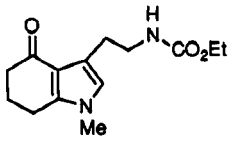
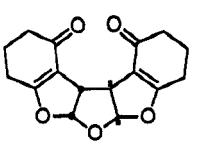


13 (72%)



14 (54%)

rhodium catalysis. The existing postulate that diazo compounds initially cyclopropanate furans and the production of both types of products from 1 suggest a unified mechanism for these reactions involving the acylcyclopropane. An explanation for the favored conversion of this adduct to the dihydrofuran product rather than a dienal is then required (eq 3). Ring opening to the zwitterion with cyclic dicarbonyls could be aided by "spiroactivation".[14] NMR experiments aimed at identifying intermediates in the cycloadditions to give 3 or 6 have thus far given no evidence for such cyclopropanes. An alternative mechanism that has been proposed previously for dipolar addition involves direct generation of the zwitterion.[1] This is difficult to reconcile with the known preference of furan for electrophilic attack at the 2-position.

(3)

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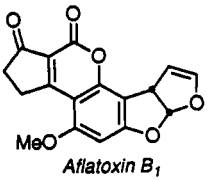
In summary, the dipolar cycloaddition of cyclic diazo 1,3-diketones provides a rapid entry into polyheterocyclic systems. The influence of ring size and breadth of application of this reaction will be established in the future. It is already apparent, however, that the method provides an expeditious synthetic route toward such natural heterocycles as aflatoxin.[15]



Aflatoxin B_1

Acknowledgment. The support of NIH grant GM-38226 and the Johnson Matthey Metals Loan Program is gratefully acknowledged.

Supplementary Material Available: Experimental procedures and spectral data, ORTEP diagrams and tables of crystallographic data, atomic positional and thermal parameters, and bond lengths and angles for 14 (12 pages); listing of observed and calculated structure amplitudes (5 pages). Ordering information is given on any current masthead page.

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Articles

Smenochromenes, Unusual Macrocyclic Sesquiterpene Hydroquinone Derivatives from a Seychelles Sponge of the Genus *Smenospongia*

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Smenochromenes A–D (2–5) are four unusual macrocyclic chromenes that can be derived by cyclization of farnesyl hydroquinone. The structure of smenochromene A (2) was determined by X-ray analysis and the structures of the remaining compounds were elucidated by interpretation of spectral data. The unusual geometry of smenochromene A gives rise to some unexpected spectral data. The sponge *Smenospongia* sp. also contains smenodiol (6), which is related to compounds previously found in this genus.

Compounds of mixed biogenesis that are based on the farnesyl hydroquinone skeleton are commonly found in Dictyoceratid sponges[2] and occasionally in brown algae of the genus Dictyopteris.[3] Some compounds in this series such as avarol (1) from *Dysidea avara*[4] have been extensively studied due to their pharmacological properties.[5] Although a wide variety of carbon skeletons derived by

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(2) There are at least 24 papers reporting this class of compounds. For reviews, see: Faulkner, D. J. *Tetrahedron* **1977**, *33*, 1421. Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 551; **1986**, *3*, 1; **1987**, *4*, 539; **1988**, *5*, 613; **1990**, *7*, 269; **1991**, *8*, 97.

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Table I. ^{13}C [50 MHz, $CDCl_3$, δ (mult)] and ^1H [500 MHz, $CDCl_3$, δ (mult, J or int)] NMR Data for Smenochromenes A–D (2–5)

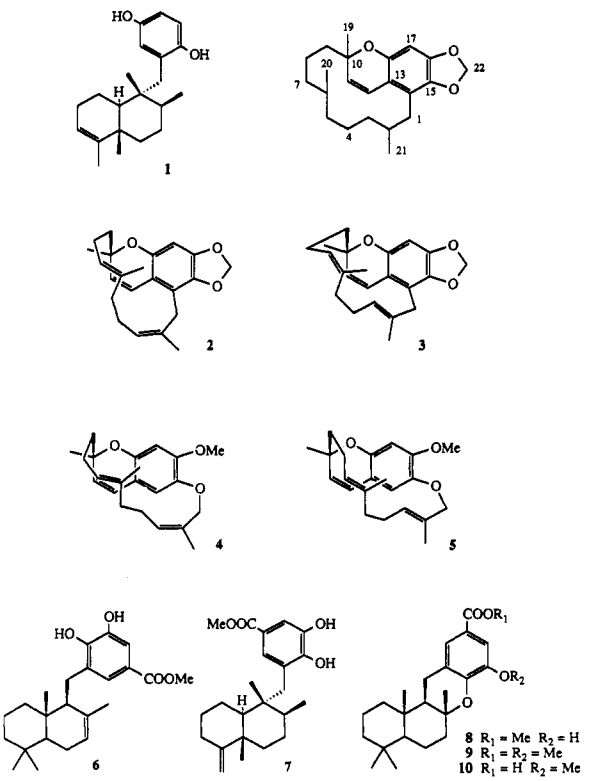
C	2		3		4		5	
1	28.3 (t)	3.01 (d, 14) 3.43 (d, 14)	24.9 (t)	3.10 (d, 16) 3.32 (d, 16)	74.0 (t)	4.25 (d, 12) 4.46 (d, 12)	80.3 (t)	4.15 (d, 11.5) 4.52 (d, 11.5)
2	132.1 (s)		131.8 (s)		129.8 (s)		129.8 (s)	
3	129.0 (d)	5.09 (t, 5.5)	124.5 (d)	4.73 (t, 7)	131.3 (d)	5.16 (d, 10)	132.0 (d)	4.82 (t, 6)
4	28.3 (t)	2.12 (m) 2.25 (m)	22.4 (t)	1.50 (m) 2.12 (m)	27.1 (t)	1.67 (m) 1.85 (m)	24.6 (t)	2.10 (m, 2 H)
5	39.3 (t)	2.00 (m, 2 H)	37.7 (t)	1.52 (m) 2.10 (m)	39.4 (t)	1.29 (m) 1.85 (m)	38.9 (t)	1.89 (m, 2 H)
6	134.1 (s)		132.4 (s)		134.2 (s)		131.8 (s)	
7	126.1 (d)	5.14 (dd, 9, 5)	127.6 (d)	5.23 (t, 7)	124.4 (d)	4.99 (t, 5.5)	126.6 (d)	4.92 (t, 5.5)
8	23.4 (t)	1.84 (m) 2.25 (m)	34.2 (t)	1.89 (m) 2.12 (m)	24.0 (t)	2.09 (m) 2.20 (m)	23.0 (t)	2.10 (m, 2 H)
9	40.0 (t)	1.31 (m) 1.51 (m)	39.6 (t)	1.28 (m)	42.2 (t)	1.29 (m, 2 H)	41.3 (t)	1.50 (m, 2 H)
10	77.7 (s)		77.8 (s)		80.1 (s)		79.0 (s)	
11	125.4 (d)	5.35 (d, 10)	125.9 (d)	5.34 (d, 10)	124.9 (d)	5.22 (d, 10)	125.7 (d)	5.32 (d, 10)
12	121.5 (d)	6.38 (d, 10)	121.4 (d)	6.17 (d, 10)	120.5 (d)	6.19 (d, 10)	119.1 (d)	6.31 (d, 10)
13	112.7 (s)		115.2 (s)		112.4 (s)		113.3 (s)	
14	117.9 (s)		116.4 (s)		122.1 (d)	6.40 (s)	123.5 (d)	6.52 (s)
15	139.5 (s)		140.0 (s)		140.6 (s)		139.3 (s)	
16	146.7 (s)		146.4 (s)		153.9 (s)		153.3 (s)	
17	96.2 (d)	6.25 (s)	97.3 (d)	6.29 (s)	99.5 (d)	6.20 (s)	99.8 (d)	6.30 (s)
18	150.0 (s)		148.6 (s)		150.3 (s)		150.3 (s)	
19	29.7 (q)	1.42 (s, 3 H)	26.9 (q)	1.48 (s, 3 H)	31.4 (q)	1.45 (s, 3 H)	30.2 (q)	1.48 (s, 3 H)
20	17.3 (q)	1.16 (s, 3 H)	17.0 (q)	1.39 (s, 3 H)	14.8 (q)	1.36 (s, 3 H)	14.4 (q)	1.39 (s, 3 H)
21	26.4 (q)	1.88 (s, 3 H)	14.3 (q)	1.67 (s, 3 H)	22.6 (q)	1.88 (s, 3 H)	14.1 (q)	1.67 (s, 3 H)
22	100.0 (t)	5.78 (d, 1) 5.85 (d, 1)	100.4 (t)	5.81 (d, 1.5) 5.88 (d, 1.5)	55.7 (q)	3.72 (s, 3 H)	55.5 (q)	3.75 (s, 3 H)

cyclization and rearrangement of the sesquiterpene chain have been reported, none are more bizarre than the macrocyclic chromenes from *Smenospongia* sp. that we have called smenochromenes A–D (**2–5**).

The ethyl acetate soluble material from a methanolic extract of the Seychelles sponge *Smenospongia* sp. was chromatographed on Sephadex LH-20 to obtain a fraction that was rich in chromenes, as indicated by UV and ^1H NMR spectroscopy. The chromene fraction was further purified by HPLC on Partisil to obtain smenochromene A (**2**, 24 mg, 0.26% dry wt), smenochromene B (**3**, 3.5 mg, 0.037% dry wt), smenochromene C (**4**, 3.6 mg, 0.037% dry wt), and smenochromene D (**5**, 3.6 mg, 0.037% dry wt). A more polar fraction from the Sephadex LH-20 chromatography was purified by chromatography on silica gel to obtain smenodiol (**6**, 30 mg, 0.3% dry wt) (Chart I).

Smenochromene A (**2**) was obtained as optically inactive, colorless crystals, mp 98 °C. The molecular formula $C_{22}H_{26}O_3$, which was determined by high resolution mass measurement, required 10 unsaturation equivalents. Six unsaturations are assigned to the chromene ring system, one to a methylenedioxy ring, and two to isolated trisubstituted olefinic bonds, leaving the final unsaturation equivalent to be accommodated as a macrocyclic ring. The UV spectrum [($CHCl_3$) 242 nm (ε 11 020), 334 (5320)] is typical of a chromene chromophore and the ^{13}C NMR spectrum supports this assignment (Table I). The ^1H NMR spectrum was difficult to assign because of some very unusual chemical shift values. The signals at δ 6.38 (d, 1 H, J = 10 Hz) and 5.35 (d, 1 H, J = 10 Hz) were assigned to the olefinic protons of the chromene system and the signal at 6.25 (s, 1 H) was assigned to an aromatic proton. The corresponding ^{13}C NMR signal occurred at δ 96.2, suggesting that the single aromatic proton was flanked by two oxygen atoms. The methylenedioxy moiety gave rise to ^1H NMR signals at δ 5.78 (d, 1 H, J = 1 Hz) and 5.85 (d, 1 H, J = 1 Hz) and a ^{13}C NMR signal at 100.0 (t). The remaining carbon atom on the aromatic ring, para to the hydrogen, must be the point of attachment for the macrocyclic ring. The HMBC experiment revealed that the isolated methylene proton signals at δ 3.43 (d, 1 H, J = 14 Hz) and 3.01 (d, 1 H, J = 14 Hz) were coupled to aromatic carbon signals at δ 112.7 (s), 117.9 (s), and 139.5 (s), to the olefinic carbon signals at 132.1 (s) and 129.0 (d), and to the methyl signal at δ 26.4 (q). The signals at δ 26.4 and 129.0 show single-bond correlations with the ^1H NMR signals at 1.88 (s, 3 H) and 5.09 (t, 1 H, J = 5.5 Hz) that were assigned to a cis double bond bearing methyl and methylene groups attached to the quaternary carbon. Although both the ^{13}C NMR spectrum, which was assigned by analysis of the HMQC and HMBC experiments, and biosynthetic considerations correctly led us to the con-

Chart I



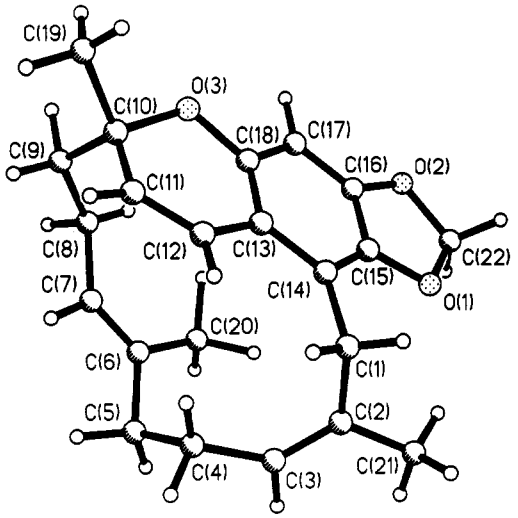


Figure 1. Computer-generated perspective drawing of the final X-ray model of smenochromene A (**2**). The naturally occurring material is racemic.

clusion that smenochromene A (**2**) contained a regular terpenoid chain as part of the macrocyclic ring, it was difficult to reconcile the chemical shift value of the ^{1}H NMR signal at δ 1.19 (s, 3 H) with a methyl group on a trisubstituted olefin. We therefore chose to perform an X-ray crystallographic study of this unusual molecule.

A computer-generated perspective drawing of the final X-ray model of smenochromene A (**2**) is given in Figure 1. One structural feature is noteworthy: Me-20 is directly under the center of the aromatic rings and is only 3.61 Å away. This places the vinyl methyl group (Me-20) well inside the ring current of the aromatic ring system and accounts for the unusual upfield shift of the corresponding ^{1}H NMR signal to 1.19 ppm. A molecular model generated by with the PC Model program was almost identical with the X-ray model and gave a distance of 3.64 Å between Me-20 and the plane of the aromatic rings. Examination of a Dreiding model of **2** did not exclude a conformation in which the Δ^7 double bond is rotated by about 180° so that H-7 lies within the ring current and Me-20 is outside: remarkably, empirical force-field calculations predict that both conformations are of approximately equal energy but the energy barrier for interconversion is very high. Another interesting feature of smenochromene A (**2**) is that, unlike other compounds of this series, it is racemic.

Smenochromene B (**3**), $[\alpha]_D$ +6.4°, is an isomer of smenochromene A (**2**). The ^{1}H and ^{13}C NMR data for smenochromene B (**3**) were assigned by interpretation of COSY and XHCORR experiments. Comparison of the NMR data with those of smenochromene A revealed that the C-21 signal was at δ 14.3 (q) in **3** instead of 26.4 (q) in **2**, indicating the 2*E* geometry in smenochromene B. The chemical shift of the Me-20 signal at δ 1.39 (s, 3 H) indicates that the methyl group is located within the ring current of the chromene system but is further away from the plane of the aromatic ring system. This conclusion is supported by empirical force-field calculations that indicate a distance of 5.23 Å between Me-20 and the plane of the aromatic ring system.

Smenochromene C (**4**), $[\alpha]_D$ −217°, was obtained as a colorless crystalline solid, mp 52 °C. The molecular formula $C_{22}H_{28}O_3$, which was determined by high resolution mass measurement of the molecular ion at m/z = 340.2841, required 9 unsaturation equivalents. An initial examination of the NMR spectrum of **4** suggested that it was quite closely related to **2**. The "missing" unsaturation equivalent is that due to the methylenedioxy ring; in its place, smenochromene C (**4**) has a methoxyl group that gave rise to a ^{1}H NMR signal at δ 3.72 (s, 3 H), and a ^{13}C NMR signal at 55.7 (q). The presence of two para-substituted aromatic proton signals at δ 6.40 (s, 1 H) and 6.20 (s, 1 H) required the second aromatic proton to be at the position occupied by the terpenoid chain in **2**. The terpenoid chain was in turn attached to an oxygen through a methylene group that gave rise to ^{1}H NMR signals at δ 4.25 (d, 1 H, J = 12 Hz) and 4.46 (d, 1 H, J = 12 Hz). Since the NMR data indicated that the terpenoid chain and chromene ring were intact, there were two possible structures for **4**, one as drawn and the other with *O*-methyl and *O*-methylene groups reversed. Three NOEDS measurements clearly defined the structure; irradiation of the methoxyl signal at δ 3.72 caused a 9.5% enhancement of the H-17 signal at 6.20 and irradiation of the H-14 signal at 6.40 caused enhancements of H-12 (3.8%) and the H-2 signals at 4.46 (1.8%). The 2*Z*,6*E* geometry was deduced from the chemical shifts of the methyl signals at δ 22.6 (q, C-21), which is shifted upfield from the usual position by the effect of a γ-oxygen, and 14.8 (q, C-20).

Smenochromene D (**5**), $[\alpha]_D$ −68.5°, is an isomer of smenochromene C (**4**) and has an identical structure except that the chemical shifts of the C-20 and C-21 signals at δ 14.4 (q) and 14.1 (q) require the 2*E*,6*E* geometry.

Smenodiol (**6**), $[\alpha]_D$ −53.5°, was obtained as a white crystalline solid, mp 185 °C. The molecular formula $C_{23}H_{32}O_4$ was established by high resolution mass measurement. A preliminary analysis of the spectral data clearly indicated that smenodiol was not closely related to the smenochromenes. The molecular formula is the same as that of dictyoceratin A (**7**),[6] which appears to have the same structure as smenospondiol from a Red Sea species of *Smenospongia*.[7] The ^{1}H NMR spectrum contained signals at δ 7.49 (br s, 1 H), and 7.26 (br s, 1 H), that were assigned to meta-substituted protons on an aromatic ring. The signal at δ 3.85 (s, 3 H), together with ^{13}C NMR signals at δ 167.9 (s) and 51.8 (q), suggested that one of the substituents on the aromatic ring was a carbomethoxy group. The UV spectrum showed a strong bathochromic shift (293 nm → 317 nm) on treatment with base, which, together with the IR band at 3450 cm^{-1} and the chemical shifts of the ^{13}C NMR signals in the aromatic region, suggested that the two remaining oxygen atoms were present as phenolic groups. The sesquiterpene portion of smenodiol was easily identified as a drimane residue by analysis of the NMR data. In particular, the ^{1}H NMR signals at δ 5.35 (br s, 1 H), and 1.40 (br s, 3 H) were indicative of a cyclic methyl-substituted olefin and the ^{13}C NMR spectrum, which included olefinic signals at δ 135.4 (s) and 122.9 (d), was diagnostic for the Δ^7-drimene ring system.[8]

The location of the olefinic bond and the substitution pattern on the aromatic ring were confirmed by treatment of **6** with *p*-toluenesulfonic acid in benzene to obtain cyclic ether **8**, followed by methylation with dimethyl sulfate/potassium carbonate in acetone to prepare methyl ester **9**, which was hydrolyzed in methanolic potassium hydroxide solution to form the acid **10**. The ^{1}H NMR spectrum of the acid **10** contained aromatic signals at δ 7.53

(6) Nakamura, H.; Deng, S.; Kobayashi, J.; Ohizumi, Y. *Tetrahedron* **1986**, *42*, 4197.
(7) Kondracki, M.-L.; Davoust, D.; Guyot, M. *J. Chem. Res., Synop.* **1989**, 74.
(8) See Figure 1 in Nishiwa et al. (Nishiwa, M.; Takenaka, H.; Hayashi, Y. *J. Org. Chem.* **1986**, *51*, 806) and footnote 5 in Sullivan, B. W.; Faulkner, D. J.; Matsumoto, G. K.; He, C.-h.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 4568.

(d, 1 H, J = 1.5 Hz) and 7.40 (d, 1 H, J = 1.5 Hz) and a methoxyl signal at 3.89 (s, 3 H). Two NOEDS experiments established the substitution pattern: irradiation of the signal at δ 3.89 caused enhancement of only one aromatic signal at 7.40 while irradiation of the H-11 methylene signal at 2.67 (m, 2 H) resulted in enhancement of the other aromatic signal at 7.53. Since the phenolic group that was involved in ether formation is ortho to the methylene group, the substitution pattern about the aromatic ring must be as shown. The stereochemistry of the methyl group at C-8 must be axial because irradiation of the methyl signal at δ 1.24 (s, 3 H) caused enhancement of the C-13 methyl signal at 0.84 (s, 3 H). In contrast with the antimicrobial activity reported for dictyoceratin A (7)[6] and smenospondiol,[7] smenodiol did not exhibit any appreciable antimicrobial activity.

Experimental Section

Collection, Extraction, and Isolation Procedures. The sponge *Smenospongia* sp. (9.6 g of dry wt, collection no. 90-087) was collected by hand using SCUBA (-20 m) at Therese Island, Seychelles, in May 1990. The specimen was stored in methanol at -4 °C for 4 months, at which time the methanol was decanted and the sponge was repeatedly extracted by being soaked in methanol at room temperature. The combined methanol extracts were evaporated under reduced pressure and the residue was partitioned between ethyl acetate (3 × 200 mL) and water (200 mL). The ethyl acetate extract was dried over anhydrous sodium sulfate and the solvent evaporated to obtain the crude organic extract (1.3 g). The organic extract was chromatographed on Sephadex LH-20 using a 1:1 mixture of methanol/dichloromethane as eluant to obtain a fraction that gave an unusual ^{1}H NMR spectrum. This fraction was separated by HPLC on Partisil using 2.5% ethyl acetate in hexane as eluant to obtain smenochromene A (**2**, 24 mg, 0.26% dry wt), smenochromene B (**3**, 3.5 mg, 0.037% dry wt), smenochromene C (**4**, 3.6 mg, 0.037% dry wt), and smenochromene D (**5**, 3.6 mg, 0.037% dry wt). A more polar fraction from the LH-20 Sephadex column was further purified by silica gel chromatography to yield smenodiol (**6**, 30 mg, 0.031% dry wt).

Smenochromene A (2): colorless crystals, mp 98 °C; $[\alpha]_D$ = 0° (c 0.22, CH_2Cl_2); IR (KBr) 1615, 1455, 940 cm^{-1}; UV ($CHCl_3$) 242 nm (ϵ 11 000), 334 (5320); ^{1}H NMR (500 MHz, $CDCl_3$) see Table I; ^{13}C NMR (50 MHz, $CDCl_3$) see Table I; mass spectrum, m/z 338 (100), 323 (15), 255 (76), 202 (57); HREIMS, obsd m/z = 338.1896, $C_{22}H_{26}O_3$ requires m/z = 338.1882.

Smenochromene B (3): colorless crystals, mp 80–82 °C; $[\alpha]_D$ = 6.4° (c 0.35, CH_2Cl_2); IR (neat) 2920, 1620, 1460, 940 cm^{-1}; UV ($CHCl_3$) 243 nm (ϵ 11 980), 333 (6900); ^{1}H NMR (500 MHz, $CDCl_3$) see Table I; ^{13}C NMR (50 MHz, $CDCl_3$) see Table I; mass spectrum, m/z 338 (100), 323 (17), 255 (68), 202 (67); HREIMS, obsd m/z = 338.1872, $C_{22}H_{26}O_3$ requires m/z = 338.1882.

Smenochromene C (4): colorless crystals, mp 52 °C; $[\alpha]_D$ = -217° (c 0.3, CH_2Cl_2); IR (neat) 1610, 1505 cm^{-1}; UV ($CHCl_3$) 242 nm (ϵ 11 260), 320 (6400); ^{1}H NMR (500 MHz, $CDCl_3$) see Table I; ^{13}C NMR (50 MHz, $CDCl_3$) see Table I; mass spectrum, m/z 340 (77), 257 (31), 191 (100), 190 (76), 161 (38); HREIMS, obsd m/z = 340.2041, $C_{22}H_{28}O_3$ requires m/z = 340.2038.

Smenochromene D (5): colorless glass; $[\alpha]_D$ = -68.5° (c 0.35, CH_2Cl_2); IR (neat) 2920, 1615, 1505, cm^{-1}; UV ($CHCl_3$) 242 nm (ϵ 11 125), 322 (5760); ^{1}H NMR (500 MHz, $CDCl_3$) see Table I; ^{13}C NMR (50 MHz, $CDCl_3$) see Table I; mass spectrum, m/z 340 (100), 227 (11), 191 (40), 190 (65); HREIMS, obsd m/z = 340.2027, $C_{22}H_{28}O_3$ requires m/z = 340.2038.

Smenodiol (6): colorless crystals (MeOH); mp 185 °C; $[\alpha]_D$ = +53.5° (c 0.37, MeOH); IR (KBr) 3460, 1685, 1600, 1440 cm^{-1}; UV (MeOH) 217 nm (ϵ 4470), 267 (1675), 293 (sh, 810), (MeOH + OH$^-$) 202 (11 415), 239 (2600), 289 (sh, 1000), 317 (1925); ^{1}H NMR (200 MHz, $CDCl_3/CD_3OD$) δ 7.49 (br s, 1 H), 7.26 (br s, 1 H), 5.35 (br s, 1 H), 3.85 (s, 3 H), 2.65 (m, 2 H), 2.40 (m, 1 H), 1.89 (m, 2 H), 1.40 (s, 3 H), 1.18–1.34 (m, 6 H), 0.88 (s, 6 H), 0.86 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3/CD_3OD$) δ 167.9 (s), 147.6 (s), 143.0 (s), 135.4 (s), 129.6 (s), 122.9 (d), 122.0 (d), 120.3 (s), 112.6 (d), 53.6 (d), 51.8 (q), 50.6 (d), 42.0 (t), 39.2 (t), 36.7 (s), 33.1 (q), 32.9 (s), 25.6 (t), 23.6 (t), 22.1 (q), 21.8 (q), 18.8 (t), 13.7 (q); mass spectrum, m/z 372 (37), 248 (22), 233 (28), 191 (100), 109 (48); HREIMS, obsd m/z = 372.2262, $C_{22}H_{28}O_3$ requires m/z = 372.2300.

Single-Crystal X-ray Analysis of Smenochromene A (2). A colorless block with dimensions 0.2 × 0.4 × 0.4 mm was selected for all further analysis. Preliminary photographs showed monoclinic symmetry, and accurate lattice constants of a = 8.217 (4), b = 21.907 (8), and c = 10.727 (5) Å and β = 106.40 (3)° were obtained from diffractometer measured 2θ values. Systematic extinctions were uniquely consistent with space group $P2_1/c$, and one molecule of composition $C_{22}H_{26}O_3$ gave a plausible density of 1.21 g/cm^3. The space group requires that naturally occurring smenochromene A be achiral or a racemic mixture. All unique reflections with $2\theta \leq 116°$ were collected on a computer-controlled diffractometer using Cu K$\bar{\alpha}$ radiation (1.54178 Å) and 2θ–θ scans. A total of 2521 reflections were used in the analysis. The structure was solved easily and refined with full-matrix least-squares refinement using anisotropic non-hydrogen atoms and fixed isotropic riding hydrogens. The final crystallographic residuals were R = 5.60% and R_w = 6.57%. Additional crystallographic details are in the supplementary material.

Conversion of Smenodiol (6) into the Acid 10. A crystal of p-toluenesulfonic acid was added to a solution of smenodiol (**6**, 5 mg) in dry benzene (10 mL), and the solution was boiled under reflux for 2 h. The cooled solution was washed with dilute sodium bicarbonate solution and dried over sodium sulfate, and the solvent was evaporated to obtain a quantitative yield of the ether **8**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38 (s, 2 H), 3.85 (s, 3 H), 2.63 (m, 2 H), 1.21 (s, 3 H), 0.94 (s, 3 H), 0.90 (s, 3 H), 0.89 (s, 3 H).

The ether **8**, which was used without purification, was dissolved in acetone (5 mL) to which dimethyl sulfate (5 mg) and potassium carbonate (5 mg) were added. The stirred solution was boiled under gentle reflux for 8 h. The cooled solution was evaporated and the residue was partitioned between dichloromethane (2 × 10 mL) and water (5 mL). The combined organic extracts were dried over sodium sulfate and the solvent evaporated to obtain a single product, the methyl ether **9**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, 1 H, J = 2 Hz), 7.34 (d, 1 H, J = 2 Hz), 3.88 (s, 3 H), 3.87 (s, 3 H), 2.65 (m, 2 H), 1.22 (s, 3 H), 0.89 (s, 3 H), 0.88 (s, 3 H), 0.84 (s, 3 H).

The methyl ether **9** was dissolved in 10% methanolic potassium hydroxide solution (5 mL) and the solution was boiled under gentle reflux for 12 h. The solvent was evaporated and the product was partitioned between dichloromethane (2 × 10 mL) and 1 N hydrochloric acid (5 mL). The combined organic extracts were washed with water and dried over sodium sulfate and the solvent was evaporated to obtain the acid **10** (4 mg, 80% theoretical): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, 1 H, J = 1 Hz), 7.40 (d, 1 H, J = 1 Hz), 3.89 (s, 3 H), 2.67 (m, 2 H), 1.24 (s, 3 H), 0.90 (s, 6 H), 0.84 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$ + CD_3OD) δ 167.8, 147.9, 146.7, 124.4, 122.2, 120.6, 109.7, 78.4, 55.7, 55.4, 51.3, 41.3, 40.3, 38.7, 36.5, 32.8, 32.7, 21.8, 21.0, 20.2, 19.3, 18.0, 14.4; EIMS, m/z 372 (34), 357 (15), 191 (100); HRMS, obsd m/z = 372.2289, $C_{22}H_{28}O_3$ requires m/z = 372.2300.

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Supplementary Material Available: Tables of fractional coordinates, bond distances, bond angles, and temperature factors for smenochromene A and ^{13}C NMR spectra for smenochromenes A–D and smenodiol (10 pages). Ordering information is given on any current masthead page.