 201 spectrometer. IR spectra were recorded on a Jasco FT-IR 5300 infrared spectrophotometer. FABMS were obtained with a VG Quattro GC/MS spectrometer. The NMR spectra were recorded on a Varian Unity INOVA 500 FT-NMR at 500 MHz for ^{1}H and 125 MHz for ^{13}C or on a Bruker AMX-400 FT-NMR at 400

MHz for ^{1}H and 100 MHz for ^{13}C, respectively, in acetone-d_6 or $CDCl_3$ using TMS as an internal standard. HRFABMS was recorded on a JEOL JMS-SX/SX 102A mass spectrometer. Silica gel (Merck, 230−400 mesh) was used for column chromatography. Precoated silica gel plates (Merck, Kieselgel 60 F_{254}, 0.2 mm) were used for analytical TLC. High-performance liquid chromatography (HPLC) was achieved on a Hitachi L-7100 apparatus equipped with a Bischoff refractive index detector and a Hitachi L-7400 UV detector and with the Thermo column (250 × 4.6 mm 5 μm Hypersil HS silica).

Organism. The gorgonian *Briareum excavatum* was collected by hand using scuba along the coast of southern Taiwan, in July 1995, at depths of 4−5 m, and was stored in a freezer until extraction. A voucher specimen was deposited in the Department of Marine Resources, National Sun Yat-Sen University (specimen no. KTSC-103).

Extraction and Isolation. The extraction scheme followed the standard procedures of our previous reports.[1,2] The freeze-dried material (1.9 kg) was minced and extracted exhaustively with EtOAc. The organic extract was evaporated to give a residue, which was separated by silica gel column chromatography using hexanes and hexanes−EtOAc mixtures of increasing polarity to afford a series of fractions. The fractions containing diterpenoids **1**−**4** were further separated on silica gel using CH_2Cl_2 or mixtures of *n*-hexane and EtOAc. Diterpenoid **4** was eluted with pure CH_2Cl_2. Diterpenoids **2** and **1** were separated with silica gel by HPLC using *n*-hexane−EtOAc (3:1) and *n*-hexane−EtOAc (2:1), respectively. The most polar compound, diterpenoid **3**, was purified with silica gel by HPLC using *n*-hexane−EtOAc (3:2).

Briaexcavatolide S (1): white powder (1.5 mg); mp 227−229 °C; $[\alpha]_D^{27}$ −79° (*c* 0.1, acetone); IR (neat, $CHCl_3$) ν_{max} 3449, 1780, and 1732 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m*/*z* 523 [0.8, (M + H)$^+$], 463 (0.3), 445 (0.1), 403 (0.3), 385 (0.6), 367 (0.1), 343 (0.5), and 325 (0.4); HRFABMS *m*/*z* 523.2177 (calcd for $C_{26}H_{35}O_{11}$, 523.2180).

Briaexcavatolide T (2): white powder (2.0 mg); mp 195−197 °C; $[\alpha]_D^{27}$ +19° (*c* 0.1, $CHCl_3$); UV (MeOH) λ_{max} 221 nm (log ϵ 4.02); IR (neat, $CHCl_3$) ν_{max} 3495, 1780, 1730, and 1688 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m*/*z* 405 [0.2, (M + H)$^+$], 345 (0.2), and 327 (0.3); HRFABMS *m*/*z* 405.1920 (calcd for $C_{22}H_{29}O_7$, 405.1914).

Briaexcavatolide U (3): white powder (1.1 mg); mp 110−111 °C; $[\alpha]_D^{27}$ +48° (*c* 0.1, $CHCl_3$); IR (neat, $CHCl_3$) ν_{max} 3588, 1782, and 1738 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m*/*z* 583 [1, (M + H)$^+$], 565 (0.9), 523 (1), 463 (1), 445 (1), 403 (1), 385 (1), 343 (2), 325 (1), and 307 (5); HRFABMS *m*/*z* 583.2386 (calcd for $C_{28}H_{39}O_{13}$, 583.2391).

Briaexcavatolide V (4): white powder (4.6 mg); mp 173−175 °C; $[\alpha]_D^{27}$ +49° (*c* 1.8, $CHCl_3$); IR (neat, $CHCl_3$) ν_{max} 3395, 1774, and 1728 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; FABMS *m*/*z* 537 [0.2, (M + H)$^+$], 477 (0.2), 417 (0.1), 389 (0.3), 371 (0.1), 329 (2), and 311 (0.8); HRFABMS *m*/*z* 537.2709 (calcd for $C_{28}H_{41}O_{10}$, 537.2700).

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