Bioactive Compounds from the Gorgonian *Briareum polyanthes*. Correction of the Structures of Four Asbestinane-Type Diterpenes

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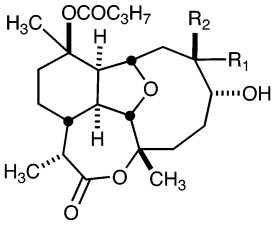
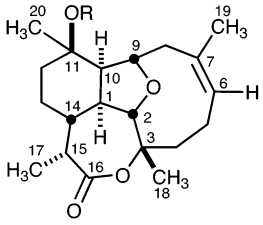
Our extended chemical investigation of the crude MeOH−$CHCl_3$ extract of the gorgonian octocoral *Briareum polyanthes* from Puerto Rico has led to the isolation of three eunicellin-type diterpenoids, **1**−**3**, along with five (**4**−**8**) diterpenoids of the asbestinane-type and one (**9**) of the briarane-type of polycyclized diterpenes. The structures and relative stereochemistry of the new compounds **1**−**9** were established on the basis of spectroscopic analysis (^{1}H NMR, ^{13}C NMR, HMQC, HMBC, NOESY). The biological activity of these compounds against pathogenic microbes responsible for various human infectious diseases was investigated. In addition, new data recorded for four known asbestinin diterpenes also isolated during this investigation and further analysis through chemical reactions have prompted us to revise our original structural assignments for these compounds.

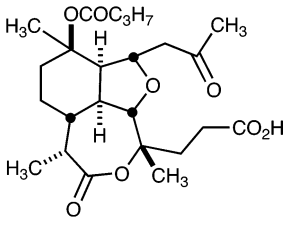
Briareum polyanthes Duchassaing & Michelotti (Gorgoniidae) is a West Indian gorgonian species that occurs commonly in the Greater Antilles.[1] Extracts of this octocoral and its constituents are reported to exhibit a wide spectrum of biological activities including insecticidal, antiviral, antihelminthic, antimicrobial, antiinflammatory, and antiplasmodial.[2] A previous investigation on the chemical composition of *B. polyanthes* collected in Puerto Rican waters showed that it is also a rich source of eunicellin-based (briarellins) diterpenoids.[3] In the present study, we report the isolation of briarellin Q (**1**), briarellin R (**2**), and *seco*-briarellin R (**3**), new eunicellin-type diterpenoids, along with five new asbestinane-based diterpenoids [asbestinins-24 (**4**), -25 (**5**), and -26 (**6**), *seco*-asbestinin B (**7**), and *nor*-asbestinin A (**8**)] and the new briarane diterpenoid **9**. Their structures were determined mainly through the use of 1D and 2D NMR techniques. In the course of isolating compounds **1**−**9**, we also found and identified four known asbestinane diterpenes, namely, asbestinin-10, asbestinin-20, asbestinin-21, and 11-acetoxy-4-deacetoxyasbestinin F.[4,5] In this paper, we discuss new analytical data for the latter compounds that have led us to revise their previously assigned structures.



1 R_1 = OH; R_2 = CH_3
10 R_1 = CH_3; R_2 = OH



2 R = COC_3H_7
11 R = $COCH_3$



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Results and Discussion

The HRESIMS (positive mode) of briarellin R (**2**) displayed a quasimolecular ion peak at *m*/*z* 405.2654 (calcd 405.2641), which corresponds to the molecular formula $C_{24}H_{37}O_5$. The IR spectrum showed an intense absorption band at 1720 cm^{-1} (ester carbonyl group). The ^{1}H NMR spectrum of **2** indicated the presence of five methyl groups with three-proton singlets at δ 1.74, 1.59, and 1.31, one doublet at δ 1.34, and one triplet at δ 0.92. It also exhibited a broad triplet with large splitting at δ 5.63 (1H, J = 8.5 Hz) ascribed to the trisubstituted olefin group. A set of nearly overlapped signals at δ 4.04 and 4.01, each integrating for one proton, were assignable to H-9 and H-2, respectively. Another set of nearly coalescent one-proton broad singlets at δ 2.65 and 2.67 were attributable to H-1 and H-10. Appropriate ^{13}C NMR signals were observed at δ 26.7 (C-19), 23.1 (C-18), 28.7 (C-20), 17.6 (C-17), 13.6 (C-24), 130.0 (C-6), 80.8 (C-9), 91.7 (C-2), 45.8 (C-1), and 49.9 (C-10). The ^{1}H and ^{13}C NMR data of **2** (Table 1) were closely comparable to those of known briarellin J (**11**), except that **2** showed signals corresponding to an 11-butyryloxyl substituent in lieu of an acetoxyl group.[3] On the basis of the above data, including data from a NOESY experiment,[6] briarellin R (**2**) was concluded to be the *n*-butanoyl analogue of **11** with the relative stereochemistry as described by formula **2**.

Briarellin Q (**1**), obtained as a white, amorphous solid, displayed 24 signals in the ^{13}C NMR spectrum (two ester carbonyls, three other nonprotonated carbons bearing oxygen, seven methines, seven methylenes, and five methyls) and gave a pseudomolecular ion peak at *m*/*z* 439.2701 in the HRFABMS (positive mode) attributed to the $[M + H]^+$ ion, suggesting it to be an isomer of known briarellin O (**10**) ($C_{24}H_{38}O_7$).[3] The IR spectrum showed strong absorption bands at 3457 (hydroxyl group) and 1732 and 1716 (ester carbonyls) cm^{-1}. The ^{1}H NMR spectrum (Table 1) had many signals comparable to those of the latter, viz., a pair of 1H signals at δ 2.67 and 2.60 assignable to bridgehead methines H-1 and H-10, a pair of oxymethine resonances at δ 3.65 and 3.95 for H-2 and H-9, respectively, and signals for an *n*-butanoyl system involving C-11.

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Table 1. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) Spectral Data for Compounds **1**−**4**[a]

	briarellin Q (**1**)		briarellin R (**2**)		*seco*-briarellin R (**3**)		asbestinin-24 (**4**)	
atom	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult
1	2.67, br d, 9.2	44.8 (CH)	2.65, br s	45.8 (CH)	2.57, m	44.3 (CH)	2.59, q, 9.5	37.7 (CH)
2	3.65, br s	95.6 (CH)	4.01, br s	91.7 (CH)	4.06, d, 5.2	87.9 (CH)	3.84, d, 8.6	94.7 (CH)
3		85.8 (qC)		85.0 (qC)		83.4 (qC)		77.6 (qC)
4α	2.57, m	35.3 (CH_2)	1.71, m	34.4 (CH_2)	2.05, m	29.9 (CH_2)	1.18, m	27.6 (CH_2)
4*β*	1.78, m		2.10, m		2.32, m		2.02, m	
5α	2.05, m	29.9 (CH_2)	2.34, m	22.8 (CH_2)	2.46, m	28.7 (CH_2)	2.16, m	25.4 (CH_2)
5*β*	2.05, m		1.84, m		2.46, m		1.70, m	
6	3.95, d, 7.1	78.9 (CH)[b]	5.63, br t, 8.5	130.0 (CH)		177.0 (qC)	3.19, br d, 7.4	82.6 (CH)
7		73.9 (qC)		131.2 (qC)		206.6 (qC)	1.70, m	37.2 (CH)
8α	2.26, m	46.8 (CH_2)	2.10, m	38.4 (CH_2)	2.74, m	50.0 (CH_2)	1.03, m	38.1 (CH_2)
8*β*	1.66, m		2.51, br d, 14.0		2.65, dd, 2.3, 13.5		1.97, m	
9	3.95, d, 7.1	79.6 (CH)	4.04, m	80.8 (CH)	4.17, dt, 2.3, 8.7	77.8 (CH)	4.06, dd, 4.3, 12.3	82.0 (CH)
10	2.60, m	54.2 (CH)	2.67, br s	49.9 (CH)[b]	2.45, m	52.4 (CH)	1.73, m	48.0 (CH)
11		81.3 (qC)		81.3 (qC)		80.4 (qC)	5.37, dd, 2.0, 5.8	73.4 (CH)
12α	2.05, m	30.1 (CH_2)	2.02, m	30.1 (CH_2)	2.05, m	30.1 (CH_2)	2.10, m	31.3 (CH)
12*β*	2.05, m		2.02, m		2.05, m			
13α	1.85, m	17.1 (CH_2)	1.84, m	16.7 (CH_2)	1.87, m	16.2 (CH_2)	1.47, m	31.4 (CH_2)
13*β*	1.85, m		1.84, m		2.02, m		1.03, m	
14	1.72, m	38.3 (CH)	1.66, m	37.3 (CH)	1.58, m	36.1 (CH)	1.87, m	38.2 (CH)
15	2.99, dq, 4.8, 7.3	46.3 (CH)	2.91, dq, 4.6, 7.4	46.1 (CH)	2.91, dq, 4.7, 7.5	45.8 (CH)	1.64, m	36.3 (CH)
16α		176.0 (qC)		176.1 (qC)		175.8 (qC)	3.46, dd, 2.7, 13.0	68.0 (CH_2)
16*β*							3.76, d, 13.0	
17	1.34, d, 7.6	17.5 (CH_3)	1.34, d, 7.6	17.6 (CH_3)	1.37, d, 7.4	17.6 (CH_3)	0.92, d, 7.1	11.0 (CH_3)
18	1.40, s	23.4 (CH_3)	1.59, s	23.1 (CH_3)	1.46, s	20.7 (CH_3)	1.33, s	22.8 (CH_3)
19	1.35, s	25.4 (CH_3)	1.74, s	26.7 (CH_3)[b]	2.21, s	31.3 (CH_3)	1.00, d, 7.3	23.0 (CH_3)
20	1.31, s	28.7 (CH_3)	1.31, s	28.7 (CH_3)	1.29, s	28.8 (CH_3)	0.90, d, 7.2	17.0 (CH_3)
21		172.3 (qC)		172.3 (qC)		172.7 (qC)		171.3 (qC)
22	2.33, t, 7.5	37.2 (CH_2)	2.19, t, 7.4	37.4 (CH_2)	2.23, m	37.2 (CH_2)	2.08, s	21.4 (CH_3)
23	1.63, m	18.3 (CH_2)	1.54, m	18.4 (CH_2)	1.63, m	18.5 (CH_2)	3.29, s	56.5 (CH_3)
24	0.96, t, 7.4	13.6 (CH_3)	0.92, t, 7.4	13.6 (CH_3)	0.95, t, 7.3	13.7 (CH_3)		

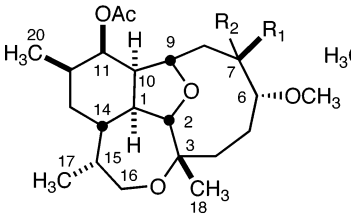
[a] Data recorded in $CDCl_3$ at 25 °C. Assignments were aided by ^{1}H−^{1}H COSY, DEPT, HMBC, HMQC, and NOESY NMR experiments. [b]Broad, low-intensity resonance line.

The major difference was in the signals for H-6 and H-9 (resonating as a pair of overlapped doublets at *δ* 3.95), which appeared upfield in **1** by 0.52 and 0.31 ppm, respectively. This was accompanied by a downfield shift of 0.22 ppm for H_3-19, which suggests that the relative stereochemistry at C-7 may be reversed in **1**, thus pointing to the presence of a cis *vic*-glycol functionality involving C-6 and C-7. The upfield shift of C-7 (2.4 ppm) and the downfield shift of C-19 (3.0 ppm) observed in the ^{13}C NMR spectrum of **1** can then be rationalized on the basis of this peculiarity. Detailed analysis of the 2D NMR spectra provided further confirmation that **1** is simply a C-7 epimer of briarellin O (**10**). Strong NOE correlations (recorded in C_6D_6) involving H-6 and the C-18 and C-19 methyl protons reveal that the latter are positioned on the same face (interestingly, whereas in briarellin O there exist NOE correlations between H-6 and H_3-18, no such correlations exist between H-6 and H_3-19). The C-7 (*S**) stereochemistry in **1** was also evident from key NOESY correlations between H-9 and H_3-19.

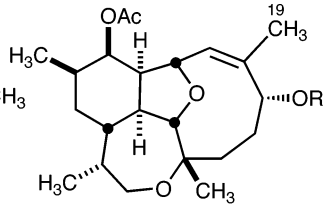
seco-Briarellin R (**3**) showed a pseudomolecular ion peak at *m*/*z* 453 $[M + H]^+$ in the FABMS spectrum (positive mode), and the molecular formula, $C_{24}H_{37}O_8$, was established by HRFABMS [*m*/*z* 453.2487, $(M + H)^+$, Δ +0.1 mmu]. Broad IR absorptions implied the presence of hydroxyl (3500−3000 cm^{-1}) and carbonyl (1717 cm^{-1}) functionalities, indicating the presence of a carboxylic acid moiety. The ^{1}H and ^{13}C NMR spectra of **3** (Table 1) were analogous to those of **2** except for the following observation: two sp^2 quaternary carbons (δ_C 206.6 and 177.0) bearing an oxygen atom for **3** were observed in place of the olefin carbons of **2**. The positions of these carbonyl carbons were deduced to be C-7 and C-6 by HMBC correlations for H_3-19, H_2-8, and H-9 to C-7, and H_2-4 and H_2-5 to C-6. The relative stereochemistry of **3** was deduced from NOESY correlations.[7] On the basis of our proposed structure, it appears that **3** might arise biogenetically from the oxidation/cleavage of the C-6/C-7 bond of briarellin R (**2**). Compound **3**, with these uncommon structural features, represents the second example of such ether-cyclized diterpenoids known as *seco*-eunicellins.[8]

Compounds **4**−**6** were quickly identified as terpenoids based on the asbestinane carbon skeleton because their ^{13}C NMR spectra did not contain a signal for a tetrasubstituted carbon atom bearing carbon substituents (as found at the carbocyclic ring junction in the briarein series), nor did these compounds reveal a signal near 17−21 ppm ascribable to the C-13 methylene group, as found in the eunicellin (briarellin) series.[9] To the best of our knowledge, this is the first time that diterpenes based on the asbestinane carbon skeleton are reported from *B. polyanthes*.

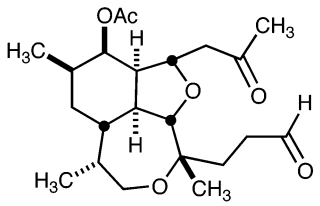
Compound **4**, named asbestinin-24, was obtained as a white semisolid, and its HREIMS exhibited a molecular ion at *m*/*z* 394.2722, consistent with a molecular formula of $C_{23}H_{38}O_5$. A sharp IR absorption band at 1736 cm^{-1} implied the presence of a single ester carbonyl functionality. Unlike compounds **1**−**3**, the ^{1}H NMR spectrum of **4** indicated the presence of a doublet at *δ* 3.76 (*J* = 13.0 Hz, H-16*β*) and a doublet of doublets at *δ* 3.46 (*J* = 2.7, 13.0 Hz, H-16α), each integrating for one proton, attributable to an oxymethylene group. It also revealed signals for four oxymethines at *δ* 5.37 (H-11), 4.06 (H-9), 3.84 (H-2), and 3.19 (H-6), three methyl doublets at *δ* 1.00 (H_3-19), 0.92 (H_3-17), and 0.90 (H_3-20), and three methyl singlets at *δ* 3.29 (H_3-23), 2.08 (H_3-22), and 1.33 (H_3-18). The ^{13}C NMR spectrum showed signals for two oxygenated quaternary carbons [*δ* 171.3 (C-21) and 77.6 (C-3)], four oxygenated methines [*δ* 94.7 (C-2), 82.6 (C-6), 82.0 (C-9), 73.4 (C-11)], one oxygenated methylene (*δ* 68.0, C-16), and an oxygenated methyl (*δ* 56.5, C-23). Additionally, there were characteristic signals for six nonoxygenated methines at *δ* 37.7 (C-1), 37.2 (C-7), 48.0 (C-10), 31.3 (C-12), 38.2 (C-14), and 36.3 (C-15). Comparison of the ^{1}H and ^{13}C NMR spectra of **4** with those of known 11-acetoxy-4-deoxyasbestinin D (previously reported from the Caribbean gorgonian *B. asbestinum*)[9] made evident the similarities between these structures, but most importantly, revealed the presence of some



4 $R_1 = CH_3$; $R_2 = H$
5 $R_1 = OH$; $R_2 = CH_3$



6 R = H
12 R = Ac



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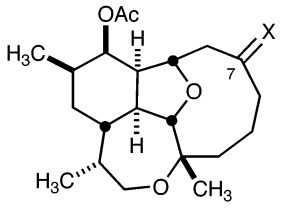
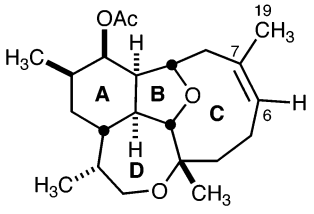


8 X = O
13 X = CH_2



11-acetoxy-4-deoxyasbestinin D

features unique to **4**. While the complex tetracyclic ring system along with the acetate functionality at C-11 were shown to be intact in **4**, asbestinin-24, however, did not show the olefin carbon signals ascribable to C-6 and C-7. Instead, asbestinin-24 contained new signals at δ 82.6 (CH) and 37.2 (CH) for C-6 and C-7, respectively. Moreover, the signals ascribable to H-6 and H_3-19 in analogues of the 4-deoxyasbestinin series having a Δ^6 olefin were replaced in **4** by new signals at δ 3.19 (1H, br d, $J = 7.4$ Hz, H-6) and 1.00 (3H, d, $J = 7.3$ Hz, H_3-19), respectively. These combined spectroscopic data led us to propose structure **4** for asbestinin-24. The complete planar structure of asbestinin-24 and the unambiguous assignment of all its ^{1}H and ^{13}C NMR signals were thus achieved by analysis of COSY, DEPT, HMQC, and HMBC spectroscopic data (Table 1). The relative stereochemistry of most stereogenic centers of **4**, as determined from a NOESY experiment, was identical with that of all of the previously known diterpenoids in the 4-deoxyasbestinin series.[9] On the other hand, NOE correlations of H_3-19 with H-9 and H-6 established the β-orientation of these protons.

Asbestinin-25 (**5**) was isolated as an optically active colorless oil whose IR spectrum showed strong absorption bands at 3540 and 1737 cm^{-1} (hydroxyl and ester groups). The HRFABMS (positive mode) showed a sodiated quasimolecular ion at *m*/*z* 433.2570, consistent with a molecular formula of $C_{23}H_{38}O_6$. However, the ^{13}C NMR spectrum acquired in $CDCl_3$ at 75 MHz showed 23 pairs of closely spaced resonance lines, suggesting the occurrence at 25 °C of two stable conformers of **5** in a 1:1 ratio. Thus, we elected to continue the structure determination of **5** using C_5D_5N whereby a single set of 23 resonance lines was obtained. Interestingly, the ^{13}C NMR spectrum showed signals that correlated easily with those of the complex tetracyclic array of compound **4**. The number and types of the ^{1}H and ^{13}C NMR signals (Table 2) associated with the asbestinin skeleton were essentially the same as those of asbestinin-24 (**4**), with only small differences in their chemical shifts. The only major difference between their ^{1}H NMR spectra involved the methyl doublet at δ 1.00 ascribable to H_3-19 in **4**, which was replaced in compound **5** by a sharp three-proton singlet at δ 1.35. This observation, coupled with the appearance of a new signal for an additional oxygenated quaternary carbon at δ 75.3 (C-7) in the ^{13}C NMR spectrum of **5**, pointed to the presence of a methyl-substituted tertiary alcohol involving C-7. The location of the new hydroxyl group at C-7 was evident from the HMBC correlation of the latter carbon with the H_3-19 signal. The methyl group at C-7 showed a strong NOE interaction with H-10; the former must therefore be α-oriented. Absence of any NOE correlations further indicated that H_3-19 is trans to both H-6 and H-9.

The molecular formula of asbestinin-26 (**6**) was determined as $C_{22}H_{34}O_5$, on the basis of its $[M + 1 - H_2]^+$ fragment ion at *m*/*z* 377.2333 in the HRFABMS (positive mode). IR absorptions implied the presence of hydroxyl (3467 cm^{-1}) and ester carbonyl (1736 cm^{-1}) functionalities. The ^{1}H and ^{13}C NMR spectra of **6** (Table 2) were analogous to those of known 11-acetoxy-4-deoxyasbestinin E (**12**) (previously isolated from *B. asbestinum*)[5] except for the following observations: H-6 appeared shifted upfield to δ 5.40 in **6** (vs δ 6.36 in **12**) and the acetate methyl signal present in the ^{1}H NMR spectrum of **12** was missing in the case of compound **6**. These data pointed to the presence of a hydroxyl group at C-6 in asbestinin-26 (**6**). Comparison of the overall physical and spectral data of **6** with those reported for compound **12** indicated that these compounds were otherwise identical. Due to the very small amounts of pure compound obtained, which were mainly used for evaluating its biological activities, no attempt was made to chemically correlate compounds **6** and **12**.

seco-Asbestinin B (**7**) had the molecular formula $C_{22}H_{34}O_6$ as determined by HREIMS. The ^{13}C NMR spectrum of **7** (Table 2) displayed signals indicating three carbonyl carbons (of a ketone, aldehyde, and ester groups), five methyls, five methylenes, eight sp^3 methines, and one oxygenated sp^3 quaternary carbon. These facts implied that **7** could be a natural product arising from oxidative cleavage of 11-acetoxy-4-deoxyasbestinin D at the Δ^6 position. Extensive analysis of the HMQC, ^{1}H−^{1}H COSY, and HMBC spectra of **7** enabled us to outline its planar structure, which had the A-, B-, and D-rings identical with those of compounds **4**−**6**. The loci of the ketone and aldehyde groups were deduced to be C-7 and C-6, respectively, by HMBC correlations for H_3-19, H_2-8, and H-9 to C-7, and H_2-4 and H_2-5 to C-6. The relative stereochemistry of *seco* derivative **7** was routinely demonstrated by NOESY; the correlations of H-2/H_3-18, H-2/H-9, H-2/H-14, H-14/H-15, and H-14/H_3-20 indicated that H-2, H-9, H-14, H-15, H_3-18, and H_3-20 were above the molecular plane and were assigned as having a β-configuration. Moreover, NOESY interactions of H-1 with H-10, H-11, and H_3-17 suggested that these protons were α-oriented. A structurally similar *seco*-asbestinin was previously isolated from *B. asbestinum*.[10]

nor-Asbestinin A (**8**), a minor compound, was obtained as a colorless oil whose molecular formula was established as $C_{21}H_{32}O_5$ by HREIMS. Its IR spectrum showed absorptions at 1736 and 1697 cm^{-1}, typical for saturated ester and ketone functionalities. The ^{1}H NMR spectrum of **8** contained signals for an acetate ester [δ 2.09 (3H, s)], the presence of which was also in full agreement with the $[M - CH_3CO_2H]^+$ fragment at *m*/*z* 304 observed in the EIMS. Therefore, compound **8** was a *nor*-diterpene. The planar structure of *nor*-asbestinin A (**8**) was deduced from analysis of 1D- and 2D-NMR spectra. The ^{1}H and ^{13}C NMR spectra of **8** had many features in common with those of analogues **4**−**6**, and indeed, ^{1}H−^{1}H COSY and HMQC experiments confirmed many of the same partial structures, although the chemical shifts of the respective protons and carbons of **8** (Table 2) differed somewhat. Nevertheless, distinctively different spectroscopic features were observed in the NMR spectra, which ultimately indicated that the methyl group connected to C-7 in compounds **4**−**6** had been replaced in **8** by a ketone functionality. Critically, the ^{13}C NMR spectrum of **8** lacked the methyl carbon signal typically ascribed to C-19 and also

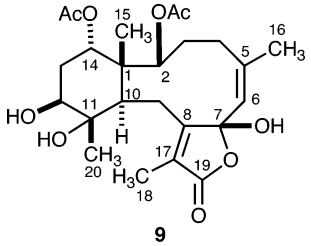
Table 2. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) Spectral Data for Compounds **5**−**8**

	asbestinin-25 (**5**)[a]		asbestinin-26 (**6**)[b]		*seco*-asbestinin B (**7**)[b]		*nor*-asbestinin A (**8**)[b]	
atom	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult	δ_H, mult, *J* in Hz	δ_C, mult
1	2.57, q, 9.8	37.7 (CH)	2.44, q, 9.7	37.2 (CH)	2.19, m	38.0 (CH)	2.35, m	38.7 (CH)
2	4.02, br d, 7.5	92.5 (CH)	3.78, d, 7.3	93.3 (CH)	3.52, d, 9.2	92.5 (CH)	3.84, d, 11.2	93.9 (CH)
3		77.7 (qC)		77.8 (qC)		75.5 (qC)		76.6 (qC)
4α	1.60, m	34.6 (CH_2)	1.30, m	32.8 (CH_2)	1.91, m	28.3 (CH_2)	1.61, m	35.5 (CH_2)[c]
4*β*	2.05, m		1.61, m		1.71, m		1.61, m	
5α	1.47, m	27.0 (CH_2)	1.85, m	30.5 (CH_2)	2.38, m	38.5 (CH_2)	1.61, m	34.4 (CH_2)[c]
5*β*	2.10, m		1.45, m		2.56, m		1.61, m	
6α		85.8 (CH)		69.7 (CH)	9.73, dd, 1.3, 2.4	203.5 (CH)	2.28, m	48.1 (CH_2)
6*β*	4.44, br d, 10.3		5.40, m				2.53, m	
7		75.3 (qC)		137.7 (qC)		206.8 (qC)		214.4 (qC)
8α	1.72, m	47.6 (CH_2)	5.09, br d, 1.4	127.6 (CH)	2.68, d, 1.7	48.3 (CH_2)	2.28, m	48.2 (CH_2)
8*β*	1.72, m				2.70, s		3.00, dd, 5.1, 11.7	
9	3.95, m	79.6 (CH)	4.71, br s	82.6 (CH)	3.90, ddd, 1.2, 5.6, 12.7	76.7 (CH)	4.24, dt, 2.0, 4.5	80.9 (CH)
10	1.72, m	48.7 (CH)	2.00, br d, 9.6	50.4 (CH)	2.02, m	47.9 (CH)	2.50, m	45.3 (CH)
11	5.50, br d, 4.0	73.4 (CH)	5.41, m	73.6 (CH)	5.19, t, 3.5	72.3 (CH)	5.32, dd, 2.6, 5.5	73.8 (CH)
12	1.39, m	31.7 (CH)	2.09, m	31.4 (CH)	1.83, m	31.5 (CH)	2.15, m	31.1 (CH)
13α	0.94, m	31.4 (CH_2)	1.50, m	31.4 (CH_2)	1.60, m	30.8 (CH_2)	1.51, m	31.5 (CH_2)
13*β*	2.05, m		1.02, dd, 2.5, 13.3		1.08, m		1.00, m	
14	1.98, m	38.6 (CH)	1.89, m	38.3 (CH)	1.97, m	37.7 (CH)	1.84, m	37.9 (CH)
15	1.51, m	37.1 (CH)	1.60, m	36.6 (CH)	1.60, m	36.5 (CH)	1.61, m	36.7 (CH)
16α	3.49, br d, 12.7	67.9 (CH_2)	3.46, dd, 2.8, 13.1	67.8 (CH_2)	3.45, dd, 3.2, 12.8	67.7 (CH_2)	3.45, dd, 2.9, 13.0	67.7 (CH_2)
16*β*	3.87, d, 12.7		3.79, m		3.67, d, 12.8		3.76, d, 13.0	
17	0.99, d, 6.7	11.4 (CH_3)	0.90, d, 7.0	10.9 (CH_3)	0.87, d, 7.0	11.2 (CH_3)	0.90, d, 7.1	10.9 (CH_3)
18	1.44, s	22.6 (CH_3)	1.27, s	22.2 (CH_3)	1.23, s	23.1 (CH_3)	1.32, s	24.0 (CH_3)[c]
19	1.35, s	24.2 (CH_3)	1.64, br d, 1.4	17.2 (CH_3)	2.16, s	30.7 (CH_3)	0.91, d, 7.2	17.5 (CH_3)
20	0.90, d, 7.2	17.4 (CH_3)	0.91, d, 7.2	17.3 (CH_3)	0.93, d, 7.0	18.7 (CH_3)		171.3 (qC)
21		171.0 (qC)		171.3 (qC)		171.1 (qC)	2.09, s	21.3 (CH_3)
22	2.00, s	21.2 (CH_3)	2.08, s	21.4 (CH_3)	2.12, s	21.2 (CH_3)		
23	3.27, s	57.7 (CH_3)						

[a] Data recorded in C_5D_5N at 25 °C. [b]Data recorded in $CDCl_3$ at 25 °C. Assignments were aided by ^{1}H−^{1}H COSY, DEPT, HMBC, HMQC, and NOESY NMR experiments. [c]Due to the broad, low-intensity nature of this resonance line, the chemical shift value shown has been estimated.

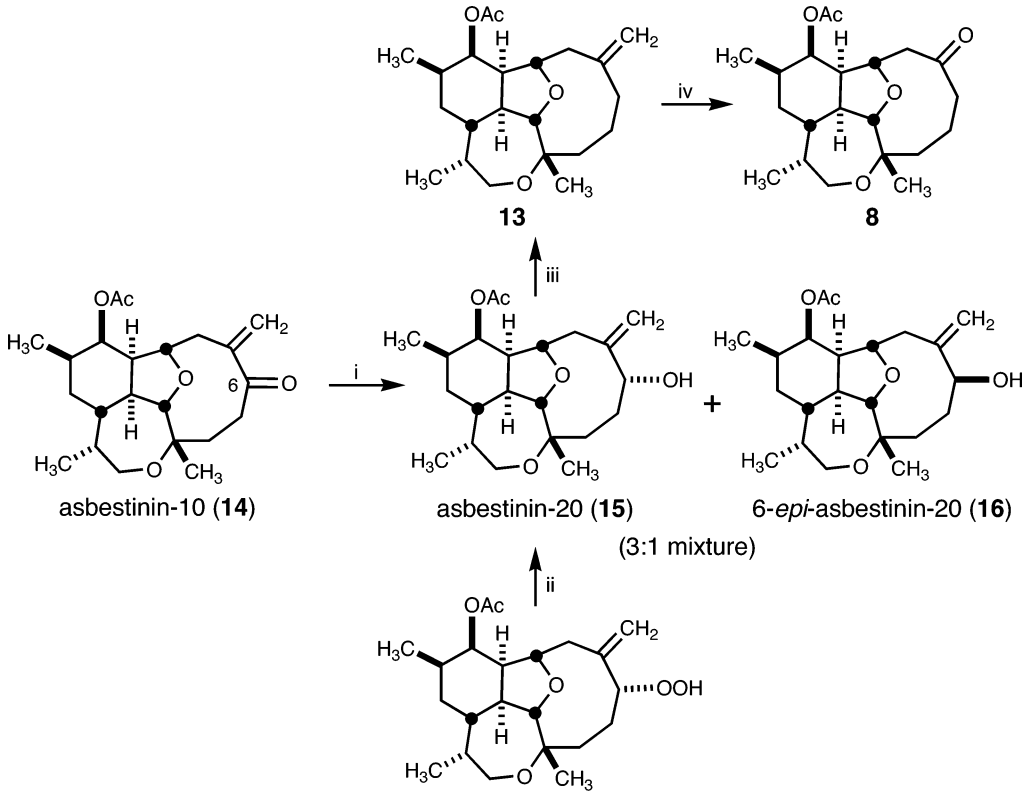
revealed the presence of a new carbonyl carbon at δ 214.4. This peculiarity suggested that **8** must be the oxidative cleavage product of an asbestinin diterpene such as **13** (Figure 1). On the basis of this assumption the structure of **8** was confirmed through the following reaction sequence. Treatment of known asbestinin-20 (**15**)[5] with $LiClO_4/(CH_3)_3SiH$ in ether at 25 °C, followed by ozonolysis of the ensuing product 6-deoxyasbestinin-20 (**13**) in EtOAc solution at −78 °C, gave, upon oxidative workup, the expected ketone **8**, which was identical to the natural product with respect to its GLC-MS and TLC retention time and mass spectral fragmentation patterns.

A previous investigation of the gorgonian coral *B. asbestinum* (Pallas) from Puerto Rico that led to the discovery of 10 briarane diterpenoids greatly helped us to quickly recognize compound **9** as the only briarane-based diterpenoid isolated during this investigation.[11] Briarein **9** was isolated as a colorless oil whose HRESIMS did not show a molecular ion species, but a $[M - H_2O + Na]^+$ fragment ion at *m*/*z* 471.2017 implying that **9** had the molecular formula $C_{24}H_{34}O_9$. The IR spectrum revealed broad absorption bands for hydroxyl (3431 cm^{-1}) and ester carbonyl (1739 cm^{-1}) groups. The ^{1}H NMR spectrum showed resonances due to two acetates [δ 2.09 (3H, s) and 1.97 (3H, s)], two olefinic methyls [δ 2.00 (3H, s) and 1.70 (3H, s)], two quaternary methyls [δ 1.63 (3H, s) and 1.30 (3H, s)], an olefinic proton [δ 5.31 (1H, br s)], and three oxymethine signals [δ 5.16 (1H, br t, J = 2.7 Hz), 4.87 (1H, dd, J = 2.0, 8.7 Hz), and 3.87 (1H, br s)]. The ^{13}C NMR spectrum revealed the presence of tetrasubstituted [δ 160.1 (qC) and 127.9 (qC)] and trisubstituted [δ 145.8 (qC) and 124.8 (CH)] double bonds, a hemiketal carbon [δ 106.2 (qC)], two acetate carbonyls [δ 170.6 (qC) and 169.0 (qC)], one α,*β*-unsaturated-*γ*-lactone carbonyl [δ 171.4 (qC)], one tetrasubstituted carbon atom bearing carbon substituents [δ 44.3 (qC)], and four mono-oxygenated carbons [δ 77.9 (qC), 77.2 (CH), 76.1 (CH), and 75.6 (CH)]. The ^{1}H−^{1}H COSY, HMQC, and HMBC experiments readily located the acetates at C-2 and C-14 and revealed that C-11 and C-12 each had a free hydroxyl group. The connectivities from C-1 to C-8 and to C-17 and the vicinity of the latter to C-18 and C-19 were easily traced. The environment of the C-11/C-12 *vic*-glycol was established by HMBC correlations of C-12 to H-14 and H_3-20 and of C-11 to H_2-9 and H_3-20. In addition, the C-10 bridgehead methine showed HMBC correlations with H_3-15 and H_3-20. Complete ^{1}H and ^{13}C NMR assignments for compound **9** are given in the Experimental Section. NOESY measurements were carried out in order to deduce the relative stereochemical features of **9**. Thus, H-10 gave correlations with H-2 and H-12, but not with H_3-15, indicating that H-2, H-10, and H-12 are located on the same face (assigned as the α-face) and that H_3-15 lies on the opposite, *β*-face. In addition, H_3-15 gave NOE correlations with H-14 and H_3-20, confirming the *β*-orientation for these protons. The relative configuration at C-7 was inferred from molecular modeling studies wherein the most stable conformation of **9**, consistent with all of the NOE interactions observed, required the *S** stereochemistry.



9

In this paper, we also report the isolation from *B. polyanthes* of four known asbestinin analogues, namely, asbestinin-10, asbestinin-

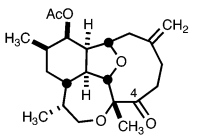
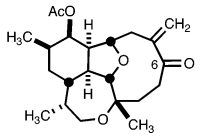
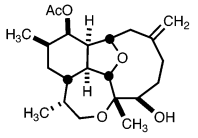
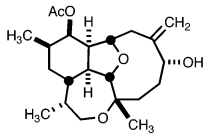
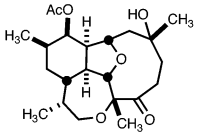
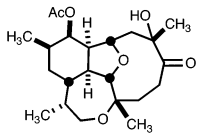
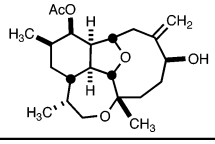
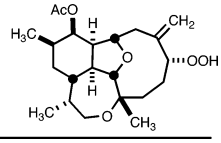


i. $NaBH_4$ in MeOH, 25 °C, 90 min (74%); ii. $NaBH_4$ in MeOH, 25 °C, 110 min (75%); iii. $LiClO_4$ in ether, $(Et)_3SiH$, 25 °C, 42 h (52%); iv. O_3 in EtOAc, 30% H_2O_2, 105 °C, 4h (100%).

Figure 1. Chemical interconversion studies aimed at establishing the molecular structures of compounds **8**, **14**, **15**, and **17** unambiguously.

20, asbestinin-21, and 11-acetoxy-4-deacetoxyasbestinin F. These compounds were first reported between 1993 and 1994, and their structures were elucidated by extensive spectroscopic studies.[4,5] However, upon reisolation of these compounds, we acquired new spectroscopic data that were not in accordance with the reported structures (Table 3). Further analysis through chemical reactions allowed us to revise their structures (Figure 1). Critically, the ketone group in asbestinin-10 should be placed at C-6 (not at C-4 as originally reported) from HMBC correlations between the carbonyl signal at δ 206.4 (qC) and the H_2-19 exomethylene protons at δ_H 5.15 and 5.25. In addition, HMBC correlations between the ^{13}C NMR signal at δ_C 35.8 (CH_2) and H_3-18 at δ_H 1.25 unambiguously established the position of this methylene group at C-4. Interestingly, the UV spectrum of asbestinin-10 shows only end absorption, suggesting that the ketone and exocyclic methylene moieties are not coplanar. To confirm this idea, asbestinin-10 (**14**) was reduced using $NaBH_4$ in MeOH to produce a 3:1 mixture of epimeric alcohols **15** and **16** (Figure 1). The spectroscopic data for **15** were identical with those already reported for asbestinin-20, indicating that these compounds are the same.[5] The relative stereochemistry at C-6 of epimers **15** and **16** was confidently established from their NOESY spectra. Thus, the NOESY spectrum of **15** exhibited correlations of H-6 with H_3-18 and H-9. In compound **16** H-6 should be α because of the NOE interactions of H-6 with H-10 and the absence of NOE cross-peaks between H-6 and H_3-18. Treatment of 11-acetoxydeacetoxyasbestinin F (**17**) with $NaBH_4$ in MeOH gave asbestinin-20 (**15**) as the sole product, providing evidence for the presence of a hydroperoxyl group in **17** (Figure 1). Moreover, newly acquired MS data for **17** (HRFABMS) showed a pseudomolecular ion species $[M + Na]^+$ at *m/z* 417.2265 consistent with the molecular formula $C_{22}H_{34}O_6Na$ (not $C_{22}H_{34}O_5$ as originally reported from earlier HREIMS data).[5] Examination of the HMBC data for asbestinin-21 showed correlations between H_3-19 at δ_H 1.29 and the carbonyl group at δ_C 210.8, suggesting that the latter functionality must be located at C-6 (not at C-4). From the above data and further HMBC correlations between C-4 [δ_C 34.0 (CH_2)] and the proton signals ascribable to H-2 and H_3-18, we concluded that in asbestinin-21 there must be a carbonyl at C-6 and a methylene group at C-4, not the other way around as originally

Table 3. Original and Revised Structures for Four Asbestinin Diterpenes

Compound name	Original structure	Revised structure
asbestinin-10[4]		
asbestinin-20[5]		
asbestinin-21[5]		
11-acetoxy-4-deacetoxyasbestinin F[5]		

reported (Table 3).[5] Thus, the earlier reported structures of these four asbestinin analogues were not correct and their structures should be revised as shown in Table 3. The proposed structural revisions suggest that there exists a strong possibility that other asbestinin structures with similar features might also require revision. A list of six additional asbestinin structures likely to require revision, along with their presumably correct structures, is provided as Supporting Information (Table 4).

Briarellin Q (**1**) demonstrated significant in vitro antiplasmodial activity against chloroquine-resistant *Plasmodium falciparum* W2 (IC_{50} 3 μg/mL), while briarellin R (**2**) (IC_{50} 15 μg/mL) and *seco*-briarellin R (**3**) (IC_{50} 20 μg/mL) were less potent. On the other hand, briarellin R (**2**) inhibited growth of human leukemia CCRF-CEM cells (IC_{50} 8.9 μg/mL), and when tested for in vitro antituberculosis activity against *Mycobacterium tuberculosis* H_{37}-Rv, briarellin R (**2**) strongly inhibited mycobacterial growth by 91% whereas briarellin Q (**1**) marginally inhibited growth by 43% at a concentration of 128 μg/mL. Compound **2** showed no toxicity against the West Nile, HCV, Flu A (H1N1 and H3N2), and Flu B viruses. Although asbestinin-25 (**5**) was inactive against *P. falciparum* (IC_{50} value $\geq$ 50 μg/mL), asbestinin analogues **4**, **6**, **8**, **14**, **15**−**17**, and asbestinin-21 were moderately active (IC_{50} values 16, 18, 14, 9, 13, 17, 13, and 18 μg/mL, respectively). On the other hand, none of the asbestinin analogues tested showed antiviral activity against the VEE, West Nile, Yellow Fever, Dengue Type 2, Flu A (H1N1 and H3N2), Flu B, RSV A, HBV, or HBC viruses, nor were they active against the *M. tuberculosis* bacterium at a concentration of 128 μg/mL. However, when subjected to in vitro antiviral testing against Epstein−Barr (EBV) virus, asbestinin-10 (**14**) was found to be very active (IC_{50} 0.25 μg/mL). Additionally, briarein **9** demonstrated moderate in vitro antiplasmodial activity (IC_{50} = 8 μg/mL).

Experimental Section

General Experimental Procedures. Optical rotations were measured with a Perkin-Elmer polarimeter model 243B. IR spectra were recorded with a Nicolet Magna 750 FT-IR spectrophotometer. All NMR spectra were recorded with a Bruker DPX-300 (^{1}H, 300 MHz; ^{13}C, 75 MHz) spectrometer. ^{1}H−^{1}H COSY, NOESY, HMQC, and HMBC spectra were measured using standard Bruker pulse sequences. Chemical shifts are given on a δ (ppm) scale with $CHCl_3$ (^{1}H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm) as the internal standard. Mass spectra were taken at the Mass Spectrometry Laboratory of the University of Illinois at Urbana−Champaign.

Animal Material. The gorgonian octocoral *Briareum polyanthes* (Duchassaing & Michelotti) (order Gorgoniidae, phylum Cnidaria, family Briareidae) was collected from a coral reef off Cabo Rojo, Puerto Rico, at a depth of 10−15 m on October 4, 2000. A voucher specimen has been deposited at the Department of Chemistry, University of Puerto Rico, Río Piedras, Puerto Rico (deposit number BPPR01-1).

Extraction and Isolation. General extraction procedures were as described in our previous publication.[3] The *n*-hexane extract (27.8 g) was purified by size exclusion chromatography on a Bio-Beads SX-2 column with toluene to yield 12 fractions (1−12). Fraction 7 was concentrated to an orange oil (1.5 g) and chromatographed over Si gel (50 g) with 10% EtOAc in *n*-hexane to yield 21 subfractions, denoted A−T. Subfraction S (192 mg) was purified further by CC over Si gel (10 g) with 0.5% MeOH in $CHCl_3$ to give briarein **9** (6 mg). Fraction 9 was concentrated to a yellow oil (2.8 g) and chromatographed over Si gel (100 g) with 10% EtOAc in *n*-hexane to yield 30 subfractions, denoted I−XXX. Subfractions XV (106 mg) and XVI (39 mg) were combined and chromatographed over Si gel (10 g) with 1% MeOH in $CHCl_3$ to give briarellin R (**2**) (28 mg). Purification of subfraction XVII (12 mg) by CC over Si gel (7 g) with 0.3% MeOH in $CHCl_3$ gave *nor*-asbestinin A (**8**) (8.1 mg). Subfraction XX was identified as known asbestinin-10 (18.3 mg).[4] Briarellin Q (**1**) (4.0 mg) was isolated from subfraction XXI (176 mg) by successive Si gel CC with 1% MeOH in $CHCl_3$ and 3% acetone in $CHCl_3$. Subfraction XXIII (283 mg) was chromatographed over Si gel (10 g) and eluted with 0.5% MeOH in $CHCl_3$ to give known 11-acetoxy-4-deacetoxyasbestinin F (44.2 mg).[5] Purification of subfraction XXIV (110 mg) over a Si gel column (7 g) with 1% MeOH in $CHCl_3$ gave asbestinin-26 (**6**) (7.2 mg). Subfraction XXVIII (293 mg) was chromatographed successively over Si gel (10 g) using 0.5% MeOH in $CHCl_3$ and then 10% acetone in $CHCl_3$ to yield *seco*-briarellin R (**3**) (5.0 mg). Fraction 10 (0.70 mg) was fractionated over Si gel (30 g) with 10% EtOAc in *n*-hexane to yield 32 subfractions, denoted 1−32. Subfractions 14 and 23 were identified, respectively, as asbestinin-24 (**4**) (8.1 mg) and known asbestinin-10 (36 mg).[4] Subfraction 24 (53 mg) was purified by successive Si gel CC using 1% MeOH in $CHCl_3$ and then 2% acetone in $CHCl_3$ to give *seco*-asbestinin B (**7**) (14 mg). Subfraction 25 (73 mg) was chromatographed over Si gel (5 g) with 0.5% MeOH in $CHCl_3$ to give additional quantities of known 11-acetoxy-4-deacetoxyasbestinin F (7 mg) and asbestinin-25 (**5**) (56 mg).[5] Fraction 11 (0.90 g) was purified by CC over Si gel (40 mg) with 10% EtOAc in *n*-hexane to yield 20 subfractions, denoted A−T. Subfraction Q (93 mg) was chromatographed over a Si gel (5 g) column with 1% *n*-hexane in $CHCl_3$ to give known asbestinin-21 (9 mg).[5] Subfraction R was identified as the known asbestinin-20 (84 mg).[5]

Briarellin Q (1): white solid; $[\alpha]^{20}_D$ −17.0 (*c* 1.0, $CHCl_3$); IR (neat) 3457, 2967, 2934, 1732, 1716, 1379, 1251, 1173, 1076, 1009, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 1; HRFABMS (magic bullet) *m*/*z* $[M + H]^+$ 439.2701 (calcd for $C_{24}H_{39}O_7$, 439.2696).

Briarellin R (2): colorless oil; $[\alpha]^{20}_D$ −9.0 (*c* 1.0, $CHCl_3$); IR (neat) 2965, 2933, 1720, 1378, 1251 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 1; HRESIMS *m*/*z* $[M + H]^+$ 405.2654 (calcd for $C_{24}H_{37}O_5$, 405.2641).

***seco*-Briarellin R (3):** colorless oil; $[\alpha]^{20}_D$ −16.7 (*c* 0.6, $CHCl_3$); IR (neat) 3500−3000, 2965, 2937, 2880, 1717, 1456, 1377, 1253, 1171, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 1; HRFABMS (magic bullet) *m*/*z* $[M + H]^+$ 453.2487 (calcd for $C_{24}H_{37}O_8$, 453.2488).

Asbestinin-24 (4): white semisolid; $[\alpha]^{20}_D$ +10.0 (*c* 1.1, $CHCl_3$); IR (neat) 2966, 2928, 2875, 1736, 1460, 1370, 1236, 1093, 1069, 1012 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 1; EIMS *m*/*z* 394 $[M]^+$ (1), 334 (59), 323 (54), 302 (33), 175 (40), 146 (53), 133 (79), 93 (91), 55 (100); HREIMS *m*/*z* $[M]^+$ 394.2722 (calcd for $C_{23}H_{38}O_5$, 394.2719).

Asbestinin-25 (5): colorless oil; $[\alpha]^{20}_D$ +9.2 (*c* 1.3, $CHCl_3$); $[\alpha]^{20}_D$ +5.2 (*c* 1.7, C_5H_5N); IR (neat) 3540, 2964, 2932, 2876, 1737, 1464, 1384, 1372, 1239, 1074, 1019, 993, 753 cm^{-1}; ^{1}H NMR (C_5D_5N, 300 MHz) and ^{13}C NMR (C_5D_5N, 75 MHz), see Table 2; EIMS *m*/*z* 410 $[M]^+$ (1), 392 (12), 350 (5), 339 (17), 277 (17), 174 (36), 133 (59), 98 (100), 55 (80); HRFABMS (3-NBA) *m*/*z* $[M + Na]^+$ 433.2570 (calcd for $C_{23}H_{38}O_6Na$, 433.2566).

Asbestinin-26 (6): colorless oil; $[\alpha]^{20}_D$ −7.5 (*c* 1.2, $CHCl_3$); IR (neat) 3467, 2962, 2936, 2875, 1736, 1461, 1372, 1240, 1080, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 2; HRFABMS (magic bullet) *m*/*z* $[M + 1 - H_2]^+$ 377.2333 (calcd for $C_{22}H_{33}O_5$, 377.2328).

***seco*-Asbestinin B (7):** colorless oil; $[\alpha]^{20}_D$ +32.5 (*c* 0.4, $CHCl_3$); IR (neat) 2962, 2929, 2874, 2817, 2720, 1733, 1718, 1459, 1372, 1238, 1080, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 2; EIMS *m*/*z* 394 $[M]^+$ (2), 336 (11), 277 (20), 234 (54), 176 (70), 149 (100), 133 (48), 105 (42), 55 (41); HREIMS *m*/*z* $[M]^+$ 394.2357 (calcd for $C_{22}H_{34}O_6$, 394.2355).

***nor*-Asbestinin A (8):** colorless oil; $[\alpha]^{20}_D$ −29.0 (*c* 1.0, $CHCl_3$); IR (neat) 2962, 2932, 2871, 1736, 1697, 1462, 1375, 1234, 1073 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) and ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 2; EIMS *m*/*z* 364 $[M]^+$ (2), 304 (30), 252 (32), 192 (58), 174 (100), 133 (79), 113 (70); HREIMS *m*/*z* $[M]^+$ 364.2254 (calcd for $C_{21}H_{32}O_5$, 364.2250).

Briarein (9): colorless oil; $[\alpha]^{20}_D$ −30.9 (*c* 1.1, $CHCl_3$); IR (neat) 3431, 2968, 2938, 2873, 1739, 1670, 1436, 1375, 1246, 1196, 1051, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.87 (dd, J = 2.0, 8.7 Hz, H-2), 1.85 (m, H-3α), 2.30 (m, H-4α), 3.27 (m, H-4β), 5.31 (s, H-6), 2.58 (m, H-9α), 3.27 (m, H-9β), 2.97 (d, J = 10.7 Hz, H-10), 3.87 (br s, H-12), 2.02 (m, H-13α), 2.63 (m, H-13β), 5.16 (br t, J = 2.7 Hz, H-14), 1.30 (s, H_3-15), 1.70 (s, H_3-16), 2.00 (s, H_3-18), 1.63 (s, H_3-20), 1.97 (s, H_3-22), 2.08 (s, H_3-24); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.3 (qC, C-1), 77.2 (CH, C-2), 30.7 (CH_2, C-3), 28.4 (CH_2, C-4), 145.8 (qC, C-5), 124.8 (CH, C-6), 106.2 (qC, C-7), 160.1 (qC, C-8), 25.1 (CH_2, C-9), 39.5 (CH, C-10), 77.9 (qC, C-11), 76.1 (CH, C-12), 26.8 (CH_2, C-13), 75.6 (CH, C-14), 13.2 (CH_3, C-15), 22.9 (CH_3, C-16),

127.9 (qC, C-17), 9.9 (CH_3, C-18), 171.4 (qC, C-19), 30.9 (CH_3, C-20), 170.6 (qC, C-21), 21.2 (CH_3, C-22), 169.0 (qC, C-23), 21.4 (CH_3, C-24); HRESIMS *m/z* $[M - H_2O + Na]^+$ 471.2017 (calcd for $C_{24}H_{32}O_8Na$, 471.1995).

Conversion of Asbestinin-10 (14) into Asbestinin-20 (15). A mixture of asbestinin-10 (130.0 mg, 0.35 mmol) and $NaBH_4$ (52.6 mg, 1.38 mmol) in MeOH (6.0 mL) was stirred at 25 °C for 90 min. The reaction mixture was quenched with 5 N HCl and concentrated in vacuo, and the residue obtained was partitioned between $CHCl_3$ and H_2O. The dried ($MgSO_4$) organic extract was concentrated to give an oil (95 mg), which was purified by HPLC (Chiracel OD, elution with 2% 2-propanol in hexane), affording pure asbestinin-20 (**15**) (28.0 mg, 56% yield) and 6-*epi*-asbestinin-20 (**16**) (9.2 mg, 18% yield).

6-*epi*-Asbestinin-20 (16): colorless oil; $[\alpha]^{20}_D$ −30.0 (*c* 0.5, $CHCl_3$); IR (neat) 3442, 2966, 2933, 2875, 1733, 1646, 1461, 1373, 1237, 1112, 1077, 1017, 968, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.28 (m, H-1), 3.85 (d, J = 8.5 Hz, H-2), 1.51 (m, H-4α), 1.02 (dd, J = 2.1, 13.5 Hz, H-4β), 1.88 (m, H-5αβ), 4.27 (br s, H-6), 2.16 (m, H-8αβ), 4.16 (ddd, J = 1.5, 4.3, 8.8 Hz, H-9), 2.20 (m, H-10), 5.36 (dd, J = 2.5, 5.3 Hz, H-11), 2.16 (m, H-12), 1.51 (m, H-13α), 1.02 (dd, J = 2.1, 13.5 Hz, H-13β), 1.88 (m, H-14), 1.61 (m, H-15), 3.46 (m, H-16α), 3.76 (d, J = 13.2 Hz, H-16β), 0.89 (d, J = 7.8 Hz, H_3-17), 1.30 (s, H_3-18), 5.36 (br s, H-19α), 5.07 (br d, J = 6.4 Hz, H-19β), 0.92 (d, J = 7.4 Hz, H_3-20), 2.09 (s, H_3-22); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.8 (CH, C-1), 94.1 (CH, C-2), 76.0 (qC, C-3), 31.6 (CH_2, C-4), 27.4 (CH_2, C-5), 76.0 (CH, C-6), 156.9 (qC, C-7), 31.6 (CH_2, C-8), 83.0 (CH, C-9), 45.8 (CH, C-10), 73.9 (CH, C-11), 31.3 (CH, C-12), 31.6 (CH_2, C-13), 38.0 (CH, C-14), 36.7 (CH, C-15), 67.5 (CH_2, C-16), 10.9 (CH_3, C-17), 23.5 (CH_3, C-18), 114.9 (CH_2, C-19), 17.5 (CH_3, C-20), 171.3 (qC, C-21), 21.3 (CH_3, C-22); HRESIMS *m/z* $[M + H]^+$ 379.2489 (calcd for $C_{22}H_{35}O_5$, 379.2484).

Conversion of 11-Acetoxy-4-deacetoxyasbestinin F (17) into Asbestinin-20 (15). Fresh $NaBH_4$ (8.1 mg, 0.11 mmol) was added to a solution of 11-acetoxy-4-deacetoxyasbestinin F (21 mg, 0.053 mmol) in MeOH (3.0 mL), and the resulting mixture was stirred at 25 °C for 110 min. After the addition of 1 N HCl the reaction mixture was concentrated in vacuo and the residue obtained was suspended in H_2O and extracted with $CHCl_3$. The dried ($MgSO_4$) organic layer was concentrated to dryness to yield asbestinin-20 (15 mg, 75% yield).

Deoxygenation of Asbestinin-20 (15) to Yield 6-Deoxyasbestinin-20 (13). After stirring a mixture of $LiClO_4$ (6.0 mg, 0.056 mmol) and asbestinin-20 (19.4 mg, 0.051 mmol) in dry ether (2.0 mL) at 25 °C for 2 min under nitrogen, triethylsilane (25 μL, 0.154 mmol) was added at once. Upon stirring at 25 °C for another 42 h the mixture was quenched with H_2O and extracted with diethyl ether (3 × 5 mL). The dried ($MgSO_4$) organic layer was concentrated in vacuo, and the residue obtained was purified by Si gel CC (elution with 25% EtOAc in *n*-hexane) to give 8.4 mg (43% yield) of unreacted asbestinin-20 and pure 6-deoxyasbestinin-20 (**13**) (5.5 mg, 52% yield).

6-Deoxyasbestinin-20 (13): colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.41 (m, H-1), 3.75 (d, J = 6.7 Hz, H-2), 2.15 (br d, J = 13.3 Hz, H-8α), 3.36 (dd, J = 6.8, 13.3 Hz, H-8β), 4.04 (dd, J = 4.3, 6.5 Hz, H-9), 2.20 (m, H-10), 5.26 (m, H-11), 2.06 (m, H-12), 1.88 (m, H-14), 1.41 (m, H-15), 3.49 (dd, J = 2.8, 13.0 Hz, H-16α), 3.77 (br s, H-16β), 0.92 (d, J = 7.1 Hz, H_3-17), 1.28 (s, H_3-18), 5.18 (br s, H-19α), 5.27 (br s, H-19β), 0.94 (d, J = 7.2 Hz, H_3-20), 2.08 (s, H_3-22); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.1 (CH, C-1), 93.3 (CH, C-2), 77.2 (qC, C-3), 35.9 (CH_2, C-4), 37.6 (CH_2, C-5), 31.6 (CH_2, C-6), 146.7 (qC, C-7), 41.6 (CH_2, C-8), 80.0 (CH, C-9), 47.9 (CH, C-10), 73.1 (CH, C-11), 31.2 (CH, C-12), 29.7 (CH_2, C-13), 37.4 (CH, C-14), 36.7 (CH, C-15), 68.2 (CH_2, C-16), 11.0 (CH_3, C-17), 24.0 (CH_3, C-18), 114.1 (CH_2, C-19), 18.1 (CH_3, C-20), 171.1 (qC, C-21), 21.2 (CH_3, C-22); HRFABMS (magic bullet) *m/z* $[M + H]^+$ 363.2534 (calcd for $C_{22}H_{35}O_4$, 363.2535).

Microozonolysis of 6-Deoxyasbestinin-20 (13) to Yield *nor*-Asbestinin A (8). A stream of ozone in oxygen was bubbled into a solution of 6-deoxyasbestinin-20 (1 mg, 0.003 mmol) in EtOAc (1 mL) kept at −78 °C until the solution turned blue. The solution was stirred for another 5 min and then was allowed to warm to 25 °C while the excess ozone was removed (and the sample concentrated) with a stream of nitrogen. After addition of H_2O (2.5 mL) and a few drops of 30% H_2O_2 the ozonide obtained was refluxed to 105 °C for 4 h, then allowed to cool, and extracted with $CHCl_3$ (3 × 5 mL). The dried ($MgSO_4$) organic layer was concentrated, and the oily product was analyzed by TLC and GLC-MS. On the basis of its retention time and mass spectral fragmentation patterns the product obtained was identified as *nor*-asbestinin A (**8**).

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Supporting Information Available: List of six asbestinin diterpenoids isolated from *Briareum asbestinum* (during prior work) whose molecular structures are likely to require revision (Table 4). This material is available free of charge via the Internet at http://pubs.acs.org.

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