4.88-5.84, m, 5 H; 6.68, dd, J = 11, 18 Hz, 1 H. IR (CCl_4) cm^{-1}: 1705, 1640, 1600, 890. MS m/z (%): 232 (8), 150 (10), 137 (72), 122 (100). Anal. ($C_{16}H_{24}O$) C, H.

Ketone 2. Two separate Pyrex tubes were charged with 4 mL each of a solution of 1.44 g of **3** in 8 mL of toluene. Methylene blue (50 mg) was added to each. The tubes were sealed and maintained at 170 °C for 68 h. After cooling, the tubes were opened and the contents combined, concentrated in vacuo, and chromatographed on 50 g of silica gel with 3% EtOAc-petroleum ether to give 654 mg (65% based on E diene in **3**) of **2** as a thick oil, R_f (10% EtOAc-hexane) 0.37. VPC analysis ($^1/_8$ in. × 6 ft 3% OV-17, 190 °C, 120 mL/min) showed six peaks, with retention times of 3.5, 3.9, 4.7, 5.0, 6.1, and 6.8 min. The 6.1-min peak (ketone **2**) accounted for 73% of the total. Three crystallizations of the ketone mixture from petroleum ether (-78 °C, 6, 2, and 2 mL/g of mixture) gave 367 mg (77% recovery) of **2** as a white solid, mp 65-70 °C. This material was pure by VPC. NMR ($CDCl_3$): δ 0.85, s, 3 H; 1.0-2.6, m, 17 H; 1.66, s, 3 H; 5.33, bs, 1 H. IR (CCl_4) cm^{-1}: 1705. MS m/z (%): 232 (100), 217 (33), 203 (47), 122 (86), 121 (86), 106 (96). ^{13}C NMR:[27] 11.78 (q), 21.36 (q), 22.39 (t), 22.88 (d), 24.94 (t), 25.75 (t), 26.40 (t), 34.37 (t), 36.04 (s), 41.68 (t), 47.8 (t), 49.64 (d), 53.81 (d), 120.72 (d), 134.53 (s), 213.68 ppm (s). Anal. ($C_{16}H_{24}O$) C, H.

Enone 16. To a solution of lithium diisopropylamide prepared from 101 mg (1.0 mmol) of diisopropylamine and 300 mL (0.8 mmol) of 2.66 M n-butyllithium in 8 mL of THF in a 25-mL flame-dried round-bottom flask stirred magnetically in a dry ice-acetone bath was added **2** (156 mg, 0.67 mmol) in 2 mL of THF dropwise over 3 min. Stirring was continued for 5 min: then acetaldehyde (0.5 mL, large excess) was added in one portion. Stirring was continued for an additional 5 min. The reaction mixture was then diluted with aqueous HCl and extracted with CH_2Cl_2. The combined extracts were dried over K_2CO_3 and concentrated in vacuo.

The resulting oil was taken up in 10 mL of ethylene chloride, 30 mg of p-toluenesulfonic acid monohydrate added, and the solution refluxed for 10 min. The reaction mixture was diluted with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined extracts were dried over K_2CO_3 and concentrated in vacuo. The residue was chromatographed on 5 g of silica gel with 2% EtOAc-petroleum ether to give 47 mg of unreacted **2** and 66 mg (59% based on unrecovered **2**) of **16** as oil, R_f (10% EtOAc-hexane) 0.43. NMR ($CDCl_3$): δ 0.78, s, 3 H; 1.0-3.0, m, 15 H; 1.62, s, 3 H; 1.72, d, J = 7 Hz, 3 H; 5.36, bs, 1 H; 6.62, bq, J = 7 Hz, 1 H. IR (CCl_4) cm^{-1}: 1675, 1605. MS m/z (%): 258 (90), 243 (12), 229 (15), 134 (87), 122 (100). Anal. ($C_{18}H_{26}O$) C, H.

Isopropyl Ketone 17. Methyllithium (2.22 mL of 1.80 M in Et_2O, 4.0 mmol) was added to CuI·Me_2S 26 (630 mg, 2.5 mmol) in 5 mL Et_2O in a 25-mL round-bottom flask stirred magnetically under N_2 in an ice-water bath, to give a thick yellow suspension. Enone **16** (60 mg, 0.23 mmol) in 2 mL of Et_2O was added dropwise over 1 min. Stirring was continued for 5 min. The mixture was quenched with aqueous HCl, rendered alkaline with aqueous NH_4OH, diluted with saturated aqueous NaCl, and extracted with Et_2O. The combined extracts were dried over K_2CO_3 and concentrated in vacuo. The residue was chromatographed on 5 g of silica gel with 20% CH_2Cl_2-petroleum ether to give 36 mg (56%) of **17** as an oil, R_f (30% CH_2Cl-hexane) 0.27. NMR ($CdCl_3$): δ 0.82, s, 3 H; 0.92, m, 6 H; 1.0-2.4, m, 17 H; 1.60, s, 3 H; 5.32, bs, 1 H. IR (CCl_4) cm^{-1}: 1700, 1370, 1360. MS m/z (%): 274 (100), 259 (33), 147 (39), 132 (45), 121 (88), 106 (71). Anal. ($C_{19}H_{30}O$) C, H.

Fichtelite (1). To ketone **17** (29 mg, 0.11 mmol) in 5 mL of hexane in a 25-mL round-bottom flask stirred magnetically under N_2 was added diisobutylaluminum hydride (0.5 mL of 1.0 M, excess). Stirring was continued for 5 min. The reaction mixture was diluted with aqueous HCl and extracted with CH_2Cl_2. The combined extracts were dried over K_2CO_3 and concentrated in vacuo.

To the residue in 5 mL of CH_2Cl_2 in a 25-mL round-bottom flask stirred magnetically under N_2 in a -10 °C bath (dry ice-brine) was added pyridine (300 mL) followed by sulfuryl chloride (80 mL, 1.0 mmol). Stirring was continued for 20 min. Dimethylamine in CH_2Cl_2 (prepared by adding 0.5 mL of 25% aqueous dimethylamine to 2 mL of CH_2Cl_2, followed by repetitive drying with K_2CO_3) was added. The cooling bath was removed and stirring continued for 20 min. The mixture was then diluted with aqueous HCl and extracted with CH_2Cl_2. The combined extracts were dried over K_2CO_3 and concentrated in vacuo.

The residue was transferred with 5 mL of THF to a 100-mL three-neck round-bottom flask. Liquid ammonia (30 mL) was distilled in, the solution stirred magnetically, and sodium metal (washed with hexane) added in small pieces, until a solid blue solution with blue foam was maintained. Methanol was added to discharge the color, and the ammonia was evaporated under a stream of nitrogen. The residue was diluted with water and extracted with petroleum ether. The combined extracts were dried over K_2CO_3 and concentrated in vacuo.

PtO_2 (10 mg) suspended in 1 mL of acetic acid was exposed to an atmosphere of hydrogen for 15 min. The above residue in 1 mL of acetic acid was added and stirring continued for 1 h. The mixture was diluted with water and extracted with petroleum ether. The combined extracts were washed with aqueous $NaHCO_3$, dried over K_2CO_3, and concentrated in vacuo. The residue was filtered through 300 mg of silica gel with petroleum ether. Evaporation of the solvent left 17 mg (61%) of a colorless oil, R_f (petroleum ether) 0.85. This material showed two peaks on VPC ($^1/_8$ in. × 5 ft, 3% OV-1, 180 °C, 35 mL/min, 4.7 and 5.2 min) in a ratio of 1:2. The latter was identical (t_R, MS) with authentic fichtelite. A pure sample isolated by preparative VPC gave a ^1H FT NMR[27] spectrum that was identical with that of authentic fichtelite recorded under the same conditions: 0.80, s, 3 H; 0.83, d, J = Hz, 6 H; 0.89, d, J = 7 Hz, 3 H.

Acknowledgments. We wish to express our appreciation to Professor William S. Johnson for supplying a sample of authentic fichtelite. This investigation was supported by Grant CA 22757, awarded by the National Cancer Institute, DHEW, and by a Biomedical Research Support Grant, S07-RR05424, DHEW, for the FT NMR and mass spectrometric instrumentation.

(27) These spectra were recorded on a JEOLCO FX-90Q spectrometer, in $CDCl_3$ with Me_4Si as internal standard.

The Asbestinins, a Novel Class of Diterpenes from the Gorgonian *Briareum asbestinum*

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Abstract: The gorgonian *Briareum asbestinum* contained two classes of diterpenes, the briareins and the asbestinins. The structure of asbestinin-1 (**3**) was determined from a single-crystal X-ray diffraction study on the corresponding diol **8**. The structures of asbestinins-2, -3, -4, and -5 (**4**-**7**) were determined by analysis of spectral data. The relationships between asbestinins-2, -3, -4, and -5 (**4**-**7**) and asbestinin-1 (**3**) were confirmed by chemical interconversions.

The gorgonian coral *Briareum asbestinum* is a common inhabitant of shallow Caribbean reefs. Previous studies of the metabolites of *B. asbestinum* led to the isolation of a series of chlorinated diterpenes,[1,2] one of which, briarein A (**1**), has been

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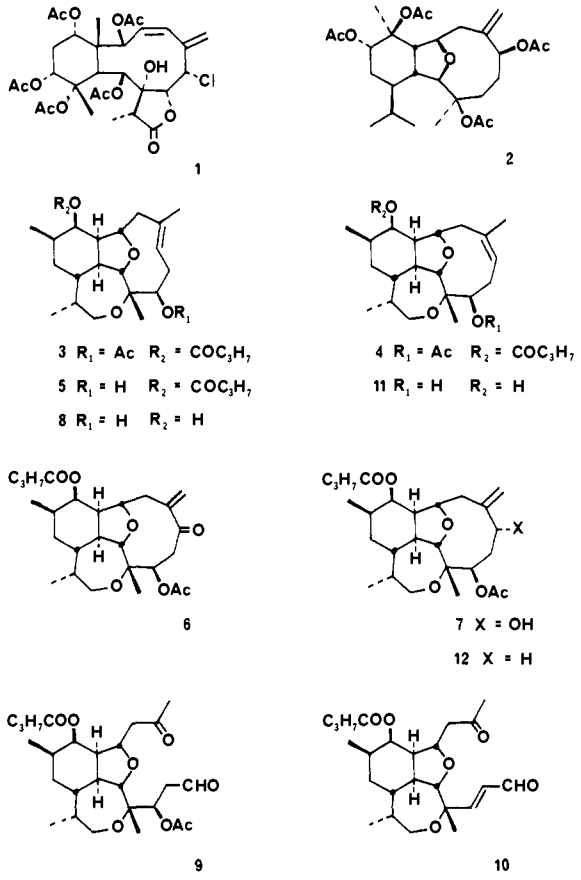
(1) Hyde, R. W. Thesis, University of Oklahoma, 1966.

0002-7863/80/1502-5088$01.00/0

Chart I



identified by an X-ray diffraction study.[3] We have isolated briarein B, an analogue of briarein A (**1**) with a butyrate ester replacing one of the acetate groups, as the major chlorinated diterpene (0.45% dry weight) from a sample of *B. asbestinum* collected in Belize. Cooccuring with briarein B were found a series of nonchlorinated diterpenes having a new carbon skeleton that was more closely related to that of eunicellin (**2**).[4]

Repeated chromatography of the ethyl acetate soluble material from a methanolic extract of *B. asbestinum* provided a number of diterpenes, both chlorinated and nonchlorinated. We have isolated and identified five of the more abundant nonchlorinated diterpenes **3**–**7** which we have named the asbestinins. In the samples of *B. asbestinum* that we have examined, the asbestinins were as abundant as the briareins.

Asbestinin-1 (**3**) (0.1% dry weight) had the molecular formula $C_{26}H_{40}O_6$. The infrared spectrum contained an ester band at 1740 cm^{-1}. The ^1H NMR spectrum contained an acetate signal at δ 2.07 and signals for a butyrate ester group at δ 0.98 (t, 3 H, J = 7 Hz), 1.67 (m, 2 H), and 2.36 (t, 2 H, J = 7 Hz). The ^{13}C NMR spectrum contained signals at δ 173.2 (s) and 169.9 (s) for two ester carbonyls, at δ 129.5 (s) and 125.6 (d), assigned to a trisubstituted olefin, and at δ 94.8 (d), 81.0 (d), 79.4 (s), 73.4 (d), 72.9 (d), and 67.6 (t), assigned to carbon atoms bearing oxygen. Asbestinin-1 (**3**) therefore contained two ether rings and two carbocyclic rings. Since the ^{13}C NMR spectrum did not contain a signal for a tetrasubstituted carbon atom bearing carbon substituents, as found at the carbocyclic ring junction in briarein A, asbestinin-1 could not be assigned a structure based on the briarein carbon skeleton.

Although asbestinin-1 (**3**) could not be crystallized, the corresponding diol **8**, resulting from reduction of **3** with lithium aluminum hydride in ether at 25 °C, crystallized from ether/hexane, mp 154–156 °C. The results of a single-crystal X-ray diffraction study of diol **8** are presented in Figure 1. This molecule crystallizes such that two independent molecules form the asymmetric unit. These independent molecules have the same structure and are related by the noncrystallographic symmetry operation $x^* \cong 1.00 - x$, $y^* \cong y + 0.05$, $z^* \cong 1.22 - z$. The mean difference in dihedral angle between the two crystallographically independent molecules is 3.3° with a maximum value of 14° for C(20)–C(12)–C(13)–C(14). The experiment described here did not distinguish enantiomers and the molecule drawn in Figure 1 was chosen to facilitate comparison with earlier work. The correct stereochemical descriptors are C1(S^*), C2(S^*), C3(S^*), C4(R^*), C9(S^*), C10(S^*), C11(R^*), C12(R^*), C14(S^*), and C15(R^*). The C6–C7 double bond has the *E* configuration. During the refinement of the structure we were particularly concerned about the possible misassignment of atomic types for O4 and C20. This was a concern since, if the methyl and hydroxy were switched, the carbon skeleton would be identical with the well-known eunicellin-type molecules. When the identity of these atoms was reversed, the crystallographic residual rose to 0.116 from 0.074 and was not reduced by further refinement. Also during refinement of this reversed structure it was noted that the temperature factors of the "carbon" atom decreased and that of the "oxygen" increased, as would be expected if they were improperly assigned. There also appear to be two hydrogen bonds involving O4 of 3.01 and 2.83 Å. If O4 were a methyl carbon, these would be unacceptably short contacts.

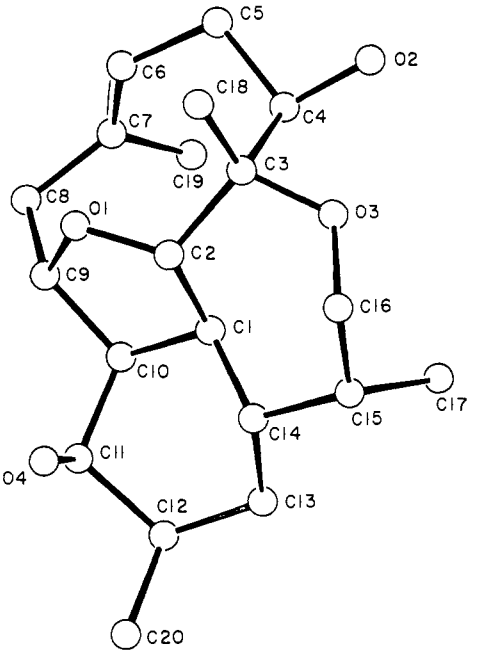


Figure 1. Computer-generated perspective drawing of the final X-ray model of diol **8**. Hydrogens are omitted for clarity and no absolute configuration is implied.

The structure itself is a complicated tetracyclic array. The tetrahydrofuran is incorporated in such a way that the two α-hydrogens are cis to each other as are the two β-hydrogens but the α–β relationships are trans. The cyclohexane ring is in a boat conformation with O4 in a flagpole and C15 in a bowsprit position. In general, all distances and angles agree well with accepted values.

The relative positions of the acetate and butyrate groups in asbestinin-1 (**3**) were determined through the following reaction sequence. Ozonolysis of asbestinin-1 (**3**) in ethyl acetate solution at −78 °C, followed by catalytic hydrogenation of the ozonide, gave the expected keto aldehyde **9**. Treatment of the keto aldehyde **9** with DBU in ether caused β elimination of acetic acid, yielding the unsaturated aldehyde **10**. The ^1H NMR spectrum of **10** contained signals at δ 9.60 (d, 1 H, J = 8 Hz), 6.87 (d, 1 H, J = 15 Hz), and 6.44 (dd, 1 H, J = 15, 8 Hz) for the protons on

(2) Bartholome, C. Thesis, Université Libre de Bruxelles, 1974.
(3) Burk, J. E.; Van der Helm, D.; Chang, C. Y.; Ciereszko, L. S. *Acta. Crystallogr., Sect. B* **1977**, *33*, 704.
(4) Kennard, O.; Watson, D. G.; Riva de Sanseverino, L.; Tursch, B.; Bosmans, R.; Djerassi, C. *Tetrahedron Lett.* **1968**, 2879.

the α,β-unsaturated aldehyde functionality and at δ 2.16 due to a methyl ketone. Asbestinin-1 (**3**) therefore had an acetate ester on the 10-membered carbocyclic ring and a butyrate ester on the cyclohexane ring.

Asbestinin-2 (**4**) (0.05% dry weight) was shown to be an isomer of asbestinin-1 (**3**). The ^{1}H NMR spectrum of **4** contained signals for an acetate ester [δ 2.09 (s, 3 H)] and a butyrate ester [δ 0.99 (t, 3 H, J = 7 Hz), 1.68 (m, 2 H), and 2.35 (t, 2 H, J = 7 Hz)]. Reduction of asbestinin-2 (**4**) with lithium aluminum hydride in ether at room temperature gave a diol **11** that was not identical with diol **8**. Comparison of the ^{1}H NMR spectra of asbestinin-1 (**3**) and asbestinin-2 (**4**) revealed that the major differences were associated with the carbocyclic 10-membered ring. In the spectrum of asbestinin-1 (**3**) the α-acetoxy, α-butyroxy, and olefinic protons all overlapped at δ 5.31, whereas the spectrum of asbestinin-2 (**4**) contained an olefinic signal at δ 5.74 (m, 1 H), an α-acetoxy signal at δ 4.88 (d, 1 H, J = 7 Hz), and an unchanged α-butyroxy signal at δ 5.31 (dd, 1 H, J = 3, 2 Hz). The presence of an allylic proton signal at δ 3.20 (m, 1 H) coupled to both the olefinic proton signal and the α-acetoxy proton signal suggested that asbestinin-2 (**4**) contained a Δ^6 olefinic bond and must therefore be a geometrical isomer of asbestinin-1 (**3**).

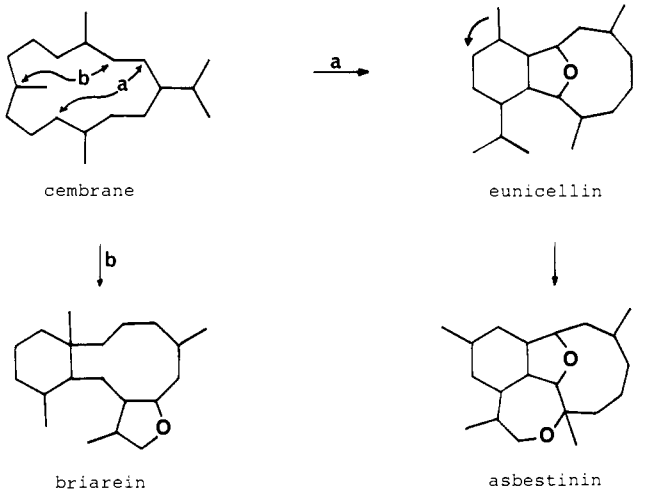
The structure of asbestinin-2 (**4**) was confirmed by ozonolysis in ethyl acetate solution at −78 °C, followed by catalytic hydrogenation of the resulting ozonide, to obtain the keto aldehyde **9**, identical in all respects with the product of ozonolysis of asbestinin-1 (**3**). Treatment of asbestinin-1 (**3**) with boron trifluoride etherate in benzene solution gave a 2:1 mixture of asbestinin-2 (**4**) and a third isomer **12** having an exocyclic methylene group [^{1}H NMR signals at δ 4.89 (brs, 1 H) and 5.15 (brs, 1 H)].

Asbestinin-3 (**5**), obtained from a second collection of *B. asbestinum* (0.4% dry weight), mp 156–158 °C, had the molecular formula $C_{24}H_{38}O_5$. The ^{1}H NMR spectrum of **5** did not contain an acetate signal and was almost identical with that of asbestinin-1 (**3**), with the exception that one of the overlapping signals at δ 5.31 in the spectrum of asbestinin-1 (**3**) now occurred at δ 3.90 (dd, 1 H, J = 11, 7 Hz). Treatment of asbestinin-3 (**5**) with lithium aluminum hydride in ether gave the diol **8**, indicating that asbestinin-3 (**5**) was a deacetylated derivative of asbestinin-1 (**3**). Acetylation of asbestinin-3 (**5**) with acetic anhydride in pyridine for 48 h gave asbestinin-1 (**3**) in quantitative yield.

Asbestinin-4 (**6**) (0.2% dry weight) had the molecular formula $C_{26}H_{38}O_7$. The ^{1}H NMR spectrum again indicated the presence of an acetate group [δ 2.08 (s, 3 H)] and a butyrate group [δ 0.94 (t, 3 H, J = 7 Hz), 1.66 (m, 2 H), and 2.33 (t, 2 H, J = 7 Hz)]. The infrared spectrum contained an ester band at 1740 cm^{-1} and an unsaturated carbonyl band at 1690 cm^{-1}. The ^{13}C NMR spectrum contained signals at δ 198.7 (s), 146.8 (s), and 114.1 (t), indicating that the carbonyl was conjugated to an exocyclic methylene group. The presence of the methylene proton signals at δ 5.38 (brs, 1 H) and 5.40 (brs, 1 H) in the ^{1}H NMR spectrum confirmed this assignment. The remaining downfield proton signals were similar to those of **12**, with the exception of the presumed α-acetoxy proton signal at δ 5.77 (t, 1 H, J = 7 Hz) that was coupled to a two-proton signal at δ 2.81 (d, 2 H, J = 7 Hz) due to protons adjacent to a carbonyl group. Since the coupling constants associated with the remaining downfield signals were similar to those observed for other compounds in this series, we assigned structure **6** to asbestinin-4.

Asbestinin-5 (**7**) was a minor metabolite (0.01% dry weight) having the molecular formula $C_{26}H_{40}O_7$. The infrared spectrum contained bands at 3500 and 1740 cm^{-1}, indicative of hydroxyl and ester groups, respectively. The ^{13}C NMR spectrum contained two ester carbonyl signals at δ 173.1 and 171.8, olefinic carbon signals at δ 148.5 and 115.5, and seven signals for carbon atoms bearing oxygen at δ 93.4, 83.4, 76.9, 74.0, 73.6, 72.5, and 67.4. The ^{1}H NMR spectrum contained very broad signals for the protons that we assigned to the large ring, indicating an equilibrium between different ring conformations. A broad signal at δ 4.15 (brs, 1 H) was assigned to an allylic α-hydroxy proton; we therefore assigned structure **7** to asbestinin-5. The relationship between asbestinin-4 (**6**) and asbestinin-5 (**7**) was confirmed by allylic oxidation of asbestinin-5 (**7**) with manganese dioxide in chloroform solution to obtain asbestinin-4 (**6**) in good yield.

Scheme I. Proposed Biosynthetic Relationship between the Briarein Carbon Skeleton and the Asbestinin Carbon Skeleton



We could not assign the stereochemistry at C-6 in asbestinin-5 (**7**) from ^{1}H NMR coupling constants. However, examination of a Dreiding model of asbestinin-1 (**3**) in the conformation revealed by X-ray diffraction studies (Figure 1) indicated that one face of the Δ^6 olefinic bond was sterically hindered to attack by reagents. Asbestinin-1 (**3**) was treated with singlet oxygen, generated by photolysis of oxygen in the presence of methylene blue at 0 °C, to obtain a single hydroperoxide[5] that was reduced with sodium sulfite solution to obtain asbestinin-5 (**7**) in good yield. Asbestinin-5 (**7**) must therefore have a 6α-hydroxy group.[6] Through this series of reactions both asbestinin-4 (**6**) and asbestinin-5 (**7**) have been related to asbestinin-1 (**3**).

The carbon skeleton of the asbestinins is related to that of eunicellin (**2**)[4] and cladiellin[7] by migration of a methyl group from C11 to C12. The asbestinins also contain an additional seven-membered ether ring formed between C3 and C16. The isolation of both briareins and asbestinins in *B. asbestinum* suggests that both ring systems might be synthesized in vivo by different cyclizations of the cembrane ring skeleton. Thus the biosynthesis of the asbestinins most likely involves the cyclization of a cembrane to a "eunicellin" followed by methyl migration and ether formation (Scheme I).

Experimental Section[8]

Collection and Extraction. *Briareum asbestinum* (Pallas) was collected by hand at Lighthouse Reef, Belize, and at Carrie Bow Cay, Belize. The samples were chopped into 2-in. lengths and stored in ethanol (~1 L). The extract was decanted and the solvent evaporated in vacuo to obtain a residue that was partitioned between ethyl acetate (2 × 250 mL) and water (100 mL). The combined ethyl acetate extracts were dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain dark orange oils. The sample from Lighthouse Reef gave 15.2 g (1.5% dry weight) of crude extract while the sample from Carrie Bow Cay gave 15.3 g (1.5% dry weight) of crude extract. Neither sample was homogenized or exhaustively extracted.

Chromatography of the Sample from Lighthouse Reef. The extract (15.2 g) was chromatographed on a column (60 cm × 5 cm diameter)

(5) The hydroperoxide underwent slow thermal decomposition at 35 °C to give asbestinin-4.

(6) As expected, singlet oxygen oxidation of asbestinin-2 (**4**) gave the 6β-hydroxy derivative: ^{1}H MNR ($CDCl_3$) δ 0.84 (d, 3 H, J = 7 Hz), 0.94 (d, 3 H, J = 7 Hz), 1.00 (t, 3 H, J = 7 Hz), 1.31 (s, 3 H), 2.06 (s, 3 H), 3.44 (dd, 1 H, J = 13, 3 Hz), 3.75 (d, 1 H, J = 13 Hz), 3.90 (d, 1 H, J = 8 Hz), 4.16 (m, 1 H), 4.39 (dd, 1 H, J = 11, 4 Hz), 4.62 (t, 1 H, J = 4 Hz), 5.12 (brs, 1 H), 5.39 (dd, 1 H, J = 6, 2 Hz), 5.41 (brs, 1 H).

(7) Kazlauskas, R.; Murphy, P. T.; Wells, R. J.; Schönholzer, P. *Tetrahedron Lett.* **1977**, 4643.

(8) For general methods see: Stierle, D. B.; Faulkner, D. J. *J. Org. Chem.* **1979**, *44*, 964.

of Florisil (320 g) with eluants of increasing polarity from hexane through ether to ethyl acetate. Fractions eluted with 10% ether in hexane contained a 2:1 mixture of asbestinin-1 (**3**) and asbestinin-2 (**4**) (1.45 g, 0.15% dry weight) that was separated as needed by high-performance liquid chromatography on μ-Porasil (5% ether in hexane eluant). Fractions eluted with 20% ether in hexane were rechromatographed on a column of silica gel (100 g) to obtain two components. The first component was purified by high-performance liquid chromatography on μ-Porasil (10% ether in hexane eluant) to obtain asbestinin-4 (**6**) (200 mg, 0.02% dry weight). The second component was purified by high-performance liquid chromatography (15% ether in hexane) to give asbestinin-5 (7) (100 mg, 0.01% dry weight). Fractions eluted with ether gave briarein B (4.5 g, 0.45% dry weight).

Chromatography of the Sample from Carrie Bow Cay. The crude extract (3.5 g) was chromatographed on a column of silica gel (100 g) by using a similar eluant regime. Fractions eluted with 10% ether in hexane contained asbestinin-1 (**3**) (475 mg, 0.21% dry weight). Fractions eluted with 20% ether in hexane gave asbestinin-3 (**5**) (900 mg, 0.4% dry weight).

Asbestinin-1 (3): $[\alpha]^{20}_D$ −26.3° (*c* 3.3 $CHCl_3$); IR ($CHCl_3$) 1740, 1450, 1390, 970, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (d, 3 H, *J* = 7 Hz), 0.90 (d, 3 H, *J* = 7 Hz), 0.98 (t, 3 H, *J* = 7 Hz), 1.35 (s, 3 H), 1.67 (m, 2 H), 1.87 (brs, 3 H), 2.07 (s, 3 H), 2.36 (t, 2 H, *J* = 7 Hz), 2.46 (dd, 1 H, *J* = 13, 6 Hz), 2.71 (m, 1 H), 3.38 (dd, 1 H, *J* = 13.5, 5 Hz), 3.84 (dd, 1 H, *J* = 13.5, 2 Hz), 4.04 (d, 1 H, *J* = 8 Hz), 4.05 (m, 1 H), 5.31 (m, 3 H); ^1H NMR (C_6D_6) 0.81 (d, 3 H, *J* = 7 Hz), 0.84 (d, 3 H, *J* = 7 Hz), 0.89 (t, 3 H, *J* = 7 Hz), 1.52 (s, 3 H), 1.79 (brs, 3 H), 1.84 (s, 3 H), 2.17 (t, 2 H, *J* = 7 Hz), 2.42 (dd, 1 H, *J* = 13, 6 Hz), 2.86 (m, 1 H), 3.39 (dd, 1 H, *J* = 13, 5 Hz), 3.80 (brd, 1 H, *J* = 13 Hz), 4.16 (m, 1 H), 4.20 (d, 1 H, *J* = 8 Hz), 5.34 (m, 1 H), 5.50 (brt, 1 H, *J* = 7 Hz), 5.64 (dd, 1 H, *J* = 11, 5 Hz); ^{13}C NMR (C_6D_6) δ 173.2 (s), 169.9 (s), 129.5 (s), 125.6 (d), 94.8 (d), 81.0 (d), 79.4 (s), 73.4 (d), 72.9 (d), 67.6 (t), 48.8 (d), 44.5 (t), 38.5 (d, d), 37.6 (d), 36.6 (t), 31.6 (t), 31.3 (d), 29.7 (t), 21.1 (q), 19.7 (q), 18.8 (t, q), 18.4 (q), 13.7 (q), 11.6 (q); high-resolution mass spectrum, obsd *m/e* 448.2852, $C_{26}H_{40}O_6$ requires *m/e* 448.2824.

Asbestinin-2 (4): $[\alpha]^{20}_D$ −48.2° (*c* 1.7 $CHCl_3$); IR (CCl_4) 1740, 1450, 1360, 1170, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, 3 H, *J* = 7 Hz), 0.91 (d, 3 H, *J* = 7 Hz), 0.99 (t, 3 H, *J* = 7 Hz), 1.41 (s, 3 H), 1.79 (brs, 3 H), 2.09 (s, 3 H), 2.35 (t, 2 H, *J* = 7 Hz), 2.69 (brd, 1 H, *J* = 14 Hz), 3.20 (m, 1 H), 3.50 (dd, 1 H, *J* = 13, 3.5 Hz), 3.85 (d, 1 H, *J* = 13 Hz), 3.93 (d, 1 H, *J* = 8 Hz), 4.09 (m, 1 H), 4.88 (d, 1 H, *J* = 7 Hz), 5.31 (dd, 1 H, *J* = 3, 2 Hz), 5.74 (m, 1 H); ^{13}C NMR (C_6D_6) δ 173.1, 170.0, 131.8, 127.5, 92.0, 82.1, 79.4, 77.2, 73.3, 67.7, 45.5, 41.2, 38.9, 38.2, 37.1, 36.7, 34.0, 31.7 (2 C), 29.5, 21.1, 19.6, 18.8, 18.4, 13.7, 11.0; high-resolution mass spectrum, obsd *m/e* 448.2826, $C_{26}H_{40}O_6$ requires *m/e* 448.2824.

Asbestinin-3 (5): mp 156–158 °C (1:1 ether/hexane); $[\alpha]^{20}_D$ −39.4° (*c* 3.4 $CHCl_3$); IR ($CHCl_3$) 3600, 1740, 1430, 1380, 1190, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (d, 3 H, *J* = 7 Hz), 0.93 (d, 3 H, *J* = 7 Hz), 1.00 (t, 3 H, *J* = 7 Hz), 1.28 (s, 3 H), 1.79 (brs, 3 H), 2.38 (t, 2 H, *J* = 7 Hz), 2.79 (m, 1 H), 3.48 (s, OH), 3.61 (dd, 1 H, *J* = 14, 4 Hz), 3.90 (dd, 1 H, *J* = 11, 7 Hz), 4.05 (brd, 1 H, *J* = 14 Hz), 4.05 (m, 1 H), 4.13 (d, 1 H, *J* = 8 Hz), 5.32 (m, 2 H); ^1H NMR (C_6D_6) 0.74 (d, 3 H, *J* = 7 Hz), 0.82 (t, 3 H, *J* = 7 Hz), 0.86 (d, 3 H, *J* = 7 Hz), 1.37 (s, 3 H), 1.61 (s, 3 H), 2.16 (t, 2 H, *J* = 7 Hz), 2.39 (dd, 1 H, *J* = 13, 5 Hz), 2.98 (m, 1 H), 3.31 (dd, 1 H, *J* = 13.5, 3.5 Hz), 3.46 (s, OH), 3.79 (brd, 1 H, *J* = 13.5 Hz), 3.98 (dd, 1 H, *J* = 10.5, 7 Hz), 4.09 (dd, 1 H, *J* = 6, 2 Hz), 4.14 (d, 1 H, *J* = 8 Hz), 5.27 (m, 1 H), 5.45 (brt, 1 H, *J* = 8 Hz); ^{13}C NMR (C_6D_6) δ 173.3 (s), 127.5 (s), 126.9 (d), 93.2 (d), 80.9 (d), 80.8 (s), 73.2 (d), 72.2 (d), 68.1 (t), 48.8 (d), 44.5 (t), 39.0 (d), 37.9 (d), 37.8 (d), 36.6 (t), 31.6 (t), 31.3 (d), 31.0 (t), 18.7 (q, t), 18.5 (q), 18.1 (q), 13.7 (q), 10.8 (q); high-resolution mass spectrum, obsd *m/e* 388.2603, $C_{24}H_{36}O_4$ ($M^+ - H_2O$) requires *m/e* 388.2612.

Asbestinin-4 (6): $[\alpha]^{20}_D$ −60° (*c* 2.5 $CHCl_3$); IR (CCl_4) 1740, 1690, 1360, 1240, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (d, 3 H, *J* = 7 Hz), 0.89 (d, 3 H, *J* = 7 Hz), 0.94 (t, 3 H, *J* = 7 Hz), 1.30 (s, 3 H), 2.08 (s, 3 H), 2.33 (t, 2 H, *J* = 7 Hz), 2.81 (d, 2 H, *J* = 7 Hz), 3.47 (dd, 1 H, *J* = 13, 5 Hz), 3.73 (brd, 1 H, *J* = 13 Hz), 3.84 (d, 1 H, *J* = 8 Hz), 4.00 (dd, 1 H, *J* = 7, 4 Hz), 5.30 (dd, 1 H, *J* = 4, 3 Hz), 5.38 (brs, 1 H), 5.40 (brs, 1 H), 5.77 (t, 1 H, *J* = 7 Hz); ^{13}C NMR (C_6D_6) δ 198.7 (s), 172.9 (s, s), 146.8 (s), 114.1 (t), 93,0 (d), 80.4 (d), 77.8 (s), 72.5 (d), 71.9 (d), 67.7 (t), 48.8 (d), 41.5 (t), 39.9 (t), 38.2 (d), 37.9, 37.3, 36.4 (t), 31.4 (2 C), 20.9 (q), 18.7 (t, q), 18.2 (q), 13.7 (q), 11.2 (q); high-resolution mass spectrum, obsd *m/e* 402.2426, $C_{24}H_{34}O_5$ ($M^+ - C_2H_4O_2$) requires *m/e* 402.2406.

Asbestinin-5 (7): $[\alpha]^{20}_D$ −18° (*c* 2.3 $CHCl_3$); IR (CCl_4) 3500, 1730, 1715, 1250, 1100, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (d, 3 H, *J* = 7 Hz), 0.91 (d, 3 H, *J* = 7 Hz), 0.98 (t, 3 H, *J* = 7 Hz), 1.35 (s, 3 H), 2.09 (s, 3 H), 2.32 (t, 2 H, *J* = 7 Hz), 3.03 (brd, 1 H, *J* = 15 Hz), 3.43 (dd, 1 H, *J* = 13, 4 Hz), 3.73 (d, 1 H, *J* = 13 Hz), 3.87 (d, 1 H, *J* = 8 Hz), 4.10 (brs, 1 H), 4.15 (brs, 1 H), 5.03 (brs, 1 H), 5.14 (brs, 1 H), 5.37 (dd, 1 H, *J* = 4, 2 Hz), 5.56 (brs, 1 H); ^{13}C NMR (C_6D_6) δ 173.1, 171.8, 148.5, 115.5, 93.4, 83.4, 76.9, 74.0, 73.6, 72.5, 67.4, 46.0, 39.4, 39.0, 38.9, 37.4, (2 C), 36.7, 31.7, 31.5, 21.1, 18.8, 17.8 (2 C), 13.7, 11.0; high-resolution mass spectrum, obsd *m/e* 446.2630, $C_{26}H_{38}O_6$ ($M^+ - H_2O$) requires *m/e* 446.2669.

Reaction of Asbestinin-1 (3) with Lithium Aluminum Hydride. A solution of asbestinin-1 (**3**) (50 mg, 0.11 mmol) in dry ether (5 mL) was added to a suspension of lithium aluminum hydride (30 mg) in dry ether (15 mL) and the mixture was stirred for 20 min at room temperature. Excess reagent was destroyed by addition of ethyl acetate (1 drop) followed by dropwise addition of 0.1 N hydrochloric acid (**Caution!**). The ether layer was separated and dried over sodium sulfate, and the solvent was removed to obtain a semisolid mass (46 mg, quantitative). Recrystallization from 1:1 ether/hexane gave white needles of the diol **8**: mp 154–156 °C; IR (CCl_4) 3450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (d, 3 H, *J* = 7 Hz), 1.09 (d, 3 H, *J* = 7 Hz), 1.28 (s, 3 H), 1.81 (brs, 3 H), 2.56 (dd, 1 H, *J* = 12, 6 Hz), 2.79 (m, 1 H), 3.58 (dd, 1 H, *J* = 13, 3 Hz), 3.82 (dd, 1 H, *J* = 4, 2.5 Hz), 3.91 (dd, 1 H, *J* = 11, 6 Hz), 4.04 (brd, 1 H, *J* = 13 Hz), 4.17 (d, 1 H, *J* = 8 Hz), 4.41 (dd, 1 H, *J* = 6, 2 Hz), 5.38 (brt, 1 H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 128.1 (s), 125.9 (d), 93.1 (d), 81.4 (d), 80.2 (s), 72.4 (d), 71.8 (d), 68.2 (t), 49.8 (d), 44.4 (t), 38.2 (d), 37.6 (d), 37.5 (d), 31.8 (t), 31.3 (d), 30.1 (t), 18.8 (q, q), 17.6 (q), 10.6 (q); high-resolution mass spectrum, obsd *m/e* 336.2322, $C_{20}H_{32}O_4$ requires *m/e* 336.2300.

Ozonolysis of Asbestinin-1 (3). A stream of ozone in oxygen was bubbled into a solution of asbestinin-1 (**3**) (10 mg, 0.02 mmol) in ethyl acetate (10 mL) at −78 °C until the solution became blue. The solution was stirred for an additional 5 min and then warmed to room temperature while excess ozone was removed in a stream of dry nitrogen. Ten percent palladium-on-charcoal catalyst was added to the solution which was then stirred under an atmosphere of hydrogen for 2 h. The catalyst was removed by filtration and the solvent evaporated to obtain the keto aldehyde **9** (11 mg, quantitative): IR (CCl_4) 1740, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (d, 3 H, *J* = 7 Hz), 0.96 (d, 3 H, *J* = 7 Hz), 0.98 (t, 3 H, *J* = 7 Hz), 1.27 (s, 3 H), 2.06 (s, 3 H), 2.15 (s, 3 H), 2.35 (t, 2 H, *J* = 7 Hz), 2.61 (m, 3 H), 2.77 (dd, 1 H, *J* = 16, 5 Hz), 3.49 (d, 1 H, *J* = 9 Hz), 3.54 (dd, 1 H, *J* = 13, 3 Hz), 3.69 (brd, 1 H, *J* = 13 Hz), 3.85 (dt, 1 H, *J* = 8, 8, 6.5 Hz), 5.17 (t, 1 H, *J* = 3 Hz), 5.43 (dd, 1 H, *J* = 5.5, 4 Hz), 9.72 (dd, 1 H, *J* = 3.5, 1 Hz); high-resolution mass spectrum, obsd *m/e* 420.2529, $C_{24}H_{36}O_6$ ($M^+ - C_2H_4O_2$) requires *m/e* 420.2512.

The keto aldehyde **9** (11 mg) was dissolved in dry ether (10 mL) containing 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) (10 mg), and the mixture was allowed to stand for 4 h at room temperature. The solution was washed with water (10 mL) and dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain the α,β-unsaturated aldehyde **10** (8 mg, 85% theoretical): UV (MeOH) 220 nm (ε 6300); IR (CCl_4) 1740, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (d, 3 H, *J* = 7 Hz), 0.97 (d, 3 H, *J* = 7 Hz), 1.01 (t, 3 H, *J* = 7 Hz), 1.44 (s, 3 H), 2.16 (s, 3 H), 2.38 (t, 2 H, *J* = 7 Hz), 2.64 (m, 2 H), 3.64 (dd, 1 H, *J* = 13, 2 Hz), 3.69 (brs, 1 H), 3.80 (brd, 1 H, *J* = 13 Hz), 3.97 (dt, 1 H, *J* = 6.5, 6.5, 5 Hz), 5.22 (m, 1 H), 6.44 (dd, 1 H, *J* = 15, 8 Hz), 6.87 (d, 1 H, *J* = 15 Hz), 9.60 (d, 1 H, *J* = 8 Hz); high-resolution mass spectrum, obsd *m/e* 420.2529, $C_{24}H_{36}O_6$ requires *m/e* 420.2512.

Reaction of Asbestinin-2 (4) with Lithium Aluminum Hydride. A solution of asbestinin-2 (**4**) (20 mg, 0.045 mmol) in dry ether (5 mL) was added to a suspension of lithium aluminum hydride (15 mg) in dry ether (15 mL), and the mixture was stirred for 20 min at room temperature. The reaction was worked up in the manner described above to obtain the diol **11** (18 mg, quantitative) as an oil: IR (CCl_4) 3450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (d, 3 H, *J* = 7 Hz), 1.07 (d, 3 H, *J* = 7 Hz), 1.31 (s, 3 H), 1.78 (brs, 3 H), 2.65 (brd, 1 H, *J* = 14 Hz), 3.01 (m, 1 H), 3.50 (dd, 1 H, *J* = 13.5, 4 Hz), 3.80 (m, 2 H), 3.91 (d, 1 H, *J* = 13.5 Hz), 4.00 (d, 1 H, *J* = 9 Hz), 4.44 (m, 1 H), 5.61 (brt, 1 H, *J* = 7 Hz); high-resolution mass spectrum, obsd *m/e* 336.2274, $C_{20}H_{32}O_4$ requires *m/e* 336.2300.

Ozonolysis of Asbestinin-2 (4). A stream of ozone in oxygen was bubbled into a solution of asbestinin-2 (**4**) (10 mg, 0.022 mmol) in ethyl acetate (10 mL) at −78 °C until the blue color of ozone persisted. The reaction was worked up in the manner described above to obtain the keto aldehyde **9** (10 mg, 97% theoretical) identical in all respects with the sample obtained from asbestinin-1 (**3**).

Boron Trifluoride Catalyzed Rearrangement of Asbestinin-1 (3). Boron trifluoride etherate (1 drop) was added to a solution of asbestinin-1 (**3**) (4 mg, 0.01 mmol) in dry benzene, and the solution was stirred overnight at room temperature. The reaction mixture was poured into water, the organic layer was separated and dried over sodium sulfate, and the solvent was evaporated to obtain a 2:1 mixture of products. The reaction

products were separated on preparative TLC (1:1 ether–hexane eluant) to obtain asbestinin-2 (**4**) (2 mg), identical in all respects with an authenitc sample, and the exocyclic olefin **12** (1 mg): IR (CCl_4) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (d, 3 H, J = 7 Hz), 0.88 (d, 3 H, J = 7 Hz), 0.96 (t, 3 H, J = 7 Hz), 1.29 (s, 3 H), 2.04 (s, 3 H), 3.41 (dd, 1 H, J = 13, 3 Hz), 3.70 (brd, 1 H, J = 13 Hz), 3.85 (d, 1 H, J = 8 Hz), 4.11 (m, 1 H), 4.89 (brs 1 H), 5.15 (brs, 1 H), 5.19 (m, 1 H), 5.36 (m, 1 H); high-resolution mass spectrum, obsd m/e 448.2825, $C_{26}H_{40}O_6$ requires m/e 448.2775.

Reaction of Asbestinin-3 (5) with Lithium Aluminum Hydride. A solution of asbestinin-3 (**5**) (5 mg, 0.01 mmol) in dry ether (5 mL) was added to a suspension of lithium aluminum hydride (5 mg) in dry ether (5 mL), and the reaction was allowed to proceed as described for asbestinin-1 above to give the diol **8** (4 mg), identical in all respects with the sample of diol **8** obtained from asbestinin-1 (**3**).

Acetylation of Asbestinin-3 (5). A solution of asbestinin-3 (**5**) (5 mg, 0.01 mmol) in a mixture of acetic anhydride (0.5 mL) and pyridine (1 mL) was allowed to stand for 48 h at room temperature. The reagents were evaporated under high vacuum and the residue was partitioned between ether (2 × 10 mL) and water (5 mL). The combined ether extracts were dried over sodium sulfate, and the solvent was evaporated to give asbestinin-1 (**3**) (5 mg, 90% theoretical), identical in all respects with the authentic material.

Oxidation of Asbestinin-5 (7) with Manganese Dioxide. Activated manganese dioxide (5 mg, 0.06 mmol) was added to a solution of asbestinin-5 (7) (5 mg, 0.01 mmol) in chloroform (2 mL) and the solution was stirred for 2 h at room temperature. The reagent was removed by filtration and the solvent evaporated to obtain asbestinin-4 (**6**) (4 mg, 80% theoretical), identical in all respects with an authentic sample.

X-ray Analysis of Diol 8. The diol **8** crystallized in the orthorhombic crystal system. Accurate lattice parameters, determined by a least-squares fit of 15 moderate 2θ values measured on a four-circle diffractometer, were **a** = 12.351 (1), **b** = 13.641 (2), and **c** = 22.195 (7) Å. Systematic extinctions suggested space group $P2_12_12_1$ and density considerations suggested *two* molecules of composition $C_{20}H_{32}O_4$ in the asymmetric unit. Successful solution and refinement fully justified these assumptions.

All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled diffractometer using graphite-monochromated CuKα radiation (1.541 78 Å) and variable speed, 1° ω scans. A total of 2857 reflections were measured in this fashion; after correction for Lorentz, polarization, and background effects, 2497 (87%) were judged observed ($|F_o^2| \geq 3\sigma(F_o^2)$).

A phasing model was achieved uneventfully by a multisolution, weighted tangent formula approach in which 1 general and 6 centrosymmetric reflections formed the starting set for phase permutation.[7] The resulting E synthesis showed all of the nonhydrogen atoms in the asymmetric unit. Atom types were identified by peak intensity, geometrical considerations, and behavior on refinement (vide supra). Hydrogen atoms were located on intermediate difference electron density syntheses, and full-matrix least-squares refinements have currently converged to an unweighted crystallographic residual of 0.074 for the observed reflections. Supplementary material to this paper contains additional crystallographic details.

Oxidation of Asbestinin-1 (3) with Singlet Oxygen. Asbestinin-1 (**3**) (60 mg, 0.12 mmol) and methylene blue (1 mg) were dissolved in methylene chloride (10 mL) and the solution was cooled to 0 °C. Oxygen was bubbled slowly through the solution, which was irradiated under a 200-W light bulb. The reaction was allowed to proceed at 0–10 °C for 12 h. The solvent was removed under vacuum and the residue was redissolved in methanol (5 mL). Saturated sodium sulfite solution was added dropwise to the methanolic solution until a light precipitate formed. The solution was stirred for 3 h, water (30 mL) was added, and the organic material was extracted into ethyl acetate (2 × 10 mL). The combined organic extracts were dried over sodium sulfate and the solvent was removed under vacuum to obtain an oil (50 mg). Purification by high-peformance liquid chromatography on μ-Porasil (ether eluant) gave asbestinin-5 (7) (40 mg, 65% theoretical), identical in all respects with the natural material.

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Supplementary Material Available: Fractional coordinates, temperature factors, bond distances, bond angles, intermolecular contacts, and observed and calculated structure factors for diol **8** (20 pages). Ordering information is given on any current masthead page.

(9) The following library of crystallographic programs was used: Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. B* **1970**, *24*, 274 (MULTAN); Hubbard, C. R.; Quicksall, C. O; Jacobson, R. A. "The Fast Fourier Algorithm and the Programs ALFF, ALFFDP, ALFFT and FRIEDEL", USAEC Report IS-2625; Institute for Atomic Research, Iowa State University, Ames, IA, 1971; Busing, W. R.; Martin, K. O.; Levy, H. A. "A Fortran Crystallographic Least Squares Program", USAEC Report ORNL-TM-305; Oak Ridge National Laboratory, Oak Ridge, TN, 1965; Johnson, C. "ORTEP: A Fortran Thermal-Ellipsoid Plot Program", USAEC Report ORNL-3794: Oak Ridge National Laboratory Oak Ridge, TN, 1965.