Junceellolides J−L, 11,20-Epoxybriaranes from the Gorgonian Coral *Junceella fragilis*

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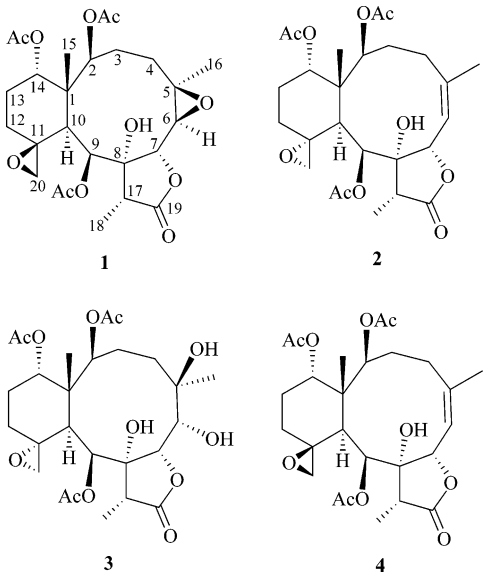
Three new 11,20-epoxybriarane diterpenoids, junceellolides J−L (**1**−**3**), along with a known metabolite, **4**, have been isolated from the gorgonian coral *Junceella fragilis*. The structures of these metabolites were elucidated using spectroscopic methods. The cyclohexane rings were found to exist in boat form in briaranes **1** and **4** and in chair form in **2** and **3**. The structure of **1** was further confirmed by chemical conversion and single-crystal X-ray diffraction analysis. The relationship between ^{13}C NMR chemical shifts and the conformation of the cyclohexane ring in briaranes possessing an 11,20-epoxy group are described. The briaranes **2** and **4** showed mild inhibitory effects on human neutrophil elastase release.

Gorgonian corals belonging to the genus *Junceella* (Cnidaria, Gorgonacea, Ellisellidae),[1−3] abundant in the coral reefs of the tropical Indo-Pacific Ocean, have been recognized as rich sources for marine natural products, most of which possess unique structural features.[4] In previous studies, various diterpenoids featuring a 3,8-cyclized cembrane (briarane) carbon skeleton were isolated from *Junceella fragilis* (Ridley).[5−13] During our continuing studies on the chemical constituents of *J. fragilis*, four 11,20-epoxybriaranes, including three new diterpenoids, junceellolides J−L (**1**−**3**), and a known metabolite, **4**,[7] were isolated from *J. fragilis*. Although a series of studies have been made on the identification of briarane derivatives in marine organisms,[14,15] little is known about the conformation of the cyclohexane ring in briarane-type natural products. The isolation, structure elucidation, and biological activity of metabolites **1**−**4** and the relationship between ^{13}C NMR chemical shifts and the conformation of the cyclohexane ring in briaranes possessing an 11,20-epoxy group are reported in this paper.

Specimens of the gorgonian *J. fragilis*, collected at the coast of southern Taiwan, were minced and extracted with EtOAc. The extract was separated using Si gel column chromatography. Junceellolide J (**1**) was obtained as colorless crystals. The FABMS of **1** displayed a pseudomolecular ion at *m*/*z* 547 (M^+ + Na), suggesting a molecular formula of $C_{26}H_{36}O_{11}$, which was confirmed by HRESIMS. Thus, nine degrees of unsaturation were deduced for **1**. IR absorptions were observed at 3339, 1780, and 1738 cm^{-1}, suggesting the presence of hydroxy, γ-lactone, and ester groups in **1**. The FABMS of **1** exhibited peaks at *m*/*z* 547 (M^+ + Na), 507 (M^+ + H − H_2O), 465 (M^+ + H − AcOH), 447 (M^+ + H − H_2O − AcOH), 405 (M^+ + H − 2AcOH), 387 (M^+ + H − H_2O − 2AcOH), 345 (M^+ + H − 3AcOH), and 327 (M^+ + H − H_2O − 3AcOH), indicating the presence of a hydroxy and three acetoxy groups in **1**. Resonances in the ^{13}C NMR spectrum of **1** at δ 175.6 (q, C), 170.8 (q, C), 169.8 (q, C), and 169.6 (q, C) supported the presence of a γ-lactone and three additional ester groups (Table 1). The esters were identified as acetates by the presence of three



methyl resonances in the ^{1}H NMR spectrum at δ 2.21 (3H, s), 2.03 (3H, s), and 2.01 (3H, s) (Table 2). On the basis of above data, briarane **1** was found to be pentacyclic. An epoxide containing a methyl substituent was confirmed from the signals of two oxygen-bearing carbons at δ 62.5 (q, C-5) and 60.1 (CH-6) and from the proton signal of a methyl singlet resonating at δ 1.64 (3H, s, H_3-16). Furthermore, the carbon resonances at δ 62.6 (q, C-11) and 59.3 (CH_2-20) indicated the presence of an exocyclic epoxy group in **1**. The proton chemical shifts of H_2-20 (δ 3.01, 1H, d, J = 3.2 Hz; 2.94, 1H, d, J = 3.2 Hz) confirmed the presence of this group. Moreover, a methyl doublet (δ 1.19, 3H, d, J = 7.2 Hz, H_3-18), a methyl singlet (δ 1.11, 3H, s, H_3-15), two aliphatic methine protons (δ 2.37, 1H, q, J = 7.2 Hz, H-17; 2.11, 1H, d, J = 6.0 Hz, H-10), four pairs of methylene protons (δ 2.27, 1H, m, H-3; 1.57, 1H, m, H-3′; 2.24, 1H, m, H-4; 1.86, 1H, m, H-4′; 2.36, 1H, m, H-12; 1.19, 1H, m, H-12′; 2.17, 1H, m, H-13; 1.80, 1H, m, H-13′), five oxymethine protons (δ 5.72, 1H, d, J = 6.0 Hz, H-9; 5.08, 1H, d, J = 5.6 Hz, H-2; 4.84, 1H, d, J = 4.4 Hz, H-14; 4.30, 1H, d, J = 9.2 Hz, H-7; 3.39, 1H, d, J = 9.2 Hz, H-6), and a hydroxy proton (δ 5.19, 1H, d, J = 1.2 Hz, OH-8) were observed in the ^{1}H NMR spectrum of **1**.

Comparison of the spectral data of **1** with those of the known metabolite **4** showed that the carbon−carbon double bond between

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Table 1. ^{13}C NMR Chemical Shifts for Diterpenoids **1**−**4**[a]

position	**1**		**2**		**3**		**4**			
1	47.0	(q,C)[b]	48.5	(q,C)	48.7	(q,C)	47.0	(q,C)	47.4	(q,C)[c]
2	74.4	(CH)	75.8	(CH)	79.5	(CH)	74.9	(CH)	73.4	(CH)
3	27.8	(CH_2)	31.3	(CH_2)	29.1	(CH_2)	29.0	(CH_2)	31.9	(CH_2)
4	31.5	(CH_2)	29.6	(CH_2)	35.0	(CH_2)	32.3	(CH_2)	28.7	(CH_2)
5	62.5	(q,C)	146.2	(q,C)	89.6	(q,C)	144.0	(q,C)	135.6	(q,C)
6	60.1	(CH)	118.9	(CH)	82.7	(CH)	121.1	(CH)	120.7	(CH)
7	80.4	(CH)	77.9	(CH)	89.7	(CH)	78.3	(CH)	77.9	(CH)
8	79.9	(q,C)	81.5	(q,C)	92.6	(q,C)	80.5	(q,C)	80.1	(q,C)
9	67.1	(CH)	65.3	(CH)	73.0	(CH)	67.8	(CH)	77.6	(CH)
10	42.3	(CH)	38.5	(CH)	42.8	(CH)	39.9	(CH)	39.6	(CH)
11	62.6	(q,C)	59.9	(q,C)	56.8	(q,C)	62.6	(q,C)	62.6	(q,C)
12	23.7	(CH_2)	29.4	(CH_2)	30.1	(CH_2)	24.0	(CH_2)	23.6	(CH_2)
13	24.2	(CH_2)	25.1	(CH_2)	24.7	(CH_2)	24.6	(CH_2)	24.3	(CH_2)
14	73.3	(CH)	75.8	(CH)	75.0	(CH)	73.6	(CH)	67.4	(CH)
15	14.2	(CH_3)	15.0	(CH_3)	14.7	(CH_3)	14.8	(CH_3)	14.5	(CH_3)
16	26.7	(CH_3)	28.0	(CH_3)	30.5	(CH_3)	28.3	(CH_3)	28.1	(CH_3)
17	42.7	(CH)	43.5	(CH)	46.9	(CH)	42.5	(CH)	42.3	(CH)
18	6.5	(CH_3)	6.8	(CH_3)	9.7	(CH_3)	6.9	(CH_3)	6.5	(CH_3)
19	175.6	(q,C)	176.2	(q,C)	176.7	(q,C)	176.7	(q,C)	176.8	(q,C)
20	59.3	(CH_2)	51.2	(CH_2)	51.3	(CH_2)	59.4	(CH_2)	59.1	(CH_2)
acetate methyls	21.7	(CH_3)	21.9	(CH_3)	22.1	(CH_3)	21.9	(CH_3)	21.7	(CH_3)
	21.1	(CH_3)	21.7	(CH_3)	21.7	(CH_3)	21.2	(CH_3)	20.9	(CH_3)
	20.9	(CH_3)	21.5	(CH_3)	21.3	(CH_3)	21.2	(CH_3)	20.8	(CH_3)
acetate carbonyls	170.8	(q,C)	170.9	(q,C)	171.0	(q,C)	170.9	(q,C)	170.6	(q,C)
	169.8	(q,C)	170.2	(q,C)	170.8	(q,C)	170.2	(q,C)	170.2	(q,C)
	169.6	(q,C)	170.0	(q,C)	170.7	(q,C)	169.8	(q,C)	169.9	(q,C)

[a] Spectra recorded at 100 MHz in $CDCl_3$ at 25 °C. [b] Multiplicity deduced by DEPT. The values are downfield in ppm from TMS. [c] Data were reported by García et al. (see ref 7).

Table 2. ^1H NMR Chemical Shifts for Diterpenoids **1**−**4**[a]

position	**1**	**2**	**3**	**4**	
2	5.08 d (5.6)[b]	5.08 dd (4.0, 1.6)	5.58 dd (4.0, 2.0)	4.64 d (4.8)	4.71 br d (4.9)[c]
3	2.27 m	2.89 td (15.2, 5.6)	3.17 br t (14.4)	2.43 m	2.51 m
3′	1.57 m	1.46 m	1.23 m	2.02 m	1.71 m
4	2.24 m	2.14 m	2.09 m	2.39 m	2.01 m
4′	1.86 m	2.08 m	1.86 m	1.56 m	1.05 m
6	3.39 d (9.2)	5.47 d (9.6)	4.22 br s	5.54 dd (10.0, 1.2)	5.60 br d (10.2)
7	4.30 d (9.2)	5.03 d (9.6)	4.63 s	5.08 d (10.0)	5.13 d (10.2)
9	5.72 d (6.0)	4.78 d (3.2)	5.36 s	5.55 d (5.6)	4.84 d (4.9)
10	2.11 d (6.0)	2.95 d (3.2)	2.92 s	2.33 d (5.6)	2.17 s
12	2.36 m	2.42 dd (14.3, 6.0)	2.15 m	2.23 m	1.81 m
12′	1.19 m	1.04 m	1.19 m	1.08 m	1.05 m
13	2.17 m	1.85 m	1.89 m	2.07 m	2.4 m
13′	1.80 m	1.62 m	1.79 m	1.70 m	2.1 m
14	4.84 d (4.4)	4.71 br s	4.96 br s	4.76 d (4.8)	5.63 br d (5.4)
15	1.11 s	0.94 s	1.15 s	1.03 s	1.10 s
16	1.64 s	2.05 s	1.25 s	1.95 d (1.2)	2.02 s
17	2.37 q (7.2)	2.26 q (7.2)	2.82 q (6.8)	2.29 q (7.2)	2.37 q (7.1)
18	1.19 d (7.2)	1.08 d (7.2)	1.37 d (6.8)	1.07 d (7.2)	1.15 d (7.1)
20a	3.01 d (3.2)	3.43 br s	2.62 d (2.8)	2.90 d (4.0)	2.98 br d (4.1)
20b	2.94 d (3.2)	2.52 d (2.4)	2.37 d (2.8)	2.79 d (4.0)	2.86 br d (4.1)
OH-8	5.19 d (1.2)			4.83 s	
acetates	2.21 s	2.12 s	2.11 s	2.16 s	2.23 s
	2.03 s	2.00 s	2.04 s	1.94 s	2.02 s
	2.01 s	1.94 s	1.99 s	1.90 s	1.97 s

[a] Spectra recorded at 400 MHz in $CDCl_3$ at 25 °C. [b] *J* values (in Hz) in parentheses. [c] Data were reported by García et al. (see ref 7).

C-5 and C-6 in **4** (δ_H 5.54, 1H, dd, J = 10.0, 1.2 Hz, H-6; δ_C 144.0, q, C-5; 121.1, CH-6) was replaced by an epoxy group in **1** (δ_H 3.39, 1H, d, J = 9.2 Hz, H-6; δ_C 62.5, q, C-5; 60.1, CH-6). This observation and the planar structure of **1** could be determined essentially from the $^1H-^1H$ COSY and HMBC correlations cited in Figure 1 and supported by chemical interconversion from **4**. Thus, briarane **4** was submitted to epoxidation with *m*-CPBA in dichloromethane to give a compound whose spectral data (IR, ^1H and ^{13}C NMR) and optical rotation value were coincident with those of natural product **1**. The structure of **1** was further confirmed by single-crystal X-ray diffraction analysis (Figure 2). The X-ray structure shows the twist-boat conformation of the cyclohexane in **1**, and this observation was also supported by the NOESY correlations of **1** (Figure 3). The absolute structure of the known metabolite **4** has been established;[7] therefore, we are able to assign the absolute configurations of all the chiral centers of **1** as 1*R*,2*S*,5*R*,6*S*,7*S*,8*R*,9*S*,10*S*,11*S*,14*S*,17*R*, by comparison with those of **4**. Moreover, by comparison of the ^{13}C NMR data with those of **1** (δ_C 62.6, q, C-11; 59.3, CH_2-20), the stereochemistry of the 11,20-epoxide in the known metabolites **4** (δ_C 62.6, q, C-11; 59.4, CH_2-20)[7] and junceellolide F (δ_C 62.4, q, C-11; 59.1, CH_2-20)[8] should be redrawn as being of β-orientation. The configurations of C-11 in briaranes **1** and **4** are worthy of comment. In the previous study, the absolute configuration of C-11 in the known briarane **4** was assigned as *R*.[7] However, due to the definition of the *R* and *S* configurations of chiral carbons[16] and by comparison of its ^{13}C NMR data with those of two unnamed known briaranes isolated from a Japanese octocoral *Ellisella* sp.,[17] the configuration of C-11

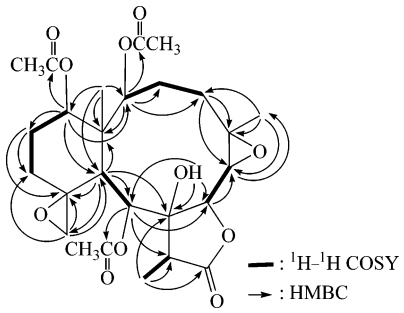

Figure 1. ^{1}H−^{1}H COSY and selective HMBC correlations of **1**.

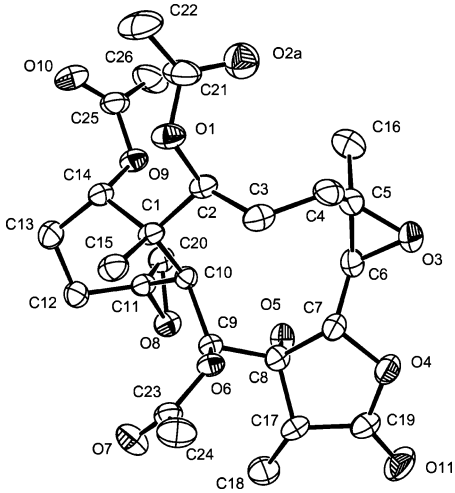

Figure 2. Computer-generated ORTEP plot of **1** showing the relative configuration.

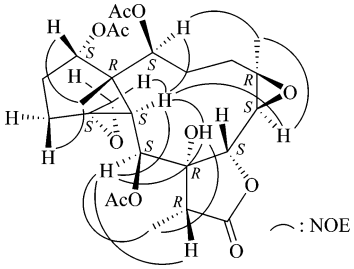

Figure 3. Selective NOESY correlations of **1**.

for the known briarane **4** should be reassigned as *S*. On the basis of detailed analysis of 1D and 2D NMR data, the ^{13}C and ^{1}H NMR chemical shifts for the known briarane **4** were reassigned in this study (Tables 1 and 2).

Junceellolide K (**2**) had the same molecular formula as that of **4**, $C_{26}H_{36}O_{10}$, as determined by HRESIMS, with nine degrees of unsaturation. Through detailed spectral analysis (IR, MS, ^{1}H and ^{13}C NMR) it was found that the structure of **2** was similar to that of **4**. Comparison of the ^{13}C NMR chemical shifts of C-11 and C-20 of **2** (δ 59.9, q, C-11; 51.2, CH_2-20) with those of **1** (δ 62.6, q, C-11; 59.3, CH_2-20) and **4** (δ 62.6, q, C-11; 59.4, CH_2-20) showed that the relative stereochemistry of C-11 in **2** is of *R* form, leading to the configuration of cyclohexane in the chair form.

Junceellolide L (**3**) had the molecular formula $C_{26}H_{38}O_{12}$ as determined by FABMS and NMR data, implying eight degrees of unsaturation. By comparison of the MS and ^{1}H and ^{13}C NMR data with those of **2**, briarane **3** was found to be the 5,6-dihydroxy derivative of **2**. The relative stereochemistry of **3** was determined from a NOESY experiment (Figure 4). In the NOESY spectrum of **3**, H-7 showed NOE interactions with H-6 and H-17, suggesting that H-6 and H-7 are β-oriented. H_3-16 was found to show an NOE correlation with H-6, but not with H-7, indicating that this methyl

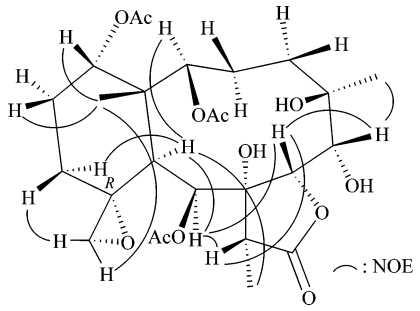

Figure 4. Selective NOESY correlations of **3**.

group is α-oriented. Furthermore, comparison of the ^{13}C NMR chemical shifts of C-11 and C-20 of **3** (δ 56.8, q, C-11; 51.3, CH_2-20) with those of **2** (δ 59.9, q, C-11; 51.2, CH_2-20) and **1** (δ 62.6, q, C-11; 59.3, CH_2-20) indicated that the epoxy group in **3** was also 11*R*, and the cyclohexane ring of **3** should be presented as having a chair conformation.

From the characteristics of chemical shifts it was known that the briarane derivatives contained an 11,20-epoxy group. We summed up the chemical shifts for C-11 and C-20; these appear at δ 62−63 and 58−60 ppm, respectively, while the epoxy group existed in 11*S* form and led the cyclohexane rings to show a boat conformation (Table 3).[7,8,17] Furthermore, if the epoxy group was found to exist in the 11*R* configuration, the ^{13}C NMR data for C-11 and C-20 were shifted upfield and appeared at δ 55−61 and 47−52 ppm, and the cyclohexane rings were found to exist in the chair conformation (Table 4).[6,13,18−32]

In the biological activity testing, briaranes **2** and **4** were found to exhibit mild activity inhibiting human neutrophil elastase release at 10 μg/mL (Table 5).

Experimental Section

General Experimental Procedures. Melting points were determined on a Fargo apparatus and are uncorrected. Optical rotation values were measured in $CHCl_3$ or CH_2Cl_2 with a JASCO P-1010 digital polarimeter at 25 °C. Infrared spectra were obtained on a Varian DIGLAB FTS 1000 FT-IR spectrometer. Low-resolution mass data were obtained by FAB with a VG QUATTRO GC/MS spectrometer. HRMS data were recorded by ESI FT-MS on a Bruker APEX II mass spectrometer. NMR spectra were recorded on a Varian Mercury PLUS 400 FT-NMR at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively, in $CDCl_3$ using TMS as an internal standard. Column chromatography was performed on Si 60 (230−400 mesh) (Merck, Darmstadt, Germany). TLC spots (Si gel 60 F_{254}, Merck) were detected with a UV_{254} lamp and by 10% H_2SO_4 followed by heating at 120 °C for 5 min. All solvents used were either freshly distilled or of analytical grade.

Animal Material. A specimen of *J. fragilis* was collected by hand using scuba at the southern Taiwan coast in December 2002, at a depth of −10 m. Living reference specimens are being maintained in the authors' tanks, and the voucher specimen was deposited in the National Museum of Marine Biology and Aquarium (NMMBA). This organism was identified from descriptions.[1−3]

Extraction and Isolation. The organism (wet weight 780 g) was collected and freeze-dried. The freeze-dried material (570 g) was minced and extracted with EtOAc. The remaining mixture was separated by silica gel column chromatography, using *n*-hexane and *n*-hexane−EtOAc mixtures of increasing polarity. Briarane **4** was eluted with *n*-hexane−EtOAc (3:1), **2** with *n*-hexane−EtOAc (5:2), **1** with *n*-hexane−EtOAc (2:1), and **3** with *n*-hexane−EtOAc (1:1).

Junceellolide J (1): colorless crystals (18.7 mg); mp 254−255 °C; $[\alpha]^{25}_D$ −82 (*c* 0.7, $CHCl_3$); IR (neat) ν_{max} 3339, 1780, 1738, 1375, 1219 cm^{-1}; ^{13}C ($CDCl_3$, 100 MHz) and ^{1}H ($CDCl_3$, 400 MHz) NMR data, see Tables 1 and 2; FABMS *m*/*z* 547 (M^+ + Na, 0.1), 507 (0.1), 465 (0.9), 447 (0.1), 405 (0.2), 387 (0.2), 345 (0.3), 327 (1.1); HRESIMS *m*/*z* 547.2152 (calcd for $C_{26}H_{36}O_{11}$ + Na, 547.2155).

Junceellolide K (2): white powder (7.5 mg); mp 265−268 °C; $[\alpha]^{25}_D$ −28 (*c* 0.3, $CHCl_3$); IR (neat) ν_{max} 3358, 1775, 1738, 1256, 1219 cm^{-1}; ^{13}C ($CDCl_3$, 100 MHz) and ^{1}H ($CDCl_3$, 400 MHz) NMR

Table 3. 11,20-Epoxy ^{13}C NMR Chemical Shifts for Briaranes Possessing a Cyclohexane Ring in the Boat Form

compound	C-11*S* (q,C)	C-20 (CH_2)	ref
junceellolide J (**1**)	62.6	59.3	
(−)-11β,20β-epoxy-4-deacetoxyjunceellolide D (**4**)	62.6	59.4	
(+)-11α,20α-epoxyjunceellolide D[a]	62.3	59.1	7
(−)-11α,20α-epoxy-4-deacetyljunceellolide D[a]	62.3	59.1	7
(−)-11α,20α-epoxy-4-deacetoxyjunceellolide D[a]	62.6	59.1	7
junceellolide F[a]	62.4	59.1	8
unnamed briarane analogue[b]	62.7	58.3	17
unnamed briarane analogue[c]	62.2	58.2	17

[a] The stereochemistry of the 11,20-epoxy group in these four metabolites should be revised as having a β-orientation. [b] This metabolite was reported as compound **3** in ref 17. [c] This metabolite was reported as compound **4** in ref 17.

Table 4. 11,20-Epoxy ^{13}C NMR Chemical Shifts for Briaranes Possessing a Cyclohexane Ring in the Chair Form

compound	C-11*R* (q,C)	C-20 (CH_2)	ref
junceellolide K (**2**)	59.9	51.2	
junceellolide L (**3**)	56.8	51.3	
junceellonoid C	57.0	51.7	13
juncenolide A	57.1	51.4	18
juncenolide B[a]	58.3	50.1	19
juncenolide C	58.3	49.0	19
juncenolide D	58.2	49.0	19
juncenolide E	58.0	50.1	20
juncenolide F	57.4	50.5	21
juncenolide G	57.2	49.9	21
praelolide	56.2	51.3	22
junceellin B	55.4	50.2	23
nui-inoalide A	55.5	51.1	24
nui-inoalide B	60.2	48.4	24
umbraculolide B	57.9	50.1	25
juncin H	57.8	50.7	26
(+)-gemmacolide A	56.8	50.4	26
(+)-gemmacolide B	56.9	50.4	26
gemmacolide A	56.8	50.4	27
gemmacolide B	56.8	50.4	27
gemmacolide C	57.5	50.3	27
gemmacolide D	59.1	48.8	27
gemmacolide E	59.5	48.9	27
gemmacolide F	57.9	49.2	27
juncin A	59.3	50.5	28
juncin C	57.9	49.7	28
juncin D	57.8	49.5	28
juncin E	57.1	49.5	28
juncin I	58.2	48.7	29
juncin J	58.4	48.9	29
juncin K	59.2	49.0	29
juncin L	56.8	50.5	29
juncin M	57.5	50.7	29
juncin O	56.4	49.3	30
juncin P	56.5	50.0	30
juncin Q	60.4	47.5	30
juncenolide B[a]	56.8	50.8	31
junceellolide C	57.2	50.1	6
unnamed briarane analogue[b]	58.1	50.8	32

[a] These two briaranes are designated as juncenolide B by two research groups, respectively (see refs 19 and 31). [b] This metabolite was reported as (1*R*,2*R*,5*Z*,7*R*,8*S*,9*R*,10*R*,11*R*,14*R*,17*S*)-2,14-diacetoxy-8,17:11,20-bis-epoxy-9-hydroxy-briar-5-en-18-one.

data, see Tables 1 and 2; FABMS *m*/*z* 509 ($M^+ + H$, 0.1), 449 (0.2), 431 (0.1), 389 (0.2), 371 (0.2), 329 (0.6), 311 (0.6); HRESIMS *m*/*z* 531.2207 (calcd for $C_{26}H_{36}O_{10}$ + Na, 531.2206).

Junceellolide L (3): white powder (13.0 mg); mp 243−245 °C; $[\alpha]^{25}_D$ +43 (*c* 0.7, $CHCl_3$); IR (neat) ν_{max} 3418, 1780, 1734, 1373, 1238 cm^{-1}; ^{13}C ($CDCl_3$, 100 MHz) and ^1H ($CDCl_3$, 400 MHz) NMR data, see Tables 1 and 2; FABMS *m*/*z* 465 ($M^+ + H - AcOH - H_2O$, 1.4), 429 (0.1), 405 (0.2), 387 (0.1), 327 (0.7), 309 (0.2); HRESIMS *m*/*z* 465.2125 (calcd for $C_{26}H_{38}O_{12} + H - AcOH - H_2O$, 465.2124).

(−)-11β,20β-Epoxy-4-deacetoxyjunceellolide D (4): white powder (36.8 mg); mp 123−125 °C; $[\alpha]^{25}_D$ −57 [*c* 0.9, CH_2Cl_2 (lit.[7] $[\alpha]^{22}_D$ −53.1 (*c* 0.5, CH_2Cl_2)]; IR (neat) ν_{max} 3295, 1775, 1740, 1252, 1219 cm^{-1}; ^{13}C ($CDCl_3$, 100 MHz) and ^1H ($CDCl_3$, 400 MHz) NMR data, see Tables 1 and 2; FABMS *m*/*z* 509 ($M^+ + H$, 0.4), 491 (0.1), 449 (0.5), 431 (0.2), 389 (0.7), 371 (0.3), 329 (1.4), 311 (1.2).

Table 5. Inhibitory Effects of Briaranes **1**−**4** on Superoxide Generation and Elastase Release by Human Neutrophil in Response to fMet-Leu-Phe/Cytochalasin B

	superoxide generation	elastase release
compound	Inh (%)[a]	Inh (%)[a]
1	7.66 ± 5.34	5.17 ± 2.71
2	13.89 ± 4.64[b]	15.04 ± 5.54[b]
3	5.55 ± 3.50	5.52 ± 4.11
4	22.62 ± 6.76[b]	15.36 ± 3.34[b]

[a] Percentage of inhibition (Inh %) at 10 μg/mL concentration. Results are presented as average ± SEM (n = 3 or 4). [b] $P < 0.05$ compared with control (DMSO).

Reaction of 4 with *m*-CPBA. Epoxidation of **4** was carried out according to a previous procedure.[7] The reaction product was separated by column chromatography on silica gel to give pure briarane **1**; physical (mp and optical rotation values) and spectral (IR, ^1H and ^{13}C NMR) data were in full agreement with those of the natural product **1**.

Single-Crystal X-ray Crystallographic of 1.[33] Suitable colorless prisms of **1** were obtained from a solution of a mixture of EtOAc and $CHCl_3$ (2:1). The crystal (0.6 × 0.4 × 0.2 mm) belongs to the monoclinic system, space group *C*2 (# 5) with a = 27.019(5) Å, b = 9.372(2) Å, c = 11.729(2) Å, V = 2962(1) Å^3, Z = 4, D_{calcd} = 1.254 g/cm^3, λ (Mo Kα) = 0.71073 Å. Intensity data were measured on a Rigaku AFC7S diffractometer up to $2\theta_{max}$ of 52°. All 3108 unique reflections were collected. The structure was solved by direct methods and refined by a full-matrix least-squares procedure. The non-hydrogen atoms were given anisotropic thermal parameters. The refined structural model converged to a final R = 0.0544, R_w = 0.1453 for 1774 observed reflections [$I > 2\sigma(I)$] and 372 variable parameters.

Human Neutrophil Superoxide 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 the procedures described previously.[34] 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-Valp-nitroanilide as the elastase substrate.

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Supporting Information Available: Crystallographic data of compound **1**. These materials are available free of charge via the Internet at http://pubs.acs.org.

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