# 8,17-Epoxybriarane Diterpenoids, Briaranolides A−J, from an Okinawan Gorgonian *Briareum* sp.

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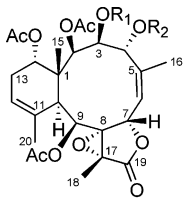
Ten new 8,17-epoxybriarane diterpenoids, briaranolides A−J (**1**−**10**), were isolated from an Okinawan gorgonian *Briareum* sp. The structure of the diterpenoids was determined on the basis of spectroscopic analysis, chemical conversions, and X-ray analysis.

A characteristic feature of briarane diterpenoids is the presence of a highly substituted bicyclo[8.4.0]tetradecane skeleton.[1] More than 300 briarane diterpenoids have previously been discovered from marine organisms, and the number is still increasing.[2] Some of these possess interesting biological properties such as cytotoxic,[3] anti-inflammatory,[4−6] antiviral,[6,7] insecticidal,[8] immunomodulation,[9] and multidrug resistance reversing activity.[10] The chemical structures of these compounds have mainly been determined on the basis of spectroscopic analyses. However, elucidation of functional group stereochemistry remains problematic due to the flexible configuration of the cyclodecane moiety.[11] In fact, reports detailing the determination of an absolute configuration remain sparse.[1,5,10,12]

During the course of our investigations on the chemical constituents of Okinawan marine invertebrates,[13] 10 new 8,17-epoxybriarane diterpenoids, briaranolides A−J (**1**−**10**), were isolated from an Okinawan gorgonian *Briareum* sp. The isolation and structural elucidation of these new briarane diterpenoids, including determination of absolute configuration based on chemical conversions and X-ray analysis, are presented below.

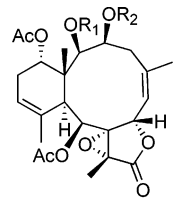


**1** $R_1$=$R_2$=Ac

**2** $R_1$=Ac, $R_2$=$CO(CH_2)_2CH_3$

**3** $R_1$=$CO(CH_2)_2CH_3$, $R_2$=$CO(CH_2)_2CH_3$

**4** $R_1$=H, $R_2$=$CO(CH_2)_2CH_3$

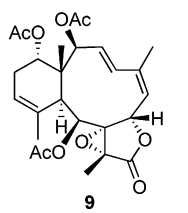


**5** $R_1$=$R_2$=Ac

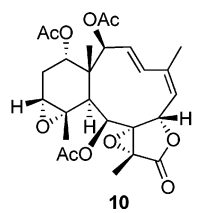
**6** $R_1$=Ac, $R_2$=$CO(CH_2)_2CH_3$

**7** $R_1$=Ac, $R_2$=H

**8** $R_1$=$COCH_2CH_3$, $R_2$=$CO(CH_2)_2CH_3$



**9**



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## Results and Discussion

The gorgonian specimens of *Briareum* sp., obtained in June 2002 from the coral reef of Hatoma Island, Okinawa, Japan, were extracted with MeOH and then with acetone. The extracts were combined and then partitioned between water and EtOAc. The EtOAc-soluble portion was partitioned between 80% aqueous MeOH and *n*-hexane. Repeated chromatographic separation of the 80% aqueous MeOH-soluble portion led to the purification and subsequent characterization of 10 new 8,17-epoxybriaranes, briaranolides A−J (**1**−**10**).

Briaranolide A (**1**) was found to have the molecular formula $C_{30}H_{38}O_{13}$ as determined from high-resolution ESIMS. The IR spectrum of **1** suggested the presence of a $\gamma$-lactone moiety (1793 $cm^{-1}$) and ester group (1744 and 1238 $cm^{-1}$). From $^1H$ and $^{13}C$ NMR analyses, **1** was found to possess five acetoxy groups and one $\gamma$-lactone moiety [$\delta_H$ 2.19 (3H, s), 2.09 (3H, s), 2.08 (3H, br s), 2.03 (3H, s), 1.99 (3H, s), $\delta_C$ 170.8 (C), 170.2 (C), 169.3 (C), 169.2 (C), 169.2 (C), 169.0 (C)], in addition to two trisubstituted olefins [$\delta_H$ 5.47 (1H, br d, $J$ = 9.2 Hz), 5.46 (1H, br s), $\delta_C$ 140.7 (C), 131.2 (C), 124.3 (CH), 122.0 (CH)] (Tables 1 and 2). $^1H$ and $^{13}C$ NMR correlations were evident from inspection of the HMQC spectrum. The planar structure of **1** was determined essentially from $^1H-^1H$ COSY and HMBC correlations cited in Figure 1. The presence of an 8,17-epoxide was established by the absence of hydroxy group-derived IR absorptions, the molecular formula, and the C-8 ($\delta_C$ 71.3) and C-17 ($\delta_C$ 62.1) $^{13}C$ NMR chemical shifts.

Briaranolides B (**2**), C (**3**), and D (**4**) were found to have a molecular formula of $C_{32}H_{42}O_{13}$, $C_{34}H_{46}O_{13}$, and $C_{30}H_{40}O_{12}$, respectively, based on high-resolution mass spectrometry and elemental analysis. The IR and NMR spectra (Tables 1 and 2) of **2**−**4** were similar to those of **1**. The functional groups at C-3 and/or C-4 of **2**−**4** differed from that of **1**, as determined from 1D and 2D NMR analyses together with chemical conversions. Briaranolide B (**2**) has a butyryloxy group at the C-4 position, while briaranolide D (**4**) has a hydroxy group at position C-3 and a butyryloxy group at position C-4, in lieu of the acetoxy group(s) found in **1**. Briaranolide C (**3**) was found to have two butyryloxy groups; the position of one of these was confirmed to be C-4, while the precise position of the other was difficult to ascertain by NMR analyses. This problem was solved by the butyrylation of briaranolide D (**4**) that yielded briaranolide C (**3**). Similarly, briaranolide B (**2**) was derived from briaranolide D (**4**) by acetylation. The aforementioned chemical conversions assisted in the unambiguous determination of the planar structures of **2**−**4**.

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**Table 1.** $^1$H NMR Data for Compounds **1**−**4** (*J* in Hz)

| no. | | **1**[a] | | **2**[a] | | **3**[b] | | **4**[a] | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | | 5.36 | (d, 3.1) | 5.38 | (d, 3.0) | 5.36 | (d, 3.3) | 5.43 | (br s) |
| 3 | | 5.08 | (br s) | 5.07 | (br s) | 5.09 | (br s) | 3.72 | (br s) |
| 4 | | 6.41 | (d, 1.0) | 6.43 | (d, 3.7) | 6.43 | (d, 3.8) | 6.25 | (br s) |
| 6 | | 5.47 | (br d, 9.2) | 5.46 | (br d, 9.2) | 5.45 | (d, 9.2) | 5.38 | (d, 8.6) |
| 7 | | 5.81 | (d, 9.2) | 5.82 | (d, 9.2) | 5.82 | (d, 9.2) | 5.85 | (d, 8.6) |
| 9 | | 5.44 | (d, 2.5) | 5.44 | (d, 2.2) | 5.42 | (d, 2.5) | 5.35 | (d, 2.8) |
| 10 | | 3.04 | (br s) | 3.04 | (br s) | 3.05 | (br s) | 2.88 | (br s) |
| 12 | | 5.46 | (br s) | 5.47 | (br s) | 5.47 | (br s) | 5.45 | (br s) |
| 13 | | 2.32 | (m) | 2.32 | (m) | 2.28 | (m) | 2.33 | (m) |
| | | 2.16 | (m) | 2.14 | (m) | 2.13 | (m) | | |
| 14 | | 4.78 | (dd, 8.5, 6.4) | 4.79 | (dd, 8.7, 6.6) | 4.78 | (dd, 9.0, 6.6) | 4.77 | (t, 7.4) |
| 15 | | 1.61 | (br s) | 1.60 | (br s) | 1.64 | (br s) | 1.56 | (br s) |
| 16 | | 1.82 | (br s) | 1.81 | (br s) | 1.79 | (br s) | 1.88 | (s) |
| 18 | | 1.47 | (s) | 1.48 | (s) | 1.46 | (s) | 1.48 | (s) |
| 20 | | 1.76 | (d, 0.5) | 1.76 | (br s) | 1.75 | (br s) | 1.69 | (br s) |
| 2-Ac | | 2.08 | (br s)[c] | 2.07 | (s)[c] | 2.04 | (s)[c] | 2.07 | (s) |
| 3-Ac | | 2.03 | (s)[c] | 2.03 | (s)[c] | | | | |
| 3-COPr | 2′ | | | | | 2.32 | (dt, 7.4, 1.6) | | |
| | 3′ | | | | | 1.64 | (quintet, 7.4) | | |
| | 4′ | | | | | 0.97 | (t, 7.4) | | |
| 4-Ac | | 2.09 | (s) | | | | | | |
| 4-COPr | 2″ | | | 2.34 | (t, 7.3) | 2.25 | (t, 7.4) | 2.37 | (m) |
| | 3″ | | | 1.67 | (quintet, 7.3) | 1.66 | (quintet, 7.4) | 1.70 | (quintet, 7.4) |
| | 4″ | | | 0.98 | (t, 7.3) | 0.95 | (t, 7.4) | 0.98 | (t, 7.4) |
| 9-Ac | | 2.19 | (s)[c] | 2.19 | (s)[c] | 2.18 | (s)[c] | 2.21 | (s) |
| 14-Ac | | 1.99 | (s) | 1.99 | (s) | 1.97 | (s) | 1.99 | (s) |

[a] 500 MHz in $CDCl_3$. [b] 400 MHz in $CDCl_3$. [c] Data are interchangeable in the same column.

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

| no. | | **1**[a] | | **2**[a] | | **3**[b] | | **4**[a] | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | | 42.3 | (C) | 42.3 | (C) | 42.3 | (C) | 42.2 | (C) |
| 2 | | 72.8 | (CH) | 72.7 | (CH) | 72.7 | (CH) | 72.7 | (CH) |
| 3 | | 70.7 | (CH) | 70.7 | (CH) | 70.4 | (CH) | 71.7 | (CH) |
| 4 | | 65.8 | (CH) | 65.4 | (CH) | 65.6 | (CH) | 66.2 | (CH) |
| 5 | | 140.7 | (C) | 140.9 | (C) | 140.8 | (C) | 141.1 | (C) |
| 6 | | 124.3 | (CH) | 124.1 | (CH) | 124.2 | (CH) | 123.5 | (CH) |
| 7 | | 74.7 | (CH) | 74.9 | (CH) | 74.8 | (CH) | 75.2 | (CH) |
| 8 | | 71.3 | (C) | 71.3 | (C) | 71.3 | (C) | 71.6 | (C) |
| 9 | | 72.6 | (CH) | 72.7 | (CH) | 72.7 | (CH) | 72.7 | (CH) |
| 10 | | 43.8 | (CH) | 43.9 | (CH) | 43.9 | (CH) | 43.8 | (CH) |
| 11 | | 131.2 | (C) | 131.2 | (C) | 131.1 | (C) | 131.0 | (C) |
| 12 | | 122.0 | (CH) | 122.1 | (CH) | 122.1 | (CH) | 122.4 | (CH) |
| 13 | | 28.1 | ($CH_2$) | 28.2 | ($CH_2$) | 28.1 | ($CH_2$) | 28.2 | ($CH_2$) |
| 14 | | 73.9 | (CH) | 73.8 | (CH) | 73.7 | (CH) | 74.5 | (CH) |
| 15 | | 17.6 | ($CH_3$) | 17.5 | ($CH_3$) | 17.4 | ($CH_3$) | 17.3 | ($CH_3$) |
| 16 | | 17.4 | ($CH_3$) | 17.5 | ($CH_3$) | 17.5 | ($CH_3$) | 16.9 | ($CH_3$) |
| 17 | | 62.1 | (C) | 62.2 | (C) | 62.1 | (C) | 62.2 | (C) |
| 18 | | 10.2 | ($CH_3$) | 10.3 | ($CH_3$) | 10.2 | ($CH_3$) | 10.2 | ($CH_3$) |
| 19 | | 170.8 | (C) | 170.8 | (C) | 170.8 | (C) | 170.8 | (C) |
| 20 | | 22.1 | ($CH_3$) | 22.1 | ($CH_3$) | 22.0 | ($CH_3$) | 22.6 | ($CH_3$) |
| 2-Ac | | 169.3 | (C)[c] | 169.4 | (C)[c] | 169.2 | (C)[c] | 169.5 | (C)[c] |
| | | 20.8 | ($CH_3$)[d] | 20.8 | ($CH_3$)[d] | 20.8 | ($CH_3$)[d] | 21.0 | ($CH_3$) |
| 3-Ac | | 169.2 | (C)[c] | 169.3 | (C)[c] | | | | |
| | | 20.5 | ($CH_3$)[d] | 20.5 | ($CH_3$)[d] | | | | |
| 3-COPr | 1′ | | | | | 171.6 | (C) | | |
| | 2′ | | | | | 35.8 | ($CH_2$) | | |
| | 3′ | | | | | 18.0 | ($CH_2$) | | |
| | 4′ | | | | | 13.6 | ($CH_3$) | | |
| 4-Ac | | 169.0 | (C)[c] | | | | | | |
| | | 20.5 | ($CH_3$) | | | | | | |
| 4-COPr | 1″ | | | 171.6 | (C) | 171.8 | (C) | 171.4 | (C) |
| | 2″ | | | 36.0 | ($CH_2$) | 35.9 | ($CH_2$) | 35.9 | ($CH_2$) |
| | 3″ | | | 18.4 | ($CH_2$) | 18.4 | ($CH_2$) | 18.5 | ($CH_2$) |
| | 4″ | | | 13.7 | ($CH_3$) | 13.6 | ($CH_3$) | 13.6 | ($CH_3$) |
| 9-Ac | | 169.2 | (C)[c] | 169.3 | (C)[c] | 169.2 | (C)[c] | 169.3 | (C)[c] |
| | | 20.8 | ($CH_3$)[d] | 20.8 | ($CH_3$)[d] | 20.7 | ($CH_3$)[d] | 20.9 | ($CH_3$) |
| 14-Ac | | 170.2 | (C)[c] | 170.2 | (C)[c] | 170.2 | (C)[c] | 170.2 | (C)[c] |
| | | 21.0 | ($CH_3$)[d] | 21.0 | ($CH_3$)[d] | 20.9 | ($CH_3$)[d] | 20.9 | ($CH_3$) |

[a] 125 MHz in $CDCl_3$. [b] 100 MHz in $CDCl_3$. [c,d] Data are interchangeable in the same column.

The absolute configuration of briaranolides A−D (**1**−**4**) was determined by the use of X-ray analysis together with chemical conversions. As mentioned above, the chemical conversion of briaranolide D (**4**) yielded briaranolides B (**2**) and C (**3**). Hydrolysis of the ester groups in briaranolide D (**4**) followed by acetylation yielded briaranolide A (**1**). The absolute configuration of the *p*-bromobenzoate **11** (Figure 2) derived from briaranolide D (**4**) was determined to be

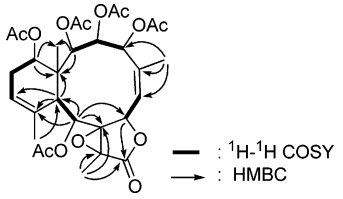
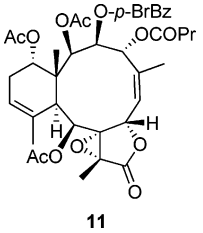



**Figure 1.** Selective $^1$H−$^1$H COSY and HMBC correlations of **1**.




**11**

**Figure 2.** Structure of *p*-bromobenzoate **11**.

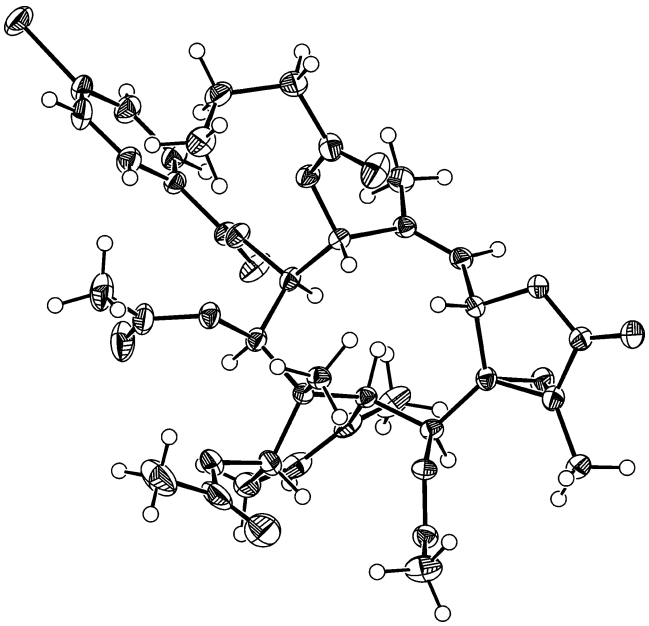


**Figure 3.** ORTEP drawing of *p*-bromobenzoate **11**.

1*R*,2*R*,3*S*,4*R*,7*S*,8*S*,9*S*,10*S*,14*S*,17*R* on the basis of the Flack parameter [−0.002 (6)] in the X-ray analysis (Figure 3).[14,15] These results clearly indicated that each of the briaranolides A−D (**1**−**4**) possess the same 1*R*,2*R*,3*S*,4*R*,-7*S*,8*S*,9*S*,10*S*,14*S*,17*R* configuration.

Briaranolide E (**5**) was shown to have the molecular formula $C_{28}H_{36}O_{11}$ as determined by high-resolution ESIMS. The spectral data of **5** were similar to that of briaranolide A (**1**) except that one methylene was detected in the NMR spectrum in lieu of the acyloxylated methine of **1**. The planar structure of **5** was determined by 2D NMR (HMQC, $^1$H−$^1$H COSY, and HMBC), the molecular formula, and the C-8 ($\delta_C$ 71.6) and C-17 ($\delta_C$ 62.2) $^{13}$C NMR chemical shifts (Figure 4).

The molecular formulas of briaranolides F−H (**6**−**8**) were determined as $C_{30}H_{40}O_{11}$, $C_{26}H_{34}O_{10}$, and $C_{31}H_{42}O_{11}$, respectively, from high-resolution ESIMS. The IR and NMR spectra of **6**−**8** were similar to those of **5** (Tables 3 and 4). The functional groups at C-2 and/or C-3 of compounds **6**−**8** differed from that of **5**, as determined from 1D and 2D NMR analyses. Briaranolide F (**6**) possesses a butyryloxy group at the C-3 position, briaranolide G (**7**) possesses a hydroxy group at the C-3 position, while briaranolide H (**8**) possesses propyonyloxy and butyryloxy groups at the C-2 and C-3 positions, respectively, in lieu of the acetoxy group(s) of **5**.

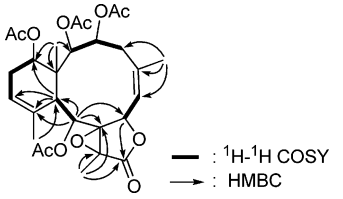



**Figure 4.** Selective $^1$H−$^1$H COSY and HMBC correlations of **5**.

The absolute configuration of briaranolides E−H (**5**−**8**) was determined by the use of X-ray analysis together with chemical conversions. Briaranolide E (**5**) was derived from briaranolides F (**6**) and H (**8**) by hydrolysis followed by acetylation and also from the acetylation of briaranolide G (**7**). X-ray analysis of bis-*p*-bromobenzoate **12** (Figure 5), which was derived from briaranolide D (**6**), confirmed the absolute configuration as 1*S*,2*R*,3*S*,7*S*,8*S*,9*S*,10*S*,14*S*,17*R* on the basis of the Flack parameter [0.00(2)] (Figure 6).[14,16] Consequently, the absolute configuration of briaranolides E−H (**5**−**8**) was clearly shown to be 1*R*,2*R*,3*S*,7*S*,8*S*,9*S*,-10*S*,14*S*,17*R*.

Briaranolide I (**9**) was found to have the molecular formula $C_{26}H_{32}O_9$ on the basis of elemental analysis. The presence of a $\gamma$-lactone moiety (1786 cm$^{-1}$) and ester group (1748, 1731, and 1250 cm$^{-1}$) was suggested from the IR spectrum. From $^1$H and $^{13}$C NMR analyses, compound **9** was found to have three acetoxy groups and one $\gamma$-lactone moiety [$\delta_H$ 2.12 (3H, s), 2.05 (3H, s), 2.01 (3H, s), $\delta_C$ 170.7 (C), 170.4 (C), 169.8 (C), 169.8 (C)], in addition to one disubstituted *E*-olefin [$\delta_H$ 6.60 (1H, d, $J$ = 15.7 Hz), 5.94 (1H, dd, $J$ = 15.7, 9.9 Hz), $\delta_C$ 137.7 (CH), 126.2 (CH)] and two trisubstituted olefins [$\delta_H$ 5.52 (1H, br s), 5.31 (1H, m), $\delta_C$ 142.4 (C), 131.4 (C), 123.2 (CH), 117.4 (CH)] (Tables 5 and 6). The planar structure of **9** was determined by 2D NMR (HMQC, $^1$H−$^1$H COSY, and HMBC), the molecular formula, and the C-8 ($\delta_C$ 68.6) and C-17 ($\delta_C$ 64.1) $^{13}$C NMR chemical shifts (Figure 7).

The molecular formula of briaranolide J (**10**) was determined as $C_{26}H_{32}O_{10}$ based on high-resolution ESIMS. The presence of an 11,12-epoxide in **10** was clearly indicated following spectroscopic comparison with **9**.

The absolute configuration of briaranolide I (**9**) was determined as 1*R*,2*S*,7*S*,8*S*,9*S*,10*S*,14*S*,17*R* from the chemical conversion of briaranolide G (**7**) using the following three steps: (1) mesylation of **7**, (2) $\beta$-elimination of the mesylate by treatment with DBU, and (3) acetylation. The absolute configuration of briaranolide J (**10**) was established as 1*R*,2*S*,7*S*,8*S*,9*S*,10*S*,11*S*,12*R*,14*S*,17*R* as determined from its synthesis from briaranolide I (**9**) by epoxidation and the NOESY correlation between Me-15 and Me-20 of **10**.

Just like briaranolides I (**9**) and J (**10**), 8,17-epoxybriarane diterpenoids that possess a 3,5-diene moiety are quite rare.[17] The biological activity of the 10 new briarane diterpenoides reported here is currently under investigation.

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured with a JASCO DIP-360 polarimeter. IR spectra were recorded with a JASCO FT-IR/620 spectrometer and UV spectra with a JASCO V-550 spectrometer. $^1$H and $^{13}$C NMR spectra were taken with Bruker DPX-400 and DRX-500 spectrometers. Chemical shifts were expressed on a $\delta$ (ppm)

**Table 3.** $^1$H NMR Data for Compounds **5**–**8**[a] (*J* in Hz)

| no. | | **5** | | **6** | | **7** | | **8** | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | | 5.51 | (d, 3.4) | 5.51 | (d, 3.4) | 5.45 | (d, 3.6) | 5.55 | (d, 3.3) |
| 3 | | 4.75 | (m) | 4.77 | (m) | 3.51 | (br s) | 4.78 | (m) |
| 4 | | 3.27 | (dd, 15.6, 3.9) | 3.28 | (dd, 15.5, 3.8) | 3.25 | (dd, 15.0, 3.2) | 3.29 | (dd, 15.5, 3.7) |
| | | 2.07 | (dd, 15.6, 3.0) | 2.06 | (dd,15.5, 2.9) | 1.92 | (dd, 15.0, 2.6) | 2.07 | (dd, 15.5, 2.9) |
| 6 | | 5.38 | (br d, 8.9) | 5.38 | (br d, 9.2) | 5.33 | (br d, 9.1) | 5.39 | (br d, 9.1) |
| 7 | | 5.60 | (d, 9.2) | 5.60 | (d, 9.2) | 5.58 | (d, 9.1) | 5.61 | (d, 9.1) |
| 9 | | 5.53 | (d, 1.6) | 5.53 | (d, 1.5) | 5.48 | (d, 1.4) | 5.54 | (br s) |
| 10 | | 3.08 | (br s) | 3.09 | (br s) | 3.05 | (br s) | 3.09 | (br s) |
| 12 | | 5.48 | (br s) | 5.49 | (br s) | 5.41 | (br s) | 5.50 | (br s) |
| 13 | | 2.34 | (m) | 2.34 | (m) | 2.36 | (m) | 2.36 | (m) |
| | | 2.19 | (m) | 2.18 | (m) | 2.21 | (m) | 2.19 | (m) |
| 14 | | 4.80 | (dd, 9.3, 6.9) | 4.77 | (m) | 4.80 | (dd, 9.3, 6.9) | 4.78 | (dd, 9.5, 6.9) |
| 15 | | 1.60 | (s) | 1.60 | (s) | 1.60 | (s) | 1.60 | (s) |
| 16 | | 1.82 | (d, 0.6) | 1.81 | (br s) | 1.93 | (br s) | 1.81 | (br s) |
| 18 | | 1.47 | (s) | 1.47 | (s) | 1.46 | (s) | 1.47 | (s) |
| 20 | | 1.75 | (d, 0.7) | 1.76 | (br s) | 1.68 | (br s) | 1.76 | (br s) |
| 2-Ac | | 2.11 | (s) | 2.10 | (s)[b] | 2.14 | (s) | | |
| 2-COEt | 2′ | | | | | | | 2.36 | (m) |
| | 3′ | | | | | | | 1.19 | (t, 7.6) |
| 3-Ac | | 1.97 | (s) | | | | | | |
| 3-COPr | 2″ | | | 0.92 | (t, 7.4) | | | 2.18 | (t, 7.4) |
| | 3″ | | | 1.61 | (m) | | | 1.61 | (m) |
| | 4″ | | | 2.20 | (t, 7.4) | | | 0.92 | (t, 7.4) |
| 9-Ac | | 2.18 | (s) | 2.18 | (s)[b] | 2.18 | (s) | 2.18 | (s) |
| 14-Ac | | 1.98 | (s) | 1.97 | (s) | 2.00 | (s) | 1.95 | (s) |

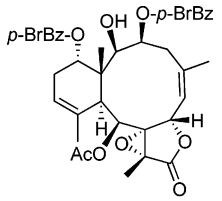
[a] 500 MHz in $CDCl_3$. [b] Data are interchangeable in the same column.

**Table 4.** $^{13}$C NMR Data for Compounds **5**–**8**[a]

| no. | | **5** | | **6** | | **7** | | **8** | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | | 41.9 | (C) | 42.0 | (C) | 42.0 | (C) | 42.0 | (C) |
| 2 | | 72.3 | (CH) | 72.3 | (CH) | 75.1 | (CH) | 72.4 | (CH) |
| 3 | | 72.5 | (CH) | 72.2 | (CH) | 72.6 | (CH) | 72.1 | (CH) |
| 4 | | 33.7 | ($CH_2$) | 33.9 | ($CH_2$) | 36.5 | ($CH_2$) | 33.9 | ($CH_2$) |
| 5 | | 142.5 | (C) | 142.5 | (C) | 143.6 | (C) | 142.5 | (C) |
| 6 | | 121.5 | (CH) | 121.5 | (CH) | 120.6 | (CH) | 121.5 | (CH) |
| 7 | | 75.9 | (CH) | 76.0 | (CH) | 76.1 | (CH) | 76.0 | (CH) |
| 8 | | 71.6 | (C) | 71.6 | (C) | 71.6 | (C) | 71.6 | (C) |
| 9 | | 72.6 | (CH) | 72.7 | (CH) | 72.7 | (CH) | 72.6 | (CH) |
| 10 | | 44.0 | (CH) | 44.0 | (CH) | 43.6 | (CH) | 44.0 | (CH) |
| 11 | | 130.9 | (C) | 130.9 | (C) | 131.5 | (C) | 130.9 | (C) |
| 12 | | 122.1 | (CH) | 122.1 | (CH) | 121.9 | (CH) | 122.2 | (CH) |
| 13 | | 28.1 | ($CH_2$) | 28.1 | ($CH_2$) | 28.2 | ($CH_2$) | 28.1 | ($CH_2$) |
| 14 | | 73.4 | (CH) | 73.4 | (CH) | 73.4 | (CH) | 73.4 | (CH) |
| 15 | | 17.0 | ($CH_3$) | 17.0 | ($CH_3$) | 16.9 | ($CH_3$) | 17.0 | ($CH_3$) |
| 16 | | 23.4 | ($CH_3$) | 23.4 | ($CH_3$) | 23.3 | ($CH_3$) | 23.4 | ($CH_3$) |
| 17 | | 62.2 | (C) | 62.2 | (C) | 62.2 | (C) | 62.2 | (C) |
| 18 | | 10.5 | ($CH_3$) | 10.5 | ($CH_3$) | 10.5 | ($CH_3$) | 10.5 | ($CH_3$) |
| 19 | | 171.3 | (C) | 171.3 | (C) | 171.3 | (C) | 171.3 | (C) |
| 20 | | 21.7 | ($CH_3$) | 21.7 | ($CH_3$) | 21.9 | ($CH_3$) | 21.7 | ($CH_3$) |
| 2-Ac | | 169.3 | (C) | 169.2 | (C)[b] | 170.9 | (C) | | |
| | | 20.9 | ($CH_3$) | 20.9 | ($CH_3$)[b] | 21.1 | ($CH_3$) | | |
| 2-COEt | 1′ | | | | | | | 172.5 | (C) |
| | 2′ | | | | | | | 27.7 | ($CH_2$) |
| | 3′ | | | | | | | 9.2 | ($CH_3$) |
| 3-Ac | | 169.6 | ($CH_3$) | | | | | | |
| | | 20.7 | (C) | | | | | | |
| 3-COPr | 1″ | | | 172.2 | (C) | | | 172.1 | (C) |
| | 2″ | | | 35.9 | ($CH_2$) | | | 35.9 | ($CH_2$) |
| | 3″ | | | 18.0 | ($CH_2$) | | | 17.9 | ($CH_2$) |
| | 4″ | | | 13.6 | ($CH_3$) | | | 13.6 | ($CH_3$) |
| 9-Ac | | 169.2 | (C) | 169.2 | (C)[b] | 169.3 | (C) | 169.2 | (C) |
| | | 20.7 | ($CH_3$) | 20.7 | ($CH_3$)[b] | 20.7 | ($CH_3$) | 20.7 | ($CH_3$) |
| 14-Ac | | 170.2 | (C) | 170.2 | (C) | 170.2 | (C) | 170.2 | (C) |
| | | 20.9 | ($CH_3$) | 20.9 | ($CH_3$) | 21.0 | ($CH_3$) | 20.9 | ($CH_3$) |

[a] 125 MHz in $CDCl_3$. [b] Data are interchangeable in the same column.

scale with tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad). EIMS spectra were obtained with a Thermo Quest TSQ 700 spectrometer and high-resolution EIMS (HREIMS) spectra, using a VG Auto Spec E spectrometer. ESIMS and high-resolution ESIMS (HRESIMS) spectra were obtained with a Micromass LCT spectrometer. Elemental analysis data were obtained with an Elemental Vavio EL. X-ray diffractions were measured




**12**

**Figure 5.** Structure of bis-*p*-bromobenzoate **12**.

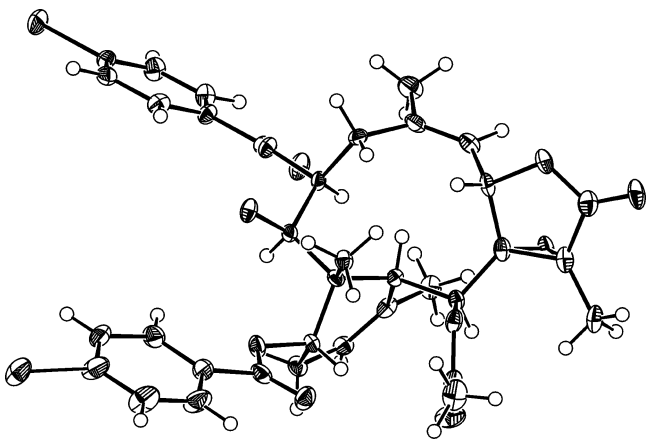


**Figure 6.** ORTEP drawing of bis-*p*-bromobenzoate **12**.

on Bruker MXC18 KHF22 and Rigaku RAXIS-RAPID diffractometers. Flash column chromatography was carried out on Kanto Chemical silica gel 60N (spherical, neutral) 40–50 $\mu$m.

**Animal Material.** The gorgonian specimens of *Briareum* sp. were obtained from the coral reef of Hatoma Island, Okinawa, Japan, at a depth of 5 m by hand using scuba, in June 2002. A voucher specimen has been deposited at Tokyo University of Pharmacy and Life Science (SC-02-10).

**Extraction and Isolation.** Wet specimens (10.3 kg) were cut into small pieces and extracted with MeOH (15.0 L × 3) and then acetone (15.0 L × 3). The combined extract (574 g) was concentrated and partitioned between EtOAc (4.0 L × 4) and water (2.0 L) to give an EtOAc-soluble portion (265 g). The EtOAc-soluble portion was partitioned between *n*-hexane (1.8 L × 4) and 80% aqueous MeOH (3.0 L) to give a *n*-hexane-

**Table 5.** $^1$H NMR Data for Compounds **9** and **10** (*J* in Hz)

| no. | **9**[a] | | **10**[b] | |
|---|---|---|---|---|
| 2 | 5.50 | (d, 9.9) | 5.45 | (d, 10.1) |
| 3 | 5.94 | (dd, 15.7, 9.9) | 5.85 | (dd, 15.7, 10.1) |
| 4 | 6.60 | (d, 15.7) | 6.60 | (d, 15.7) |
| 6 | 5.31 | (m) | 5.33 | (m) |
| 7 | 4.66 | (d, 4.4) | 4.71 | (d, 4.7) |
| 9 | 6.50 | (br s) | 6.36 | (s) |
| 10 | 2.81 | (br s) | 2.59 | (s) |
| 12 | 5.52 | (br s) | 2.93 | (br s) |
| 13 | 2.30 | (m) | 2.18 | (m) |
| | 2.00 | (m) | | |
| 14 | 4.87 | (br d, 4.4) | 4.79 | (br d, 2.5) |
| 15 | 1.12 | (s) | 1.19 | (s) |
| 16 | 1.85 | (br s) | 1.87 | (br s) |
| 18 | 1.61 | (s) | 1.67 | (s) |
| 20 | 1.89 | (br s) | 1.35 | (s) |
| 2-Ac | 2.01 | (s) | 2.00 | (s) |
| 9-Ac | 2.12 | (s) | 2.17 | (s) |
| 14-Ac | 2.05 | (s) | 2.05 | (s) |

[a] 400 MHz in $CDCl_3$. [b] 500 MHz in $CDCl_3$.

**Table 6.** $^{13}$C NMR Data for Compounds **9** and **10**

| no. | **9**[a] | | **10**[b] | |
|---|---|---|---|---|
| 1 | 45.0 | (C) | 44.9 | (C) |
| 2 | 73.9 | (CH) | 74.2 | (CH) |
| 3 | 126.2 | (CH) | 126.0 | (CH) |
| 4 | 137.7 | (CH) | 137.6 | (CH) |
| 5 | 142.4 | (C) | 142.5 | (C) |
| 6 | 117.4 | (CH) | 116.8 | (CH) |
| 7 | 77.0 | (CH) | 76.6 | (CH) |
| 8 | 68.6 | (C) | 67.8 | (C) |
| 9 | 68.1 | (CH) | 68.4 | (CH) |
| 10 | 39.3 | (CH) | 40.4 | (CH) |
| 11 | 131.4 | (C) | 58.4 | (C) |
| 12 | 123.2 | (CH) | 59.2 | (CH) |
| 13 | 28.1 | ($CH_2$) | 26.1 | ($CH_2$) |
| 14 | 71.3 | (CH) | 70.8 | (CH) |
| 15 | 13.8 | ($CH_3$) | 14.5 | ($CH_3$) |
| 16 | 23.3 | ($CH_3$) | 23.4 | ($CH_3$) |
| 17 | 64.1 | (C) | 63.4 | (C) |
| 18 | 10.8 | ($CH_3$) | 9.1 | ($CH_3$) |
| 19 | 170.7 | (C) | 170.7 | (C) |
| 20 | 24.5 | ($CH_3$) | 24.3 | ($CH_3$) |
| 2-Ac | 169.8 | (C) | 169.6 | (C) |
| | 21.2 | ($CH_3$) | 21.2 | ($CH_3$) |
| 9-Ac | 169.8 | (C) | 170.0 | (C) |
| | 21.0 | ($CH_3$) | 21.1 | ($CH_3$) |
| 14-Ac | 170.4 | (C) | 170.5 | (C) |
| | 21.1 | ($CH_3$) | 21.1 | ($CH_3$) |

[a] 100 MHz in $CDCl_3$. [b] 125 MHz in $CDCl_3$.

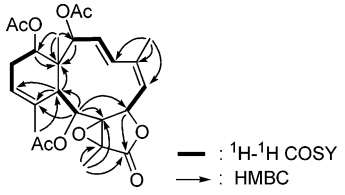



**Figure 7.** Selective $^1$H−$^1$H COSY and HMBC correlations of **9**.

soluble portion (88.0 g) and an 80% aqueous MeOH-soluble portion (171 g). The 80% aqueous MeOH-soluble portion was chromatographed on Si gel using a *n*-hexane−EtOAc (1:1, 1:3, to 0:1) gradient and MeOH as eluent to produce fractions 1 (2.60 g), 2 (113 g), 3 (45.7 g), and 4 (8.10 g). Fraction 2 was subjected to flash Si gel column chromatography (elution with *n*-hexane−EtOAc (5:4)) to give fractions 2-1 (1.10 g), 2-2 (9.20 g), 2-3 (65.4 g), and 2-4 (37.3 g). Fraction 2-2 was subjected to flash Si gel column chromatography (elution with *n*-hexane−EtOAc (5:4)) and then recrystallized from $Et_2O$−*n*-hexane to give briaranolides C (**3**) (3.36 g), H (**8**) (501 mg), and I (**9**) (1.03 g). Flash Si gel column chromatography of fraction 2-3 (elution with $CHCl_3$−EtOAc (10:1)) afforded briaranolides B (**2**) (13.1 g) and F (**6**) (44.3 g). Flash Si gel column chromatography of fraction 2-4 (elution with $CHCl_3$−EtOAc (8:1)) produced briaranolide E (**5**) (36.9 g). Fraction 3 was subjected to flash Si gel column chromatography (elution with $CHCl_3$−EtOAc (3:1)) to give fractions 3-1 (1.39 g), 3−2 (16.8 g), 3-3 (8.96 g), 3-4 (13.9 g), and 3-5 (4.34 g). Flash Si gel column chromatography of fraction 3-2 (elution with *n*-hexane−EtOAc (1:1)) afforded briaranolides A (**1**) (2.64 g) and D (**4**) (7.78 g). Fraction 3-3 was chromatographed repeatedly on flash Si gel using *n*-hexane−EtOAc (1:1) and *n*-hexane−acetone (2:1) to give briaranolides G (**7**) (346 mg) and J (**10**) (293 mg).

**Briaranolide A (1):** colorless powder; mp 230−233 °C; $[\alpha]_D^{27}$ +41.2° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 1793, 1744, 1238 cm$^{-1}$; $^1$H and$^{13}$C NMR, see Tables 1 and 2; COSY correlations (H/H) H-2/H-3; H-3/H-4; H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.32), H-13 ($\delta_H$ 2.16); H-13 ($\delta_H$ 2.32)/H-14; H-13 ($\delta_H$ 2.16)/H-14; HMBC correlations (H/C) H-2/C-1, C-3, C-4, C-10, C-14, Me-15; H-4/C-3, C-5, C-6, Me-16, C-4-Ac; H-6/C-4, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11; H-10/C-1, C-2, C-8, C-9, C-11, C-12, C-14, Me-20; H-12/C-10, C-13, Me-20; H-13 ($\delta_H$ 2.32)/C-1, C-11, C-12; H-13 ($\delta_H$ 2.16)/C-11, C-12, C-14; H-14/C-1, C-10, C-12, C-13, Me-15, C-14-Ac; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; C-4-Ac(Me)/C-4-Ac(C=O); C-14-Ac(Me)/C-14-Ac(C=O); ESIMS (*m/z*) 607 [M$^+$ + H] (30), 547 (100); HRESIMS (*m/z*) 607.2405 (calcd for $C_{30}H_{39}O_{13}$, M$^+$ + H, 607.2391).

**Briaranolide B (2):** colorless needles; mp 224−228 °C; $[\alpha]_D^{24}$ +50.4° (*c* 0.4, $CHCl_3$); IR (KBr) $\nu_{max}$ 1793, 1743, 1240 cm$^{-1}$; $^1$H and$^{13}$C NMR, see Tables 1 and 2; COSY correlations (H/H) H-2/H-3; H-3/H-4; H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.32), H-13 ($\delta_H$ 2.14); H-13 ($\delta_H$ 2.32)/H-14; H-13 ($\delta_H$ 2.14)/H-14; H-2″/H-3″; H-3″/Me-4″; HMBC correlations (H/C) H-2/C-1, C-3, C-4, C-14, Me-15; H-4/C-3, C-5, C-6, Me-16, C-4-COPr; H-6/C-4, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11; H-10/C-1, C-8, C-11, C-12, C-14, Me-20; H-12/C-10, C-13, C-14, Me-20; H-13 ($\delta_H$ 2.26)/C-1, C-11, C-12; H-13 ($\delta_H$ 2.14)/C-11, C-12, C-14; H-14/C-1, C-2, C-10, C-13, Me-15, C-14-Ac; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; H-2″/C-1″, C-3″, Me-4″; H-3″/C-1″, C-2″, Me-4″; Me-4″/C-2″, C-3″; C-14-Ac(Me)/C-14-Ac(C=O); ESIMS (*m/z*) 657 [M$^+$ + Na] (60), 652 (100), 635 (25), 575 (38), 385 (68), 325 (80); HRESIMS (*m/z*) 657.2535 (calcd for $C_{32}H_{42}O_{13}Na$, M$^+$ + Na, 657.2523).

**Briaranolide C (3):** colorless pillars; mp 149−152 °C; $[\alpha]_D^{25}$ +44.3° (*c* 1.1, $CHCl_3$); IR (KBr) $\nu_{max}$ 1795, 1745, 1244 cm$^{-1}$; $^1$H and$^{13}$C NMR, see Tables 1 and 2; COSY correlations (H/H) H-2/H-3; H-3/H-4; H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.28), H-13 ($\delta_H$ 2.13); H-13 ($\delta_H$ 2.28)/H-14; H-13 ($\delta_H$ 2.13)/H-14; H-2′/H-3′; H-3′/Me-4′; H-2″/H-3″; H-3″/Me-4″; HMBC correlations (H/C) H-2/C-1, C-3, C-4, C-14, Me-15; H-4/C-3, C-5, C-6, Me-16, C-4-COPr; H-6/C-4, C-5, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11; H-10/C-1, C-8, C-11, C-12, C-14, Me-20; H-12/C-10, C-13; H-13 ($\delta_H$ 2.28)/C-11; H-13 ($\delta_H$ 2.13)/C-11, C-14; H-14/C-1, C-13, C-14-Ac; Me-15/C-1, C-10; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; H-2′/C-1′, C-3′; H-3′/C-1′, C-2′, Me-4′; Me-4′/C-2′, C-3′; H-2″/C-1″, C-3″; H-3″/C-1″, C-2″, Me-4″; Me-4″/C-2″, C-3″; C-14-Ac(Me)/C-14-Ac(C=O); EIMS (*m/z*) 663 [M$^+$ + H] (10), 603 (45), 575 (72), 515 (100); *anal.* C 61.55%, H 7.04%, calcd for $C_{34}H_{46}O_{13}$, C 61.62%, H 7.00%.

**Briaranolide D (4):** colorless amorphous solid; $[\alpha]_D^{23}$ +53.0° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 3452, 1790, 1740, 1245 cm$^{-1}$; $^1$H and$^{13}$C NMR, see Tables 1 and 2; COSY correlations (H/H) H-6/H-7, H-9/H-10; H-12/H-13; H-13/H-14; H-2″/H-3″; H-3″/Me-4″; HMBC correlations (H/C) H-4/C-3, C-5, C-6, Me-16, C-4-COPr; H-6/C-5, C-7, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11, C-9-Ac; H-10/C-1, C-2, C-8, C-11, C-12; H-12/C-13, Me-20; H-13/C-11, C-12, C-14; H-14/C-1, C-10, C-12, C-13, Me-15, C-14-Ac; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; H-2″/C-1″, C-3″, Me-4″; H-3″/C-1″, C-2″, Me-4″; Me-4″/C-2″, C-3″; C-2-Ac(Me)/C-2-Ac(C=O); C-9-Ac(Me)/C-9-Ac(C=O); C-14-Ac(Me)/C-14-Ac(C=O); ESIMS (*m/z*) 593 [M$^+$+H] (10), 575 (100), 533 (20); HRESIMS (*m/z*) 593.2614 (calcd for $C_{30}H_{41}O_{12}$, M$^+$ + H, 593.2598).

**Briaranolide E (5):** colorless needles; mp 183−187 °C; $[\alpha]_D^{26}$ −26.0° (*c* 1.0, $CH_2Cl_2$); IR (KBr) $\nu_{max}$ 1790, 1745, 1242 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 3 and 4; COSY correlations (H/H) H-2/H-3, H-3/H-4 ($\delta_H$ 3.27), H-4 ($\delta_H$ 2.07); H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.34), H-13 ($\delta_H$ 2.19); H-13 ($\delta_H$ 2.34)/H-14; H-13 ($\delta_H$ 2.19)/H-14; HMBC correlations (H/C) H-2/C-1, C-4, C-14, Me-15, C-2-Ac; H-4 ($\delta_H$ 3.27)/C-3, C-5, C-6, Me-16; H-4 ($\delta_H$ 2.07)/C-3, C-5, C-6; H-6/C-4, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11, C-9-Ac; H-10/C-1, C-8, C-11, C-12, C-14, Me-20; H-13 ($\delta_H$ 2.34)/C-1, C-11, C-12; H-13 ($\delta_H$ 2.19)/C-14; H-14/C-1, C-2, C-13, Me-15, C-14-Ac; Me-15/C-1, C-2, C-10, C-14; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; C-2-Ac(Me)/C-2-Ac(C═O); C-3-Ac(Me)/C-3-Ac(C═O); C-9-Ac(Me)/C-9-Ac(C═O); C-14-Ac(Me)/C-14-Ac-(C═O); ESIMS (*m/z*) 571 [$M^+$ + Na] (100), 369 (25), 309 (58); HRESIMS (*m/z*) 571.2125 (calcd for $C_{28}H_{36}O_{11}Na$, $M^+$ + Na, 571.2155).

**Briaranolide F (6):** colorless needles; mp 130−135 °C; $[\alpha]_D^{28}$ −50.3° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 1789, 1743, 1249 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 3 and 4; COSY correlations (H/H) H-2/H-3; H-3/H-4 ($\delta_H$ 3.28), H-4 ($\delta_H$ 2.06); H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.34), H-13 ($\delta_H$ 2.18); H-13 ($\delta_H$ 2.34)/H-14; H-13 ($\delta_H$ 2.18)/H-14; H-2″/H-3″; H-3″/Me-4″; HMBC correlations (H/C) H-2/C-1, C-4, Me-15; H-3/C-5, C-3-COPr; H-4 ($\delta_H$ 3.28)/C-2, C-3, C-5, C-6, Me-16; H-4 ($\delta_H$ 2.06)/C-2, C-3, C-5, C-6, Me-16; H-6/C-4, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11; H-10/C-1, C-2, C-8, C-11, C-12, Me-20; H-12/C-10, C-14, Me-20; H-13 ($\delta_H$ 2.34)/C-11, C-12; H-13 ($\delta_H$ 2.18)/C-11, C-12, C-14; H-14/C-1, C-2, C-13, Me-15, C-14-Ac; Me-15/C-1, C-10, C-14; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; H-2″/C-1″, C-3″, Me-4″; H-3″/C-1″, C-2″, Me-4″; Me-4″/C-2″, C-3″; C-14-Ac(Me)/C-14-Ac-(C═O); ESIMS (*m/z*) 577 [$M^+$ + H] (80), 517 (100), 457 (68), 369 (70), 309 (69); HRESIMS (*m/z*) 577.2637 (calcd for $C_{30}H_{41}O_{11}$, $M^+$ + H, 577.2649).

**Briaranolide G (7):** colorless amorphous solid; $[\alpha]_D^{25}$ +3.0° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 3465, 1788, 1742, 1246 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 3 and 4; COSY correlations (H/H) H-2/H-3, H-3/H-4 ($\delta_H$ 3.25), H-4 ($\delta_H$ 1.92); H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.36), H-13 ($\delta_H$ 2.21); H-13 ($\delta_H$ 2.36)/H-14; H-13 ($\delta_H$ 2.21)/H-14; HMBC correlations (H/C) H-2/C-4, C-10, C-14, Me-15, C-2-Ac; H-3/C-5; H-4 ($\delta_H$ 3.25)/C-2, C-5, C-6, Me-16; H-4 ($\delta_H$ 1.92)/C-2, C-6, Me-16; H-6/C-4, C-8, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-7, C-8, C-10, C-11, C-9-Ac; H-10/C-1, C-2, C-8, C-9, C-11, C-12, C-14, Me-20; H-12/C-10, C-13, C-14, Me-20; H-13 ($\delta_H$ 2.36)/C-1, C-11, C-12, C-14; H-13 ($\delta_H$ 2.21)/C-11, C-12, C-14; H-14/C-1, C-2, C-13, Me-15, C-14-Ac; Me-15/C-1, C-2, C-10, C-14; Me-16/ C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; C-2-Ac(Me)/C-2-Ac(C═O); C-9-Ac(Me)/C-9-Ac(C═O); C-14-Ac(Me)/C-14-Ac(C═O); ESIMS (*m/z*) 507 [$M^+$ + H] (100), 489 (32), 447 (87), 387 (30); HRESIMS (*m/z*) 507.2242 (calcd for $C_{26}H_{35}O_{10}$, $M^+$ + H, 507.2230).

**Briaranolide H (8):** colorless needles; mp 207−210 °C; $[\alpha]_D^{26}$ −39.8° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 1789, 1752, 1735, 1246 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 3 and 4; COSY correlations (H/H) H-2/H-3; H-3/H-4 ($\delta_H$ 3.29), H-4 ($\delta_H$ 2.07); H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.36), H-13 ($\delta_H$ 2.19); H-13 ($\delta_H$ 2.36)/H-14; H-13 ($\delta_H$ 2.19)/H-14; H-2′/H-3′; H-2″/Me-3″; H-3″/Me-4″; HMBC correlations (H/C) H-2/C-1, C-4, C-14, Me-15, C-2-COEt; H-3/C-5, C-3-COPr; H-4 ($\delta_H$ 3.29)/C-2, C-5, C-6, Me-16; H-4 ($\delta_H$ 2.07)/C-2, C-5, C-6, Me-16; H-6/C-4, Me-16; H-7/C-5, C-6, C-19; H-9/C-7, C-8, C-10, C-11, C-9-Ac; H-10/C-1, C-8, C-11, C-12, C-14, Me-20; H-12/C-10, C-14, Me-20; H-13 ($\delta_H$ 2.36)/C-1, C-11, C-12; H-13 ($\delta_H$ 2.19)/C-11, C-12, C-14; H-14/C-1, C-2, C-13, Me-15, C-14-Ac; Me-15/C-1, C-2, C-10, C-14; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; H-2′/C-1′, Me-3′; Me-3′/C-1′, C-2′; H-2″/C-1″, C-3″, Me-4″; H-3″/C-1″, C-2″, Me-4″; Me-4″/C-2″, C-3″; C-9-Ac(Me)/C-9-Ac(C═O); C-14-Ac(Me)/C-14-Ac(C═O); ESIMS (*m/z*) 591 [$M^+$ + H] (80), 531 (100), 471 (55), 369 (60), 309 (70); HRESIMS (*m/z*) 591.2809 (calcd for $C_{31}H_{43}O_{11}$, $M^+$ + H, 591.2805).

**Briaranolide I (9):** colorless prisms; mp 213−216 °C; $[\alpha]_D^{25}$ +33.6° (*c* 1.1, $CHCl_3$); IR (KBr) $\nu_{max}$ 1786, 1748, 1731, 1250 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 5 and 6; COSY correlations (H/H) H-2/H-3; H-3/H-4; H-6/H-7, H-9/H-10; H-12/H-13 ($\delta_H$ 2.30), H-13 ($\delta_H$ 2.00); H-13 ($\delta_H$ 2.30)/H-14; H-13 ($\delta_H$ 2.00)/H-14; HMBC correlations (H/C) H-2/C-1, C-3, C-4, C-14, Me-15, C-2-Ac; H-3/C-1, C-2, C-5; H-4/C-2, C-3, C-5, C-6; H-6/C-4, C-7, C-8; H-7/C-5, C-6, C-8, C-19; H-9/C-1, C-8, C-10, C-11, C-17, C-9-Ac; H-10/C-1, C-9, C-11, C-12; H-13 ($\delta_H$ 2.30)/C-11, C-12; H-13 ($\delta_H$ 2.00)/C-1, C-11; H-14/C-1, C-2, C-10, C-12, C-13, C-14-Ac; Me-15/C-1, C-2, C-10, C-14; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; C-2-Ac(Me)/C-2-Ac(C═O); C-9-Ac(Me)/C-9-Ac(C═O); C-14-Ac(Me)/C-14-Ac-(C═O); EIMS (*m/z*) 488 [$M^+$] (18), 446 (62), 386 (7), 326 (17); *anal.* C 63.81%, H 6.73%, calcd for $C_{26}H_{32}O_9$, C 63.92%, H 6.60%.

**Briaranolide J (10):** colorless amorphous; $[\alpha]_D^{24}$ +11.8° (*c* 1.0, $CHCl_3$); IR (KBr) $\nu_{max}$ 1795, 1742, 1233 $cm^{-1}$; $^1H$ and $^{13}C$ NMR, see Tables 5 and 6; COSY correlations (H/H) H-2/H-3, H-3/H-4; H-6/H-7, H-9/H-10; H-12/H-13; H-13/H-14; HMBC correlations (H/C) H-2/C-1, C-3, C-4, C-14, Me-15, C-2-Ac; H-3/C-1, C-2, C-5; H-4/C-2, C-3, C-5, C-6, Me-16; H-6/C-4, C-7, C-8, Me-16; H-7/C-5, C-6, C-19; H-9/C-1, C-8, C-10, C-11, C-17, C-9-Ac; H-10/C-1, C-8, C-9, C-11, C-14, Me-15, Me-20; H-12/C-13, C-14, Me-20; H-13/C-1, C-12, C-14; H-14/C-2, C-10, C-12, C-13, C-14-Ac; Me-15/C-1, C-2, C-10, C-14; Me-16/C-4, C-5, C-6; Me-18/C-8, C-17, C-19; Me-20/C-10, C-11, C-12; C-2-Ac(Me)/C-2-Ac(C═O); C-9-Ac(Me)/C-9-Ac(C═O); C-14-Ac(Me)/C-14-Ac-(C═O); NOESY correlations (H/H) H-2/H-4, H-10, C-14-Ac; H-3/Me-15, Me-16, C-9-Ac; H-4/Me-16; H-6/H-7, Me-16; H-7/H-9, C-9-Ac; H-9/H-10, Me-18, Me-20; H-10/Me-18; H-12/Me-15, Me-20; H-14/Me-15, C-2-Ac; Me-15/Me-20; Me-18/Me-20; ESIMS (*m/z*) 505 [$M^+$ + H] (65), 445 (100), 320 (60), 268 (32); HRESIMS (*m/z*) 505.2063 (calcd for $C_{26}H_{33}O_{10}$, $M^+$ + H, 505.2074).

**Synthesis of Briaranolide B (2) from Briaranolide D (4).** To a pyridine (200 μL) solution of **4** (10.1 mg, 17.0 μmol) was added acetic anhydride (100 μL), and the mixture was stirred at room temperature for 14 h. The reaction mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (2:1)) to give **2** (7.5 mg, 70% yield). The spectral data were identical with those of natural **2**.

**Synthesis of Briaranolide B (3) from Briaranolide D (4).** To a pyridine (170 μL) solution of **4** (19.8 mg, 33.4 μmol) was added *n*-butyryl chloride (8.7 μL, 83.5 μmol), and the mixture was stirred at room temperature. After 11 h, 4-(dimethylamino)pyridine (0.5 mg) was added, and stirring was continued for 5 h at room temperature. The reaction mixture was diluted with diethyl ether and washed with water and brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (2:1)) to give **3** (14.6 mg, 66% yield). The spectral data were identical with those of natural **3**.

**Synthesis of Briaranolide A (1) from Briaranolide D (4).** To a methanol (1.0 mL) solution of **4** (30.0 mg, 50.6 μmol) was added lithium hydroxide monohydrate (2.0 mg, 50.6 μmol), and the mixture was stirred at room temperature for 1 h. The reaction mixture was concentrated under reduced pressure. To a solution of the residue in pyridine (400 μL) were added acetic anhydride (200 μL) and 4-(dimethylamino)pyridine (3.1 mg, 25.3 μmol) followed by stirring at 60 °C for 20 h. The mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (1:1)) to give **1** (20.1 mg, 67% yield). The spectral data were identical with those of natural **1**.

**Synthesis of *p*-Bromobenzoate 11 from Briaranolide D (4).** To a pyridine (400 μL) solution of **4** (50.0 mg, 84.4 μmol) was added *p*-bromobenzoyl chloride (37.1 mg, 169 μmol), and the mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with diethyl ether and washed with water, aqueous HCl (1 M), and brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (2:1)) to give *p*-bromobenzoate **11** (49.9 mg, 76% yield): colorless

crystal; mp 103−106 °C; $[\alpha]_D^{28}$ +36.0° (*c* 1.8, $CHCl_3$); IR (KBr) $\nu_{max}$ 1794, 1740, 1591, 1375, 1271, 1243, 1224 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ ($\epsilon$) 247 (24775) nm; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ ppm 7.81 (2H, br d, $J$ = 8.6 Hz), 7.60 (2H, br d, $J$ = 8.6 Hz), 6.56 (1H, br d, $J$ = 4.7 Hz), 5.88 (1H, d, $J$ = 9.3 Hz), 5.54 (1H, br d, $J$ = 9.3 Hz), 5.50 (1H, d, $J$ = 2.9 Hz), 5.49 (1H, br s), 5.49 (1H, d, $J$ = 2.7 Hz), 5.40 (1H, br s), 4.79 (1H, t, $J$ = 7.7 Hz), 3.18 (1H, br s), 2.34 (1H, m), 2.20 (3H, s), 2.19 (3H, m), 2.11 (3H, br s), 2.00 (3H, s), 1.87 (3H, br s), 1.82 (3H, br s), 1.60 (3H, br s), 1.59 (2H, m), 1.49 (3H, s), 0.90 (3H, t, $J$ = 7.3 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ ppm 171.7, 170.8, 170.2, 169.2, 169.0, 164.0, 140.3, 131.9, 131.9, 131.4, 131.1, 131.1, 128.7, 128.2, 124.7, 122.0, 77.2, 74.5, 74.3, 72.3, 71.7, 71.2, 66.0, 62.2, 43.6, 42.7, 35.9, 28.1, 22.4, 21.1, 20.9, 20.9, 18.3, 18.1, 17.7, 13.6, 10.2; ESIMS (*m/z*) 775 [$M^+$ + H] (13), 716 (43), 686 (38); HRESIMS (*m/z*) 775.1964 (calcd for $C_{37}H_{44}O_{13}Br$, $M^+$ + H, 775.1965).

**Synthesis of Briaranolide E (5) from Briaranolide F (6).** To a methanol (170 $\mu$L) solution of **6** (5.0 mg, 8.7 $\mu$mol) was added potassium carbonate (4.8 mg, 34.8 $\mu$mol), and the mixture was stirred at room temperature for 12 h. The reaction mixture was concentrated under reduced pressure. To a solution of the residue in pyridine (170 $\mu$L) were added acetic anhydride (85 $\mu$L) and 4-(dimethylamino)pyridine (2.1 mg, 17.4 $\mu$mol) followed by stirring at 40 °C for 2 days. The mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (5:4)) to give **5** (3.0 mg, 63% yield). The spectral data were identical with those of natural **5**.

**Synthesis of Briaranolide E (5) from Briaranolide G (7).** To a pyridine (200 $\mu$L) solution of **7** (5.0 mg, 9.9 $\mu$mol) was added acetic anhydride (100 $\mu$L), and the mixture was stirred at room temperature for 63 h. The reaction mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (1:1)) to give **5** (5.4 mg, quant.). The spectral data were identical with those of natural **5**.

**Synthesis of Briaranolide E (5) from Briaranolide H (8).** To a methanol (170 $\mu$L) solution of **8** (5.0 mg, 8.3 $\mu$mol) was added potassium carbonate (46.0 mg, 332 $\mu$mol), and the mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure. To a solution of the residue in pyridine (170 $\mu$L) were added acetic anhydride (85 $\mu$L) and 4-(dimethylamino)pyridine (2.0 mg, 16.6 $\mu$mol) followed by stirring at 40 °C for 6 days. The mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (5:4)) to give **5** (1.3 mg, 28% yield). The spectral data were identical with those of natural **5**.

**Synthesis of Bis-*p*-bromobenzoate 12 from Briaranolide F (6).** To a methanol (3.5 mL) solution of **6** (101 mg, 175 $\mu$mol) was added lithium hydroxide monohydrate (7.3 mg, 175 $\mu$mol), and the mixture was stirred at room temperature for 43 h. The reaction mixture was neutralized with aqueous HCl (1 M) and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with $CHCl_3$−MeOH (14:1)) to give triol (24.0 mg, 32% yield): colorless amorphous solid; $[\alpha]_D^{24}$ +32.7° (*c* 0.9, $CHCl_3$); IR (neat) $\nu_{max}$ 3457, 1782, 1755 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ ppm 5.64 (1H, d, $J$ = 9.1 Hz), 5.35 (2H, br s), 5.31 (1H, d, $J$ = 9.1 Hz), 4.04 (1H, d, $J$ = 3.1 Hz), 3.52 (1H, dd, $J$ = 8.3, 6.8 Hz), 3.28 (1H, dd, $J$ = 14.6, 4.9 Hz), 3.27 (1H, br s), 3.06 (1H, br s), 2.48 (1H, m), 2.12 (3H, s), 2.11 (1H, m), 2.03 (1H, dd, $J$ = 14.6, 2.6 Hz), 1.95 (3H, s), 1.68 (6H, br s), 1.44 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ ppm 171.5, 168.8, 143.8, 132.0, 121.3, 120.4, 77.2, 76.0, 73.8, 73.4, 72.6, 71.4, 62.1, 43.2, 42.6, 37.4, 32.1, 23.6, 22.3, 21.0, 17.9, 10.3; ESIMS (*m/z*) 423 [$M^+$ + H] (100), 405 (60), 203 (75); HRESIMS (*m/z*) 423.2004 (calcd for $C_{22}H_{31}O_8$, $M^+$ + H, 423.2019).

To a pyridine (300 $\mu$L) solution of the above triol (14.5 mg, 34.3 $\mu$mol) was added *p*-bromobenzoyl chloride (37.7 mg, 172 $\mu$mol), and the mixture was stirred at room temperature for 1.5 h. The reaction mixture was diluted with diethyl ether and washed with water, aqueous HCl (1 M), and brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with $CHCl_3$−acetone (24:1)) to give bis-*p*-bromobenzoate **12** (12.7 mg, 47% yield): colorless crystal; mp 198−200 °C; $[\alpha]_D^{25}$ +19.1° (*c* 1.6, $CHCl_3$); IR (KBr) $\nu_{max}$ 3583, 1784, 1755, 1716, 1590, 1272 $cm^{-1}$; UV (EtOH) $\lambda_{max}$ ($\epsilon$) 245 (31903) nm; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ ppm 7.94 (2H, d, $J$ = 8.5 Hz), 7.86 (2H, d, $J$ = 8.5 Hz), 7.63 (2H, d, $J$ = 8.5 Hz), 7.57 (2H, d, $J$ = 8.5 Hz), 5.68 (1H, d, $J$ = 9.2 Hz), 5.61 (1H, d, $J$ = 2.1 Hz), 5.52 (1H, br s), 5.45 (1H, d, $J$ = 9.2 Hz), 5.12 (1H, dd, $J$ = 8.2, 6.6 Hz), 5.09 (1H, br s), 4.32 (1H, br s), 3.48 (1H, dd, $J$ = 15.4, 4.1 Hz), 3.27 (1H, br s), 2.55 (1H, m), 2.27 (3H, s), 2.19 (2H, m), 1.86 (3H, br s), 1.82 (3H, br s), 1.62 (3H, br s), 1.51 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ ppm 171.3, 169.2, 165.5, 164.5, 142.2, 132.1, 132.0, 132.0, 131.9, 131.9, 131.2, 131.2, 131.1, 131.1, 129.0, 128.8, 128.5, 128.4, 121.9, 121.5, 77.2, 75.8, 75.7, 75.2, 72.4, 71.4, 62.3, 43.9, 43.2, 33.8, 28.5, 23.8, 22.2, 20.9, 17.0, 10.5; ESIMS (*m/z*) 787 [$M^+$ + H] (10), 271 (100); HRESIMS (*m/z*) 787.0746 (calcd for $C_{36}H_{37}O_{10}Br_2$, $M^+$ + H, 787.0753).

**Synthesis of Briaranolide I (9) from Briaranolide G (7).** To a solution of **7** (9.8 mg, 19.3 $\mu$mol) in dichloromethane (100 $\mu$L) were added triethylamine (26.9 $\mu$L, 193 $\mu$mol) and methanesulfonyl chloride (7.5 $\mu$L, 96.7 $\mu$mol) followed by stirring at room temperature for 1 h. The reaction mixture was diluted with diethyl ether, washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with $CHCl_3$−acetone (19:1)) to give mesylate (11.3 mg, quant.): colorless amorphous solid; $[\alpha]_D^{24}$ −9.0° (*c* 0.6, $CHCl_3$); IR (KBr) $\nu_{max}$ 1791, 1747 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ ppm 5.63 (1H, d, $J$ = 3.1 Hz), 5.59 (1H, d, $J$ = 9.2 Hz), 5.58 (1H, d, $J$ = 1.4 Hz), 5.52 (1H, br s), 5.45 (1H, br d, $J$ = 9.2 Hz), 4.81 (1H, dd, $J$ = 9.1, 6.9 Hz), 4.55 (1H, d, $J$ = 2.2 Hz), 3.35 (1H, dd, $J$ = 15.9, 4.0 Hz), 3.01 (4H, s), 2.45 (1H, m), 2.32 (1H, dd, $J$ = 15.9, 2.6 Hz), 2.23 (1H, m), 2.18 (3H, s), 2.15 (3H, s), 2.04 (3H, s), 2.00 (3H, s), 1.77 (3H, br s), 1.59 (3H, s), 1.49 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ ppm 171.1, 170.0, 169.2, 169.2, 142.2, 131.3, 122.4, 80.0, 77.2, 75.7, 73.5, 72.9, 72.1, 71.3, 62.2, 44.1, 42.0, 39.1, 35.2, 28.2, 24.0, 21.7, 21.0, 20.9, 20.6, 16.8, 10.6; ESIMS (*m/z*) 585 [$M^+$ + H] (22), 525 (45), 489 (100), 465 (33); HRESIMS (*m/z*) 585.2012 (calcd for $C_{27}H_{37}O_{12}S$, $M^+$ + H, 585.2006).

To a toluene (190 $\mu$L) solution of the above mesylate (11.5 mg, 19.7 $\mu$mol) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (14.7 $\mu$L, 98.5 $\mu$mol), and the mixture was stirred at 100 °C for 5 h. To the reaction mixture was added acetic anhydride (18.6 $\mu$L, 197 $\mu$mol), and then the reaction mixture was stirred at room temperature for 46 h. The mixture was concentrated under reduced pressure and then purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (4:3)) to give **9** (5.4 mg, 56% yield). The spectral data were identical with those of natural **9**.

**Synthesis of Briaranolide J (10) from Briaranolide I (9).** To a cold (0 °C) solution of **9** (10.1 mg, 20.7 $\mu$mol) in dichloromethane (200 $\mu$L) were added sodium hydrogenphosphate (7.3 mg, 51.7 $\mu$mol) and *m*-chloroperbenzoic acid (6.6 mg, 24.8 $\mu$mol) followed by stirring for 2.5 h. The mixture was treated with dimethyl sulfide and allowed to warm slowly to room temperature over 1 h. The reaction mixture was diluted with diethyl ether, washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by Si gel column chromatography (elution with *n*-hexane−EtOAc (1:1)) to give **10** (7.3 mg, 70% yield). The spectral data were identical with those of natural **10**.

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**Supporting Information Available:** $^1H$ and $^{13}C$ NMR spectra of new compounds (**1**−**12**) and crystallographic data of compounds **11** and **12**. These materials are available free of charge via the Internet at http://pubs.acs.org.

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