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ISOLATION AND STRUCTURES OF SIXTEEN NEW ASBESTININ DITERPENES FROM THE CARIBBEAN GORGONIAN *BRIAREUM ASBESTINUM*

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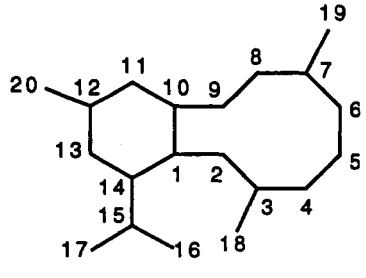
ABSTRACT.—Sixteen new diterpenoids, representative of the asbestinane skeletal class, have been isolated from shallow water colonies of the Caribbean gorgonian octocoral *Briareum asbestinum*. The structures of these secondary metabolites, named asbestinin-11 [**1**], asbestinin-12 [**3**], asbestinin-13 [**4**], asbestinin-14 [**5**], asbestinin-15 [**7**], asbestinin-16 [**8**], asbestinin-17 [**9**], asbestinin-18 [**10**], asbestinin-19 [**11**], asbestinin-20 [**12**], asbestinin-21 [**13**], asbestinin-22 [**14**], asbestinin-23 [**15**], 11-acetoxy-4-deoxyasbestinin E [**16**], 11-acetoxy-4-deoxyasbestinin F [**17**] and 4-deoxyasbestinin G [**18**], were defined by chemical and spectroscopic methods. These specimens of *B. asbestinum*, collected in Puerto Rico, yielded almost exclusively diterpenoids possessing the asbestinane carbon skeleton thus suggesting minor biosynthetic variations for this gorgonian. In this paper, we also revise the structures of the known asbestinin-6 and asbestinin-7 to asbestinanes **2** and **6**, respectively.

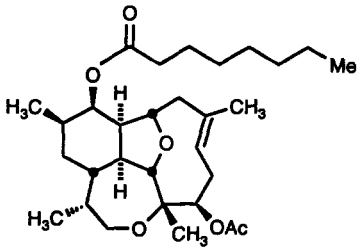
An impressive number of marine invertebrates have been found to have promising cytotoxic activity against a variety of cancer cell lines. One such invertebrate, the gorgonian octocoral *Briareum asbestinum* Pallas, has been the subject of intense investigation in our laboratory (1–3). The secondary compounds of *B. asbestinum* are unusually diverse and consist mainly of briarane and asbestinane class diterpenoids (4). Although produced by a different terpene cyclization pathway, both classes consist of bicyclic molecules with fused six- and ten-membered rings. We have recently reported the isolation and structures of nine tetracyclic diterpenes, 4-deoxyasbestinins A–D (1,2), and asbestinins 6–10 (3), from this gorgonian. These diterpenes were found to be active against several human tumor cell lines at a 1–10 μM level. As part of our continuing search for bioactive compounds, we report in this communication the isolation and structures of sixteen new diterpenes possessing the relatively uncommon asbestinane carbon skeleton, from the Caribbean gorgonian *B. asbestinum*, collected off the east and west coasts of Puerto Rico. We have found thus far that colonies of this gorgonian from these locations show minor chemical variations and are composed almost exclusively of asbestinane diterpenoids rather than a mixture of briaranes and asbestinanes (5,6).



Asbestinane skeleton

[1]Graduate student sponsored by the Agency for International Development (AID) and the FIPI Program of the University of Puerto Rico.

[2]Undergraduate student sponsored by the NIH-MBRS Program of the University of Puerto Rico, Río Piedras Campus.



Asbestinin-6 [**I**]
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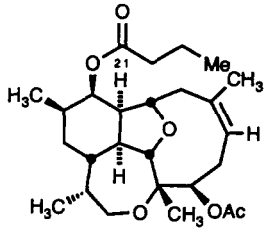
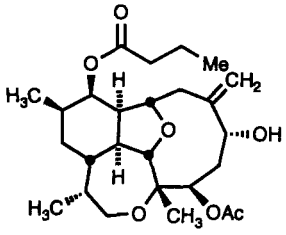
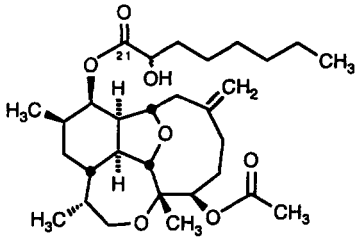


Asbestinin-2 [**II**]



Asbestinin-5 [**III**]



Asbestinin-7 [**IV**]
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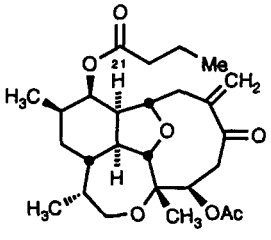
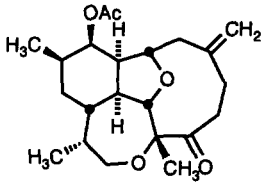


Asbestinin-4 [**V**]

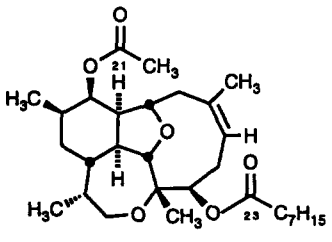


Asbestinin-10 [**VI**]

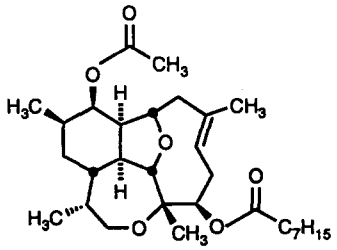
RESULTS AND DISCUSSION

The residue from the MeOH/$CHCl_3$ extract obtained from specimens of the gorgonian collected from the west coast of Puerto Rico (Mona Island) was extracted first with hexane followed by $CHCl_3$. The residue obtained from the hexane extract upon size-exclusion chromatography gave a group of fractions containing a complex mixture of several major and minor metabolites. These were separated by repeated cc and hplc to yield nine new asbestinins, asbestinins 11–19 [**1**, **3–5**, **7–11**], along with the known asbestinin-6 [**2**] and asbestinin-7 [**6**] (3). When specimens of *B. asbestinum* collected off the east coast of Puerto Rico (Palomino Island) were subjected to identical extractive procedures, four new asbestinins were isolated, namely asbestinins 20–23 [**12–15**], which were accompanied by three new 4-deoxyasbestinin diterpenes [**16–18**], and the known 4-deoxyasbestinins A–D (1). The structures as well as the chemical and spectroscopic properties of the new asbestinins are described below.

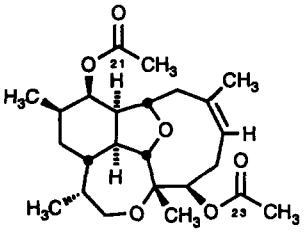
Since their ^{13}C-nmr spectra did not contain a signal for a tetrasubstituted carbon atom bearing carbon substituents, as found at the carbocyclic ring junction in the briarein series, nor did it reveal a signal near 17–21 ppm ascribable to the C-13 methylene group, as found in the eunicellin series, these asbestinin diterpenes could not be assigned a structure based on the briarein or the eunicellin carbon skeletons.



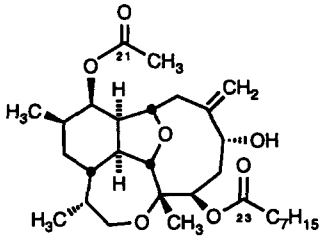
Asbestinin-11 [**1**]



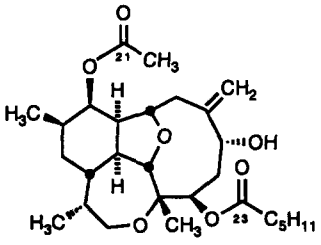
Asbestinin-6 [**2**]



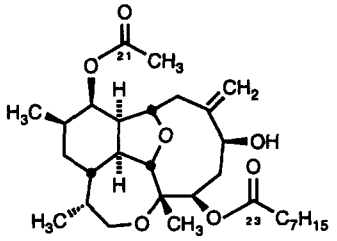
Asbestinin-12 [**3**]



Asbestinin-13 [**4**]

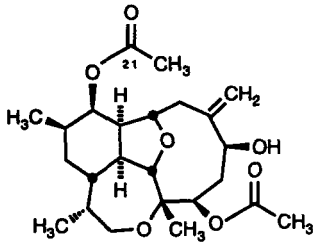


Asbestinin-14 [**5**]

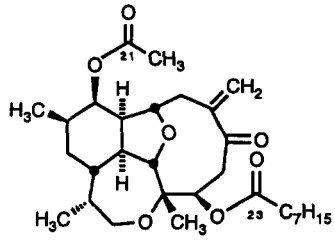


Asbestinin-7 [**6**]

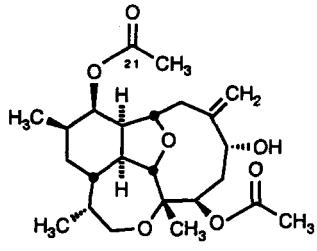
A molecular formula of $C_{30}H_{48}O_6$ was established for asbestinin-11 [**1**] from hreims which gave the highest mass peak at *m/z* 504 with fragments representing the loss of one (*m/z* 444) molecule of AcOH and one (*m/z* 360) molecule of caprylic acid. The ^{1}H-nmr spectrum of asbestinin-11 [**1**] exhibited resonances due to an acetyl methyl signal at δ 2.11, an endocyclic sp^2 methine [δ 5.75 (1H, br t, J=6.9 Hz)], two oxymethine protons [δ 3.92 (1H, d, J=9.0 Hz) and 4.10 (1H, m)], two diastereotopic oxymethylene protons [δ 3.83 (1H, d, J=13.2 Hz) and 3.46 (1H, dd, J=3.6 and 13.2 Hz)], β-capryloxy [δ 4.89 (1H, d, J=7.5 Hz)] and β-acetoxy [δ 5.27 (1H, dd, J=3.0 and 4.5 Hz)] protons, along with five methyls [δ 1.79 (3H, s), 1.41 (3H, s), 0.92 (3H, d, J=7.2 Hz), 0.87 (3H, t, J=8.0 Hz), and 0.86 (3H, d, J=7.2 Hz)]. The ^{1}H-nmr spectrum of **1** was similar to that which has been reported for asbestinin-6 [**I**], a known compound which was also present in this specimen of *B. asbestinum* (3). The only differences were the multiplicity and downfield shift of the H-6 proton (Table 1) (in **1** it appears as a br t at δ 5.75 while in asbestinin-6 it appears as a complex m at δ 5.30), and the observation that in **1** the β-acetoxy (H-11) and β-capryloxy (H-4) protons were well resolved in $CDCl_3$ solution, whereas in asbestinin-6 [**I**] H-4, H-6, and H-11 appear as three overlapping signals at δ 5.30 in $CDCl_3$. The relative positions of the acetate and caprylate groups in asbestinin-11 [**1**] were determined unambiguously through a selective INEPT nmr experiment. Selective irradiation of the signal at δ 5.27 (H-11) caused enhancement of the ^{13}C-nmr signal at δ 171.24 (C-21) while irradiation of the signal at δ 4.89 (H-4) caused a similar



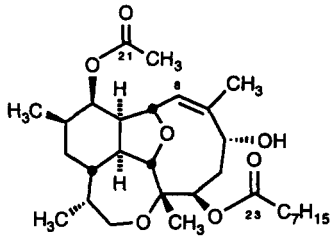
Asbestinin-15 [7]



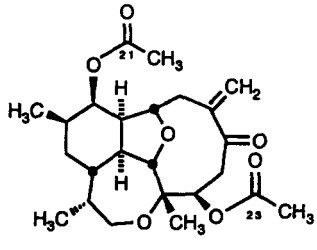
Asbestinin-16 [8]



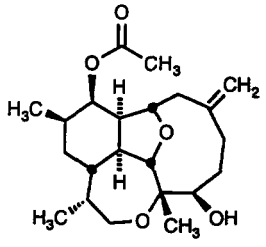
Asbestinin-17 [9]



Asbestinin-18 [10]



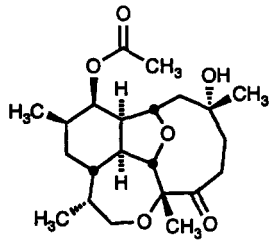
Asbestinin-19 [11]



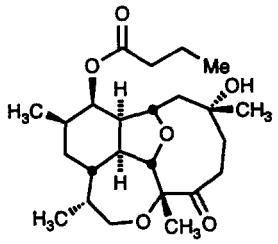
Asbestinin-20 [12]

enhancement of the ^{13}C-nmr signals at δ 173.48 (C-23), 76.76 (C-3), and 19.35 (C-18). This experiment allowed us to establish unambiguously the position of the acetate group at C-11 and that of the caprylate group at C-4. Moreover, direct comparison of the selective INEPT nmr data recorded here for asbestinin-11 with those obtained earlier by us for asbestinin-6 (in C_6D_6) suggested that the relative positions of the ester groups on the complex tetracyclic array in both compounds were in fact identical. On the basis of this comparison and reinterpretation of the spectral data recorded earlier (3), the structure reported for asbestinin-6 should be corrected to that depicted by **2**. The ^{13}C-nmr spectrum was also similar to that of asbestinin-6, showing that all common stereochemistry elements, excepting that of the geometry of the double bond, were unchanged. The *Z* stereochemistry of the former was established by the chemical shift difference of Me-19 (δ 29.51 vs. 18.79) and of the C-8 methylene carbon (δ 36.98 vs. 44.19)(1). The structure of asbestinin-11 [**1**] differed from that of the known asbestinin-2 [**II**] (7) only in the fatty acid composition with which one of the alcohols is esterified (i.e., caprylic vs. butyric), as well as in the relative positions of the ester groups about the complex tetracyclic array.

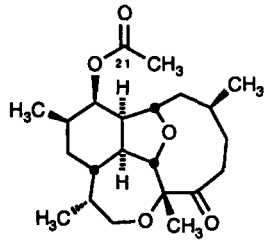
Asbestinin-12 [**3**] was a minor metabolite having the molecular formula $C_{24}H_{36}O_6$. The hreims gave the highest mass peak at *m/z* 420 with fragments indicating the loss of two (*m/z* 360 and 300) molecules of AcOH. The ^{1}H-nmr spectrum indicated the presence of two acetate groups [δ 2.11 (3H, s) and 2.08 (3H, s)], one sp^2 methine proton signal [δ 5.72 (1H, br t, J=6.6 Hz)] and two β-acetoxy protons [δ 5.25 (1H, dd, J=2.9 and



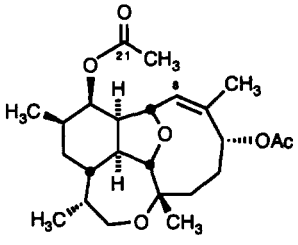
Asbestinin-21 [**13**]



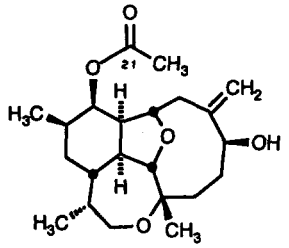
Asbestinin-22 [**14**]



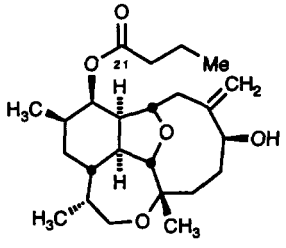
Asbestinin-23 [**15**]



11-Acetoxy-4-deoxyasbestinin E [**16**]



11-Acetoxy-4-deacetoxyasbestinin F [**17**]



4-Deoxyasbestinin G [**18**]

4.8 Hz) and 4.85 (1H, d, J=7.2 Hz)]. The remaining downfield proton signals were similar to those found for asbestinin-11 [**1**] and to those reported for the known asbestinin-2 [**II**] (7) and, since the coupling constants associated with these signals were similar to those of **II** (Table 1), structure **3** was assigned to asbestinin-12.

The analysis of the spectral data of asbestinin-13 [**4**] established a molecular formula of $C_{30}H_{48}O_7$. The ^{13}C-nmr spectrum contained two ester carbonyl signals at δ 175.43 and 171.18, olefinic carbon signals at δ 147.51 and 115.62, and seven signals for carbon atoms bearing oxygen at δ 92.93, 82.99, 76.39, 73.95, 73.85, 72.27, and 67.32. The ^{1}H-nmr spectrum contained very broad signals for the protons assigned to the largest carbocyclic ring, suggesting an equilibrium between different ring conformations (7). The relative positions of the acetate and caprylate groups in asbestinin-13 [**4**] were determined unambiguously through ^{1}H-^{1}H COSY and INAPT experiments. For instance, because in $CDCl_3$ solution H-4 and H-11 do not overlap, the ^{13}C-nmr signal assignments of carbons C-21 and C-23 were made from single-frequency on-resonance decoupling experiments by irradiating the H-4 and H-11 signals individually. Thus, selective irradiation of the signal at δ 5.34 (H-11) caused enhancement of the ^{13}C-nmr signal at δ 171.18 (C-21), while irradiation of the signal at δ 5.01 (H-4) caused a similar enhancement of the ^{13}C-nmr signal at δ 175.43 (C-23). A broad signal at δ 4.16 (1H, br s), assigned to an allylic α-hydroxy proton, was correlated to the ^{13}C-nmr signal

TABLE 1. Selected ^{1}H-Nmr (300 MHz) Data of Compounds **1**, **3–18** in $CDCl_3$.[a,b]

Proton	Compound				
	1 δ, mult., *J* (Hz)	**3** δ, mult., *J* (Hz)	**4** δ, mult., *J* (Hz)	**5** δ, mult., *J* (Hz)	**6** δ, mult., *J* (Hz)
1	2.32, m	2.23, m	2.45, m	2.34, m	2.71, m
4	4.89, d, 7.5	4.85, d, 7.2	5.01, m	5.02, m	5.52, br t, 3.1
5(α)	3.19, m	3.15, m	1.62, m	1.60, m	2.06, m
(β)	1.88, m	1.58, m	2.34, m	2.33, m	2.34, m
6	5.75, br t, 6.9	5.72, br t, 6.6	4.16, br s	4.17, m	4.53, dd, 1.5, 5.1
8(α)	2.68, d, 14.7	2.66, d, 14.7	2.32, d, 6.9	2.30, d, 3.0	2.35, d, 7.5
(β)	1.85, dd, 3.6, 14.7	1.81, dd, 3.6, 14.7	2.25, m	2.23, m	2.40, d, 7.5
9	4.10, m	4.08, m	4.15, br t, 5.4	4.17, br t, 3.9	4.15, br t, 5.7
10	2.05, m	1.97, m	2.31, m	2.31, m	2.10, m
Me-18	1.41, s	1.38, s	1.31, s	1.32, s	1.27, s
19(α)	1.79, s	1.76, s	5.56, s	5.57, br s	5.31, br s
(β)	—	—	5.11, s	5.12, br s	5.14, br s
	7	**8**	**9**	**10**	**11**
1	2.72, m	2.51, m	2.44, m	2.66, m	2.57, m
4	5.49, t, 3.6	5.75, t, 7.5	5.01, br s	5.05, dd, 2.7, 11.7	5.74, t, 7.8
5(α)	2.51, br d, 15.6	2.78, br d, 7.5	1.63, m	2.10, m	2.85, d, 8.1
(β)	2.01, d, 4.8	2.78, br d, 7.5	1.63, m	1.56, m	2.85, d, 8.1
6(α)	4.52, dd, 3.3, 5.1	—	4.14, m	5.49, dd, 6.3, 11.4	—
(β)	—	—	—	—	—
8(α)	2.37, dd, 7.5, 13.8	3.40, dd, 1.2, 13.2	2.23, m	5.12, d, 1.2	3.38, br d, 7.8
(β)	2.25, dd, 5.1, 13.8	2.13, d, 13.2	2.23, m	—	2.14, br d, 8.4
9	4.15, m	4.02, dd, 4.5, 6.9	4.14, m	4.70, d, 1.5	4.02, dd, 6.9, 4.5
10	2.19, m	2.06, m	2.11, m	2.06, m	2.10, m
Me-18	1.29, s	1.29, s	1.31, s	1.31, s	1.29, s
19(α)	5.31, br s	5.40, br s	5.53, br s	1.71, s	5.39, br s
(β)	5.14, br s	5.36, br s	5.12, br s	—	5.37, br s
	12	**13**	**14**	**15**	
1	2.47, m	2.56, m	2.54, m	2.55, m	
4	4.09, br s	—	—	—	
5(α)	2.59, br d, 5.1	2.74, dd, 3.6, 14.2	2.71, dd, 3.9, 13.8	2.52, m	
(β)	2.12, m	2.67, dd, 1.2, 5.4	2.59, dd, 0.9, 5.1	2.28, m	
6(α)	2.09, dd, 0.9, 6.9	2.30, dd, 3.2, 14.2	2.27, d, 3.9	2.23, m	
(β)	1.60, m	1.50, m	1.57, d, 2.4	1.72, m	
8(α)	2.26, m	2.20, d, 11.2	2.27, d, 7.8	2.45, m	
(β)	1.70, m	2.01, d, 3.9	2.06, d, 3.9	1.54, br d, 2.7	
9	4.02, dd, 4.2, 6.3	4.27, dd, 3.6, 11.4	4.24, dd, 3.6, 11.4	3.90, t, 4.8	
10	1.97, m	1.90, m	1.84, m	2.01, m	
Me-18	1.26, s	1.33, s	1.31 s	1.25, s	
19(α)	5.20, br s	1.29, s	1.28, s	0.99, d, 6.9	
(β)	4.89, br s	—	—	—	
	16	**17**	**18**		
1	2.42, m	2.48, m	2.26, m		
4(α)	1.67, m	1.56, m	1.56, m		
(β)	1.33, m	1.56, m	1.56, m		
5(α)	1.48, m	2.06, m	2.05, m		
(β)	1.88, m	2.10, m	2.05, m		
6(α)	6.36, dd, 5.7, 11.4	4.43, br s	4.42, br s		
(β)	—	—	—		
8(α)	5.15, br d, 0.9	1.89, m	1.89, m		
(β)	—	2.32, d, 5.4	2.45, m		
10	1.99, m	2.08, m	2.00, m		
Me-18	1.30, s	1.28, s	1.24, s		
19(α)	1.60, br s	5.29, s	5.29, br s		
(β)	—	5.16, s	5.15, br s		

[a]Assignments were aided by ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, NOESY, spin splitting patterns, selective decoupling experiments, and comparison of *J* values.

[b]The δ values are in ppm and are referenced to the residual $CHCl_3$ signal (7.26 ppm).

resonating at δ 73.85; structure **4** was therefore assigned to asbestinin-13. The relative stereochemistry for all the substituents on the complex tetracyclic array was determined to be identical to those of known asbestinin-5 [**III**] (7,8) by analysis of proton-proton coupling constants (see Table 1), nOe experiments, and ^{13}C-nmr chemical shift compari-

sons. This compound differs from asbestinin-5 [**III**] only in the fatty acid composition of one of its ester groups (i.e., caprylic vs. butyric), and the relative positions of the ester groups.

Asbestinin-14 [**5**] was isolated as a colorless oil and possessed a mass spectral molecular ion which was 28 mass units fewer than that of asbestinin-13 [**4**]. This difference is consistent with replacement of the caprylate ester moiety in **4** with a caproic ester group in **5**. A caproic ester moiety in asbestinin-14 was also evident from the ^{1}H- and ^{13}C-nmr spectra and by the presence of a major ion at *m/z* 376.22908 for $C_{22}H_{32}O_5$, which reflects a fragmentation of $M^+-C_6H_{12}O_2$ (caproic acid) from the molecular composition of $C_{28}H_{44}O_7$. The ir spectrum contained a band at 3463 cm^{-1} indicative of a hydroxyl group and a broad signal at δ 4.17 in the ^{1}H-nmr spectrum was indicative of an allylic α-hydroxy proton (H-6). The near identity of the ^{1}H- and ^{13}C-nmr shifts in **4** and **5** further suggested that these compounds differed only in their fatty acid composition at C-4.

The structure of the asbestin diterpene **6** showed it to be an isomer of asbestinin-13 [**4**]. The ^{1}H-nmr spectrum of this compound contained separate signals for an acetate ester [δ 2.07 (3H, s)] and the six methylenes and the methyl group of a caprylate ester. Ions corresponding to sequential losses of AcOH and caprylic acid from the molecular ion were evident from the mass spectrum of **6**. The locus of the caprylate vs. acetate groups in **6** followed directly from selective INEPT nmr experiments performed as described earlier for **1** and **4**. The methylene proton signals at δ 5.31 (1H, br s) and 5.14 (1H, br s) indicated that the double bond in **6** was in an exocyclic position. Comparison of the ^{1}H- and ^{13}C-nmr spectra of asbestinin-13 [**4**] and **6** (Tables 1 and 2) revealed that the major differences were associated with a change in **6** in its relative configuration at C-6. A broad signal at δ 4.53 (1H, dd, J=1.5 and 5.1 Hz), assigned to an allylic β-hydroxy proton, was correlated in the ^{13}C-nmr spectrum to a carbon resonance at δ 87.07. The stereochemistry at C-6 in **6** is based on the chemical shift difference of the C-6 carbon (δ 87.07) and the H-6 resonance (δ 4.53) which appear shifted upfield to 73.85 and 4.16 ppm, respectively, in **4**. A similar empirical relationship between the C-6 methine carbon chemical shift and the H-6 proton chemical shift with the α or β configuration of the allylic hydroxy group at C-6 has been observed for other compounds in this series throughout this work. To confirm the interpretation that **4** and **6** differed only in their relative configuration of the hydroxy group at C-6, both compounds were chemically converted to enone **8**. Separate oxidation of **4** and **6** with activated MnO_2 in $CHCl_3$ gave the same asbestinane [**8**] in high yield. Comparison of the overall physical and spectral data of **6** with those reported for asbestinin-7 [**IV**] (3) indicated that these compounds were in fact identical. On the basis of our synthetic interconversions and reinterpretation of spectral and chemical data, the structure reported for abestinin-7 [**IV**] should be corrected to that of asbestinin diterpene **6**.

A molecular formula of $C_{24}H_{36}O_7$ was established for asbestinin-15 [**7**] from hrfabms plus ^{1}H- and ^{13}C-nmr data. The ^{1}H-nmr spectrum contained signals for two acetates at 2.07 and 2.03 ppm along with its corresponding β-acetoxy proton signals at δ 5.49 (1H, t, J=3.6 Hz) and 5.37 (1H, dd, J=2.4 and 6.0 Hz). The methylene proton signals at δ 5.31 (1H, br s) and 5.14 (1H, br s) combined with the absence of a 3H singlet near δ 1.90 indicated that the double bond in **7** was shifted to an exocyclic position. A partially broad signal at δ 4.52 (1H, dd, J=3.3 and 5.1 Hz), assigned to an allylic β-hydroxy proton, was correlated in the ^{13}C-nmr spectrum to a carbon resonance at δ 86.94. We assigned the stereochemistry at C-6 in asbestinin-15 [**7**] based on the chemical shift difference of the C-6 carbon and H-6 proton which appear shifted upfield in **4** and **5** and a strong nOe response between H-6 and the H-19 exomethylene proton resonating

TABLE 2. ^{13}C-Nmr Data (75 MHz, $CDCl_3$) of Compounds **1–18**.[a]

Carbon	Compound									
	1 δ (mult.)	**3** δ (mult.)	**4** δ (mult.)	**5** δ (mult.)	**6** δ (mult.)	**7** δ (mult.)	**8** δ (mult.)	**9** δ (mult.)	**10** δ (mult.)	**11** δ (mult.)
1	40.74 (d)	40.76 (d)	39.20 (d)	39.21 (d)	38.95 (d)	38.82 (d)	39.59 (d)	39.14 (d)	37.72 (d)	39.63 (d)
2	91.46 (d)	91.32 (d)	92.93 (d)	92.95 (d)	93.63 (d)	93.47 (d)	92.44 (d)	92.88 (d)	93.71 (d)	92.44 (d)
3	76.76 (s)	76.73 (s)	76.39 (s)	76.41 (s)	77.16 (s)	77.20 (s)	77.17 (s)	76.37 (s)	77.15 (s)	77.21 (s)
4	78.79 (d)	79.21 (d)	72.27 (d)[d]	72.26 (d)	69.54 (d)	69.67 (d)	71.34 (d)	72.42 (d)	71.54 (d)	71.70 (d)
5	33.40 (t)	33.42 (t)	31.24 (t)	30.96 (t)	34.71 (t)	34.71 (t)	45.17 (t)	36.85 (t)	38.02 (t)	45.18 (t)
6	126.77 (d)	126.69 (d)	73.85 (d)	73.86 (d)	87.07 (d)	86.94 (d)	200.61 (s)	73.78 (d)	66.80 (d)	200.53 (s)
7	131.50 (s)	131.65 (s)	147.51 (s)	147.53 (s)	144.45 (s)	144.40 (s)	145.40 (s)	147.46 (s)	138.41 (s)	145.49 (s)
8	36.98 (t)	36.91 (t)	39.04 (t)	39.03 (t)	38.78 (t)	38.34 (t)	41.41 (t)	38.97 (t)	127.29 (d)	41.17 (t)
9	81.72 (d)	81.72 (d)	82.99 (d)	83.01 (d)	83.38 (d)	83.39 (d)	79.90 (d)	82.94 (d)	82.70 (d)	79.93 (d)
10	44.99 (d)	44.94 (d)	45.66 (d)	45.73 (d)	47.25 (d)	47.07 (d)	48.38 (d)	45.69 (d)	49.99 (d)	48.43 (d)
11	73.67 (d)	73.61 (d)	73.95 (d)	73.97 (d)	73.68 (d)	73.57 (d)	72.86 (d)	73.91 (d)	73.69 (d)	72.89 (d)
12	31.36 (d)	31.33 (d)	31.24 (d)	31.25 (d)	31.41 (d)	31.28 (d)	31.04 (d)	31.49 (d)	31.27 (d)	31.11 (d)
13	31.43 (t)	31.41 (t)	31.49 (t)	31.50 (t)	31.59 (t)	31.47 (t)	31.17 (t)	31.21 (t)	31.29 (t)	31.19 (t)
14	38.28 (d)	38.28 (d)	38.35 (d)	38.37 (d)	38.51 (d)	38.34 (d)	37.61 (d)	38.32 (d)	38.68 (d)	37.66 (d)
15	37.57 (d)	37.57 (d)	36.76 (d)	36.77 (d)	36.84 (d)	36.70 (d)	36.70 (d)	36.73 (d)	36.78 (d)	36.77 (d)
16	67.70 (t)	67.77 (t)	67.32 (t)	67.32 (t)	67.87 (t)	67.99 (t)	67.57 (t)	67.41 (t)	68.02 (t)	67.78 (t)
17	10.82 (q)	10.78 (q)	10.75 (q)	10.76 (q)	10.83 (q)	10.75 (q)	10.92 (q)	10.65 (q)	10.95 (q)	10.87 (q)
18	19.35 (q)	19.29 (q)	17.61 (q)	17.61 (q)	17.51 (q)	17.43 (q)	18.09 (q)	17.54 (q)	18.59 (q)	18.15 (q)
19	29.51 (q)	29.56 (q)	115.62 (t)	115.63 (t)	117.25 (t)	117.39 (t)	115.19 (t)	115.55 (t)	17.15 (q)	115.21 (t)
20	18.16 (q)	18.16 (q)	17.51 (q)	17.51 (q)	17.34 (q)	17.30 (q)	18.29 (q)	17.47 (q)	17.23 (q)	18.35 (q)
21	171.24 (s)	171.29 (s)[b]	171.18 (s)	171.20 (s)	171.08 (s)	171.19 (s)	171.04 (s)	172.43 (s)[b]	171.21 (s)	171.07 (s)[b]
22	21.27 (q)	21.62 (q)[c]	21.25 (q)	21.24 (q)	21.22 (q)	21.31 (q)	21.15 (q)	21.35 (q)[c]	21.34 (q)	21.19 (q)[c]
23	173.48 (s)	170.78 (s)[b]	175.43 (s)	171.20 (s)	172.99 (s)	170.33 (t)	173.13 (s)	171.15 (s)[b]	172.89 (s)	170.37 (s)[b]
24	34.79 (t)	21.30 (q)[c]	34.75 (t)	34.72 (t)	34.71 (t)	21.31 (q)	34.41 (t)	21.20 (q)[c]	34.60 (t)	21.14 (q)[c]
25	25.09 (t)	—	25.06 (t)	24.74 (t)	25.21 (t)	—	25.07 (t)	—	25.17 (t)	—
26	28.94 (t)	—	28.94 (t)[b]	29.01 (t)	28.99 (t)[b]	—	28.93 (t)[b]	—	29.06 (t)	—
27	28.94 (t)	—	28.78 (t)[b]	22.30 (t)	28.96 (t)[b]	—	28.89 (t)[b]	—	29.05 (t)	—
28	31.70 (t)	—	31.66 (t)	13.88 (q)	31.75 (t)	—	31.64 (t)	—	31.71 (t)	—
29	22.58 (t)	—	22.60 (t)	—	22.60 (t)	—	22.62 (t)	—	22.63 (t)	—
30	14.04 (q)	—	14.03 (q)	—	13.98 (q)	—	14.02 (q)	—	14.06 (q)	—

TABLE 2. Continued

Carbon	Compound									
	12 δ (mult.)	**13** δ (mult.)	**14** δ (mult.)	**15** δ (mult.)	**16** δ (mult.)	**17** δ (mult.)	**18** δ (mult.)			
1	38.43 (d)	38.03 (d)	37.96 (d)	40.65 (d)	38.27 (d)	—	—			
2	93.79 (d)	93.64 (d)	93.54 (d)	93.23 (d)	93.26 (d)	94.01 (d)	93.84 (d)			
3	76.39 (s)	77.21 (s)	77.21 (s)	77.20 (s)	77.75 (s)	77.10 (s)	77.19 (s)			
4	75.37 (d)	210.78 (s)	210.59 (s)	213.70 (s)	32.18 (t)	—	—			
5	27.06 (t)[d]	36.19 (t)	36.12 (t)	39.27 (t)	27.06 (t)	—	—			
6	29.04 (t)[d]	34.03 (t)	34.01 (t)	35.42 (t)	73.72 (d)	91.05 (d)[d]	91.05 (d)[d]			
7	148.07 (s)	76.29 (s)	76.26 (s)	37.42 (d)	133.59 (s)	146.40 (s)[d]	146.43 (s)			
8	38.78 (t)	49.33 (t)	49.33 (t)	42.92 (t)	129.18 (d)	—	—			
9	82.64 (d)	78.23 (d)	78.13 (d)	79.62 (d)	82.46 (d)	82.51 (d)	82.35 (d)			
10	45.97 (d)	47.73 (d)	47.73 (d)	48.30 (d)	50.31 (d)	46.74 (d)	46.67 (d)			
11	73.66 (d)	72.79 (d)	72.47 (d)	73.11 (d)	73.41 (d)	73.56 (d)	73.27 (d)			
12	31.04 (d)	31.51 (d)	31.52 (d)	31.10 (d)	31.40 (d)	31.27 (d)	31.29 (d)			
13	31.26 (t)	31.51 (t)	31.52 (t)	31.73 (t)	31.40 (t)	31.70 (t)	31.73 (t)			
14	37.71 (d)	38.03 (d)	38.15 (d)	37.23 (d)	37.23 (d)	37.87 (d)	37.94 (d)			
15	36.43 (d)	36.52 (d)	36.54 (d)	36.65 (d)	36.64 (d)	36.57 (d)	36.62 (d)			
16	67.14 (t)	68.17 (t)	68.19 (t)	68.30 (t)	67.86 (t)	68.24 (t)	68.23 (t)			
17	10.59 (q)	10.91 (q)	10.89 (q)	11.00 (q)	10.91 (q)	10.94 (q)	10.91 (q)			
18	23.12 (q)	22.50 (q)	22.44 (q)	24.29 (q)	22.14 (q)	29.69 (q)	29.22 (q)			
19	114.48 (t)	27.66 (q)	27.61 (q)	17.51 (q)	17.96 (q)	116.08 (t)[d]	115.84 (t)			
20	17.16 (q)	17.25 (q)	17.32 (q)	17.96 (q)	17.25 (q)	17.39 (q)	17.48 (q)			
21	171.01 (s)	170.84 (s)	173.39 (s)	171.01 (s)	171.19 (s)[b]	171.21 (s)	173.79 (s)			
22	20.91 (q)	21.34 (q)	36.68 (t)	21.17 (q)	21.37 (q)[c]	21.32 (q)	36.66 (t)			
23	—	—	18.37 (t)	—	170.24 (s)[b]	—	18.45 (t)			
24	—	—	13.63 (q)	—	21.24 (q)[c]	—	13.70 (q)			
25	—	—	—	—	—	—	—			
26	—	—	—	—	—	—	—			
27	—	—	—	—	—	—	—			
28	—	—	—	—	—	—	—			
29	—	—	—	—	—	—	—			
30	—	—	—	—	—	—	—			

[a]Multiplicities were obtained by an Attached Proton Test (APT) experiment. Assignments were made on the basis of heteronuclear chemical shift correlation methods, ^1H-^1H COSY, carbon atom multiplicities, chemical shift values and comparisons with known models. The δ values are in parts per million and are referenced to the $CDCl_3$ signal (77.0 ppm).

[b–c]Values with identical superscripts in each column may be interchanged.

[d]The resonance line was broad and of low intensity.

upfield at δ 5.14 (H-19β). Because the ^{1}H- and ^{13}C-nmr shifts in **7** and the coupling constants associated with all the proton signals were similar to those observed for other compounds in this series, structure **7** was assigned to asbestinin-15.

Asbestinin-16 [**8**] was shown to differ from asbestinin-4 [**V**], a known compound (7), only in the relative positions of the ester groups and in the fatty acid with which one of the alcohols is esterified, that is, caprylic vs. butyric. Asbestinin-16 had the molecular formula $C_{30}H_{46}O_7$. Thus, compound **8** possessed a mass spectral molecular ion which was only 2 mass units fewer than those of asbestinin-7 [**6**] and asbestinin-13 [**4**]. Ions corresponding to sequential losses of a caprylic acid (*m/z* 374) and of AcOH (*m/z* 314) moieties from the actual molecular ion *m/z* 518 were evident in the lreims. The ir spectrum contained an ester band at 1738 cm^{-1} and an unsaturated carbonyl band at 1693 cm^{-1}. The ^{13}C-nmr signals at δ 200.61 (s), 145.40 (s), and 115.19 (t), together with the fact that **8** was uv-active, indicated that the carbonyl was conjugated to an exocyclic methylene group. The presence of the methylene proton signals at δ 5.40 (1H, br s) and 5.36 (1H, br s) in the ^{1}H-nmr spectrum confirmed this assignment. The locus of the caprylate versus acetate groups shown in structure **8** was determined directly from selective INEPT nmr experiments similar to those described before and from the chemical interconversions of **4** and **6** into asbestinin-16. In general, the ^{1}H- and ^{13}C-nmr spectra of asbestinin-16 [**8**] were very similar to those of asbestinin-4, the only exception being the signals in **8** due to a caprylic acid rather than a butyric acid chain.

Asbestinin-17 [**9**] was obtained as a colorless oil and the molecular formula $C_{24}H_{36}O_7$ obtained from a hrfabms indicated that **9** was an isomer of **7**. Comparison of the ^{1}H- and ^{13}C-nmr spectra of **9** with those of **7** confirmed the overall similarity between their structures. However, some differences were observed: The broad multiplet at δ 4.14 in the ^{1}H-nmr spectrum, together with its corresponding signal in the ^{13}C-nmr spectrum at δ 73.78, suggested that asbestinin-17 contained instead an allylic α-hydroxy proton (H-6). The remaining spectral features (ir, ms, and nmr data) indicated that these compounds differed only in their relative configurations at C-6.

The hreims established a molecular formula for asbestinin-18 of $C_{30}H_{48}O_7$, indicating that **10** was an isomer of **4**. Like **4**, compound **10** showed ir absorptions (3447, 1735, and 1733 cm^{-1}) that indicated the presence of hydroxyl and diester functionalities and fragment ions in the hreims corresponding to M^+-18, M^+-60, and M^+-144 which confirmed the presence in **10** of the alcohol, acetate, and caprylate groups. Comparison of the ^{1}H- and ^{13}C-nmr spectra of **10** with those of asbestinin-13 [**4**] confirmed the structural similarity of these compounds and revealed the presence of one structural feature characteristic of **10**. The α-allylic hydroxyl moiety at C-6 and the acetate and caprylate groups at C-11 and C-4, respectively, were assumed to be intact in **10** on the basis of similar ir, ms, and nmr data (compare signals of related Hs and Cs in Tables 1 and 2). Asbestinin-18, however, did not show nmr signals indicating that the double bond was exocyclic between C-7 and C-19, as in **4**. Instead, ^{1}H-nmr signals at δ 1.71 (3H, s) and 5.12 (1H, d, J=1.2 Hz) and ^{13}C-nmr signals at δ 138.41 (s) and 127.29 (d) suggested that the double bond had shifted to an endocyclic position and was now located between C-7 and C-8. Moreover, the signal at δ 5.12 (H-8) was shown by COSY nmr to be coupled to both the methine proton at δ 4.70 (H-9), which appears in **10** somewhat shifted downfield (Table 1), and also to the olefinic methyl protons at δ 1.71 (Me-19). That asbestinin-18 also contains one allylic α-hydroxy group at C-6 was indicated by the ^{1}H-nmr signal at δ 5.49 (1H, dd, J=6.3 and 11.4 Hz), which was likewise shown by COSY to be coupled to both of the C-5 methylene protons at δ 2.10 and 1.56. Acetylation of **10** at 25° with Ac_2O/pyridine introduced a second acetate group into the molecule. The ^{1}H-nmr spectrum of the product showed a new methine proton signal at δ 6.45 (1H, dd, J=6.0 and 11.7 Hz) ascribable to H-6, which indicated that

the hydroxyl group in **10** was allylic. The *Z* geometry of the double bond was assigned to the Δ^7 double bond despite the chemical shift of Me-19, which appeared at δ 17.15 (rather than at 22–25 ppm) (9). A close examination of a Dreiding model of asbestinin-18 indicated that the Δ^7 olefinic bond could not adopt the *E* configuration; to do so would either introduce a great amount of ring strain or require twisting the molecule about the double bond. Moreover, a strong nOe response between the H-8 proton and the Me-19 group confirmed the *Z* orientation of the double bond.

Asbestinin-19 [**11**] was shown to differ from asbestinin-4 [**V**] only in the fatty acid with which one of the alcohols is esterified, acetic vs. butyric. Asbestinin-19 had the molecular formula $C_{24}H_{34}O_7$. Thus, compound **11** possessed a mass spectral molecular ion which was 2 mass units less than that of asbestinin-17 [**9**]. Ions corresponding to sequential losses of two AcOH molecules (*m/z* 374 and 314) from the actual molecular ion (*m/z* 434) were evident in the hreims. The ir spectrum contained two ester bands at 1737 and 1730 cm^{-1} and an unsaturated carbonyl band at 1688 cm^{-1}. The ^{13}C-nmr signals at δ 200.53 (s), 145.49 (s), and 115.21 (t), together with the fact that **11** was uv-active, indicated that the carbonyl was conjugated to an exocyclic methylene group. The presence of the methylene proton signals at δ 5.39 (1H, br s) and 5.37 (1H, br s) in the ^1H-nmr spectrum confirmed this assignment.

Asbestinin-20 [**12**] had the molecular formula $C_{22}H_{34}O_5$ (hreims, *m/z* 378.24086) and showed ir absorptions at 3447 and 1737 cm^{-1}, typical for alcohol and ester functionalities. The presence of hydroxyl and acetate moieties was also in full agreement with the $[M-H_2O]^+$ (M−18 mass units) and $[M-C_2H_4O_2]^+$ (M−60 mass units) fragments observed in the hreims. The ^1H-nmr spectrum of **12**, which contained signals for an acetate ester [δ 1.95 (3H, s)] and a β-hydroxy proton [δ 4.09 (1H, br s)], confirmed this interpretation. The presence of the methylene proton signals at δ 5.20 (1H, br s) and 4.89 (1H, br s) suggested that the methylene group was exocyclic. The relative positions of the hydroxyl and acetate functionalities were unequivocally determined by COSY nmr and ^{13}C-nmr chemical shift values to be at C-4 and C-11, respectively. That the hydroxyl group in asbestinin-20 was indeed at C-4 and not at C-6 was established by the ^1H-nmr chemical shift of the H-4 resonance [δ 4.09 (1H, br s)] together with the chemical conversion of **12** to the known asbestinin-10 [**VI**] (3) by oxidation with PCC in CH_2Cl_2, and the fact that **12** was uv-inactive. The resonance line assignments of all the protons and carbons of the molecule were assigned by a 2D ^1H-^{13}C hetero-correlation and APT nmr experiments that established all C-H connectivities and, hence, also all pairs of geminal protons. The ^{13}C-nmr resonance lines assigned to C-5 and C-6 (δ 27.06 and 29.04, respectively) were quite broad and of low intensity suggesting a very flexible ten-membered ring in **12** (7). A NOESY nmr experiment, together with the measured coupling constants, also determined the relative stereochemistry of the various chiral centers in asbestinin-20.

Compound **13**, named asbestinin-21, was isolated as a colorless oil with a molecular formula of $C_{22}H_{34}O_6$, estimated from ^1H- and ^{13}C-nmr data and confirmed by hreims. The occurrence of fragment ions corresponding to M^+-18 (*m/z* 376 due to loss of H_2O) and M^+-60 (*m/z* 334 due to loss of AcOH), strongly supported structure **13**. The ir spectrum contained absorptions for hydroxyl (3344 cm^{-1}), ester (1737 cm^{-1}), and ketone (1687 cm^{-1}) functionalities. Comparison of the ^1H- and ^{13}C-nmr spectra of **13** with those of the known asbestinin-10 [**VI**] (3) confirmed the structural similarity of these two compounds and revealed the presence of some features characteristic of **13**. The ketone and acetate functionalities at C-4 and C-11, respectively, were shown to be intact in **13** on the basis of similar ir and nmr data. Asbestinin-21, however, did not show olefinic carbon signals in the ^{13}C-nmr spectrum and instead contained new signals at δ 76.29 (s) and 27.66 (q). This compound, however, had two oxymethyl groups (vs. one in

asbestinin-10) as indicated by the ^{1}H-nmr signals at δ 1.33 (3H, s) and 1.29 (3H, s), and an exchangeable hydroxyl proton at δ 4.39 (1H, br s). These combined spectroscopic data indicated the presence in this compound of a tertiary carbinol, a feature not found in **VI**. The partial structures for **13** were deduced from ^{1}H-nmr COSY experiments and the chemical shifts of the protonated carbons were assigned by a 2D ^{1}H-^{13}C heterocorrelation nmr experiment (CSCM, J=140 Hz). The one other structural feature confirmed by a NOESY nmr experiment was the β-orientation of the methyl group at C-7; a strong nOe response between the Me-19 group [δ 1.29 (3H, s)] and the H-2 proton resonating at δ 3.80 (1H, d, J=8.7 Hz) was observed. Examination of a Dreiding model of asbestinin-10, a logical biosynthetic precursor to **13**, indicated that one face of the Δ^7 olefinic bond (the β-face) is sterically hindered to attack. Asbestinin-21 [**13**] must therefore have a 7α-hydroxyl group.

A molecular formula of $C_{24}H_{38}O_6$, estimated from ^{1}H- and ^{13}C-nmr data, was confirmed for asbestinin-22 [**14**] by hreims. The hreims gave major ions at *m/z* 404 for $C_{24}H_{36}O_5$ and *m/z* 334 for $C_{20}H_{30}O_4$, which reflect fragmentations of $[M-H_2O]^+$ and $[M-C_4H_8O_2]^+$, respectively, from the molecular ion $[M]^+$ at *m/z* 422. The ir spectrum of **14** contained absorptions for hydroxyl (3440 cm^{-1}), ester (1732 cm^{-1}), and ketone (1678 cm^{-1}) groups, the same structural features found in asbestinin-21 [**13**]. The near identity of all the ^{1}H- and ^{13}C-nmr shifts in **13** and **14** suggested that these compounds differed only in the fatty acid composition with which the C-11 alcohol is esterified, i.e., butyric vs. acetic. Although the relative stereochemistry at C-7 was unchanged, rigorous assignments of the nmr spectra of **14** (see Tables 1 and 2) were established by application of the same 2D nmr techniques described earlier.

Asbestinin-23 [**15**], obtained as a colorless oil, corresponded to a molecular formula of $C_{22}H_{34}O_5$ on the basis of its ^{13}C-nmr and hrfabms ($[M+1]^+$ *m/z* 379.24670) data and therefore contained six unsaturations. The ir spectrum contained one ester band at 1739 cm^{-1}, a strong ketone stretching absorption at 1700 cm^{-1} and indicated the absence of hydroxyl groups. The ^{1}H-nmr spectrum contained signals for an acetate at δ 2.06 (3H, s), a β-acetoxy proton [δ 5.23 (1H, dd, J=2.7 and 4.8 Hz)] along with four methyls [δ 1.25 (3H, s), 0.99 (3H, d, J=6.9 Hz), 0.96 (3H, d, J=7.2 Hz), and 0.92 (3H, d, J=7.2 Hz)]. The ^{13}C-nmr spectrum contained two carbonyl singlets at δ 213.70 and 171.01 due to ketone and ester groups, respectively, no olefinic carbon signals, and only five signals for carbon atoms bearing oxygen at δ 93.23, 79.62, 77.20, 73.11, and 68.30. These data alone suggested structure **15** for asbestinin-23. However, due to the highly congested nature of the high-field region of the ^{1}H-nmr spectrum, we could not argue the stereochemical orientation of the Me-19 group unambiguously based on spectroscopic data alone. To establish this assignment we correlated chemically the structure of asbestinin-23 with that of known asbestinin-10 [**VI**] (3). Thus, after 12 h at 25°, a mixture of asbestinin-10, EtOAc, and H_2/Pd/C at 1 atmosphere produced mainly **15** and its unnatural epimer at C-7 in trace amounts. Since the β-face of asbestinin-10 is sterically hindered to attack, asbestinin-23 must therefore have a 7β-methyl group.

The ^{1}H-nmr spectrum of compound **16** contained signals for two acetyl methyls at δ 2.08 and 2.00 (each 3H, s), an endocyclic sp^2 methine [δ 5.15 (1H, br d, J=0.9 Hz)], two oxymethine protons [δ 4.72 (1H, br s) and 3.84 (1H, d, J=9.6 Hz)], two diastereotopic oxymethylene protons [δ 3.80 (1H, br s) and 3.45 (1H, dd, J=2.7 and 13.2 Hz)], two acetoxy proton signals [δ 6.36 (1H, dd, J=5.7 and 11.4 Hz) and 5.40 (1H, dd, J=2.1 and 5.7 Hz)], and four methyl groups [δ 1.60 (3H, s), 1.30 (3H, s), 0.91 (3H, d, J=7.2 Hz), and 0.90 (3H, d, J=7.2 Hz)]. The ^{13}C-nmr spectrum showed the presence of twenty-four carbon atoms, two of which are ester carbonyl signals at δ 171.19 (s) and 170.24 (s), two are olefinic carbons at δ 133.59 (s) and 129.18 (d), and six represent signals for carbon atoms bearing oxygen at δ 93.26 (d), 82.46 (d), 77.75 (s),

73.72 (d), 73.41 (d), and 67.86 (t). The ir spectrum contained two ester bands at 1737 and 1734 cm^{-1} and the hreims gave the highest mass peak at *m/z* 360.23078 for $C_{22}H_{32}O_4$, which reflects a fragmentation of $[M-AcOH]^+$ from the actual molecular composition of $C_{24}H_{36}O_6$. The ion peak at *m/z* 360 in turn fragments to another ion peak at *m/z* 300 representing the loss of a second molecule of AcOH. The H-9 oxymethine proton resonating at δ 4.72, which showed $^1J_{CH}$ coupling to a carbon doublet resonating at δ 82.46, was readily correlated in the COSY nmr spectrum with the sp^2 methine resonating at δ 5.15. These correlations, combined with the downfield shift experienced by H-9, and the absence in the ^{13}C-nmr spectrum of resonances between 40–50 ppm that could be ascribed to a C-8 methylene, suggested that the double bond in **16** had shifted from its usual endocyclic position between C-6 and C-7 to now encompass carbons C-7 and C-8. A strong nOe response between the H-8 proton and the Me-19 group confirmed the *Z* orientation of the double bond. The geometry of the trisubstituted double bond in **16** was also assigned as *Z* [in spite of its signals in the ^{13}C-nmr spectrum which showed significant shielding of the Me-19 group (δ 17.96) (9)] on the basis of an examination of molecular models. The presence of an allylic β-acetoxy proton signal at δ 6.36 (1H, dd, *J*=5.7 and 11.4 Hz), which coupled only to a geminal methylene pair resonating at δ 1.88 and 1.48 assigned to the C-5 (δ 27.06) methylene protons, suggested also that 11-acetoxy-4-deoxyasbestinin E [**16**] contained a C-7, C-8 endocyclic olefinic bond. The α-orientation of the allylic acetoxy group at C-6 is based on the chemical shift of the C-6 carbon (δ 73.72) and on a strong nOe response between H-6 and H-9. The α-acetoxy proton resonating at δ 5.40 (1H, dd, *J*=2.1 and 5.7 Hz), ascribable to H-11, readily correlated with a complex multiplet near 2.10 ppm (H-12) (the latter in turn was correlated to a methyl doublet at δ 0.91 ascribable to Me-20) and a complex multiplet at δ 1.99 assigned as the H-10 methine proton. These correlations established unequivocally the position of the acetoxy group at C-11 in a fashion which is completely consistent with structure **16**.

Analysis of the spectral data for **17**, named 11-acetoxy-4-deoxyasbestinin F, established a molecular formula of $C_{22}H_{34}O_5$. The ir spectrum contained absorptions for hydroxyl (3440–3200 cm^{-1}, broad) and ester (1737 cm^{-1}) functional groups. Hreims of **17** gave major ions at *m/z* 378.24281 for $C_{22}H_{34}O_5$ $[M]^+$, *m/z* 360.23180 for $C_{22}H_{32}O_4$ and *m/z* 318.21894 for $C_{20}H_{30}O_3$, the latter two of which reflect fragmentations of $[M-H_2O]^+$ and $[M-AcOH]^+$, respectively, from the molecular ion. The major features of the ^{1}H-nmr spectrum were a broad signal exchangeable with CD_3OD [δ 8.24 (1H, br s)], a β-acetoxy proton [δ 5.35 (1H, dd, *J*=2.1 and 5.4 Hz)], two exomethylene protons [δ 5.29 (1H, br s) and 5.16 (1H, br s)], an allylic β-hydroxy proton [δ 4.43 (1H, br s)], two oxymethine protons [δ 3.80 (1H, d, *J*=9.3 Hz) and 4.17 (1H, m)], two diastereotopic oxymethylene protons [δ 3.74 (1H, d, *J*=12.6 Hz) and 3.48 (1H, dd, *J*=2.7 and 13.2 Hz)], an acetyl methyl signal [δ 2.08 (3H, s)], and three methyls [δ 1.28 (3H, s), 0.92 (3H, d, *J*=7.2 Hz), and 0.91 (3H, d, *J*=6.9 Hz)]. The ^{1}H-nmr spectrum of **17** showed broad lines for the Hs at positions 4, 5, 6, 8, and 19 suggesting that the ten-membered ring of **17** is quite flexible. Of the twenty-two carbons contained in **17** only fifteen were detected clearly in the ^{13}C-nmr spectrum as sharp intense signals which could be assigned to the three small rings (see Table 2) of the asbestinane carbon skeleton. The remaining seven resonances for carbon atoms C-1, C-4, C-5, C-6, C-7, C-8, and C-19 were quite broad signals of very low intensity that were assigned (except C-1) to the ten-membered ring. This peculiarity confirmed that the large ring of **17** is in equilibrium between different ring conformations. Because H-6, resonating at δ 4.43, produced a strong nOe response which correlated it with the H-19 exomethylene proton resonating upfield at δ 5.16 (H-19β), we established the orientation of this key resonance in the α orientation. This stereochemical assignment is consistent with the observation that H-6 appears

shifted downfield to 4.43 ppm and with the strong coupling response observed in the COSY nmr spectrum between H-6 and the upfield H-5α proton resonating at δ 2.06.

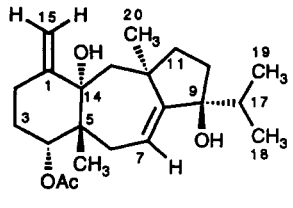
The ir spectrum of 4-deoxyasbestinin G [**18**] indicated the presence of hydroxyl and ester absorptions at 3348 cm^{-1} (broad) and 1730 cm^{-1}, respectively. This component was obtained as a colorless oil that corresponded to a molecular formula of $C_{24}H_{38}O_5$ on the basis of its hreims ($[M]^+$ *m/z* 406.26830). Among the largest ions observed in the mass spectrum were at *m/z* 388 and 318, consistent with the successive loss of H_2O plus butyric acid from the proposed molecular formula. The substitution pattern for **18** was determined to be the same as that of **17** based on the similarities of their nmr spectra. The ^{1}H-nmr and ^{13}C-nmr spectra had many broad signals consistent with the presence in 4-deoxyasbestinin G of a very flexible ten-membered ring. The ^{13}C-nmr spectrum contained only seventeen sharp, well-defined signals which were assigned to the small rings of the asbestinane skeleton. Those signals corresponding to the large ten-membered ring were broad low-intensity signals which could not always be assigned rigorously (see Table 2). The presence in the ^{13}C-nmr spectrum of signals at δ 13.70 (q), 18.45 (t), and 36.66 (t), which were not present in **17**, confirmed that **17** and **18** differed only in the fatty acid composition at the C-11 alcohol. Based on nmr data, COSY and NOESY experiments, we established that the relative stereochemistry of the C-6 hydroxyl function remained unchanged in 4-deoxyasbestinin G [**18**].

The present study also resulted in the isolation of the known diterpene **19** which is based on the dolastane carbon skeleton (10). The structure of (4*S**,9*R**,14*S**)-4-acetoxy-9,14-dihydroxydolasta-1 (15), 7-diene [**19**] was determined by spectroscopic methods, especially one- and two-dimensional nmr, and comparison to data reported for **19**. This metabolite, isolated originally from the toxic brown Caribbean seaweeds *Dictyota linearis* and *Dictyota divaricata*, is the only dolastane-type diterpenoid isolated to date from a colony of *B. asbestinum* (Mona Island) and extends knowledge of the chemical variability of this species. A possibility, however, that should not be discounted (based in part on the low yield we obtained for **19**) is that this compound may in fact stem from intertwined algae, despite our best efforts to rid *B. asbestinum* of all foreign matter prior to its extraction.

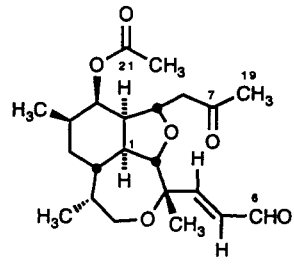
Finally, compound **20** was isolated in trace amounts during purification of compound **9** by successive ODS-Si and normal-phase hplc. With its unprecedented structural features, diterpene **20** is thus far the only known representative of the seco-asbestinin class of ether-cyclized diterpenes (11).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded on a Nicolet 600 Ft-ir spectrophotometer. ^{1}H- and ^{13}C-nmr spectra were recorded on a General Electric Multinuclear QE-300; ^{1}H-nmr chemical shifts are recorded with respect to the residual $CHCl_3$ signal (7.26 ppm) and ^{13}C-nmr chemical shifts are reported in ppm relative to $CDCl_3$ (77.0 ppm). Optical rotations were determined on a Perkin-Elmer Model 243B polarimeter. Lreims were recorded on a Hewlett-Packard 5995A spectrometer and



19



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hreims were determined at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln. Cc was performed on Analtech Si gel (35–75 mesh) and tlc analyses were carried out using Analtech glass backed precoated Si gel plates. All solvents used were either spectral grade or were distilled from glass prior to use.

COLLECTION AND EXTRACTION.—Minced and freeze-dried specimens of *B. asbestinum* (4.01 kg) collected at Mona Island, Puerto Rico, were extracted exhaustively with $CHCl_3$-MeOH (1:1) (7×1 liter) and after filtration the crude extract was evaporated under vacuum to yield a residue (300.74 g) that was partitioned between hexane and $CHCl_3$ (6×1 liter). The hexane extract was subsequently filtered and the filtrate was concentrated *in vacuo* to yield 208.38 g of a dark green oily residue. The toluene-soluble portion (156.92 g) was fractionated by size-exclusion chromatography on a Bio-Beads SX-2 column with toluene. The combined diterpene-containing fractions (tlc-guided) were concentrated to a yellow-orange oil (41.40 g) and chromatographed over a Si gel column (800 g) with 10% EtOAc in hexane. The less polar portion of the lipids was fractionated roughly into fractions A through J on the basis of tlc analyses. Successive cc of fraction B (1.78 g) by a Si gel column (60 g) with 25% EtOAc in hexane and by hplc [Ultrasphere-ODS Si gel with MeOH-H_2O (93:7)] gave pure asbestinin-11 [**1**] (22.6 mg; 0.0005% dry wt). Fraction C (1.04 g, 0.023% dry wt) consisted of pure asbestinin-6 [**2**] (3). Asbestinin-7 [**6**] (3) (31.6 mg; 0.0007% dry wt) was isolated from fraction D (3.23 g) via Si gel cc (100 g) with 30% hexane in $CHCl_3$ followed by hplc [Ultrasphere-ODS using MeOH-H_2O (85:15)]. The known dolastane diterpene **19** was isolated from fraction F (636 mg) by cc on a Si gel column (20 g; 5% $CHCl_3$/hexane as eluent) followed by reversed-phase hplc [Ultrasphere-ODS Si with MeOH-H_2O (75:25)] to yield 19.6 mg (0.00048% dry wt) of pure compound. Fraction G (1.17 g), which consisted by tlc analyses of a mixture of **3** and **8**, was dissolved in MeOH and purified through an elution gradient reversed-phase hplc [Ultrasphere-ODS Si gel with MeOH-H_2O (88:12), (85:15), and (75:25)] to give asbestinin-12 [**3**] (14.6 mg; 0.00036% dry wt) and 40.5 mg (0.001% dry wt) of analytically pure asbestinin-16 [**8**]. Fraction I (3.25 g) was chromatographed over a Si gel column (140 g) with 1% MeOH in $CHCl_3$ and separated roughly into six fractions. Purification of sub-fraction B (1.15 g) by successive cc on Si gel (20 g) with 40% EtOAc in hexane and hplc [Ultrasphere-ODS Si gel with MeOH-H_2O (75:25)] gave 37.0 mg (0.0009% dry wt) of asbestinin-13 [**4**]. Repeated hplc [Ultrasphere-ODS Si gel with MeOH-H_2O (65:35) and (90:10)] of sub-fraction C (501.2 mg) yielded 10.0 mg (0.002% dry wt) of pure asbestinin-14 [**5**]. Sub-fraction D (187.3 mg) was chromatographed by hplc [Ultrasphere-ODS Si gel with MeOH-H_2O (70:30)] to yield 27.2 mg (0.0006% dry wt) of asbestinin-15 [**7**]. Fraction J (11.34 g) was fractionated over a Si gel column (350 g) with 1% MeOH in $CHCl_3$ into thirteen fractions (1–13). Sub-fraction 3 (288 mg) was fractionated via hplc [Zorbax C-8 Si gel with 40% H_2O in MeOH] to yield pure asbestinin-19 [**11**] (8.0 mg, 0.0002% dry wt). The seco-asbestinin **20** was isolated from sub-fraction 4 (224.3 mg) by successive reversed-phase cc using ODS-Si gel [MeOH-H_2O (70:30)] and normal-phase cc (Si gel in 20% EtOAc/hexane) to give 13.0 mg (0.0002% dry wt) of the pure compound (11). Sub-fraction 5 (2.48 g) was subjected to hplc [Zorbax C-8 Si gel with MeOH-H_2O (70:30)] to yield 46.8 mg (0.0010% dry wt) of pure asbestinin-17 [**9**]. Finally, sub-fraction 6 (3.27 g) was purified by tandem hplc [Ultrasphere-Si gel with 10% isopropyl alcohol/hexane], [ODS-Si gel in MeOH-H_2O (85:15)] and by cc (Si gel using 40% EtOAc/hexane) to yield 6.1 mg (0.00015% dry wt) of asbestinin-18 [**10**].

Specimens of *B. asbestinum* collected at Palomino Island, Puerto Rico (1.58 kg, dry wt) were extracted as described above. Purification of a portion of the hexane solubles (52.3 g) by successive size-exclusion [Bio-Beads SX-2, toluene] and adsorption cc [Si gel, 30% EtOAc/hexane] produced 41 fractions. Analysis of the first 10 fractions led to the isolation of the known 4-deoxyasbestinin A, 11-acetoxy-4-deoxyasbestinin B, 4-deoxyasbestinin C, and 11-acetoxy-4-deoxyasbestinin D (5.03 g, 0.31% dry wt) (1). Fraction 11 (364.8 mg) was chromatographed using tandem hplc and cc over Si gel (15% EtOAc/hexane and 5% Me_2CO/hexane, respectively) and reversed-phase hplc [Ultrasphere-ODS Si gel (15% H_2O/MeOH)] to give 6.3 mg (0.0004% dry wt) of 11-acetoxy-4-deoxyasbestinin E [**16**]. Repeated cc of fraction 19 (227.8 mg) on Si gel (2% MeOH/$CHCl_3$) and then 15% EtOAc/hexane) yielded 22.5 mg (0.0014% dry wt) of 11-acetoxy-4-deoxyasbestinin F [**17**] and 19.7 mg (0.0012% dry wt) of 4-deoxyasbestinin G [**18**]. Fraction 24 (90 mg) was subjected to successive reversed-phase cc [ODS-Si gel (35% H_2O/MeOH)] and normal-phase Si gel cc (15% EtOAc/hexane) to give 11.0 mg (0.0007% dry wt) of pure asbestinin-23 [**15**]. Asbestinin-22 [**14**] (5.7 mg, 0.0003% dry wt) was isolated from fraction 27 (295.3 mg) via successive cc on Si gel (15% Me_2CO/hexane) and hplc [Ultrasphere-ODS MeOH-H_2O (75:25)]. Cc of fraction 34 (375.6 mg) on Si gel (20% EtOAc/hexane) yielded 120 mg (0.0075% dry wt) of analytically pure asbestinin-20 [**12**]. Asbestinin-21 [**13**] (10.8 mg, 0.0007% dry wt) was isolated by successive cc and hplc [Si gel (15% and then 30% EtOAc/hexane) and Ultrasphere-ODS MeOH-H_2O (60:40)].

Asbestinin-11 [**1**].—Colorless oil: $[\alpha]^{26}D$ −14.08° (c=6.2, $CHCl_3$); ir (neat) ν max 2959, 2928, 2874, 1737, 1731, 1454, 1367, 1234, 1178, 1069, 1020, 865, 802 cm^{-1}; hreims m/z $[M]^+$ 504.34555 (0.9) ($C_{30}H_{48}O_6$ requires 504.34506), 444 (1.5), 360 (13), 300 (8.7), 279 (10), 219 (13), 174 (3.8), 127 (8.1), 93 (10), 60 (24), 57 (100), 55 (58); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-12 [**3**].—Colorless oil: $[\alpha]^{25}D$ −24.66° (*c*=2.9, $CHCl_3$); ir ν max (neat) 2962, 2931, 2877, 1737, 1731, 1453, 1441, 1376, 1257, 1239, 1172, 1091, 1020, 964, 927, 867, 802 cm^{-1}; hreims *m/z* $[M]^+$ 420.25283 (11) ($C_{24}H_{36}O_6$ requires 420.25119), 360 (36), 300 (20), 279 (12), 232 (16), 219 (60), 193 (21), 175 (26), 174 (11), 163 (22), 161 (18), 149 (22), 147 (32), 145 (35), 135 (25), 133 (38), 121 (30), 119 (42), 107 (59), 105 (85), 93 (92), 91 (68), 79 (47), 77 (20), 71 (75), 69 (83), 67 (55), 57 (34), 55 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-13 [**4**].—Colorless oil: $[\alpha]^{26}D$ −14.59° (*c*=3.7, $CHCl_3$); ir ν max (neat) 3456, 2959, 2931, 2876, 1737, 1731, 1708, 1639, 1461, 1454, 1386, 1372, 1281, 1237, 1126, 1111, 1079, 1016, 967, 931, 802 cm^{-1}; hrfabms *m/z* $[M+Na]^+$ 543.32980 (100) ($C_{30}H_{48}O_7Na$ requires 543.32976); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-14 [**5**].—Colorless oil: $[\alpha]^{25}D$ +2.94° (*c*=4.0, $CHCl_3$); ir ν max (neat) 3463, 2959, 2932, 2874, 1736, 1730, 1644, 1456, 1429, 1374, 1282, 1242, 1126, 1112, 1079, 1018, 969, 927, 802 cm^{-1}; hreims *m/z* $[M]^+$ 492.30783 (5.0) ($C_{28}H_{44}O_7$ requires 492.30870), 474 (4.7), 376 (4.9), 316 (9.2), 298 (3.9), 279 (7.0), 249 (4.1), 245 (4.7), 232 (6.0), 220 (9.3), 219 (27), 193 (11), 175 (11), 174 (7.5), 163 (7.9), 161 (6.3), 147 (9.8), 145 (8.6), 135 (8.3), 133 (11), 122 (7.4), 119 (12), 107 (13), 105 (20), 99 (16), 93 (21), 91 (12), 81 (14), 79 (13), 71 (18), 69 (12), 67 (11), 55 (24), 43 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-15 [**7**].—Colorless oil: $[\alpha]^{26}D$ − 4.04° (*c*=2.7, $CHCl_3$); ir ν max (neat) 3365, 2961, 2934, 2878, 1737, 1731, 1715, 1643, 1453, 1427, 1372, 1283, 1238, 1125, 1111, 1078, 1053, 1019, 967, 928, 802, 755 cm^{-1}; hrfabms *m/z* $[M+Na]^+$ 459.23790 (100) ($C_{24}H_{36}O_7Na$ requires 459.23586); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-16 [**8**].—Colorless oil: $[\alpha]^{28}D$ −42.38° (*c*=3.8, $CHCl_3$); uv λ max (MeOH) nm (log ε) 206 (3.91); ir ν max (neat) 2959, 2931, 2875, 1738, 1732, 1693, 1637, 1456, 1386, 1373, 1236, 1111, 1085, 1018, 932, 802, 756 cm^{-1}; hrfabms *m/z* $[M+1]^+$ 519.33220 (96) ($C_{30}H_{47}O_7$ requires 519.33217); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-17 [**9**].—Colorless oil: $[\alpha]^{26}D$ −18.58° (*c*=16.2, $CHCl_3$); ir ν max (neat) 3452, 2961, 2934, 2878, 1737, 1731, 1707, 1641, 1455, 1429, 1371, 1283, 1236, 1126, 1111, 1079, 1060, 1049, 1016, 962, 929, 914, 750 cm^{-1}; hreims *m/z* $[M]^+$ 436.24660 (2.3) ($C_{24}H_{36}O_7$ requires 436.24608), 418 (2.5), 376 (4.4), 358 (2.3), 316 (5.2), 314 (3.2), 298 (2.1), 279 (3.9), 255 (2.1), 245 (3.6), 219 (18), 193 (12), 189 (3.3), 185 (2.0), 177 (4.6), 176 (4.3), 175 (9.6), 173 (3.4), 165 (3.2), 163 (5.4), 157 (4.5), 151 (2.3), 149 (3.9), 133 (12), 131 (4.8), 119 (8.1), 109 (5.8), 107 (9.2), 105 (18), 93 (15), 91 (11), 81 (9.6), 79 (9.7), 55 (17), 43 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-18 [**10**].—Colorless oil: $[\alpha]^{24}D$ −0.88° (*c*=2.3, $CHCl_3$); ir ν max (neat) 3447, 2956, 2926, 2873, 2856, 1735, 1733, 1721, 1699, 1463, 1456, 1388, 1373, 1259, 1237, 1171, 1128, 1104, 1086, 1049, 1011, 937, 916, 802, 743 cm^{-1}; hreims *m/z* $[M]^+$ 520.34039 (9.7) ($C_{30}H_{48}O_7$ requires 520.33997), 502 (7.2), 460 (4.3), 448 (3.7), 376 (3.8), 334 (3.9), 318 (9.1), 316 (9.7), 304 (5.2), 298 (6.4), 245 (10), 237 (4.8), 220 (5.9), 219 (16), 217 (9.1), 193 (12), 192 (13), 191 (13), 177 (8.7), 176 (11), 175 (16), 174 (18), 163 (11), 161 (10), 159 (10), 157 (9.1), 149 (9.3), 147 (14), 145 (12), 137 (10), 135 (9.6), 133 (13), 127 (21), 119 (14), 109 (15), 107 (19), 105 (24), 97 (12), 95 (18), 93 (29), 91 (17), 81 (22), 79 (17), 71 (18), 69 (22), 67 (17), 57 (100), 55 (48); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-19 [**11**].—Colorless oil: $[\alpha]^{30}D$ −48.32° (*c*=1.36, $CHCl_3$); uv λ max (MeOH) nm (log ε) 215 (3.65); ir ν max (neat) 2961, 2933, 2877, 1737, 1730, 1688, 1636, 1452, 1439, 1432, 1425, 1412, 1371, 1303, 1238, 1197, 1178, 1158, 1126, 1109, 1085, 1075, 1052, 1042, 966, 932, 916 cm^{-1}; hreims *m/z* $[M]^+$ 434.20088 (1.3) ($C_{24}H_{34}O_7$ requires 434.23043), 392 (2.7), 374 (8), 314 (11), 285 (5.2), 255 (7.2), 233 (5.8), 219 (7.1), 193 (25), 192 (10), 191 (8.3), 175 (20), 157 (7.2), 149 (8.4), 147 (12), 145 (11), 133 (25), 124 (16), 123 (22), 122 (100), 107 (10), 105 (24), 95 (13), 93 (16), 91 (14), 79 (12), 69 (9.5), 55 (19); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-20 [**12**].—Amorphous powder: $[\alpha]^{25}D$ −16.74° (*c*=5.2, $CHCl_3$); uv λ max (MeOH) nm (log ε) 206 (3.52); ir ν max (neat) 3447, 2961, 2932, 2875, 1737, 1685, 1461, 1454, 1434, 1372, 1237, 1108, 1075, 1012, 969, 950, 927, 912, 880, 666, 647 cm^{-1}; hreims *m/z* $[M]^+$ 378.24086 (4.1) ($C_{22}H_{34}O_5$ requires 378.24072), 360 (6.9), 318 (27), 300 (17), 219 (41), 193 (26), 124 (100), 69 (90), 55 (77); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-21 [**13**].—Colorless oil: $[\alpha]^{24}D$ −27.17° (*c*=1.8, $CHCl_3$); ir ν max (neat) 3344, 2962, 2931, 2875, 1737, 1732, 1687, 1461, 1454, 1427, 1373, 1242, 1183, 1110, 1072, 1020, 994, 949, 933, 918, 731 cm^{-1}; hreims *m/z* $[M]^+$ 394.23506 (1.0) ($C_{22}H_{34}O_6$ requires 394.23562), 376 (0.8), 334 (1.7), 277 (3.8), 248 (3.5), 234 (4.5), 176 (7.3), 105 (12), 93 (12), 55 (17), 43 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-22 [**14**].—Colorless oil: $[\alpha]^{22}D$ −30.61° (*c*=1.6, $CHCl_3$); ir ν max (neat) 3440, 2962, 2932, 2891, 2873, 1732, 1678, 1456, 1430, 1380, 1373, 1260, 1184, 1110, 1094, 1076, 1028, 995, 984, 948,

937, 918, 908, 876, 802, 749, 663 cm^{-1}; hreims *m/z* $[M]^+$ 422.26581 (5.8) ($C_{24}H_{38}O_6$ requires 422.26684), 404 (5.8), 365 (18), 349 (9.0), 334 (16), 320 (5.1), 319 (7.4), 316 (6.1), 306 (11), 278 (10), 277 (29), 261 (19), 248 (30), 234 (37), 221 (11), 219 (21), 209 (12), 192 (19), 191 (31), 177 (35), 176 (53), 160 (22), 149 (36), 148 (44), 147 (36), 145 (25), 133 (42), 121 (30), 119 (38), 107 (38), 105 (58), 93 (52), 91 (33), 81 (54), 71 (100), 69 (62), 57 (49), 55 (84); ^1H and ^{13}C nmr, see Tables 1 and 2.

Asbestinin-23 [**15**].—Colorless oil: $[\alpha]^{24}D$ −21.97° (*c*=2.3, $CHCl_3$); ir ν max (neat) 2960, 2926, 2873, 1739, 1700, 1684, 1456, 1390, 1373, 1239, 1107, 1081, 1018, 800 cm^{-1}; hrfabms *m/z* $[M+1]^+$ 379.24670 (100) ($C_{22}H_{35}O_5$ requires 379.24855); ^1H and ^{13}C nmr, see Tables 1 and 2.

11-Acetoxy-4-deoxyasbestinin E [**16**].—Colorless oil: $[\alpha]^{24}D$ +19.73° (*c*=1.3, $CHCl_3$); ir ν max (neat) 2961, 2925, 2874, 1737, 1734, 1457, 1452, 1384, 1248, 1174, 1085, 1021, 968, 940, 924, 811, 797 cm^{-1}; hreims *m/z* $[M]^+$ not observed ($C_{24}H_{36}O_6$ requires 420.25119), 360 (81), 318 (24), 301 (34), 300 (66), 289 (24), 241 (21), 215 (21), 213 (16), 199 (14), 192 (27), 191 (24), 187 (14), 175 (28), 174 (57), 173 (25), 163 (24), 161 (26), 149 (25), 147 (27), 145 (40), 137 (26), 135 (29), 134 (57), 133 (40), 121 (32), 119 (41), 107 (47), 105 (66), 95 (71), 93 (81), 91 (52), 81 (57), 79 (47), 77 (28), 71 (76), 69 (45), 67 (31), 57 (22), 55 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

11-Acetoxy-4-deoxyasbestinin F [**17**].—Colorless oil: $[\alpha]^{25}D$ −15.20° (*c*=4.8, $CHCl_3$); uv λ max (MeOH) (log ε) 206 (3.58) nm; ir ν max (neat) 3440–3200, 2962, 2929, 2876, 1737, 1685, 1458, 1388, 1374, 1260, 1239, 1178, 1107, 1077, 1020, 990, 918, 810 cm^{-1}; hreims *m/z* $[M]^+$ 378.24281 (0.9) ($C_{22}H_{34}O_5$ requires 378.24062), 376 (1.3), 360 (1.6), 318 (8.8), 258 (3.4), 219 (9.2), 147 (10), 124 (38), 105 (20), 55 (22), 43 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

4-Deoxyasbestinin G [**18**].—Colorless oil: $[\alpha]^{25}D$ −26.57° (*c*=7.3, $CHCl_3$); uv λ max (MeOH) (log ε) 206 (3.58) nm; ir ν max (neat) 3348, 2961, 2929, 2874, 1730, 1686, 1460, 1388, 1369, 1261, 1183, 1107, 1077, 1014, 920, 809 cm^{-1}; hreims *m/z* $[M]^+$ 406.26830 (1.3) ($C_{24}H_{38}O_5$ requires 406.27192), 404 (2.1), 388 (1.6), 376 (0.9), 318 (19), 258 (8.3), 219 (12), 193 (15), 174 (15), 147 (15), 133 (24), 124 (79), 105 (28), 71 (76), 55 (30), 43 (100); ^1H and ^{13}C nmr, see Tables 1 and 2.

ACETYLATION OF ASBESTININ-18 [**10**].—A solution of asbestinin-18 [**10**] (6.1 mg, 0.011 mmol) in a mixture of Ac_2O (0.5 ml) and pyridine (1.0 ml) was stirred at 25° for 48 h. Excess reagents were removed by evaporation *in vacuo* and the residue obtained was partitioned against Et_2O and H_2O. The combined Et_2O extract was dried over Na_2SO_4 and evaporated to give 5.5 mg of the crude diacetate. The ^1H-nmr spectrum of the product showed a methine proton signal at δ 6.45 (1H, dd, *J*=6.0 and 11.7 Hz) ascribable to H-6, which indicated that the hydroxyl group in **10** was allylic.

OXIDATION OF ASBESTININ-7 [**6**] AND ASBESTININ-13 [**4**] TO YIELD ASBESTININ-16 [**8**].—A mixture of 20.0 mg (0.038 mmol) of asbestinin-7 [**6**] and 19.0 mg (0.228 mmol) of activated MnO_2 dissolved in 2.0 ml of $CHCl_3$ was stirred for 2 h at 25° (7). The reaction mixture was filtered and after concentration the residue was passed through a short column of Si gel to give 15.45 mg of pure asbestinin-16 [**8**]. The synthetic product obtained was identical in all respects to an authentic sample of **8**.

A solution of 46.6 mg (0.089 mmol) of asbestinin-13 [**4**] dissolved in 2.0 ml of $CHCl_3$ was stirred with 44.8 mg (0.537 mmol) of activated MnO_2. The reaction was allowed to proceed as described above for asbestinin-7. After purification by cc, 31.68 mg (65% yield) of pure asbestinin-16 was obtained.

OXIDATION OF ASBESTININ-20 [**12**] TO YIELD ASBESTININ-10 [**VI**].—A suspension of PCC (23.0 mg, 0.106 mmol) in 2.50 ml of CH_2Cl_2 was added to a solution of asbestinin-20 [**12**] (20.2 mg, 0.053 mmol). The mixture was stirred for 2.5 h at 25° and then Et_2O (2.50 ml) was added to the resulting mixture. The insoluble residue was washed with Et_2O (3×2.0 ml), the combined organic extract was concentrated *in vacuo* and finally, the oily residue obtained was passed through a short Si gel column to give 14.28 mg (72% yield) of pure asbestinin-10 [**VI**]. The synthetic material was identical to the natural product with regard to ir, ms, and nmr (^1H and ^{13}C).

HYDROGENATION OF ASBESTININ-10 [**VI**].—Asbestinin-10 [**VI**] (35.4 mg, 0.094 mmol) was mixed with Pd-C (5%) (10 mg) in 15.0 ml of EtOAc at 25° under H_2 at atmospheric pressure. After the H_2 uptake ceased (12 h) the catalyst was removed by filtration and the solvent was evaporated *in vacuo* to give 32.2 mg (90% yield) of a mixture of asbestinin-23 [**15**] (major) and its unnatural epimer (minor) at C-7. After separation of the two epimers by cc on a short Si gel column the main product isolated proved to be identical in all respects to naturally occurring asbestinin-23 [**15**].

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