出國報告：其他--參加國際會議

Briaexcavatins V-Z, New Briaranes from a Cultured Octocoral *Briareum excavatum*

服務機關：國立海洋生物博物館
姓名職稱：宋秉鈞研究員
派赴國家：美國
出國期間：九十八年六月二十六日至七月三日
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出席國際學術會議心得報告

計畫編號	NSC 97-2323-B-291-001
計畫名稱	臺灣海域產四屬柳珊瑚 *Bebryce*, *Rumphella*, *Ellisella* 及 *Pinnigorgia* 及養殖型 *Briareum* 所含化學成份之與研究
出國人員姓名 服務機關及職稱	宋秉鈞 國立海洋生物博物館企劃研究組研究員
會議時間地點	Jun. 27th-July 1, **2009**, Honolulu, Hawaii (夏威夷), USA (美國)
會議名稱	The 50th Annual Meeting of the American Society of Pharmacognosy 美國生藥學會第五十屆年會
發表論文題目	Briaexcavatins V-Z, New Briaranes from a Cultured Octocoral *Briareum excavatum*

一、會議目的

美國生藥學會年會以往均為天然物化學及生藥學界每年舉辦之重要例行國際會議，今年適逢第五十屆年會，故於 2009 年六月二十七日至七月一日於美國夏威夷州的 Honolulu Sheraton Waikiki 飯店擴大舉行年會，會議由美國生藥學會(American Society of Pharmacognosy-ASP)主辦，與會人士達近貳仟人，且均為全球各國天然物化學及生藥學界研究學者。會議主要針對全球天然物化學(尤其注重海洋天然物化學方面之研究)及生藥學方面的最新研究進行交流與探討。

二、會議過程

有關海洋天然物化學之研究在會中尤受重視，各方研究學者在海洋生技製藥、海洋化學生態、海洋生物多樣性與天然物多樣性等議題上進行廣泛的討論，會中並邀請全球多名國際知名學者進行精闢的邀請演講。個人亦於會議中發表論文壹篇”Briaexcavatins V-Z, New Briaranes from a Cultured Octocoral *Briareum excavatum*”發表五個 briarane 類化合物，並針對 briarane 類化合物的結構分析作了詳盡的解釋與探討，並與參加會議的各國學者進行詳細的討論，並交換研究心得 (論文結果已另正式發表於 *Bull. Chem. Soc. Jpn.* 2009, 82, 987-996)。會中並另邀請國際海洋天然物研究學者 Prof. Higa 於九月份應海洋生物博物館之邀請訪台參與由由海生館所主辦之「The Omics in Ocean－第二屆國際海洋生物科技研討會」。並獲同意(該會議已於九月十七日至十九日於海生館召開)。

二、心得及建議事項

本次會議為一有關全球天然物化學及生藥學研究的交流會議，與會學者之研究背景廣泛，背景歧異度高，故常能在討論時有相當特殊之意見提出，對各領域之研究人員時有耳目一新之感，且邀請演講之學者均為全球知名天然物化學及生藥學界研究室之學門主持人，其熱烈參與程度相當引人注意。以在會議中可明顯看出美國的天然物化學研究上在全球仍執牛耳地位，日本在海洋天然物化學部份則表現出其極大之影響力，其他泛太平洋國家如臺灣、韓國則緊跟於後，中國大陸在論文數量上有驚人的成長，但在論文的精準度上則有進步空間。本次會議個人對美國及日本在海洋天然物方面之研究成果尤感特殊，其善盡利用國家之科技優勢發展海洋天然物之研究，而其他亞洲國家在此方面之研究水準顯然有程度上的差異，而學者們建議台灣因正處於熱帶及亞熱帶海域的交會處，生物的多樣性與歧異度極高，如能在此方面加強投入研究資源則應可能在一定時間內在海洋天然物化學的研究上建立起相對具有特色的研究學門。亦符合國家之海洋政策與發展方向。

此外，建議應加強鼓勵國內博士後研究人員及博士班學生能積極的參與此一類型之國際學術活動以增廣見聞。

附錄：會議後續相關發表 SCI 論文壹篇全文；

Sung, P.-J.*; Lin, M.-R.; Chiang, M. Y.; Hwang, T.-L. Briaexcavatins V–Z, Discovery of New Briaranes from a Cultured Octocoral *Briareum excavatum*. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 987–996.

Briaexcavatins V–Z, Discovery of New Briaranes from a Cultured Octocoral *Briareum excavatum*

Ping-Jyun Sung,*[1,2] Mei-Ru Lin,[1,3] Michael Y. Chiang,[4] and Tsong-Long Hwang[5]

[1]Graduate Institute of Marine Biotechnology, National Dong Hwa University (NDHU) and Taiwan Coral Research Center (TCRC), National Museum of Marine Biology & Aquarium (NMMBA), Checheng, Pingtung 944, Taiwan

[2]Asia-Pacific Ocean Research Center (APORC), National Sun Yat-sen University (NSYSU), Kaohsiung 804, Taiwan

[3]Department of Marine Biotechnology and Resources, National Sun Yat-sen University, Kaohsiung 804, Taiwan

[4]Department of Chemistry, National Sun Yat-sen University, Kaohsiung 804, Taiwan

[5]Graduate Institute of Natural Products, Chang Gung University, Taoyuan 333, Taiwan

Received February 12, 2009; E-mail: pjsung@nmmba.gov.tw

Five new briarane derivatives, briaexcavatins V–Z (**1**–**5**), have been isolated from a cultured octocoral *Briareum excavatum*. The structures of compounds **1**–**5** were established by spectroscopic methods. Single-crystal X-ray diffraction data for **2** confirmed the structure. Briarane **4** possesses an unprecedented 8,9-epoxy moiety. The relationships between ^{13}C NMR chemical shifts and the conformations of briaranes possessing an 11,12-epoxy group are described. Briaranes **1**, **3**, and **4** have displayed weak inhibitory effects on superoxide anion generation by human neutrophils. Briarane **1** was found to show mild inhibitory effects on human neutrophil elastase release and **5** exhibited mild activity to enhance human neutrophil elastase release.

In our continuing research on natural products from invertebrates collected in Taiwanese waters, a series of complex diterpenoid derivatives with briarane skeleton (3,8-cyclized cembranoid) have been isolated from the octocorals *Briareum* sp.,[1,2] *Briareum excavatum*,[3–10] *Ellisella robusta*,[9,11–15] *Junceella fragilis*,[7,16–23] and *Junceella juncea*.[18,23–25] The octocoral *B. excavatum* was transplanted to the National Museum of Marine Biology & Aquarium (NMMBA), Taiwan, for their interesting chemical constituents. We report herein the isolation, structure determination, and bioactivity of five new briaranes, briaexcavatins V–Z (**1**–**5**) (Chart 1), from further studies of cultured *B. excavatum*. Although over 500 briarane-type natural products have been isolated from various marine organisms,[26–28] little is known about the conformation of the cyclohexane ring in briarane analogs. The relationships between ^{13}C NMR chemical shifts and the conformation of the cyclohexane ring in briaranes possessing an 11,12-epoxy group are described. The structures of compounds **1**–**5** were established by spectroscopic methods and the structure of **2** was further supported by X-ray data analysis. Briaranes **1**, **3**, and **4** displayed weak inhibitory effects on superoxide anion generation by human neutrophils. Briarane **1** was found to show mild inhibitory effects on human neutrophil elastase release and **5** exhibited mild activity to enhance human neutrophil elastase release.

Results and Discussion

Briaexcavatin V (**1**) was obtained as a white powder and the molecular formula of **1** was determined to be $C_{24}H_{30}O_9$ by analysis of ^{13}C and ^{1}H NMR data in conjunction with DEPT results (Table 1); this conclusion was confirmed by HR-ESI-MS (m/z 485.1791, Calcd for $C_{24}H_{30}O_9 + Na$, 485.1787). Comparison of the ^{1}H NMR and DEPT data with the molecular formula indicated that there must be an exchangeable proton, requiring the presence of a hydroxy group, and this deduction was supported by a broad absorption in the IR spectrum at 3459 cm^{-1}. The IR spectrum of **1** also showed absorptions at 1767 and 1728 cm^{-1}, consistent with the presence of γ-lactone and ester groups. From the ^{13}C NMR spectrum, briarane **1** was found to possess two acetoxy groups (δ 21.3, 21.1, 2 × q; δ 170.6, 169.9, 2 × s), a γ-lactone (δ 171.5, s, C-19), a trisubstituted olefin (δ 141.5, s, C-5; 118.2, d, CH-6), and a disubstituted olefin (δ 139.0, d, CH-4; 125.6, d, CH-3). The presence of a tetrasubstituted epoxide and a trisubstituted epoxide, both containing a methyl substituent, were established from the signals of four oxygenated carbons at δ 69.4 (s, C-8), 63.7 (s, C-17), 59.5 (d, CH-12), and 58.7 (s, C-11), and further confirmed by the proton signals of two methyl singlets at δ 1.60 (3H, s, H_3-18) and 1.53 (3H, s, H_3-20) and an oxymethine proton at δ 2.97 (1H, dd, J = 1.6, 1.2 Hz, H-12). Moreover, two acetyl methyls (δ 2.05, 3H, s; 2.01, 3H, s), a methyl singlet (δ 1.26, 3H, s, H_3-15), a vinyl methyl (δ 1.88, 3H, d, J = 0.8 Hz, H_3-16), a pair of methylene protons (δ 2.20, 2H, m, H_2-13), an aliphatic methine proton (δ 2.36, 1H, s, H-10), four oxymethine protons (δ 5.43, 1H, d, J = 10.0 Hz, H-2; 5.11, 1H, d, J = 4.4 Hz, H-7; 5.20, 1H, d, J = 8.8 Hz, H-9; 4.78, 1H, ddd, J = 4.4, 1.6, 0.8 Hz, H-14), two conjugated olefin protons (δ 5.94, 1H, dd, J = 15.6, 10.0 Hz, H-3; 6.69, 1H, br d, J = 15.6 Hz, H-4), and an olefin proton (δ 5.44, 1H, ddd, J = 4.4, 1.2, 0.8 Hz, H-6), were observed in the ^{1}H NMR spectrum of **1**.

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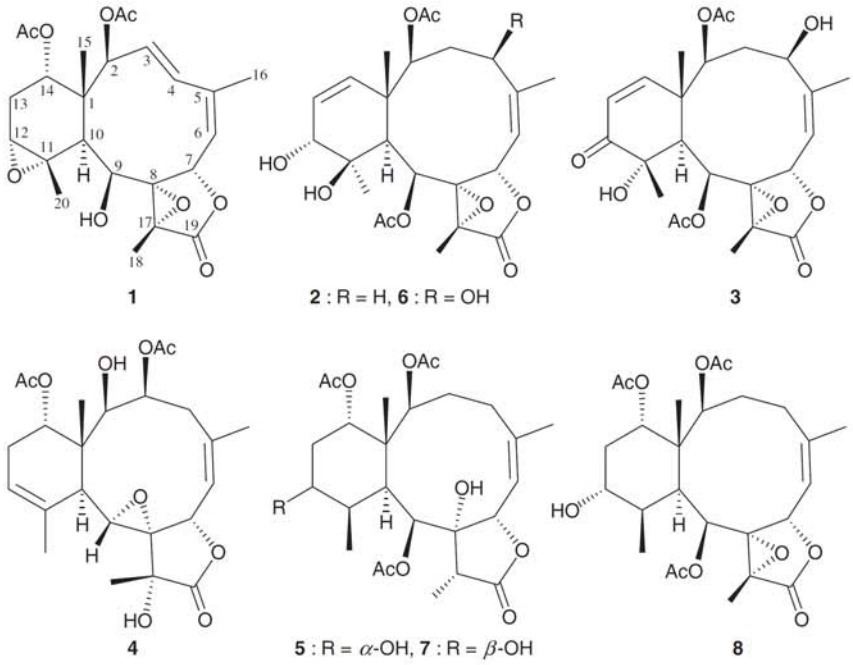

Chart 1.

Table 1. ^{1}H and ^{13}C NMR Data (δ) and HMBC Correlations (H → C) for Diterpenoid **1**

Position	^{1}H	^{13}C	HMBC
1		44.7 (s)[b)]	
2	5.43 d (10.0)[a)]	74.2 (d)	C-1, -3, -4, -14, -15, acetate carbonyl
3	5.94 dd (15.6, 10.0)	125.6 (d)	C-1, -2, -4, -5
4	6.69 br d (15.6)	139.0 (d)	C-2, -3, -5, -6
5		141.5 (s)	
6	5.44 ddd (4.4, 1.2, 0.8)	118.2 (d)	C-8, -16
7	5.11 d (4.4)	77.1 (d)	C-5, -6
8		69.4 (s)	
9	5.20 d (8.8)	68.2 (d)	C-1, -8, -10, -11, -17
10	2.36 s	41.3 (d)	C-1, -2, -8, -9, -11, -12, -14, -15
11		58.7 (s)	
12	2.97 dd (1.6, 1.2)	59.5 (d)	C-13, -14
13	2.20 m (2H)	26.5 (t)	C-1, -12, -14
14	4.78 ddd (4.4, 1.6, 0.8)	71.0 (d)	C-1, -2, -10, -12, acetate carbonyl
15	1.26 s	14.3 (q)	C-1, -2, -10, -14
16	1.88 d (0.8)	23.2 (q)	C-4, -5, -6
17		63.7 (s)	
18	1.60 s	9.2 (q)	C-8, -17, -19
19		171.5 (s)	
20	1.53 s	23.8 (q)	C-10, -11, -12
OH-9	2.43 d (8.8)		C-8, -9, -10
2-OAc		170.6 (s)	
	2.05 s	21.1 (q)	acetate carbonyl
14-OAc		169.9 (s)	
	2.01 s	21.3 (q)	acetate carbonyl

a) *J* values (in Hz) in parentheses. b) Multiplicity deduced by DEPT and HMQC spectra and indicated by usual symbols.

From the ^{1}H–^{1}H COSY spectrum of **1** (Figure 1), it was possible to establish the proton sequences from H-2/H-3, H-3/H-4, H-4/H-6 (by allylic coupling), H-6/H-7, and H-9/H-10. These data, together with the HMBC correlations between H-2/C-1, -3, -4; H-3/C-1, -2, -4, -5; H-4/C-2, -3, -5, -6; H-6/C-8; H-7/C-5, -6; H-9/C-1, -8, -10; and H-10/C-1, -2, -8, -9 (Table 1 and Figure 1), established the connectivity from C-1 to C-10 within the ten-membered ring. The vinyl methyl attached at C-5 was confirmed by the HMBC correlations between H_3-16/C-4, -5, -6 and H-6/C-16, and was further

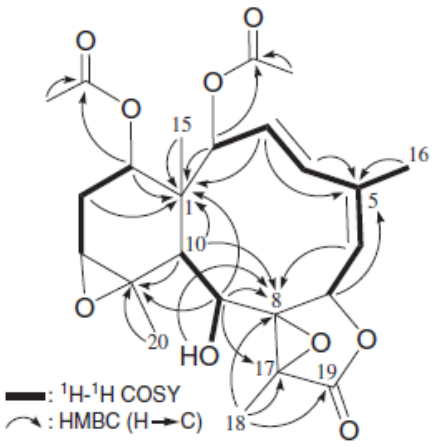

Figure 1. The ^{1}H–^{1}H COSY and selective HMBC correlations (protons and quaternary carbons) of **1**.

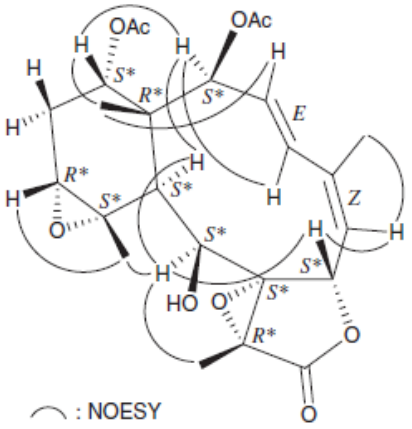

Figure 2. Selective NOESY correlations of **1**.

supported by the allylic coupling between H-4/H_3-16 and H-6/H_3-16. The methylcyclohexane ring, which is fused to the ten-membered ring at C-1 and C-10, was elucidated by the HMBC correlations between H-2/C-14; H-9/C-11; H-10/C-11, -12, -14; H_2-13/C-1; H-14/C-1, -2, -10; and H_3-20/C-10, -11, -12. The ring junction C-15 methyl was positioned at C-1 from the HMBC correlations between H_3-15/C-1, -2, -10, -14; H-2/C-15; and H-10/C-15. The HMBC correlations also indicated that the acetoxy groups are attached at C-2 and C-14. The remaining hydroxy group was positioned at C-9, as indicated by analysis of a key ^{1}H–^{1}H COSY correlation between the hydroxy proton OH-9 and H-9 and by the HMBC correlations between OH-9 and C-8, -9, -10. These data, together with the HMBC correlations between H-9/C-17 and H_3-18/C-8, -17, -19, were used to establish the molecular framework of **1**.

Based on previous surveys, all the naturally occurring briaranes have the H-10 trans to the C-15 methyl group, and these two groups are assigned as α- and β-oriented in most briarane derivatives.[26–28] The relative configuration of **1** was elucidated from the interactions observed in a NOESY experiment (Figure 2) and from vicinal ^{1}H–^{1}H coupling constant analysis. In the NOESY experiment of **1**, the correlations of H-10 with H-2 and H-9, but not with H_3-15 and H_3-20, indicated that these protons (H-2, H-9, and H-10) are situated on the same face and were assigned as α protons since the C-15 and C-20 methyls are the β-substituents at C-1 and C-11, respectively. H-14 was found to exhibit responses with H_3-15 and H-2, showing that this proton has a β-orientation. H-9 was found to show responses with H_3-18 and H_3-20, but not with H_3-15. From modeling analysis, H-9 was found to be close to H_3-18 and H_3-20 when H-9 was α-oriented in the ten-membered ring and C-18 methyl was placed on the β face in the γ-lactone moiety. H-12 exhibited a response with C-20 methyl, indicated that the C-11/12 epoxy group was α-oriented. The correlations between H-2/H-4, H-3/H_3-15, and H-6/H_3-16, suggested that $\Delta^{3,5}$ conjugated diene exists in a 3(E),5(Z) configuration. Therefore, the *s-trans*-diene moiety in **1** was elucidated. Furthermore, H-7 showed correlations with H-9 and H-6, suggesting that H-7 was on the β face. Thus, based on the above findings, the structure of **1** was established and the configurations of chiral centers of **1** were assigned as 1R*, 2S*, 7S*, 8S*, 9S*, 10S*, 11S*, 12R*, 14S*, and 17R*.

From the characteristics of chemical shifts it was known that the briarane derivatives contained an 11,12-epoxy group. We summed up the ^{13}C NMR chemical shifts for C-11 and C-12. The 11,12-epoxide was assigned as α configuration because the ^{13}C NMR chemical shifts for these two carbons were δ <60 (δ 57–60);[29] while the chiral carbons C-11 and C-12 existed in S* and R* form, respectively, and leading the epoxy group to α-orientation (Table 2).[29–38] Furthermore, if the epoxy group was found to exist in β-configuration (11R* and 12S*), the ^{13}C chemical shifts for C-11 were shifted downfield and appeared at δ 61–66, and most chemical shifts for C-12 in these briaranes were δ >60 (Table 3),[29,39–48] exclusive with those of 4-hydroxymilolide C (δ 57.4)[29] and briviolides G–I (δ 59.7, 59.9, and 59.6).[48]

Briaexcavatin W (**2**) had a molecular formula $C_{24}H_{32}O_9$ as deduced from HR-ESI-MS (*m/z* 487.1943, Calcd for $C_{24}H_{32}O_9$ + Na, 487.1944). Its IR spectrum exhibited broad OH stretch at 3497 cm^{-1}, γ-lactone at 1775 cm^{-1}, and ester carbonyls at 1728 cm^{-1}. Carbonyl resonances in the ^{13}C NMR spectrum of **2** at δ 170.6 (s, C-19) and 170.1 (2 × s) revealed the presence of a γ-lactone and two esters in **2** (Table 4). In the ^{1}H NMR spectrum of **2**, the signals for two acetyl methyls were observed at δ 2.23 (3H, s) and 2.16 (3H, s) (Table 4). It was found that the 1D and 2D NMR data of **2** (Table 4 and Figure 3) were similar with those of a known briarane, briaexcavatin K (**6**),[7] except that the signals corresponding to the 4-hydroxy group in **6** were not present in **2**. The correlations from a NOESY experiment of **2** (Figure 4) also showed that the relative stereochemistry of this metabolite is similar to those of **6**. Thus, briaexcavatin W (**2**) was found to be the 4-dehydroxy derivative of **6** and the relative configurations of chiral centers of **2** were established as 1S*, 2S*, 7S*, 8S*, 9S*, 10S*, 11R*, 12R*, and 17R*. The structure of **2** was further confirmed by a single-crystal X-ray analysis (Figure 5).

Briaexcavatin X (**3**) was obtained as a white powder. HR-ESI-MS established a molecular formula $C_{24}H_{30}O_{10}$ (*m/z* 501.1739, Calcd for $C_{24}H_{30}O_{10}$ + Na, 501.1737). The IR spectrum of **3** showed absorptions of hydroxy (ν_{max} 3459 cm^{-1}), γ-lactone (ν_{max} 1775 cm^{-1}), ester carbonyls (ν_{max} 1744 cm^{-1}), and α,β-unsaturated ketone carbonyl (ν_{max} 1696 cm^{-1}). From

Table 2. ^{13}C NMR Chemical Shifts (δ) for Natural Briaranes Possessing an 11,12-Epoxy Group in α Form[a)]

Compound	C-11(S*)	C-12 (R*)	Source	Collection site	Ref.
Briaexcavatin V (**1**)	58.7	59.5	*Briareum excavatum*	Taiwan	
Milolide C	59.2	58.5	*Briareum stechei*	Micronesia	29
Briaranolide J	58.4	59.2	*Briareum* sp.	Okinawa-Japan	30
Stylatulide	58.9	59.6	*Stylatula* sp.	Gulf of California	31,32
Minabein-10	59.0	58.7	*Minabea* sp.	Micronesia	33
Briareolide C	59.2	58.7	*Briareum* sp.	Puerto Rico-Caribbean Sea	34
Briareolide D	59.2	58.6	*Briareum* sp.	Puerto Rico-Caribbean Sea	34
Briareolate ester C	58.5	57.0	*Briareum asbestinum*	West Indies	35,36
An unnamed briarane[b)]	59.4	59.1	*Briareum asbestinum*	West Indies	35
An unnamed briarane[c)]	59.6	59.3	*Pteroeides* sp.	Indonesia	37
An unnamed briarane[c)]	59.8	59.3	*Pteroeides* sp.	Indonesia	37
Renillin D	57.7	59.3	*Renilla reniformis*	Georgia-USA	38

a) The spectral data cited in this table were measured in $CDCl_3$. b) This compound was assigned as compound **6** in Ref. 35. c) These two compounds were assigned as compounds **7** and **8**, respectively, in Ref. 37.

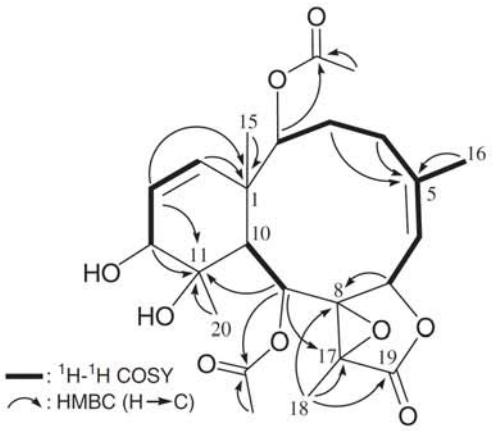

Figure 3. The ^{1}H–^{1}H COSY and selective HMBC correlations (protons and quaternary carbons) of **2**.

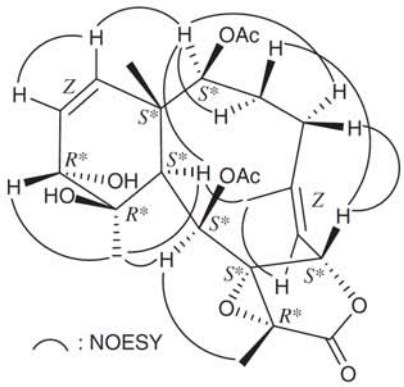

Figure 4. Selective NOESY correlations of **2**.

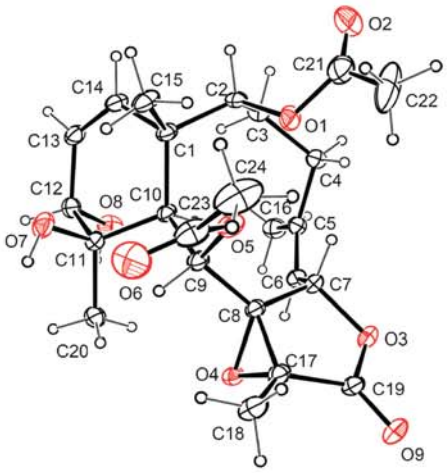

Figure 5. The ORTEP plot of **2** showing the relative configuration.

the NMR data (Table 4), an α,β-unsaturated ketone was deduced from the signals of three carbons at δ 200.7 (s, C-12), 154.0 (d, CH-14), and 123.1 (d, CH-13), and a trisubstituted olefin was found from the signals of carbons at δ 146.1 (s, C-5) and 122.9 (d, CH-6). A tetrasubstituted epoxide containing a methyl substituent was elucidated from the signals of two oxygen-bearing quaternary carbons at δ 70.4 (s, C-8) and 63.8 (s, C-17), and was further confirmed from the chemical shift of a methyl singlet resonating at δ 1.67 (3H, s, H_3-18). Three carbonyl resonances at δ 171.0 (s, C-19), 169.0 (s, ester carbonyl), and 168.2 (s, ester carbonyl) confirmed the presence of a γ-lactone and two other ester groups. In the ^{1}H NMR spectrum of **3**, two acetyl methyls were observed (δ 2.26, 3H, s; 2.15, 3H, s). From the ^{1}H–^{1}H COSY experiment of **3** (Figure 6), it was possible to establish the separate spin systems that map out the proton sequences from H-2/H_2-3/H-4; H-4/H-6 (by allylic coupling); H-6/H-7; H-6/H_3-16 (by allylic coupling); H-9/H-10; and H-13/H-14. These data, together with the HMBC correlations of **3** (Table 4 and Figure 6), established the molecular framework of **3**.

In the relative stereochemistry of **3**, the cis geometry of the C-13/14 double bond was indicated by a 10.8 Hz coupling constant between H-13 (δ 6.02) and H-14 (δ 6.37) and further confirmed by a NOESY correlation between these two protons (Figure 7). In the NOESY spectrum of **3**, a correlation was observed between H-10 and H-2, but not with H_3-15 and H_3-20; and H_3-20 exhibited a response with H_3-15, indicating that H-2, H-10, and the 11-hydroxy group should be placed on the

Table 3. ^{13}C NMR Chemical Shifts (δ) for Natural Briaranes Possessing an 11,12-Epoxy Group in β Form[a)]

Compound	C-11 (R*)	C-12 (S*)	Source	Collection site	Ref.
Milolide A	63.4	60.3	*Briareum stechei*	Micronesia	29
16-Acetoxymilolide A	63.4	60.4	*Briareum stechei*	Micronesia	29
16-Hydroxymilolide A	63.5	60.1	*Briareum stechei*	Micronesia	29
Milolide B	65.2	61.1	*Briareum stechei*	Micronesia	29
16-Chloromilolide B	65.0	61.2	*Briareum stechei*	Micronesia	29
16-Acetoxymilolide B	64.9	61.1	*Briareum stechei*	Micronesia	29
4-Hydroxymilolide C	61.0	57.4	*Briareum stechei*	Micronesia	29
An unnamed briarane[b)]	62.7	60.4	*Briareum stechei*	Great Barrier Reef	39
An unnamed briarane[c)]	62.9	60.7	*Briareum stechei*	Great Barrier Reef	39
An unnamed briarane[d)]	62.8	60.7	*Briareum stechei*	Great Barrier Reef	39
An unnamed briarane[e)]	62.8	60.7	*Briareum stechei*	Great Barrier Reef	39
An unnamed briarane[f)]	63.4	61.3	*Briareum* sp.	Great Barrier Reef	40
An unnamed briarane[g)]	63.4	61.3	*Briareum* sp.	Great Barrier Reef	40
An unnamed briarane[h)]	62.6	60.3	*Briareum* sp.	Great Barrier Reef	40
Stecholide A	62.4	61.4	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide A acetate	63.5	60.9	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide B	63.6	61.4	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide B acetate	63.5	60.9	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide C	63.6	61.4	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide C acetate	63.5	60.8	*Solenopodium stechei*	Great Barrier Reef	41
16-Acetoxystecholide A acetate	63.3	61.2	*Solenopodium stechei*	Great Barrier Reef	41
16-Acetoxystecholide B acetate	63.3	61.2	*Solenopodium stechei*	Great Barrier Reef	41
16-Acetoxystecholide C acetate	63.3	61.2	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide D	63.5	60.8	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide D butyrate	63.5	60.9	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide E	63.3	62.5	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide E acetate	63.5	60.8	*Solenopodium stechei*	Great Barrier Reef	41
Stecholide F	63.8	61.4	*Solenopodium stechei*	Great Barrier Reef	41
3-Acetoxystecholide E	64.0	61.3	*Solenopodium stechei*	Great Barrier Reef	41
16-Hydroxystecholide C acetate	63.8	61.4	*Solenopodium excavatum*	Papua New Guinea	42
Stecholide K	62.4	61.1	*Solenopodium excavatum*	Papua New Guinea	42
Stecholide L	63.6	64.2	*Solenopodium excavatum*	Papua New Guinea	42
Stecholide M	63.7	64.2	*Solenopodium excavatum*	Papua New Guinea	42
2β-Acetoxy-2-(debutyryloxy)stecholide E	64.1	61.5	*Briareum* sp.	Taiwan	43
2β-Acetoxy-2-(debutyryloxy)stecholide E acetate	63.5	60.8	*Briareum* sp.	Indonesia	43,44
Malayenolide A	63.0	60.7	*Veretillum malayense*	Indonesia	45
Malayenolide D	63.1	60.8	*Veretillum malayense*	Indonesia	45
Excavatolide P	63.6	60.7	*Briareum excavatum*	Western Australia	46
Excavatolide R	63.5	60.8	*Briareum excavatum*	Western Australia	46
Excavatolide S	62.0	61.1	*Briareum excavatum*	Western Australia	46
Brianthein C	62.4	60.5	*Briareum excavatum*	Indonesia	47
Briviolide F	61.8	61.1	*Briareum* sp.	Kagoshima-Japan	48
Briviolide G	61.8	59.7	*Briareum* sp.	Kagoshima-Japan	48
Briviolide H	61.0	59.9	*Briareum* sp.	Kagoshima-Japan	48
Briviolide I	62.5	59.6	*Briareum* sp.	Kagoshima-Japan	48

a) The spectral data cited in this table were measured in $CDCl_3$. b) This compound was named as (1*R**,2*S**,3*R**,5*Z*,7*S**,8(17)*Z*,10*R**,-11*R**,12*S**,14*S**)-3,14-diacetoxy-11,12-epoxy-18-oxobriara-5,8(17)-dien-2-yl butanoate. Please see Ref. 39. c) This compound was named as (1*R**,2*R**,5*Z*,7*S**,8(17)*Z*,10*R**,11*R**,12*S**,14*S**)-14-acetoxy-11,12-epoxy-18-oxobriara-5,8(17)-dien-2-yl butanoate. Please see Ref. 39. d) This compound was named as (1*R**,2*R**,4*R**,5*Z*,7*S**,8(17)*Z*,10*R**,11*R**,12*S**,14*S**)-4,14-diacetoxy-11,12-epoxy-18-oxobriara-5,8(17)-dien-2-yl butanoate. Please see Ref. 39. e) This compound was named as (1*R**,2*R**,4*R**,5*Z*,7*S**,8(17)*Z*,10*R**,-11*R**,12*S**,14*S**)-4,14-diacetoxy-11,12-epoxy-18-oxobriara-5,8(17)-dien-2-yl propanoate. Please see Ref. 39. f) This compound was named as (1*R**,2*R**,3*R**,5*Z*,7*S**,8*S**,9*S**,10*S**,11*R**,12*S**,14*S**,17*R**)-2,3,14-triacetoxy-8,17:11,12-bisepoxy-9-hydroxybriar-5-en-18-one. Please see Ref. 40. g) This compound was named as (1*R**,2*R**,3*R**,5*Z*,7*S**,8*S**,9*S**,10*S**,11*R**,12*S**,14*S**,17*R**)-3,14-diacetoxy-2-butyryloxy-8,17:11,12-bisepoxy-9-hydroxybriar-5-en-18-one. Please see Ref. 40. h) This compound was named as (1*R**,2*R**,3*R**,5*Z*,7*S**,8(17)*Z*,10*R**,11*R**,12*S**,14*S**)-2,3,14-triacetoxy-11,12-epoxybriara-5,8(17)-dien-18-one. Please see Ref. 40.

Table 4. ^{1}H and ^{13}C NMR Data (δ) and HMBC Correlations (H → C) for Diterpenoids **2** and **3**

Position	**2**			**3**		
	^{1}H	^{13}C	HMBC	^{1}H	^{13}C	HMBC
1		45.7 (s)[b]			46.9 (s)	
2	4.77 dd (7.2, 2.8)[a]	71.8 (d)	C-14, acetate carbonyl	4.60 d (7.2)	77.2 (d)	C-1, -3, -4, -10, -15, acetate carbonyl
3α	1.76 m	21.8 (t)	C-2, -5	2.15 ddd (15.2, 7.2, 5.6)	40.5 (t)	C-2, -4, -5
β	1.99 m		n.o.	2.84 dd (15.2, 12.4)		C-1, -4, -5
4α	1.90 m	27.0 (t)	C-2, -5, -6, -16	4.14 (12.4, 5.6)	70.7 (d)	C-6, -16
β	2.50 dd (14.4, 7.2)		C-2, -5, -6, -16			
5		145.6 (s)			146.1 (s)	
6	5.38 dd (10.0, 1.2)	119.4 (d)	C-4	5.43 dd (8.0, 1.6)	122.9 (d)	C-4
7	5.66 d (10.0)	74.5 (d)	C-8, -9	6.00 d (8.0)	73.3 (d)	C-5
8		71.0 (s)			70.4 (s)	
9	5.68 d (4.8)	68.7 (d)	C-11, -17, acetate carbonyl	5.90 d (3.2)	66.1 (d)	C-8, -10, -11, -17, acetate carbonyl
10	3.02 br s	40.7 (d)	n.o.	2.51 d (3.2)	48.5 (d)	C-1, -2, -8, -9, -11, -15
11		74.5 (s)			75.2 (s)	
12	3.74 d (5.6)	71.8 (d)	C-11, -13, -14, -20		200.7 (s)	
13	5.83 dd (10.0, 5.6)	124.1 (d)	C-1, -11, -12	6.02 d (10.8)	123.1 (d)	C-1, -11
14	5.36 d (10.0)	139.5 (d)	C-1, -2, -12	6.37 d (10.8)	154.0 (d)	C-2, -10, -12, -15
15	1.15 s	20.6 (q)	C-1, -2, -14	1.35 s	14.7 (q)	C-1, -2, -10, -14
16	1.84 d (1.2)	25.6 (q)	C-4, -5, -6	1.98 d (1.6)	25.8 (q)	C-4, -5, -6
17		62.4 (s)			63.8 (s)	
18	1.53 s	10.0 (q)	C-8, -17, -19	1.67 s	9.9 (q)	C-8, -17, -19
19		170.6 (s)			171.0 (s)	
20	1.41 s	27.5 (q)	C-10, -11, -12	1.36 s	24.3 (q)	C-10, -11, -12
OH-11	n.o.[c]			3.44 s		C-10, -11, -12, -20
2-OAc		170.1 (s)			169.0 (s)	
	2.16 s	21.8 (q)	acetate carbonyl	2.15 s	21.0 (q)	acetate carbonyl
9-OAc		170.1 (s)			168.2 (s)	
	2.23 s	21.3 (q)	acetate carbonyl	2.26 s	21.5 (q)	acetate carbonyl

a) *J* values (in Hz) in parentheses. b) Multiplicity deduced by DEPT and HMQC spectra and indicated by the usual symbols. c) n.o.: not observed.

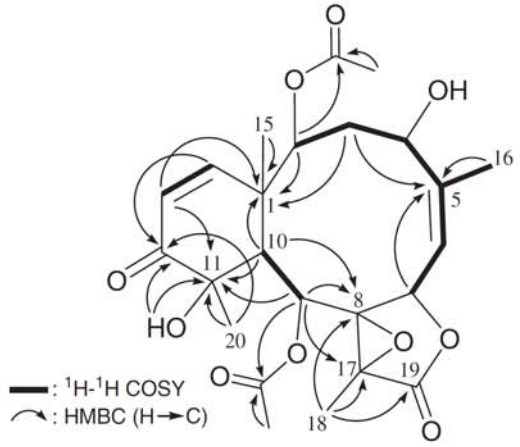

Figure 6. The ^{1}H–^{1}H COSY and selective HMBC correlations (protons and quaternary carbons) of **3**.

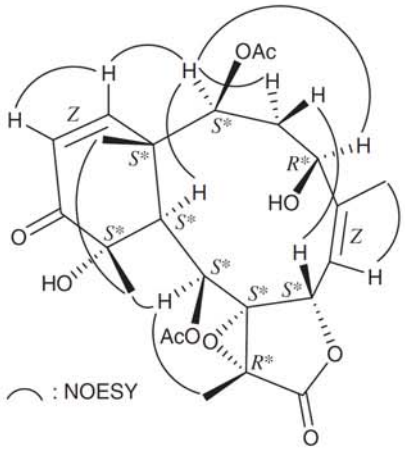

Figure 7. Selective NOESY correlations of **3**.

α face in **3**. One proton attached to C-3 and resonating at δ 2.15 was found to exhibit a correlation with H-2 and was assigned as H-3α proton. Since H-4 exhibited an interaction with H-2, the C-4 hydroxy group should attach to the β face. H-7 showed a correlation with H-3β (δ 2.84), confirming the β-orientation for H-7. Furthermore, H-9 showed correlations with H_3-18 and H_3-20, and, from molecular models, was found to be reasonably close to C-18 and C-20 methyls; therefore, H-9 should be placed on the α face in **3** and C-18 methyl is β-oriented in the γ-lactone moiety. The Z configuration of the C-5/6 double

Table 5. ^{1}H and ^{13}C NMR Data (δ) and HMBC Correlations (H → C) for Diterpenoids **4** and **5**

Position	**4**			**5**		
	^{1}H	^{13}C	HMBC	^{1}H	^{13}C	HMBC
1		42.7 (s)[b)]			45.6 (s)	
2	3.56 d (12.4)[a)]	83.5 (d)	C-1, -3, -4, -10, -14	5.11 br s	75.5 (d)	C-4, -15, acetate carbonyl
3α	5.63 d (9.2)	74.0 (d)	C-5, acetate carbonyl	1.58 m	30.9 (t)	C-5
β				2.71 m		n.o.
4α	1.95 d (14.8)	35.0 (t)	C-2, -3, -5, -6	2.03 m[d)]	28.4 (t)	C-5, -6, -16
β	2.97 dd (14.8, 9.2)		C-2, -3, -5, -6, -16	2.51 m		C-2
5		140.8 (s)			146.9 (s)	
6	5.35 dd (5.2, 1.2)	120.9 (d)	n.o.[c)]	5.37 d (10.0)	118.0 (d)	C-4, -7, -8, -16
7	5.57 dd (5.2, 1.2)	75.6 (d)	C-6, -8, -17	5.25 d (10.0)	78.8 (d)	C-5, -6
8		70.7 (s)			82.4 (s)	
9	3.43 dd (10.4, 1.2)	65.9 (d)	C-8, -11	5.29 d (2.0)	75.3 (d)	C-1, -7, -8, -10, acetate carbonyl
10	3.53 d (10.4)	36.4 (d)	C-1, -14	2.91 dd (5.2, 2.0)	33.7 (d)	C-1, -2, -8, -9, -11, -12, -15, -20
11		131.2 (s)		2.03 m[d)]	45.2 (d)	n.o.
12	5.35 m	118.6 (d)	C-10	3.70 br s	71.3 (d)	n.o.
13α	2.14 m	28.5 (t)	n.o.	1.83 m	29.2 (t)	C-1
β	2.42 br d (18.8)		n.o.	1.98 m		C-11
14	4.77 br s	77.0 (d)	C-12	4.88 dd (3.6, 3.2)	76.6 (d)	C-12, acetate carbonyl
15	1.14 s	16.4 (q)	C-1, -2, -10, -14	1.15 s	15.6 (q)	C-1, -2, -10, -14
16	1.97 br s	22.6 (q)	C-4, -5, -6	1.99 s	27.3 (q)	C-4, -5, -6
17		71.7 (s)		2.51 q (7.6)	43.4 (d)	C-8, -18, -19
18	1.52 s	21.7 (q)	C-8, -17, -19	1.20 d (7.6)	6.6 (q)	C-8, -17, -19
19		175.8 (s)			176.4 (s)	
20	1.67 d (1.2)	22.0 (q)	C-10, -11, -12	1.11 d (6.8)	15.6 (q)	C-10, -11, -12
OH-2	4.11 d (12.4)		C-2			
2-OAc					170.5 (s)	
				2.03 s[d)]	21.6 (q)	acetate carbonyl
3-OAc		170.0 (s)				
	2.06 s	21.4 (q)	acetate carbonyl			
9-OAc					169.1 (s)	
				2.21 s	21.7 (q)	acetate carbonyl
14-OAc		170.6 (s)			170.0 (s)	
	2.12 s	21.9 (q)	acetate carbonyl	2.03 s[d)]	21.6 (q)	acetate carbonyl

a) J values (in Hz) in parentheses. b) Multiplicity deduced by DEPT and HMQC spectra and indicated by usual symbols. c) n.o.: not observed. d) Signals overlapped.

bond was elucidated by a response between H-6 and H_3-16. On the basis of the above observations, the structure of **3** was elucidated and the chiral centers of **3** were assigned as 1S*, 2S*, 4R*, 7S*, 8S*, 9S*, 10S*, 11S*, and 17R*.

The HR-ESI-MS data of **4** (briaexcavatin Y) exhibited a molecular ion peak at m/z 487.1948 ($[M + Na]^+$) with a molecular formula $C_{24}H_{32}O_9$. The IR absorptions were observed at 3454, 1790, and 1727 cm^{-1}, suggesting the presence of hydroxy, γ-lactone, and ester groups. The structure of this compound was deduced from its ^{13}C NMR and DEPT spectra, which showed that this compound has 24 carbons, including six methyls, two sp^3 methylenes, two sp^2 methines, six sp^3 methines (including five oxymethines), three sp^3 quaternary carbons (including two oxygenated quaternary carbons), and five sp^2 quaternary carbons. From ^{1}H and ^{13}C NMR spectra (Table 5), **4** was found to possess two acetoxy groups and a γ-lactone moiety [δ_H 2.12, 2.06, each 3H × s; δ_C 175.8 (s, C-19), 170.6 (s), 170.0 (s)], in addition to two trisubstituted olefins [δ_H 5.35 (1H, dd, $J = 5.2$, 1.2 Hz, H-6), 5.35 (1H, m, H-12); δ_C 140.8 (s, C-5), 131.2 (s, C-11), 120.9 (d, CH-6), 118.6 (d, CH-12)]. A trisubstituted epoxide was elucidated from the NMR signals of an oxymethine (δ_H 3.43, 1H, dd, $J = 10.4$, 1.2 Hz, H-9; δ_C 65.9, d, CH-9) and an oxygenated quaternary carbon (δ 70.7, s, C-8).

From the ^{1}H–^{1}H COSY spectrum of **4** (Figure 8), it was possible to identify the separate spin systems between H-2/H-3/H_2-4, H_2-4/H-6 (by allylic coupling), H-6/H-7, H-6/H_3-16 (by allylic coupling), H-7/H-9 (by long range w coupling), H-9/H-10, H-12/H_2-13/H-14, and H-12/H_3-20 (by allylic coupling), which were assembled with the assistance of an HMBC experiment (Table 5 and Figure 8). Key HMBC correlations between H-2/C-1, -3, -4, -10, -14; H-3/C-5; H_2-4/C-2, -3, -5, -6, -16; H-7/C-6, -8, -17; H-9/C-8, -11; H-10/C-1, -14; H-12/C-10; H-14/C-12; H_3-15/C-1, -2, -10, -14; H_3-16/C-4, -5, -6; H_3-18/C-8, -17, -19; and H_3-20/C-10, -11, -12, permitted connection of carbon skeleton. An acetoxy group positioned at C-3 was confirmed from the HMBC correlation between H-3 (δ 5.63) and the ester carbonyl carbon at δ 170.0 (s). The hydroxy proton signal at δ 4.11 (1H, d, $J = 12.4$ Hz) was revealed by its ^{1}H–^{1}H COSY correlation with H-2 and confirmed by the HMBC correlation with C-2, indicating its attachment to C-2. The remaining acetoxy and hydroxy groups

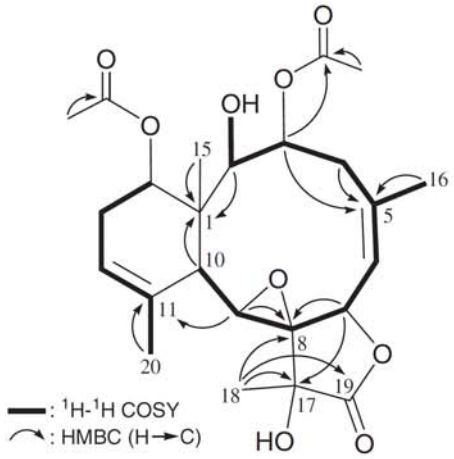

Figure 8. The ^{1}H–^{1}H COSY and selective HMBC correlations (protons and quaternary carbons) of **4**.

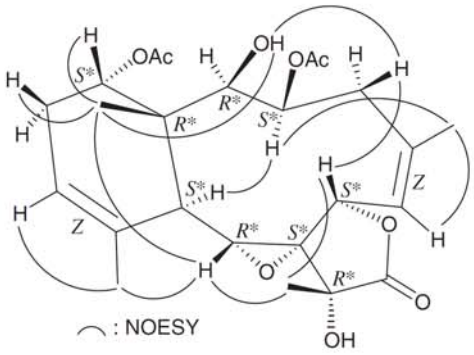

Figure 9. Selective NOESY correlations of **4**.

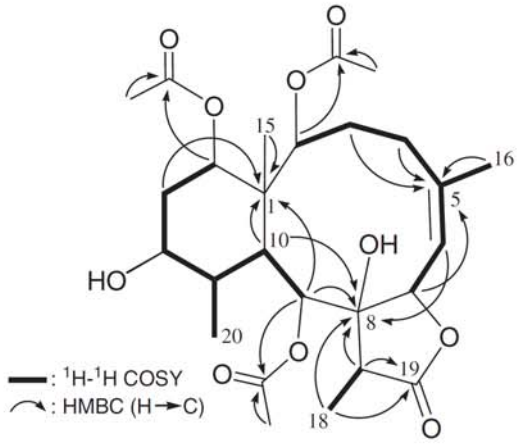

Figure 10. The ^{1}H–^{1}H COSY and selective HMBC correlations (protons and quaternary carbons) of **5**.

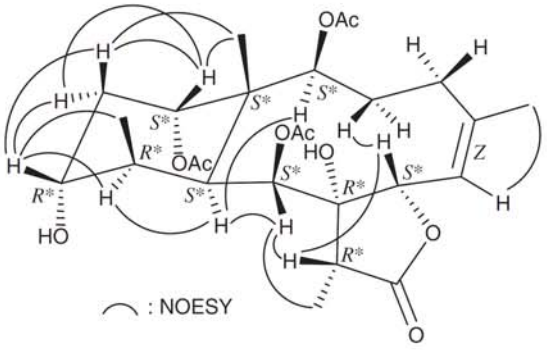

Figure 11. Selective NOESY correlations of **5**.

were positioned at C-14 and C-17, respectively, as indicated by analysis of key ^{1}H–^{1}H COSY correlations and characteristic NMR signals analysis.

The relative stereochemistry of **4** was elucidated by analysis of NOESY correlations as shown in Figure 9 and by vicinal proton coupling constant analysis. The correlations between H-10 and H-3 indicated that these two protons are situated on the same face and were arbitrary assigned as α protons since C-15 methyl group is β-oriented and did not show correlation with H-10. H-14 was found to exhibit response with H_3-15, but not with H-10, revealing the β-orientation of this proton. One of the methylene protons at C-4 (δ 2.97) exhibited a correlation with OH-2 but not with H-3 and was assigned as H-4β while the other was denoted as H-4α (δ 1.95). The correlations between H-4β/H-7 and H-7/H_3-18 reflected the β-orientation of H-7 and C-18 methyl. The correlations of H_3-16 with H-6; and H_3-20 with H-12, revealed the Z geometry of C-5/6 and C-11/12 double bonds. H-9 was found to show correlations with H_3-15, H_3-18, and H_3-20; and a large coupling constant (10.4 Hz) was found between H-9 and H-10, indicating the dihedral angle between H-9 and H-10 is approximately 180° and H-9 has a β-orientation at C-9. From the above results, the configurations of chiral centers of **4** were assigned as 1R*, 2R*, 3S*, 7S*, 8S*, 9R*, 10S*, 14S*, and 17R*.

Briaexcavatin Z (**5**) was isolated as a white powder and had the molecular formula $C_{26}H_{38}O_{10}$ on the basis of HR-ESI-MS (see Experimental). The IR spectrum of **5** showed bands at 3455, 1771, and 1736 cm^{-1}, consistent with the presence of hydroxy, γ-lactone, and ester carbonyl groups. It was found that the spectral data of **5** were very similar to those of known briarane metabolites, pachyclavulide A (**7**)[49] and briareolide F (**8**).[34] However, by comparison of the ^{1}H and ^{13}C NMR chemical shifts of C-12 oxymethine of **5** (δ_H 3.70, 1H, br s; δ_C 71.3, d) (Table 5) with those of **7** (δ_H 3.98, 1H, td, J = 4.4, 11.3 Hz; δ_C 66.9, d) and **8** (δ_H 3.70, 1H, m; δ_C 71.2, d), it was shown that the hydroxy group in **5** attached at C-12 is α-oriented, and this compound should possess a structure as represented by formula **5**. The structure of **5** was further confirmed by 2D NMR experiments (Table 5 and Figure 10) and the chiral centers for this compound were assigned as 1S*, 2S*, 7S*, 8R*, 9S*, 10S*, 11R*, 12R*, 14S*, and 17R* by its NOESY experiment (Figure 11).

It is noteworthy to mention that briaexcavatin Y (**4**) represents the first example of a briarane possessing a C-8/9 epoxy group. The 3(E),5(Z)-conjugated diene system as shown in briaexcavatin V (**1**) is rarely found in briarane analogs.[30,50] In biological activity testing, briaranes **1**, **3**, and **4** have displayed weak inhibitory effects on superoxide anion gen-

Table 6. Inhibitory Effects of Briaranes **1**–**5** on Superoxide Anion Generation and Elastase Release by Human Neutrophils in Response to fMet–Leu–Phe/Cytochalastin B

Compound	Speroxide generation	Elastase release
	Inh./%[a)]	Inh./%[a)]
1	11.39 ± 1.26	23.27 ± 8.65
2	4.17 ± 1.04	−0.64 ± 4.93
3	13.69 ± 3.84	3.24 ± 3.85
4	17.47 ± 0.85	1.56 ± 3.86
5	0.67 ± 2.09	−28.95 ± 7.39

a) Percentage of inhibition at 10 μg mL^{-1}. Results are presented as means ± SEM ($n = 3$ or 4).

eration by human neutrophils. Briarane **1** was found to show mild inhibitory effects on human neutrophil elastase release and **5** exhibited mild activity to enhance human neutrophil elastase release (Table 6).

Experimental

General Experimental Procedures. Melting points were determined on FARGO apparatus and were uncorrected. Optical rotation values were measured with a JASCO P-1010 digital polarimeter. Infrared spectra were obtained on a VARIAN DIGLAB FTS 1000 FT-IR spectrophotometer. NMR spectra were recorded on a VARIAN MERCURY PLUS 400 FT-NMR at 400 MHz for ^{1}H and 100 MHz for ^{13}C, in $CDCl_3$. Proton chemical shifts were referenced to the residual $CHCl_3$ signal (δ 7.26). ^{13}C NMR spectra were referenced to the center peak of $CDCl_3$ at δ 77.1. ESI-MS and HR-ESI-MS data were recorded on a BRUKER APEX II mass spectrometer. Column chromatography was performed on silica gel (230–400 mesh, MERCK, Darmstadt, Germany). TLC was carried out on precoated Kieselgel 60 F_{254} (0.25 mm, MERCK) and spots were visualized by spraying with 10% H_2SO_4 solution followed by heating. HPLC was performed using a system comprising a HITACHI L-7100 pump, a HITACHI photo diode array detector L-7455, and a RHEODYNE 7725 injection port. A preparative reverse phase column (Hibar 250 × 25 mm, LiChrospher 100 RP-18e, 5 μm, MERCK) was used for HPLC.

Animal Material. Specimens of the cultured octocoral *B. excavatum* were collected in 0.6-ton cultivating tanks located in the NMMBA, Taiwan, in December 2006. This organism was identified by comparison with previous descriptions.[51–53]

Extraction and Isolation. The freeze-dried and minced material of *B. excavatum* (wet weight 672 g, dry weight 270 g) was extracted with a mixture of MeOH and CH_2Cl_2 (1:1). The residue was partitioned between EtOAc and H_2O. The EtOAc layer was separated on Sephadex LH-20 and eluted using MeOH/CH_2Cl_2 (2:1) to yield fractions A–C. Fraction C was separated on silica gel and eluted using hexane/EtOAc (stepwise, 20:1–pure EtOAc) to yield fractions 1–9. Fraction C9 was separated by column chromatography on silica gel and eluted using CH_2Cl_2/acetone (stepwise, 10:1–3:1) to afford fractions C9-1 to C9-8. Fraction C9-2 was repurified by reverse phase C-18 column chromatography using MeOH/H_2O (1:1) to afford fractions C9-2-1 to C9-2-6. Fractions C9-2-1, C9-2-2, C9-2-4, and C9-2-6 were repurified by reverse phase HPLC, respectively, using MeOH/CH_3CN/H_2O to afford briaranes **3** (49:1:50), **2** (47:1:52), **1** (54:1:45), and **4** (64:1:35). Fraction C9-7 was further chromatographed on reverse phase C-18 column chromatography using MeOH/H_2O to afford **5** (1:1).

Briaexcavatin V (1): White powder (1.5 mg); mp 262–264 °C; $[\alpha]_D^{24}$ −17 (*c* 0.08, $CHCl_3$); IR (neat) ν_{max} 3459, 1767, 1728 cm^{-1}; ^{1}H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR data, see Table 1; ESI-MS *m/z* 485 (M + Na)$^+$; HR-ESI-MS *m/z* 485.1791 (calcd for $C_{24}H_{30}O_9$ + Na, 485.1787).

Briaexcavatin W (2): White powder (2.3 mg); mp 247–249 °C; $[\alpha]_D^{24}$ −99 (*c* 0.12, $CHCl_3$); IR (neat) ν_{max} 3497, 1775, 1728 cm^{-1}; ^{1}H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR data, see Table 4; ESI-MS *m/z* 487 (M + Na)$^+$; HR-ESI-MS *m/z* 487.1943 (calcd for $C_{24}H_{32}O_9$ + Na, 487.1944).

Briaexcavatin X (3): White powder (1.3 mg); mp 192–194 °C; $[\alpha]_D^{24}$ −16 (*c* 0.07, $CHCl_3$); IR (neat) ν_{max} 3459, 1775, 1744, 1696 cm^{-1}; ^{1}H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR data, see Table 4; ESI-MS *m/z* 501 (M + Na)$^+$; HR-ESI-MS *m/z* 501.1739 (calcd for $C_{24}H_{30}O_{10}$ + Na, 501.1737).

Briaexcavatin Y (4): White powder (1.8 mg); mp 137–139 °C; $[\alpha]_D^{24}$ +12 (*c* 0.05, $CHCl_3$); IR (neat) ν_{max} 3454, 1790, 1727 cm^{-1}; ^{1}H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR data, see Table 5; ESI-MS *m/z* 487 (M + Na)$^+$; HR-ESI-MS *m/z* 487.1948 (calcd for $C_{24}H_{32}O_9$ + Na, 487.1944).

Briaexcavatin Z (5): White powder (3.4 mg); mp 175–176 °C; $[\alpha]_D^{24}$ +47 (*c* 0.16, $CHCl_3$); IR (neat) ν_{max} 3455, 1771, 1736 cm^{-1}; ^{1}H ($CDCl_3$, 400 MHz) and ^{13}C ($CDCl_3$, 100 MHz) NMR data, see Table 5; ESI-MS *m/z* 533 (M + Na)$^+$; HR-ESI-MS *m/z* 533.2359 (calcd for $C_{26}H_{38}O_{10}$ + Na, 533.2362).

Single-Crystal X-ray Crystallography of Briaexcavatin W (2). Suitable colorless prisms of **2** were obtained from a solution of MeOH. The crystal (0.38 × 0.30 × 0.38 mm) belongs to the orthorhombic system, space group $P2_12_12_1$ (# 19), with a = 8.768(2) Å, b = 17.340(4) Å, c = 31.059(6) Å, V = 4722(2) Å^3, $Z = 8$, D_{calcd} = 1.307 g cm^{-3}, λ (Mo Kα) = 0.71073 Å. Intensity data were measured on a Bruker diffractometer up to $2\theta_{max}$ of 50°. All 36438 reflections were collected. The structure was solved by direct methods and refined by a full-matrix least-squares procedure. The refined structural model converged to a final $R1$ = 0.0479; $wR2$ = 0.119 for 6204 observed reflections [$I > 2\sigma(I)$] and 610 variable parameters.

Crystallographic data for the structure of briaexcavatin W (**2**) has been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 711606. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

Human Neutrophil Superoxide Anion Generation and Elastase Release. Human neutrophils were obtained by means of dextran sedimentation and Ficoll centrifugation. Superoxide generation and elastase release were carried out according to procedures described previously.[54,55] Briefly, superoxide anion production was assayed by monitoring the superoxide dismutase-inhibitable reduction of ferricytochrome *c*. Elastase release experiments were performed using MeO–Suc–Ala–Ala–Pro–Val–*p*-nitroanilide as the elastase substrate.

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