Briareins C–L, 10 New Briarane Diterpenoids from the Common Caribbean Gorgonian *Briareum asbestinum*[1]

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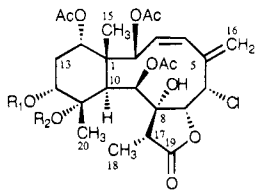
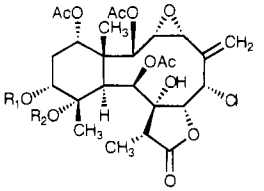
Ten new diterpenoid representatives from the briarane skeletal class have been isolated from shallow water colonies of the Caribbean gorgonian octocoral *Briareum asbestinum* collected at Mona Island near Puerto Rico. The structures of the new secondary metabolites, named briareins C–L (**3**–**12**), were defined by chemical and spectroscopic methods. In addition, two known diterpenoids, briareins A (**1**) and B (**2**), were among the most abundant compounds isolated. Traces of another known diterpenoid, briarane methyl ester (**13**), were also isolated from the same gorgonian extracts. In this paper we also establish unambiguously structure **2** for the known diterpene briarein B.

The common Caribbean gorgonian octocoral *Briareum asbestinum* (Pallas) (phylum Cnidaria, class Anthozoa, subclass Alcyonaria, order Gorgonaceae, family Briareidae), produces diterpenes of three skeletal types, the briareins, the asbestinins, and the eunicellins.[2] Although produced by a different terpene cyclization pathway, all three classes consist of bicyclic molecules with fused six- and ten-membered rings. The majority of these metabolites are endowed with biological activity that ranges from cytotoxic to anti-inflammatory, antibacterial, and antiviral activity.[2,3] Studies on the chemistry of this interesting species began in the early 1960s with the discovery of a carbonyl-containing crystalline solid from a specimen of *B. asbestinum* collected in Jamaica, which was eventually named briarein A (**1**).[4–6] The X-ray structure of briarein A (**1**) was published in 1977, and its physical and chemical properties were subsequently reported.[7,8] The ^{1}H-NMR spectral data for a tetra-acetate monobutyrate analogue of **1**, named briarein B, have also been reported.[8,9] Although the ^{1}H-NMR spectrum of briarein A has been fully assigned,[10] neither the complete assignment of its ^{13}C-NMR spectral data nor a detailed structure for briarein B (**2**) has yet been described in the literature. Extracts of *B. asbestinum* collected off the coast of Tobago and the Bahamas have afforded six diterpenes that belong also to the briarane class.[11,12] In addition, a species of *Briareum* from Puerto Rico, which was identified as either *B. asbestinum* or *B. polyanthes*, contained nine further briarane diterpenes (briareolides A–I).[13] Including the latter work, a total of 17 briarane diterpenoids have been reported thus far from Caribbean specimens of *B. asbestinum*. Nonetheless, briareins have been isolated from other Caribbean species of gorgonian, namely, *B. polyanthes* and *Erythropodium caribaeorum*.[13–19] Diterpenes with the same skeleton as briarein A have also been reported from octocorals of the order Pennatulacea in addition to octocorals belonging to the order Gorgonaceae.[3]

Our previous studies of *B. asbestinum* from Puerto Rico yielded almost exclusively diterpenoids possessing the asbestinane carbon skeleton.[20–23] Subsequent studies on the same gorgonian extracts led to the isolation of 10 new eunicellin-based diterpenes (briarellins A–I) along with briarein A (**1**).[24,25] Our investigation of *B. asbestinum* has continued further, and reported herein are the isolation and identification of 10 new briarane diterpenoids, along with the complete ^{13}C-NMR spectrum assignment of briarein A (**1**), the first unambiguous structure assignment for briarein B (**2**), and the isolation of the known briarane methyl ester (**13**).[26] *B. asbestinum* specimens were collected from Mona Island, Puerto Rico, and their combined organic-soluble extracts were partitioned following a scheme described previously.[22] ^{1}H- and ^{13}C-NMR analyses indicated that, by far, the $CHCl_3$ solubles contained the briarein-type diterpenes. Gel permeation chromatography of these extracts on Bio-Beads SX-2, then silica gel CC, gave fractions enriched in these diterpenes. Separation and purification of the diterpenes was readily accomplished by successive silica gel CC. In this collection, which provided 13 briareins, briareins A (**1**) and B (**2**) were among the more abundant briarein-type diterpenoids. Ten of these briareins (i.e., **3**–**12**), all of which appeared closely related to briarein A (**1**), were new.



Briarein A (**1**) R_1= R_2= Ac
Briarein B (**2**) R_1= COC_3H_7; R_2= Ac
Briarein C (**3**) R_1= COC_3H_7; R_2= H



Briarein D (**4**) R_1= R_2= Ac
Briarein E (**5**) R_1= Ac; R_2= H
Briarein G (**7**) R_1= COC_3H_7; R_2= Ac

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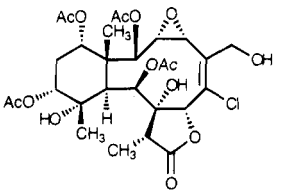
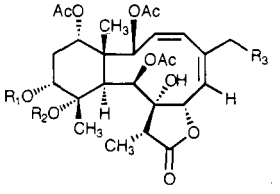


Briarein F (6)



Briarein H (8) R_1= Ac; R_2= H; R_3= OAc
Briarein I (9) R_1= Ac; R_2= H; R_3= $OCOC_7H_{15}$
Briarein J (10) R_1= Ac; R_2= H; R_3= Cl
Briarein K (11) R_1= COC_7H_{15}; R_2= H; R_3= $OCOC_3H_7$
Briarein L (12) R_1= COC_3H_7; R_2= R_3= OAc

Results and Discussion

Examination of the spectral data for **1** and **2** showed them to be briarein A and briarein B, respectively. Interestingly, although the absolute structure of one of these, briarein A (**1**), has been determined by X-ray (some of its spectral properties including ^{1}H and ^{13}C NMR have been reported in the literature), the structure of briarein B, which has been loosely described as the tetra-acetate monobutyrate analogue of briarein A,[8,9] has never been proposed [only the unassigned ^{1}H-NMR (100-MHz, $CDCl_3$) spectral properties of briarein B have been described]. After extensive analysis of all the 2D-NMR data accumulated, we obtained the complete unambiguous assignment of all the hydrogen and carbon atoms of briarein A (see Tables 1 and 2). We begin the discussion of the present work with a description for the structure of briarein B (**2**).

A molecular formula of $C_{32}H_{43}O_{13}Cl$, estimated from ^{1}H- and ^{13}C-NMR data, was confirmed for **2** by HR-FABMS. The intensity of the M + 2 isotope peak and the occurrence of a fragment ion corresponding to M^+ − 35 were strong indications of the presence of a chlorine atom in **2**. The IR spectrum of **2** contained absorptions for the same structural features found in briarein A (**1**). The conjugated diene functionality was supported by a UV absorption at λ_{max} (MeOH) 208 (ϵ 5400) and the ^{1}H-NMR signals at δ 5.76 (1H, t, J = 10.2 Hz, H-3) and 5.94 (1H, d, J = 12.3 Hz, H-4). Comparison of the ^{1}H- and ^{13}C-NMR spectra of **2** (see Tables 1 and 2) with those of briarein A confirmed the structural similarity of these two compounds. Briarein B (**2**), however, had only four acetate groups (vs. five in briarein A) as indicated by ^{1}H signals at δ 2.19 (3H, s), 1.95 (3H, s), 1.93 (3H, s), and 1.92 (3H, s). Also, resonances at δ 171.4 (s), 36.3 (t), 18.2 (t), and 13.7 (q) in the ^{13}C-NMR spectrum and at δ 2.15 (2H, m), 1.58 (2H, m), and 0.91 (3H, t, J = 7.5 Hz) in the ^{1}H-NMR spectrum of **2** indicated the presence in this compound of a butyrate moiety, a feature not found in **1**. A selective INEPT NMR experiment positioned the butyrate group on C-12. Enhancement of the ^{13}C-NMR signals at δ 171.4 (C-23), 19.6 (C-20), 72.2 (C-14), 25.9 (C-13), and 38.4 (C-10) upon irradiation of the signal for H-12 (δ 5.67) allowed this assignment unambiguously. As predicted on the basis of the similarities in their ^{1}H- and ^{13}C-NMR data, the relative stereochemistry in briarein B (**2**) was identical with that in briarein A (**1**). NOE measurements confirmed this assignment (see Table 3).

HRFABMS established a molecular formula for **3** of $C_{30}H_{41}O_{12}Cl$, two carbon, two hydrogen, and one oxygen atoms less than in the molecular formula of briarein B (**2**). Like **2**, compound **3** showed IR absorptions that indicated the presence of OH, γ-lactone, and ester functionalities. The ^{1}H-NMR spectrum of **3** was almost identical to that of **2** (see Table 1), except for having only three acetate groups. Likewise, the ^{13}C-NMR spectra of **2** and **3** were nearly identical, the only major difference being the presence of additional resonances in the spectrum of **2** at δ 168.3 (s) and 20.8 (q). These NMR data suggested that briarein C (**3**) is briarein B (**2**) with one acetyl group less. The site of disattachment of this group was determined to be at C-11 based on the high field chemical shift experienced by that carbon in the ^{13}C-NMR spectrum (79.3 ppm in **2** vs. 74.7 ppm in **3**).

The major metabolite, briarein D (**4**), was deduced to be the C-3,4 epoxy analogue of **1**. This compound exhibited ^{1}H- and ^{13}C-NMR spectra nearly identical to those of **1** (see Tables 1 and 2), the only difference being the presence in its ^{1}H-NMR and ^{13}C-NMR spectra of resonances associated with an epoxide function. HR-FABMS established a molecular formula for **4** of $C_{30}H_{39}O_{14}Cl$, one oxygen atom more than in the molecular formula of briarein A (**1**). Like **1**, compound **4** showed IR absorptions (3560, 1783, and 1743 cm^{-1}) that indicated the presence of OH, γ-lactone, and ester functionalities. The ^{1}H-NMR spectrum of briarein D contained five acetate methyl signals and did not have the signals for the olefinic methine protons of the diene group. Instead, a new signal at around δ 3.63 was observed, and it was clear that there were two overlapped signals at this resonance. One of these was assigned as the signal for H-3 from its coupling with H-2 as indicated in the COSY spectrum. The other signal (assigned to H-4) was likewise shown by COSY to be coupled only to H-3. Because all the other signals had already been assigned from COSY to be those for protons on the six- and ten-membered ring systems, the two-proton signal near δ 3.63 in the spectrum of **4** could only be those for the oxymethine protons of the C-3,4 epoxide group. This information, along with the presence of two oxymethine carbon signals in the ^{13}C-NMR spectrum of **4** at δ 60.3 and 61.2 [replacing signals at δ 130.6 (d) and 127.8 (d) in **1**], was consistent with having a C-3,4 epoxide in **4** instead of a conjugated diene group. This was also supported by the absence of absorptions in the UV spectrum of briarein D, for which only end absorption was evident. The relative stereochemistry of **4** was determined to be identical to that of **1** on the basis of NOE data (Table 3). The stereochemistry of the C-3,4 epoxide was also determined by NOE measurements. Thus, irradiation of the proton at C-3 (δ 3.61) in briarein D resulted in enhancement of the C-4 epoxide methine proton (δ 3.65) and the C-15 β-methyl group (δ 1.47).

Compound **5** (briarein E; $C_{28}H_{37}O_{13}Cl$, as deduced from HRFABMS, ^{1}H- and ^{13}C-NMR data) was easily identified as the 11-hydroxyl analogue of **4** from comparison of their ^{1}H- and ^{13}C-NMR spectra. The ^{1}H-NMR

Table 1. ^{1}H-NMR (300 MHz) Spectral Data of the Briareins A–L and Methyl Ester **13** in $CDCl_3$[a]

H	briarein A (**1**) (δ, mult, *J* (Hz), int)	briarein B (**2**) (δ, mult, *J* (Hz), int)	briarein C (**3**) (δ, mult, *J* (Hz), int)	briarein D (**4**) (δ, mult, *J* (Hz), int)	briarein E (**5**) (δ, mult, *J* (Hz), int)	briarein F (**6**) (δ, mult, *J* (Hz), int)	briarein G (**7**) (δ, mult, *J* (Hz), int)
2	6.08, d, 10.2, 1H	6.05, d, 10.2, 1H	6.31, d, 9.9, 1H	5.26, d, 8.7, 1H	5.27, d, 9.3, 1H	4.90, bs, 1H	5.25, d, 9.0, 1H
3	5.79, d, 10.8, 1H	5.76, t, 10.2, 1H	5.65, t, 10.5, 1H	3.61, m, 1H	3.51, dd, 9.3, 3.6, 1H	3.49, dd, 1H	3.64, d, 6.0, 1H
4	5.94, d, 11.1, 1H	5.94, d, 12.3, 1H	5.92, d, 11.4, 1H	3.65, m, 1H	3.66, d, 3.6, 1H	4.15, d, 8.0, 1H	3.62, d, 6.0, 1H
6	5.07, bs, 1H	5.07, d, 2.4, 1H	5.08, d, 0.6, 1H	5.19, d, 2.7, 1H	5.24, d, 3.3, 1H		5.20, d, 3.0, 1H
7	4.81, bs, 1H	4.79, bs, 1H	4.85, d, 3.9, 1H	4.94, d, 3.3, 1H	4.98, d, 3.9, 1H	5.47, bs, 1H	4.95, d, 3.6, 1H
9	5.77, bs, 1H	5.52, bs, 1H	5.74, d, 2.4, 1H	5.61, bs, 1H	5.83, d, 3.6, 1H	5.88, d, 4.2, 1H	5.59, bs, 1H
10	3.78, bs, 1H	3.77, bs, 1H	3.18, d, 2.1, 1H	3.89, s, 1H	3.20, d, 3.6, 1H	3.09, d, 4.2, 1H	3.88, bs, 1H
12	5.74, bt, 3.6, 1H	5.67, bs, 1H	4.86, bs, 1H	5.70, d, 2.1, 1H	4.86, t, 2.4, 1H	4.98, bs, 1H	5.69, bs, 1H
13	2.21, m, 1H	2.26, m, 1H	2.09, t, 4.2, 1H	2.34, t, 2.4, 1H	2.16, d, 3.0, 1H	2.12, d, 2.7, 1H	2.31, t, 2.1, 1H
13′	2.21, m, 1H	2.04, bt, 5.1, 1H	2.09, t, 4.2, 1H	2.19, t, 2.3, 1H	2.16, d, 3.0, 1H	2.12, d, 2.7, 1H	2.10, t, 2.4, 1H
14	4.82, bs, 1H	4.80, bs, 1H	4.76, bs, 1H	4.83, bs, 1H	4.70, t, 2.4, 1H	4.67, bs, 1H	4.81, bs, 1H
15	1.37, s, 3H	1.36, s, 3H	1.12, s, 3H	1.47, s, 3H	1.22, s, 3H	1.14, s, 3H	1.46, s, 3H
16	5.42, s, 1H	5.59, bs, 1H	6.03, bs, 1H	5.70, d, 2.1, 1H	5.95, d, 2.7, 1H	5.08, s, 1H	5.68, d, 2.1, 1H
16′	5.67, s, 1H	5.42, bs, 1H	5.82, bs, 1H	5.53, d, 1.8, 1H	5.90, d, 2.1, 1H	5.08, s, 1H	5.52, d, 1.5, 1H
17	3.10, q, 7.8, 1H	3.07, q, 8.1, 1H	2.75, q, 7.5, 1H	3.09, q, 8.1, 1H	2.83, q, 7.2, 1H	2.46, q, 6.7, 1H	3.07, q, 7.5, 1H
18	1.34, d, 7.8, 3H	1.31, d, 7.8, 3H	1.18, d, 7.2, 3H	1.35, d, 7.8, 3H	1.23, d, 7.2, 3H	1.19, d, 7.2, 3H	1.33, d, 7.8, 3H
20	1.51, s, 3H	1.49, s, 3H	1.38, s, 3H	1.54, s, 3H	1.42, s, 3H	1.57, s, 3H	1.52, s, 3H
22	1.94, s, 3H	2.19, s, 3H	2.26, t, 7.8, 2H	2.27, s, 3H	1.98, s, 3H	2.27, s, 3H	2.26, s, 3H
24	1.96, s, 3H	2.15, m, 2H	1.63, m, 2H	2.02, s, 3H	2.04, s, 3H	2.08, s, 3H	2.16, t, 7.5, 2H
25		1.58, m, 2H	0.94, t, 7.2, 3H				1.57, m, 2H
26	1.97, s, 3H	0.91, t, 7.5, 3H	2.17, s, 3H	2.00, s, 3H	2.24, s, 3H	2.04, s, 3H	0.91, t, 7.5, 3H
28	1.98, s, 3H	1.92, s, 3H	1.98, s, 3H	1.96, s, 3H	2.07, s, 3H	2.01, s, 3H	2.00, s, 3H
30	2.21, s, 3H	1.93, s, 3H	1.95, s, 3H	1.93, s, 3H			1.98, s, 3H
32		1.95, s, 3H					1.90, s, 3H

H	briarein H (**8**) (δ, mult, *J* (Hz), int)	briarein I (**9**) (δ, mult, *J* (Hz), int)	briarein J (**10**) (δ, mult, *J* (Hz), int)	briarein K (**11**) (δ, mult, *J* (Hz), int)	briarein L (**12**) (δ, mult, *J* (Hz), int)	methyl ester (**13**) (δ, mult, *J* (Hz), int)
2	5.57, d, 9.9, 1H	5.55, d, 9.9, 1H	5.52, d, 9.9, 1H	5.58, d, 9.9, 1H	5.53, d, 9.9, 1H	4.77, bs, 1H
3	5.64, d, 9.9, 1H	5.61, d, 10.2, 1H	5.93, d, 8.4, 1H	5.62, d, 9.9, 1H	5.65, d, 10.2, 1H	1.91, m, 2H
4	6.26, dd, 10.2, 0.9, 1H	6.24, d, 9.9, 1H	6.35, d, 11.1, 1H	6.25, dd, 9.9, 1.2, 1H	6.29, d, 10.5, 1H	2.58, m, 2H
6	5.73, dd, 8.1, 1.8, 1H	5.69,dd, 8.4, 2.7, 1H	5.69, d, 10.2, 1H	5.71, dd, 8.4, 1.8, 1H	5.70, d, 10.5, 1H	6.73, d, 9.9, 1H
7	5.00, d, 8.7, 1H	4.98, d, 8.1, 1H	4.98, d, 8.1, 1H	4.99, d, 9.3, 1H	5.06, d, 8.4, 1H	5.36, d, 10.2, 1H
9	5.77, d, 3.9, 1H	5.75, d, 3.9, 1H	5.77, d, 4.2, 1H	5.76, d, 3.9, 1H	5.76, bs, 1H	6.04, bs, 1H
10	3.10, d, 4.2, 1H	3.08, d, 3.9, 1H	3.08, d, 3.9, 1H	3.10, d, 4.2, 1H	3.24, d, 3.0, 1H	3.00, bs, 1H
12	4.93, t, 2.4, 1H	4.90, bs, 1H	4.94, t, 2.4, 1H	4.95, t, 2.7, 1H	5.75, bt, 5.4, 1H	5.38, bt, 6.3, 1H
13	2.09, t, 3.9, 1H	1.96, bs, 1H	2.15, m, 1H	2.08, bs, 1H	2.34, m, 1H	2.62, m, 1H
13′	2.09, t, 3.9, 1H	2.14, bs, 1H	2.15, m, 1H	2.08, bs, 1H	1.94, bs, 1H	1.64, m, 1H
14	4.76, t, 2.4, 1H	4.73, bs, 1H	4.76, t, 3.3, 1H	4.76, t, 2.4, 1H	4.83, bt, 2.4, 1H	4.94, d, 8.1, 1H
15	1.08, s, 3H	1.06, s, 3H	1.09, s, 3H	1.08, s, 3H	1.17, s, 3H	0.95, s, 3H
16	5.19, d, 15.0, 1H	5.16, d, 15.3, 1H	4.63, d, 12.3, 1H	5.21, d, 15.0, 1H	5.17, d, 15.6, 1H	
16′	4.65, d, 14.7, 1H	4.64, d, 15.3, 1H	4.43, d, 12.6, 1H	4.65, d, 15.0, 1H	4.62, d, 15.3, 1H	
17	2.38, q, 6.9, 1H	2.34, q, 6.9, 1H	2.38, q, 6.6, 1H	2.32, m, 1H	2.43, q, 7.2, 1H	2.53, m, 1H
18	1.17, d, 6.9, 3H	1.13, d, 7.2, 3H	1.16, d, 7.2, 1H	1.15, d, 6.9, 3H	1.23, d, 6.3, 3H	1.24, d, 7.2, 3H
20	1.53, s, 3H	1.49, s, 3H	1.53, s, 3H	1.52, s, 3H	2.06, s, 3H	1.97, s, 3H
22	2.20, s, 3H	2.18, s, 3H	2.20, s, 3H	2.35, m, 2H	2.22, s, 3H	1.96, s, 3H
23				1.64, m, 2H		
24	2.12, s, 3H	2.06, s, 3H	2.11, s, 3H	1.26, m, 2H	2.29, m, 2H	1.89, s, 3H
25				1.26, m, 2H	1.60, m, 2H	2.17, s, 3H
26	2.04, s, 3H	2.00, s, 3H	2.01, s, 3H	1.26, m, 2H	0.94, t, 7.2, 3H	
27				1.26, m, 2H		3.77, s, 3H
28	1.93, s, 3H	1.90, s, 3H	1.95, s, 3H	0.86, t, 7.2, 3H	2.12, s, 3H	
30		2.34, t, 7.5, 2H		1.92, s, 3H	1.97, s, 3H	
31	2.11, s, 3H	1.60, m, 2H				
32		1.25, m, 2H		2.04, s, 3H	1.81, s, 3H	
33		1.25, m, 2H				
34		1.25, m, 2H		2.19, s, 3H	1.91, s, 3H	
35		1.25, m, 2H				
36		0.84, t, 6.3, 3H		2.35, m, 2H		
37				1.64, m, 2H		
38				0.95, t, 7.5, 3H		

[a] Assignments were aided by ^{1}H-^{1}H COSY, spin splitting patterns, selective decoupling experiments and comparisons to known models. The δ values are in ppm and are referenced to the residual $CHCl_3$ signal (7.26 ppm). The numbering of atoms for the ester side-chains starts with the ester group at position C-11 and continues on encompassing the ester groups at position C-12, C-14, C-2, C-9, and C-16.

spectrum of **5** contained four acetate methyl signals and lacked the characteristic signals for the propyl group of a butyrate ester. Corresponding differences in the ^{13}C-NMR spectra of **4** and **5** were observed, which further supported the structure of **5** (see Tables 1 and 2). Briarein E (**5**) appears to be somewhat unstable in $CDCl_3$. For example, during an overnight NOESY experiment with **5** in $CDCl_3$, there was detectable decomposition. After the sample decomposed, we found a product that still contained chlorine and was identical with briarein F (**6**), a new natural product isolated from the same $CHCl_3$ solubles (see below).

Data from HRFABMS and ^{13}C-NMR spectrometry (Table 2) established a molecular formula of $C_{28}H_{37}O_{14}Cl$ for compound **6**, one oxygen atom more than in the molecular formula of briarein E (**5**). Carbonyl resonances in the ^{13}C-NMR spectrum of **6** at δ 174.9, 173.0, 170.6, 169.6, and 169.3 confirmed the presence of a lactone and four other esters. In the ^{1}H-NMR spectrum (Table 1) of briarein F, four acetate methyl resonances

Table 2. ^{13}C-NMR (75 MHz) Spectral Data of Briareins A–L and Methyl Ester **13** in $CDCl_3$[a]

C	briarein A (**1**) (δ (m))	briarein B (**2**) (δ (m))	briarein C (**3**) (δ (m))	briarein D (**4**) (δ (m))	briarein E (**5**) (δ (m))	briarein F (**6**) (δ (m))	briarein G (**7**) (δ (m))
1	46.1 (s)	46.0 (s)	45.8 (s)	45.1 (s)	44.6 (s)	44.9 (s)	45.2 (s)
2	71.8 (d)	71.5 (d)	72.9 (d)	71.0 (d)	72.7 (d)	75.2 (d)	71.1 (d)
3	130.6 (d)	130.6 (d)	130.0 (d)	60.3 (d)	60.6 (d)	59.0 (d)	60.2 (d)
4	127.8 (d)	127.7 (d)	128.2 (d)	61.2 (d)	59.1 (d)	59.1 (d)	61.2 (d)
5	137.0 (s)	137.0 (s)	136.7 (s)	134.1 (s)	133.9 (s)	133.6 (s)	134.2 (s)
6	64.8 (d)	64.8 (d)	62.9 (d)	63.3 (d)	61.6 (d)	131.8 (s)	63.3 (d)
7	79.4 (d)	79.4 (d)	78.9 (d)	78.3 (d)	77.7 (d)	75.9 (d)	78.3 (d)
8	84.3 (s)	84.3 (s)	81.2 (s)	83.9 (s)	81.5 (s)	82.0 (s)	84.0 (s)
9	83.4 (d)	83.3 (d)	75.5 (d)	82.4 (d)	75.7 (d)	69.0 (d)	82.4 (d)
10	38.5 (d)	38.4 (d)	38.9 (d)	38.4 (d)	38.8 (d)	38.3 (d)	38.4 (d)
11	79.4 (s)	79.3 (s)	74.7 (s)	79.5 (s)	74.7 (s)	72.5 (s)	79.5 (s)
12	70.7 (d)	70.4 (d)	74.0 (d)	70.5 (d)	74.2 (d)	73.7 (d)	70.3 (d)
13	25.8 (t)	25.9 (t)	26.5 (t)	26.0 (t)	26.1 (t)	26.0 (t)	26.1 (t)
14	72.2 (d)	72.2 (d)	73.0 (d)	72.0 (d)	72.5 (d)	72.1 (d)	72.1 (d)
15	16.0 (q)	16.0 (q)	14.6 (q)	16.9 (q)	15.0 (q)	14.3 (q)	16.9 (q)
16	116.2 (t)	116.1 (t)	116.4 (t)	116.2 (t)	118.0 (t)	76.5 (t)	116.1 (t)
17	49.1 (d)	49.1 (d)	47.6 (d)	48.3 (d)	47.7 (d)	44.4 (d)	48.3 (d)
18	10.7 (q)	10.6 (q)	8.1 (q)	10.9 (q)	8.4 (q)	6.7 (q)	10.8 (q)
19	176.5 (s)	176.5 (s)	175.7 (s)	176.0 (s)	175.2 (s)	174.9 (s)	176.0 (s)
20	19.7 (q)	19.6 (q)	24.5 (q)	19.5 (q)	25.0 (q)	25.8 (q)	19.5 (q)
21	168.7 (s)	168.3 (s)	174.0 (s)	168.3 (s)	169.2 (s)	169.6 (s)	168.3 (s)
22	20.8 (q)[b]	20.8 (q)[b]	36.6 (t)	22.0 (q)[b]	20.9 (q)[b]	21.6 (q)[b]	20.9 (q)[b]
23	168.9 (s)	171.4 (s)	18.3 (t)	168.7 (s)	169.4 (s)	170.6 (s)	171.3 (s)
24	20.9 (q)[b]	36.3 (t)	13.7 (q)	21.3 (q)[b]	21.2 (q)[b]	21.2 (q)[b]	36.4 (t)
25	170.3 (s)	18.2 (t)	170.2 (s)	170.2 (s)	171.7 (s)	173.0 (s)	18.2 (t)
26	21.3 (q)[b]	13.7 (q)	21.2 (q)[b]	20.9 (q)[b]	21.4 (q)[b]	21.3 (q)[b]	13.7 (q)
27	168.5 (s)	170.2 (s)	169.4 (s)	168.9 (s)	170.4 (s)	169.3 (s)	170.2 (s)
28	21.4 (q)[b]	21.3 (q)[b]	21.3 (q)[b]	20.9 (q)[b]	21.4 (q)[b]	21.0 (q)[b]	20.9 (q)[b]
29	169.8 (s)	168.5 (s)	169.8 (s)	169.4 (s)			168.9 (s)
30	22.0 (s)[b]	21.4 (q)[b]	21.4 (q)[b]	20.8 (q)[b]			21.3 (q)[b]
31		169.8 (s)					169.4 (s)
32		22.0 (q)[b]					22.0 (q)[b]

C	briarein H (**8**) (δ (m))	briarein I (**9**) (δ (m))	briarein J (**10**) (δ (m))	briarein K (**11**) (δ (m))	briarein L (**12**) (δ (m))	methyl ester (**13**) (δ (m))
1	45.4 (s)	45.3 (s)	45.4 (s)	45.4 (s)	45.9 (s)	44.0 (s)
2	75.3 (d)	75.6 (d)	75.2 (d)	75.4 (d)	75.1 (d)	73.2 (d)
3	132.3 (d)	132.1(d)	127.3 (d)	132.1 (d)	132.3 (d)	26.8 (t)
4	127.5 (d)	127.4 (d)	127.8 (d)	127.6 (d)	127.9 (d)	22.4 (t)
5	139.0 (s)	139.0 (s)	139.1 (s)	139.0 (s)	140.5 (s)	138.5 (s)
6	124.0 (d)	123.8 (d)	131.9 (d)	123.9 (d)	123.4 (d)	133.3 (d)
7	80.0 (d)	80.0 (d)	81.1 (d)	79.9 (d)	80.2 (d)	78.1 (d)
8	81.1 (s)	81.0 (s)	79.7 (s)	81.0 (s)	87.9 (s)	82.6 (s)
9	69.1 (d)	69.0 (d)	69.1 (d)	69.1 (d)	69.2 (d)	70.2 (d)
10	38.1 (d)	37.9 (d)	38.1 (d)	38.0 (d)	39.6 (d)	41.0 (d)
11	76.3 (s)	75.3 (s)	76.0 (s)	76.2 (s)	81.8 (s)	134.5 (s)
12	73.8 (d)	73.5 (d)	73.7 (d)	73.4 (d)	69.9 (d)	120.4 (d)
13	26.3 (t)	26.2 (t)	26.3 (t)	26.4 (t)	25.5 (t)	31.4 (t)
14	72.9 (d)	72.9 (d)	72.9 (d)	72.9 (d)	72.5 (d)	73.9 (d)
15	14.1 (q)	14.0 (q)	14.0 (q)	14.2 (q)	15.0 (q)	14.0 (q)
16	63.8 (t)	63.6 (t)	46.1 (t)	63.6 (t)	63.7 (t)	168.5 (s)
17	44.8 (d)	44.7 (d)	44.8 (d)	44.8 (d)	44.6 (d)	43.9 (d)
18	6.6 (q)	6.5 (q)	6.6 (q)	6.6 (q)	7.3 (q)	6.9 (q)
19	176.1 (s)	176.3 (s)	175.9 (s)	176.1 (s)	175.2 (s)	176.0 (s)
20	25.6 (q)	25.0 (q)	25.7 (q)	25.4 (q)	22.5 (q)	24.2 (q)
21	168.8 (s)	172.1 (s)	172.8 (s)	175.5 (s)	167.1 (s)	170.1 (s)
22	21.5 (q)[b]	21.0 (q)[b]	21.5 (q)[b]	34.2 (t)	21.5 (q)	20.9 (q)[b]
23	172.9 (s)	170.4 (s)	170.4 (s)	24.9 (t)	171.7 (s)	171.2 (s)
24	21.3 (q)[b]	21.2 (q)[b]	21.3 (q)[b]	28.9 (t)	36.2 (t)	21.2 (q)[b]
25	170.5 (s)	168.7 (s)	169.1 (s)	29.1 (t)	18.2 (t)	169.6 (s)
26	21.3 (q)[b]	21.2 (q)[b]	21.3 (q)[b]	31.6 (t)	13.7 (q)	21.4 (q)[b]
27	169.5 (s)	169.6 (s)	169.5 (s)	22.5 (t)	170.0 (s)	52.6 (q)
28	21.2 (q)[b]	21.4 (q)[b]	21.2 (q)[b]	14.0 (q)	21.3 (q)	
29	170.3 (s)	173.0 (s)		170.6 (s)	168.7 (s)	
30	20.9 (q)[b]	34.0 (t)		21.1 (q)[b]	21.2 (q)[b]	
31		24.8 (t)		168.8 (s)	169.3 (s)	
32		28.8 (t)		21.3 (q)[b]	20.9 (q)[b]	
33		28.9 (t)		169.6 (s)	170.3 (s)	
34		31.5 (t)		21.5 (q)[b]	20.9 (q)[b]	
35		22.4 (t)		173.0 (s)		
36		13.9 (q)		36.5 (t)		
37				18.4 (t)		
38				13.6 (q)		

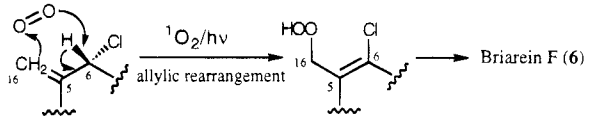
[a] Multiplicities were obtained by an Attached Proton Test (APT) experiment. Assigments were made on the basis of heteronuclear chemical shift correlation methods, carbon atom multiplicities and chemical shift values. The δ values are in parts per million and are referenced to the $CDCl_3$ signal (77.0 ppm). The numbering of atoms for the ester side-chains starts with the ester group at position C-11 and continues on encompassing the ester groups at position C-12, C-14, C-2, C-9, and C-16. [b] Values with identical superscripts in each column may be interchanged.

Table 3. Selected NOE Data for Briareins B–L[a]

proton	briarein B	briarein C	briarein D	briarein E	briarein F	briarein G	briarein H	briarein I	briarein J	briarein K	briarein L
2	H10	H10	H10	H10	H10	H10	H10	H10	H10	H10	H10
3	H15	H15	H6, H7, H15	H15	H4, H15	H4, H6, H15	H4, H15	H4, H15		H4, H15	H15
4	H6, H7	H6, H7	H6, H7	H6, H7	H3, H7	H3, H6, H7	H3, H6, H7	H3, H7	H3	H3, H7	H6, H7
6	H4	H4	H3, H4	H4		H4, H7	H4	H7			H4
7	H4	H4, H17	H3, H4	H4	H4	H4, H6	H4	H4, H6, H17		H4, H17	H4, H17
9	H10, H17, H20	H10, H17, H18, H20	H10, H17	H10, H17, H20	H17, H18, H20	H10, H17, H20	H17, H18, H20	H10, H17, H18, H20	H18, H20	H10, H17, H18, H20	H10, H17, H18, H20
10	H2	H2, H9	H2, H9, H17	H2, H9	H2, H9	H2, H9	H2	H2, H9	H2	H2, H9	H2, H9
12	H20	H20	H20	H20	H20	H20	H20	H20	H20	H20	H20
14	H15	H15	H15	H15	H15	H15	H15	H15	H15	H15	H15
15	H3, H14	H3, H14	H3, H14	H3, H14	H3, H14	H3, H14	H3, H14	H3, H14	H14	H3, H14	H3, H14
17	H9	H7, H9	H9, H10	H9		H9	H9	H7, H9		H7, H9	H7, H9
18		H7, H9			H9		H9	H9	H9	H9	H9
20	H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12	H9, H12

[a] Spectra were recorded at room temperature in $CDCl_3$ solutions.

Scheme 1



were observed. Thus, 13 of the 14 oxygen atoms in the molecular formula of compound **6** were accounted for by the same γ-lactone, hydroxyl, epoxide, and ester functionalities found in compound **5**. The remaining oxygen atom was lastly assigned as an allylic primary alcohol based on ^{13}C-NMR evidence [δ 76.5 (t)] and ^{1}H-NMR data [δ 5.08 (2H, brs)]. Additional signals in the ^{13}C-NMR spectrum of **6** at δ 133.6 (s, C-5) and 131.8 (s, C-6) suggested the presence of a tetrasubstituted double bond, the latter being that of a chlorine-bearing quaternary sp^2 carbon. On the basis of favorable NMR comparisons to briarein E (**5**) and considering results from COSY and NOESY experiments, we assigned the structure **6** to briarein F. Comparison of the spectral features of briareins E and F demonstrated their close structural relationship. Because compound **5** was found to decompose to briarein F (**6**) via autoxidation in $CDCl_3$ solution (see Scheme 1), we cannot discount the possibility that the latter compound may in fact be an artifact. This decomposition, which appears to take place in unstabilized $CDCl_3$ solution only, is noteworthy. No appreciable decomposition was detected when **5** was stirred at 25 °C in stabilized $CHCl_3$ for several months.

Briarein G (**7**), another major metabolite, also showed many spectral features in common with briarein E (**5**). A molecular formula of $C_{32}H_{43}O_{14}Cl$ was established for briarein G from HRFABMS and ^{13}C-NMR spectrometry (Table 2). In comparison to briarein D (**4**), only four acetate methyls were accounted for by close inspection of the ^{1}H-NMR spectrum of briarein G. The most obvious difference between briareins D and G, however, was the presence of a butyrate ester in **7** based on ^{1}H-NMR studies including 2D COSY and spin decoupling of a series of seven contiguous protons [δ 0.91 (3H, t, J = 7.5 Hz), 1.57 (2H, m), and 2.16 (2H, t, J = 7.5 Hz)] and the loss of one molecule of butyric acid in the LRFABMS spectrum of **7**. In comparison to briarein E (**5**), the C-12 acetate methine proton, observed in **5** at δ 4.86, was observed at lower field in the spectrum of **7** at δ 5.69. Thus, briarein G was perceived to be the C-12 butyrate analogue of briarein D (**4**).

Briarein H (**8**) was isolated as a white semi-solid whose molecular formula, $C_{30}H_{40}O_{14}$, was established by HRFABMS. The most obvious difference between briarein H (**8**) and all the other compounds in this series was its lack of a chlorine atom and an exocyclic methylene group. These groups were replaced by an acetoxymethylene group [δ 4.65 (1H, d, J = 14.7 Hz, H-16′) and 5.19 (1H, d, J = 15.0 Hz, H-16); 63.8 (t, C-16)] and a trisubstituted olefin [δ 5.73 (1H, dd, J = 8.1, 1.8 Hz, H-6); 124.0 (d, C-6)]. The presence of a conjugated diene functionality was supported by a UV absorption at λ_{max} (MeOH) 232 (ϵ 21860). The ^{1}H-NMR spectrum contained five acetate signals and, more significantly, two additional *cis*-oriented olefinic signals at δ 5.64 (1H, d, J = 9.9 Hz, H-3) and 6.26 (1H, dd, J = 10.2, 0.9 Hz, H-4), the former being coupled to the H-2 signal at δ 5.57 (1H, d, J = 9.9 Hz) and the latter to the signals ascribed to H-16. Many of the remaining spectral features were reminiscent of those of the C-7 to C-14 portion of briarein E (**5**) and, after further examination of the ^{1}H- and ^{13}C-NMR spectra, we concluded that compounds **5** and **8** had an identical substitution pattern on the cyclohexane ring. Additional NOESY measurements (Table 3) allowed the full stereochemistry of briarein H to be defined as shown in structure **8**.

Once the structure of briarein H was fully defined, the structure of a closely related metabolite, briarein I (**9**), could be assigned based on spectral comparison with **8**. Its molecular formula, $C_{36}H_{52}O_{14}$, was established by HRFABMS and both the ^{13}C- and ^{1}H-NMR spectral data indicated the presence of four acetate groups. The NMR features of briarein I (Tables 1 and 2) were also analogous to those observed for compound **8**. Metabolite **9**, however, possessed a capryloxy group in place of the acetate at C-16. The locus of the caprylate ester was established through a selective INEPT NMR experiment wherein the coupling between the H-16′s and C-29 [δ 173.0 (s)] was clearly demonstrated. The stereochemistry of the substituents in briarein I was confirmed in the same manner used for **8** using NOE measurements (Table 3) and coupling constant analysis.

Another component of the lipid extract, briarein J (**10**), differed from briareins H (**8**) and I (**9**) only in the functionality at C-16. Compound **10**, which possesses the same UV chromophore as **8** and **9**, has a molecular formula of $C_{28}H_{37}O_{12}Cl$ established from HRFABMS and ^{13}C-NMR spectrometry. Further consideration of the NMR data for compound **10** suggested the absence of an alkanoyloxymethylene group at position C-16. In

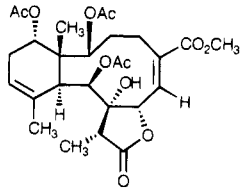
its place, a resonance line corresponding to an allylic methylene bearing chlorine in the ^{13}C-NMR spectrum [δ 46.1 (t)] was observed. In the ^{1}H-NMR spectrum, the allylic methylene protons, resonating as doublets near δ 4.62 and 5.20 in compounds **8** and **9**, had moved upfield to δ 4.43 (1H, d, J = 12.6 Hz) and 4.63 (1H, d, J = 12.3 Hz) in compound **10**. The stereochemical assignments were confirmed by the observed NOE enhancements throughout the briarane skeleton (see Table 3).

Briarein K (**11**) was isolated as a white semi-solid following purification by normal-phase silica gel CC. Data from HRFABMS and ^{13}C-NMR spectrometry (Table 2) established a molecular formula of $C_{38}H_{56}O_{14}$ for this compound. In the ^{1}H-NMR spectrum (Table 1) of briarein K, only three acetate methyl resonances were observed. The two remaining esters were determined to be a caprylate and a butyrate, based on ^{1}H-NMR studies (including 2D COSY and spin decoupling) and the presence of ion peaks in the LRFABMS of **11**, representing the loss of one molecule each of caprylic acid ($C_8H_{16}O_2$) and butyric acid ($C_4H_8O_2$). A major problem confronted in assigning the structure of **11**, however, was to ascertain the location of the caprylate and butyrate esters. A detailed analysis of the ^{1}H-NMR data showed that C-12 and C-16 both were esterified. From NMR data alone, however, we could not determine which carbon bore the caprylate and which the butyrate functionality. Evidence to assign the locations of these esters was obtained through a selective INEPT NMR experiment wherein the coupling between H-12 and C-21 (δ 175.5) and between H-16 and C-35 (δ 173.0) was clearly demonstrated (these carbonyl carbons were assigned as those of a caprylate and butyrate esters, respectively, based on their considerable differences in chemical shifts and on careful spectral comparisons with related model compounds).[21,22] In addition to NOE results (Table 3), coupling constants analysis was useful in assigning the stereochemistry of the six-membered ring.

HRFABMS established a molecular formula of $C_{34}H_{46}O_{15}$ for briarein L (**12**). Observation of the IR spectrum suggested that this compound possessed the same functional groups as those found in compounds **8**–**11**; that is, hydroxyl, γ-lactone, and ester carbonyls. The difference in structure between **11** and **12** was evident from comparison of their ^{1}H- and ^{13}C-NMR spectra. The signals for the caprylate group in the ^{13}C-NMR spectrum of **11** were replaced in the spectrum of **12** by resonances for two additional acetyl groups. Therefore, the ^{1}H-NMR spectrum of **12** contained five acetate methyl signals (as opposed to three in **11**) and lacked the characteristic signals for the heptyl group of a caprylate ester. The ^{13}C-NMR spectrum of briarein L contained seven carbonyl carbons between δ 175.2 and 167.1, one of which, δ 171.7, was assigned as the butyrate carbonyl signal (C-23) from its chemical shift value. A selective INEPT NMR experiment revealed that this signal was coupled with the oxymethine signal at δ 5.75 (1H, br t, J = 5.4 Hz) ascribable to H-12. Therefore, the location of the butyrate (and each of the acetate groups) was assigned definitively from evidence provided by this long-range ^{1}H-^{13}C COSY experiment. The stereochemical assignments made on the basis of NOE data were proven to be identical to those found in analogues **8**–**11**.

Compound **13** was isolated as a yellowish semi-solid substance after purification by silica gel CC, and it was among the least polar of the compounds reported in this series. Comparison of the ^{1}H- and ^{13}C-NMR, HR-FABMS, IR, and UV spectra with those of a known *Stylatula* (sea pen, Order Pennatulacea) metabolite suggested their identity.[26] That these two compounds were in fact the same could be shown by their almost identical specific rotations, $[\alpha]^{25}_{D}$ = −30.3° (*c* 2.90, $CHCl_3$) vs. $[\alpha]^{20}_{D}$ = −31° (*c* 1.0, $CHCl_3$).

The new briarane diterpenes reported here possess certain structural features so far unreported in the literature for compounds of this type previously isolated from Caribbean specimens of *B. asbestinum*. Briareins D–G (**4**–**7**) have a 3(*R**),4(*R**)-epoxy moiety in the 10-membered macrocycle, while briareins H–L (**8**–**12**) have an endocyclic 3,5-diene functionality. Briareins H (**8**), I (**9**), K (**11**), and L (**12**) contain an unusual alkanoyloxymethylene group at C-16, whereas briarein J (**10**) contains a chlorine atom at that position, establishing it as the first briarein derivative with such structural feature. All of the briareins, except briareins H–L (**8**–**12**), are chlorinated at the C-6 position. Briarein F (**6**) is unique among the compounds in this series in having a C-5,6 vinyl chlorine and a hydroxyl substituent at C-16. Two of the briareins, briarein I (**9**) and briarein K (**11**), possess a caprylate ester group, another structural feature so far unreported in the literature for compounds of this type. In contrast, none of the 10 new briarein derivatives reported here possesses an α,β-unsaturated γ-lactone or an α,β-epoxy γ-lactone, a feature found in many other briarane diterpenes isolated from *Briareum* spp.[13] The known methyl ester **13**,[26] the least oxygenated briarein derivative isolated from any *Briareum* spp., lacks functionality at positions C-3 and C-4, does not contain chlorine, and is devoid of oxygenated substituents at C-11 or C-12 (a $\Delta^{11,12}$ compound). Only minor structural variations in the briareins A–L (**1**–**12**) series occur in the substitution pattern around the six-membered ring.



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Experimental Section

General Experimental Procedures. ^{1}H and ^{13}C NMR were measured at 300 and 75 MHz, respectively, with a General Electric QE-300 spectrometer. IR spectra were determined in a Nicolet 600 FT-IR spectrophotometer, and UV spectra were recorded in a Hewlett-Packard Chem Station 8452A spectrometer. Optical rotations were recorded on a Perkin-Elmer Polarimeter (Model 243B). CC was performed in silica gel (35–75 mesh) and TLC analyses were carried out using glass precoated silica gel plates. All solvents used were spectral grade.

Collection and Extraction of *Briareum asbestinum*. *B. asbestinum* was collected near Mona Island in April 1992, at a depth of 2 ft. A voucher specimen (BAMI-001) is stored at the chemistry department of the University of Puerto Rico. The dry animal (ca. 4.01 kg) was blended with MeOH:$CHCl_3$ (1:1), and after filtration the crude extract was evaporated *in vacuo* to yield a green residue (ca. 301 g). The crude extract was suspended in H_2O and then extracted with hexane (4 × 1L) and then with $CHCl_3$ (3 × 1L). The $CHCl_3$ extract (ca. 15.3 g) was fractionated over silica gel (870 g) using a gradient of 15–100% hexane–EtOAc into 42 fractions. Fraction 25 (ca. 1.78 g) was purified subsequently over silica gel (90 g) using 4% $CHCl_3$–MeOH to yield seven subfractions (A–G). Subfraction B (ca. 1.09 g) was cromatographed over silica gel (45 g) with 35% hexane–Me_2CO to give four fractions (I–IV), the most polar (fraction IV) being briarein A (**1**) (87.6 mg, 0.0022% dry wt). Although we isolated **1** previously from the $CHCl_3$ extract in very small amounts,[24] we found it at higher concentration in other fractions. Fraction III (ca. 830 mg) was purified further by successive CC over silica gel (20g) with 4% CH_2Cl_2–Me_2CO yielding briarein G (**7**) (522.7 mg, 0.013% dry wt) and with silica gel (5 g) with 13% $CHCl_3$–EtOAc to give pure briarein L (**12**) (17.7 mg, 0.00044% dry wt). Subfraction D (ca. 216 mg) was purified by CC over silica gel (10 g) using 30% hexane–Me_2CO to yield briarein I (**9**) (72.2 mg, 0.0018% dry wt) and briarein C (**3**) (40.5 mg, 0.001% dry wt). Fraction 23 (ca. 525 mg) was likewise fractionated over silica gel (20 g) with 30% hexane–Me_2CO. Some of the fractions obtained were re-chromatographed over silica gel (10 g) with 7% $CHCl_3$–Me_2CO, yielding briarein B (**2**) (257.7 mg, 0.0064% dry wt) and methyl ester **13** (32.3 mg, 0.0008% dry wt). Fraction 24 (ca. 936 mg), which was purified further by CC [silica gel (70 g) with 30% hexane–Me_2CO], produced briarein K (**11**) (23.1 mg, 0.00058% dry wt) and briarein F (**6**) (18 mg, 0.00045% dry wt). Fractions 26–28 (ca. 1.85 g), were fractionated by successive CC over silica gel using mixtures of hexane–Me_2CO or Me_2CO–$CHCl_3$ as eluent to yield briarein D (**4**) (611.0 mg, 0.015% dry wt) and briarein J (**10**) (36.0 mg, 0.0009% dry wt). The last fraction studied, fraction 31 (ca. 1.15 g), was chromatographed over silica gel (79 g) with 5% CH_2Cl_2–Me_2CO, yielding briarein E (**5**) (179.0 mg, 0.0045% dry wt) and briarein H (**8**) (274.0 mg, 0.0068% dry wt).

Briarein A (1): white semi-solid; $[\alpha]^{25}_D = -58.2°$ (*c* 2.08, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2. The remaining physical and spectral properties of **1** have already been described in the literature.[8,10]

Briarein B (2): white solid; mp 202.7 °C (d), $[\alpha]^{25}_D$ −77.6° (*c* 5.54, $CHCl_3$); UV λ max (MeOH) 208 (ϵ 5400) nm; IR υ max (neat) 3548, 3447, 3010, 2964, 2939, 2879, 1783, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 693.2263 (100%) (calcd for $C_{32}H_{43}O_{13}ClNa$, 693.2289).

Briarein C (3): white solid; mp 131.5–134 °C, $[\alpha]^{25}_D$ −9.5° (*c* 2.41, $CHCl_3$); UV λ max (MeOH) 214 (ϵ 5097) nm; IR υ max (neat) 3540, 2962, 2918, 2849, 1781, 1738, 1731, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 651.2176 (100%) (calcd for $C_{30}H_{41}O_{12}ClNa$, 651.2184).

Briarein D (4): white semi-solid; $[\alpha]^{25}_D$ −48.0° (*c* 1.33, $CHCl_3$); IR υ max (neat) 3560, 3487, 2960, 2922, 2650, 1783, 1743 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 681.1923 (100%) (calcd for $C_{30}H_{39}O_{14}ClNa$, 681.1926).

Briarein E (5): white solid; mp 160.2–161.8 °C, $[\alpha]^{26}_D$ +10.7° (*c* 3.36, $CHCl_3$); IR υ max (neat) 3458, 3338, 2985, 2855, 1783, 1743, 1652 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + H]^+$ 617.1868 (100%) (calcd for $C_{28}H_{38}O_{13}Cl$, 617.2001). A solution of **5** in $CHCl_3$ was stirred at 25 °C while being exposed intentionally to air and indirect sunlight. After two months, no appreciable decomposition was detected by TLC or ^1H-NMR analyses.

Briarein F (6): white semi-solid; $[\alpha]^{25}_D$ −26.9° (*c* 1.96, $CHCl_3$); IR υ max (neat) 3540–3100, 3014, 2961, 2030, 2879, 1783, 1738, 1731, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 655.1759 (100%) (calcd for $C_{28}H_{37}O_{14}ClNa$, 655.1769).

Briarein G (7): white solid; mp 238 °C (d), $[\alpha]^{25}_D$ −28.0° (*c* 1.50, $CHCl_3$); IR υ max (neat) 3560, 3016, 2963, 2930, 2878, 2851, 1784, 1744, 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 709.2264 (100%) (calcd for $C_{32}H_{43}O_{14}ClNa$, 709.2239).

Briarein H (8): white semi-solid; $[\alpha]^{25}_D$ +18.3° (*c* 1.53, $CHCl_3$); UV λ max (MeOH) 232 (ϵ 21860) nm; IR υ max (neat) 3550, 3538, 2955, 2922, 2871, 2651, 1776, 1738 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Li]^+$ 631.2572 (100%) (calcd for $C_{30}H_{40}O_{14}Li$, 631.2578).

Briarein I (9): white semi-solid; $[\alpha]^{25}_D$ +3.5° (*c* 5.94, $CHCl_3$); UV λ max (MeOH) 206 (ϵ 5385) nm; IR υ max (neat) 3451, 3335, 2960, 2918, 2871, 2850, 1777, 1738, 1732, 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Li]^+$ 715.3515 (100%) (calcd for $C_{36}H_{52}O_{14}Li$, 715.3517).

Briarein J (10): white semi-solid; $[\alpha]^{25}_D$ +5.5° (*c* 1.45, $CHCl_3$); UV λ max (MeOH) 208 (ϵ 11727) nm; IR υ max (neat) 3454, 2962, 2956, 2920, 1774, 1734, 1701 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 623.1866 (100%) (calcd for $C_{28}H_{37}O_{12}ClNa$, 623.1871).

Briarein K (11): white semi-solid; $[\alpha]^{25}_D$ −1.6° (*c* 1.90, $CHCl_3$); UV λ max (MeOH) 206 (ϵ 7194) nm; IR υ max (neat) 3680–3100, 2961, 2927, 2880, 2851, 1773, 1740, 1736 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 759.3563 (100%) (calcd for $C_{38}H_{56}O_{14}Na$, 759.3567).

Briarein L (12): white semi-solid; $[\alpha]^{25}_D$ −19.8° (*c* 2.27, $CHCl_3$); UV λ max (MeOH) 207 (ϵ 6774) nm; IR υ max (neat) 3508, 2962, 2921, 2872, 2850, 1772, 1739, 1734 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Li]^+$ 701.3007 (100%) (calcd for $C_{34}H_{46}O_{15}Li$, 701.2997).

Methyl Ester 13. This known metabolite has been identified from its spectral properties:[26] yellowish semi-

solid; $[\alpha]^{25}_D$ −30.3° (*c* 2.90, $CHCl_3$); UV λ max (MeOH) 208 (ε 8287) nm; IR *v* max (neat) 3440, 2948, 2938, 2855, 1780, 1734 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) see Table 2; HRFABMS *m/z* $[M + Na]^+$ 559.2143 (100%) (calcd for $C_{27}H_{36}O_{11}$-Na, 559.2155).

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References and Notes

(1) This article is dedicated to Professor Paul J. Scheuer on the occasion of his 80th birthday.
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