Registry No. (±)-**3**, 72985-39-8; (-)-**3**, 73037-12-4; (+)-**3**, 73037-13-5; (±)-**4**, 72985-40-1; (+)-**4**, 73037-14-6; (-)-**4**, 73037-15-7; (±)-**5**, 73037-16-8; (+)-**5**, 36325-37-8; **7**, 41047-91-0; **8**, 72985-10-5; **9**, 72985-11-6; **10**, 54379-36-1; **11**, 72985-12-7; **12**, 72985-13-8; **13**, 72985-14-9; **14**, 72985-15-0; **15**, 72985-16-1; **16**, 72985-17-2; **17**, 72985-18-3; **18**, 610-72-0; **19**, 72985-19-4; **20**, 72985-20-7; **21**, 72985-21-8; **22**, 72985-22-9; **23**, 72985-23-0; **24**, 72985-24-1; **25**, 72985-25-2; **26**, 72985-26-3; **27**, 72985-27-4; **28**, 626-15-3; **29**, 22072-45-3; **30**, 28746-20-5; **31**, 5425-44-5; **32**, 53178-41-9; **33**, 72985-28-5; **34**, 72984-98-6; **35**, 72984-99-7; **36**, 72985-00-3; (±)-**37**, 72985-01-4; (+)-**37**, 73037-04-4; (±)-**38**, 72985-02-5; (-)-**38**, 73037-05-5; (±)-**39**, 73037-06-6; (-)-**39**, 73037-07-7; (-)-**40**, 72985-03-6; (±)-**41**, 72985-04-7; (+)-**41**, 73037-08-8; (±)-**42**, 73037-09-9; (-)-**42**, 73037-10-2; (-)-**43**, 73002-60-5; (±)-**44**, 72985-05-8; (-)-**44**, 73037-11-3.

Some Metabolites of the Marine Sponges *Smenospongia aurea* and *Smenospongia* (≡*Polyfibrospongia*) *echina*

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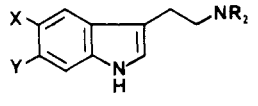
The antimicrobial metabolite of the marine sponge *Smenospongia aurea* was found to be 5-bromo-*N*,*N*-dimethyltryptamine (**4**). The same sponge also contained aureol (**6**), an unusual sesquiterpene–hydroquinone derivative. A second sample of *S. aurea* contained 8-epichromazonarol (**20**) and the indole **27**. Two samples of *Smenospongia echina* were examined and were shown to contain the antimicrobial constituent 5,6-dibromo-*N*,*N*-dimethyltryptamine (**3**), with small amounts of the phenol **25** in one sample. The structure of aureol (**6**) was determined by X-ray analysis while those of the remaining compounds were determined from spectroscopic data, particularly ^{13}C NMR spectra, and chemical interconversions.

A chemotaxonomic ideal is the assignment of a discrete class of secondary metabolites to a particular group of organisms, primarily at the genus level. Some marine sponges have been reported to contain so many different types of metabolites that they appear to defy chemotaxonomic classification. For example, *Disidea herbacea* has been reported to contain brominated phenols,[1] sesquiterpenes,[2] and some unusual chlorinated metabolites.[3] In this paper we will describe an unusual array of metabolites that have been isolated from *Smenospongia aurea* and *Smenospongia echina* (≡*Polyfibrospongia echina*), two closely related Caribbean sponges.

The sponge previously known as *Spongia fenestra* D + M or *Aplysina aurea* Hyatt has recently been reclassified as *Smenospongia aurea* (Hyatt).[4] Rützler[5] has suggested that *Polyfibrospongia echina* Laubenfels be reclassified as *Smenospongia echina* (Laubenfels). Chemical studies support Rützler's suggestion and furthermore provide evidence that *Polyfibrospongia maynardii* might also be reclassified as a *Smenospongia* species. Van Lear et al.[6] have reported the isolation of the antibacterial metabolites 5,6-dibromotryptamine (**1**) and 5,6-dibromo-*N*-methyltryptamine (**2**) from *P. maynardii*. We have isolated 5,6-dibromo-*N*,*N*-dimethyltryptamine (**3**) and 5-bromo-*N*,*N*-dimethyltryptamine (**4**) from *Smenospongia echina* and *S. aurea*, respectively.



1	R = H	X = Y = Br
2	R = H,Me	X = Y = Br
3	R = Me	X = Y = Br
4	R = Me	X = Br Y = H
5	R = Me	X = Y = H

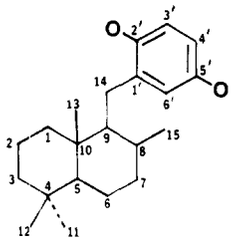
Shipboard antimicrobial screening of the Caribbean sponges *Smenospongia echina* and *Smenospongia aurea*, collected at Glover and Lighthouse Reefs, Belize, showed that the crude extracts inhibited the growth of *Staphylococcus aureus* and *Candida albicans*. Silica gel chromatography of the ethanol extract of *Smenospongia echina* gave 5,6-dibromo-*N*,*N*-dimethyltryptamine (**3**; 0.95% dry weight). The dibromoindole **3**, mp 113–115 °C, had the molecular formula $C_{12}H_{14}N_2Br_2$. The structure was deduced from the ^1H NMR spectrum which showed a six-proton singlet at δ 2.27 due to the *N*-methyl groups and signals at δ 2.59 (t, 2 H, J = 7 Hz) and 2.86 (t, 2 H, J = 7 Hz) for the side-chain methylene groups, at δ 7.18 (br s, 1 H) due to the proton at C-2, and at δ 7.70 (s, 1 H) and 7.86 (s, 1 H) due to protons at C-7 and C-4, respectively, of a 5,6-disubstituted indole. Exchange of the NH proton by deuterium caused the signal at δ 7.18 to sharpen as expected. Hydrogenation of the dibromoindole **3** gave *N*,*N*-dimethyltryptamine (**5**).[7]

Silica gel chromatography of the ethanol extract of *Smenospongia aurea* gave 5-bromo-*N*,*N*-dimethyltryptamine (**4**; 0.88% dry weight). The bromoindole **4**, mp 98–99 °C, had the molecular formula $C_{12}H_{15}N_2Br$ and was obviously related to the dibromoindole **3**. It also gave *N*,*N*-dimethyltryptamine (**5**) on hydrogenation. The

(1) Sharma, G. M.; Vig, B. *Tetrahedron Lett.* **1969**, 1715.
(2) Kazlauskas, R.; Murphy, P. T.; Wells, R. J. *Tetrahedron Lett.* **1978**, 4949. Charles, C.; Braekman, J. C.; Daloze, D.; Tursch, B.; Declercq, J. P.; Germain, G.; Van Meerssche, M. *Bull. Soc. Chim. Belg.* **1978**, *87*, 481.
(3) Hofheinz, W.; Oberhänsli, W. E. *Helv. Chim. Acta* **1977**, *60*, 660. Kazlauskas, R.; Lidgard, R. O.; Wells, R. J.; Vetter, W. *Tetrahedron Lett.* **1977**, 3183. Charles, C.; Braekman, J. C.; Daloze, D.; Tursch, B.; Karlsson, R. *Ibid.* **1978**, 1519. Kazlauskas, R.; Murphy, P. T.; Wells, R. J. *Ibid.* **1978**, 4945.
(4) Wiedenmayer, F. *Experientia, Suppl.* **1977**, *No. 28*, 69.
(5) Rützler, K., personal communication. This is a new combination based on Wiedenmayer's definition of the genus *Smenospongia*. Until this combination is published in a taxonomic monograph, it must be regarded as temporary, and both genera should be used to refer to this sponge, i.e., *Smenospongia* (≡*Polyfibrospongia*) *echina*.
(6) Van Lear, G. E.; Morton, G. O.; Fulmor, W. *Tetrahedron Lett.* **1973**, 299.
(7) "Merck Index", 8th ed; Merck: Rahway, NJ, 1968; p 379.

0022-3263/80/1945-1435$01.00/0

Table I. ^{13}C NMR Spectra (δ) of Compounds 6, 14, 15, 20, and 21

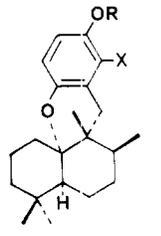


	6[a]	14[b]	15[b]	20[a]	21[a]
C_1	37.4	40.4	40.4	39.9	39.1
C_2	18.4	18.8	18.9	18.1	18.5
C_3	33.9	42.0	42.4	40.5	41.0
C_4	33.9	33.3	33.6	33.0	33.1
C_5	44.0	56.2	56.1	55.1	56.0
C_6	22.2	20.7	18.9	18.3	19.7
C_7	29.3	44.4	43.2	41.8	41.8
C_8	39.3	73.4	72.9	75.2	76.9
C_9	38.1	62.9	59.0	49.4	52.0
C_{10}	82.4	39.7	39.4	38.1	36.7
C_{11}	31.9	33.5	33.8	33.5	33.3
C_{12}	20.2	21.7	22.2	21.7	21.5
C_{13}	17.3	15.6	15.6	14.1	14.7
C_{14}	27.9	25.2	23.8	22.7	22.4
C_{15}	29.8	24.8	31.8	27.0	20.6
$C_{1'}$	122.2	134.8	135.0	123.3	123.2
$C_{2'}$	145.8	151.4	151.8	148.5	148.7
$C_{3'}$	117.2	118.1	117.2	117.3	117.3
$C_{4'}$	115.2	111.8	111.4	113.8	114.4
$C_{5'}$	148.2	154.5	154.5	148.2	146.6
$C_{6'}$	114.1	110.7	109.8	114.8	116.0

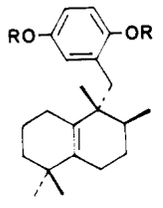
[a] $CDCl_3$. [b] C_6D_6.

position of the bromine atom at C-5 was determined by comparison of the aromatic proton signals in the ^1H NMR spectrum of **4** at δ 7.13 (d, 1 H, J = 7 Hz), 7.25 (d, 1 H, J = 7 Hz), and 7.70 (s, 1 H) with those of 5-bromoindole-3-carboxaldehyde at δ 7.37 (d, 1 H, J = 7 Hz), 7.51 (d, 1 H, J = 7 Hz), and 8.23 (s, 1 H) and 6-bromoindole-3-carboxaldehyde at δ 7.36 (d, 1 H, J = 7 Hz), 7.73 (s, 1 H), and 8.14 (d, 1 H, J = 7 Hz).[8]

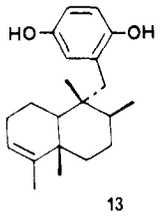
Less polar fractions from the chromatography of the ethanol extract of *S. aurea* contained aureol (**6**; 0.036% dry weight). Aureol (**6**), mp 144–144.5 °C, had the molecular formula $C_{21}H_{30}O_2$. The infrared spectrum contained a hydroxyl band at 3300 cm^{-1}. Acetylation of aureol (**6**) with acetic anhydride in pyridine gave a monoacetate **7** having an infrared band at 1760 cm^{-1}, typical of a phenolic acetate. The ^1H NMR spectrum of aureol (**6**) contained three aromatic proton signals at δ 6.62 (m, 2 H) and 6.50 (br s, 1 H), four methyl signals at δ 1.11 (d, 3 H, J = 7 Hz), 1.06 (s, 3 H), 0.92 (s, 3 H), and 0.78 (s, 3 H), and signals at δ 3.38 (d, 1 H, J = 16 Hz) and 1.96 (d, 1 H, J = 16 Hz) due to an isolated methylene group. These data led to the conclusion that aureol was a sesquiterpene hydroquinone ether, similar to chromazonarol (**21**)[9] but having a secondary methyl at C-8 and a methyl at C-9, resulting from rearrangement of the drimane skeleton. The ^{13}C NMR spectrum of aureol (Table I) supported this conclusion but the lack of methine signals above δ 44 implied that we were not dealing with a familiar carbon skeleton.



6 R = X = H
7 R = Ac X = H
8 R = Ac X = Br



9 R = Ac
10 R = H
11 R = Me (=12?)



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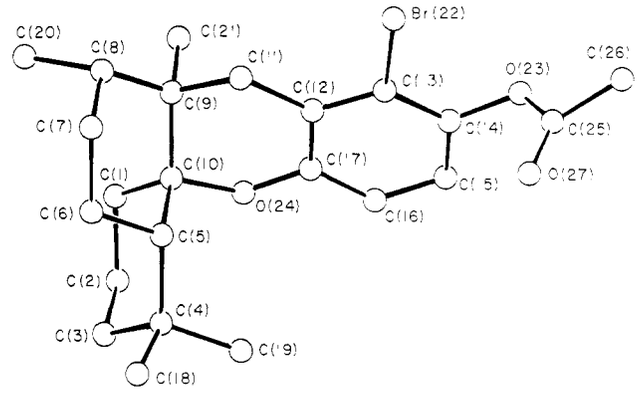


Figure 1. Computer-generated perspective drawing of bromoaureol acetate. The hydrogens are omitted for clarity.

The structure of aureol (**6**) was determined by X-ray diffraction analysis of the corresponding brominated acetate **8** prepared by treatment of aureol with bromine in carbon tetrachloride followed by acetylation of the bromophenol. Figure 1 is a computer-generated perspective drawing of the final X-ray model of bromoaureol acetate **8**. As can be seen, the structure can be formally dissected into a C_{15} sesquiterpene fragment and a brominated hydroquinone. The two cyclohexane rings of the sesquiterpene fragment are cis fused and are in the chair conformation. The absolute configurations are 5*S*, 8*S*, 9*R*, and 10*S* as would be expected if the biosynthesis of aureol (**6**) had involved axial migrations of the C-9 proton and the C-10 methyl of a drimane intermediate. The presence of a cis-fused decalin ring system explains the ^{13}C NMR spectrum which has been assigned on the basis of comparisons with model compounds (Table I).

As part of our chemical studies of aureol **6**, the compound was treated with boron trifluoride etherate in acetic anhydride to obtain diacetate **9**. The ^{13}C NMR spectrum of the diacetate **9** indicated the presence of an additional olefinic bond. The $\Delta^{5,10}$ olefinic bond was indicated by the absence of vinyl proton or vinyl methyl signals in the ^1H NMR spectrum. A similar carbon skeleton had been obtained from avarol by treatment of the corresponding dimethyl ether with hydrochloric acid in acetic acid.[10] In order to compare products, we reduced the diacetate **9** to the hydroquinone **10** with lithium aluminum hydride in ether and methylated the product with dimethyl sulfate–potassium carbonate in acetone. The dimethyl ether **11**,

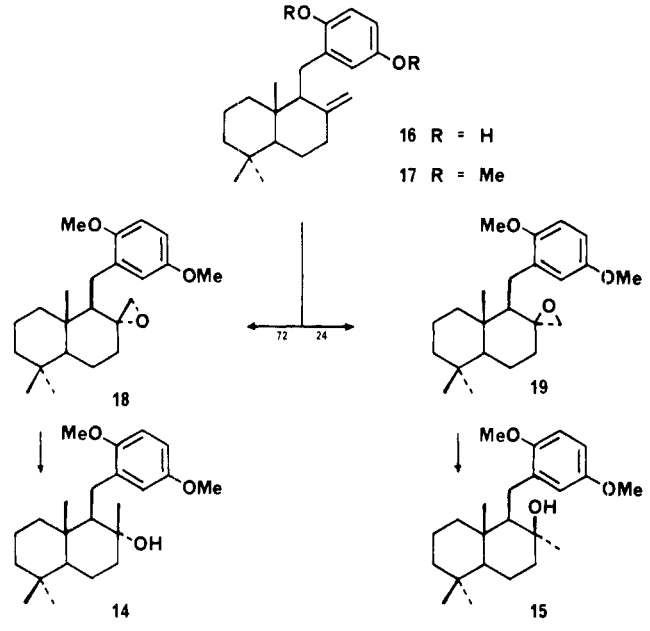
(8) Wratten, S. J.; Wolfe, M. S.; Andersen, R. J.; Faulkner, D. J. *Antimicrob. Agents Chemother.* **1977**, *11*, 411.

(9) Cimino, G.; De Stefano, S.; Minale, L. *Experientia* **1975**, *31*, 1117 and references cited therein.

(10) Minale, L.; Riccio, R.; Sodano, G. *Tetrahedron Lett.* **1974**, 3401.

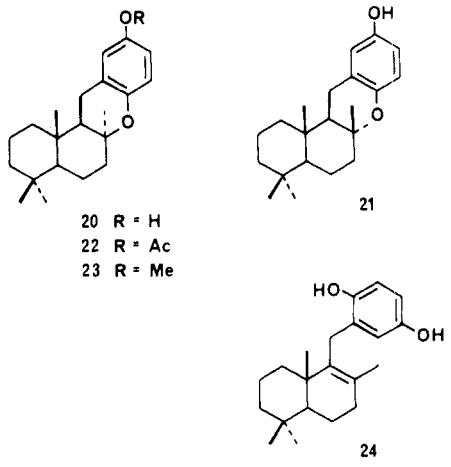
mp 73–73.5 °C, generated from aureol **6** was *not* identical with the dimethyl ether **12**, mp 58–60 °C, from avarol (**13**). We suspect that the two dimethyl ethers **11** and **12** differed in the stereochemistry at C-8, in which case the ^{13}C NMR analysis on which the stereochemistry of avarol **13** was based may not be correct.[11]

In order to determine whether ^{13}C NMR spectroscopy could be used to determine the stereochemistry at C-8 in other drimane derivatives, we synthesized the epimeric alcohols **14** and **15** from zonarol **16** by using the procedure



outlined by Ochi et al.,[12] who had obtained only the major alcohol **14**. Zonarol **16** was converted into its dimethyl ether **17** in 98% yield. Treatment of the dimethyl ether **17** with *m*-chloroperbenzoic acid in dichloromethane gave a mixture of two epoxides. The mixture was separated by LC to obtain the α-epoxide **18** in 72% yield and the β-epoxide **19** in 24% yield. The epoxides **18** and **19** were each reduced with lithium aluminum hydride in refluxing ether to obtain the alcohols **14** and **15** in quantitative yields. As expected, the 1,3-diaxial interaction experienced by the axial methyl group at C-8 in alcohol **14** caused the ^{13}C NMR signal for that methyl group to be 7 ppm upfield from the corresponding methyl signal in alcohol **15**.

These ^{13}C NMR data were directly applicable to the structural elucidation of 8-epichromazonarol (**20**), which was isolated (2.2% dry weight) from a second sample of *Smenospongia aurea*. 8-Epichromazonarol (**20**), mp 132–134 °C, had the molecular formula $C_{21}H_{30}O_2$ and, like chromazonarol (**21**),[9] formed a monoacetate, **22**, and a methyl ether, **23**. The ^1H NMR spectrum ($CDCl_3$) contained three aromatic proton signals at δ 6.57 (m, 3 H), which could be differentiated in C_6D_6 solution as signals at δ 6.36 (br d, 1 H, J = 8 Hz), 6.46 (br s, 1 H), and 6.84 (d, 1 H, J = 8 Hz), and four methyl singlets at δ 0.72, 0.82, 0.90, and 1.16. A major difference in the ^1H NMR spectra of chromazonarol[13] and 8-epichromazonarol was the appearance of the C-14 methylene proton signals: a doublet (2 H, J = 7 Hz) at δ 2.47 for chromazonarol (**21**) and the



AB portion of an ABX system at δ 2.72 (d, 1 H, J = 17 Hz) and 2.89 (dd, 1 H, J = 17, 7 Hz) for 8-epichromazonarol (**20**). The ^{13}C NMR spectra of chromazonarol and epichromazonarol were remarkably similar (Table I) with the exception of the C-15 methyl signals. The axial methyl group at C-8 in chromazonarol (δ 20.6) was 6.4 ppm upfield from the corresponding equatorial methyl group in 8-epichromazonarol (27.0). The chemical shifts of these methyl groups agree with predicted values based on alcohols **14** and **15** as model compounds.[14] The stereochemistry at C-8 in chromazonarol had not previously been established.[9]

In order to confirm this spectral assignment, we treated 8-epichromazonarol with boron tribromide in dichloromethane, a reagent known to cleave the *O*-alkyl bond in phenyl alkyl ethers.[15] This reaction gave at least six products from which only the hydroquinone **24** could be separated in pure form. The structure of the hydroquinone was based on interpretation of the ^1H NMR spectrum which contained a vinyl methyl signal at δ 1.54 but lacked a vinyl proton signal. The major fraction from chromatography of the reaction product was a 2:1 mixture of 8-epichromazonarol (**20**) and chromazonarol (**21**). The products were identified by comparison of the ^1H NMR spectrum of the mixture with spectra of authentic samples, and the identifications were confirmed by gas chromatographic comparison.

We recently obtained a sample of *Smenospongia echina* from Puerto Morelos, Mexico, that contained 5,6-dibromo-*N*,*N*-dimethyltryptamine (**3**; 0.88% dry weight) and a new phenol **25** (0.04% dry weight). The phenol **25** had the molecular formula $C_{23}H_{34}O_3$. The infrared (3600 cm^{-1}) and ultraviolet [291 nm (ϵ 4900)] spectra were characteristic of a phenol. The ^1H NMR spectrum contained two aromatic proton signals at δ 6.30 (d, 1 H, J = 3 Hz) and 6.35 (d, 1 H, J = 3 Hz), which were shifted to δ 6.32 and 6.38 in the corresponding acetate, and two methoxy signals at δ 3.74 and 3.84. Since the two aromatic protons must be meta to the hydroxyl and the aromatic ring cannot be symmetrically substituted, a 2-alkyl-4,6-dimethoxyphenol must be present.

We assumed that the remaining 15-carbon residue was of sesquiterpene origin since the ^1H NMR spectrum contained four methyl signals at δ 0.95 (d, J = 7 Hz), 1.3 (s), 1.63 (s), and 1.72 (s). The ^{13}C NMR spectrum contained signals at δ 122.6 (d), 123.1 (d), 137.4 (s), and 147.2 (s), indicating the presence of two trisubstituted olefinic bonds and implying that the sesquiterpene residue was mono-

(11) Cf.: de Rosa, S.; Minale, L.; Riccio, R.; Sodano, G. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1408. We hesitate to correct the stereochemistry of avarol on the basis of an apparent difference in physical data between two compounds that were both derived through acid-catalyzed rearrangements.

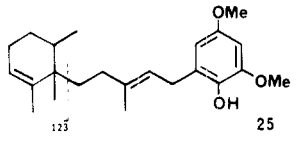
(12) Ochi, M.; Kotsuki, H.; Muraoka, K.; Tokoroyama, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 629.

(13) Measured on a sample of chromazonarol prepared from zonarol by the method of W. Fenical, personal communication.

(14) Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden: London, 1976; p 37.

(15) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1968; p 66.

cyclic. One olefinic proton signal at δ 5.32 (br t, 1 H, J = 7 Hz) was coupled to a benzylic methylene signal at 3.35 (d, 2 H, J = 7 Hz); this required that an isopentenyl unit be joined to the aromatic ring. Consideration of the spectral data led to the conclusion that the monocyclic ring system in the phenol **25** was the same as that in microcionin-2 **26**.[16] Both compounds have the same base peak



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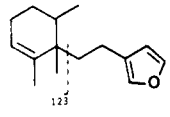

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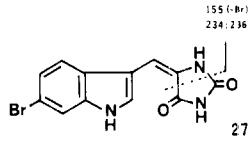

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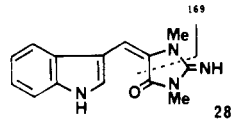

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(m/e 123) due to the cleavage shown, and the methyl signals in the ^{1}H NMR spectra are in good agreement. We are reluctant to assign the relative stereochemistry at the two asymmetric centers on the basis of spectral data[17] and were unable to pursue the question of stereochemistry since the phenol **25** was not amenable to selective oxidation.

The sample of *Smenospongia aurea* that contained 8-epichromazonarol (**20**) did not contain either of the brominated dimethyltryptamines. The only brominated compound to be isolated, albeit in small quantities, was the brominated indole **27**, mp >300 °C dec, that precipitated from the aqueous phase after solvent extraction had been completed. The bromoindole **26** had the molecular formula $C_{12}H_8N_3O_2Br$. Since we had encountered a brominated derivative of aplysinopsin (**28**)[18] elsewhere,[19] we were able to assign a structure from the spectral data without difficulty. The mass spectrum of the bromoindole **27** contained major fragment ions at m/e 155 and 234/236 resulting from the fragmentations shown. The ^{1}H NMR spectrum contained signals at δ 6.72 (s, 1 H), 7.26 (d, 1 H, J = 8 Hz), 7.63 (s, 1 H), 7.77 (d, 1 H, J = 8 Hz), and 8.16 (s, 1 H). Comparison of the three aromatic signals at δ 7.26, 7.63, and 7.77 with those of 5-bromoindole-3-carboxaldehyde and 6-bromoindole-3-carboxaldehyde (see above) and with those of a synthetic sample of 5-bromoaplysinopsin[19] led to the conclusion that the bromine atom was at C-6 on the indole ring.

These results are difficult to explain from a chemotaxonomic perspective. We have examined two samples of *S. aurea* and two of *S. echina*. Both samples of *S. aurea* contained closely related sesquiterpene phenols, but only one sample contained the brominated tryptamine **4** that we initially had expected to be a chemotaxonomic marker.[20] The other sample contained the brominated indole **26** that was closely related to compounds that we had previously found in *Dercitus* sp. The situation for *S. echina* is no less confusing: both samples contained the dibromotryptamine **3**, but only one sample contained a sesquiterpene phenol.

The sesquiterpene phenols have previously been found in other sponges of the other Dictyoceratida as well as in *Halichondria panicea* of the order Halichondrida and in brown algae of the order Dictyotales.[21] The brominated tryptamines have only been found in *Smenospongia* (or related species which may require reclassification) yet are not always found in every sample.[22] Since we must accept the taxonomist's identification of sponges, we must also accept that chemotaxonomic relationships are useful for the preliminary identification of a sponge but cannot be relied upon exclusively.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. Ultraviolet spectra were recorded on a Perkin-Elmer Model 124 double beam spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter using a 10-cm microcell. ^{1}H NMR spectra were recorded on a Varian HR-220 NMR spectrometer, and ^{13}C spectra were recorded on a Varian CFT-20 NMR spectrometer; all chemical shifts are reported with respect to Me_4Si (δ = 0). Low resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High resolution mass spectra were supplied by the Chemistry Department, U.C.L.A. Melting points were determined on a Fisher-Johns apparatus and are reported uncorrected. All solvents used were either spectral grade or distilled from glass prior to use.

Collection and Extraction. *Smenospongia echina* [reference no. 77-113] and two samples of *S. aurea*, [77-107] and [77-062], were collected by hand using SCUBA (-20 m) at Glover and Lighthouse Reefs, Belize, and were stored in ethanol prior to extraction. *S. echina* [79-019] was collected in a similar manner at Puerto Morelos, Mexico, and stored in ethanol. For each sample, the solvent was decanted and the sponge homogenized and Soxhlet extracted with ethanol. The extracts were evaporated, and the residue was partitioned between ethyl acetate (2 × 250 mL) and water (100 mL). The ethyl acetate extracts were dried over sodium sulfate, and the solvent was evaporated to yield dark brown oils: [77-113] 1.4 g (1.5% dry weight), [77-107] 4.9 g (2.4% dry weight), [77-062] 3.55 g (5.7% dry weight), [79-019] 3.1 g (1.24% dry weight).

5,6-Dibromo-*N,N*-dimethyltryptamine (3). The crude extract of *S. echina* [77-113] (1.4 g) was chromatographed on silica gel (200 g) by using eluants of increasing polarity from 30% ethyl acetate in hexane to 1% methanol in ethyl acetate. Fractions eluted with ethyl acetate contained 5,6-dibromo-*N,N*-dimethyltryptamine (**3**; 480 mg, 0.95% dry weight), which was crystallized from aqueous methanol: mp 113–115 °C; IR ($CHCl_3$) 3500–3100, 1450 cm^{-1}; UV (MeOH) 230 nm (ε 40 100), 285 (4900), 300 (3300); ^{1}H NMR (acetone-d_6) δ 2.27 (s, 6 H), 2.59 (t, 2 H, J = 7 Hz), 2.86 (t, 2 H, J = 7 Hz), 7.18 (br s, 1 H), 7.70 (s, 1 H), 7.86 (s, 1 H); ^{13}C NMR (C_6D_6) δ 139.6 (s), 131.6 (s), 127.5 (d), 125.5 (d), 119.0 (d and s), 116.1 (s), 115.2 (s), 62.9 (m), 47.3 (q, 2 C), 25.7 (m); mass spectrum, m/e (relative intensity) 348, 346, 344 (5), 290, 288, 286 (5), 266, 264 (5), 58 (100); high-resolution mass spectrum, found m/e 343.9525, $C_{12}H_{14}N_2{}^{79}Br_2$ requires m/e 343.9525.

5-Bromo-*N,N*-dimethyltryptamine (4) and Aureol (6). The crude extract of *S. aurea* [77-107] (1.0 g) was chromatographed on silica gel by using eluants of increasing polarity from hexane through ether and ethyl acetate to 10% methanol in ethyl acetate. Fractions eluted with ethyl acetate contained 5-bromo-*N,N*-dimethyltryptamine (**4**; 253 mg, 0.63% dry weight) which was crystallized from aqueous methanol: mp 98–99 °C; IR ($CHCl_3$) 3500–3200, 1475 cm^{-1}; UV (MeOH) 225 nm (ε 39 000), 285 (4400), 305 (2700); ^{1}H NMR (acetone-d_6) δ 2.34 (s, 6 H), 2.59 (t, 2 H, J = 7 Hz), 2.86 (t, 2 H, J = 7 Hz), 6.97 (br s, 1 H), 7.13 (d, 1 H, J = 7 Hz), 7.25 (d, 1 H, J = 7 Hz), 7.70 (s, 1 H); ^{13}C NMR (C_6D_6) δ 139.0 (s), 132.7 (s), 127.5 (d), 127.3 (d), 124.1 (d), 116.4 (d and

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(17) Reexamination of the published[16] LIS data for the microcionin-2 epoxides using a semiquantitative analysis method led us to conclude that the data did not clearly define the stereochemistry of microcionin-2.

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(21) Minale, L. In "Marine Natural Products: Chemical and Biological Perspectives"; Scheuer, P. J., Ed.; Academic Press: New York, 1977; Vol. 1, pp 218–32.

(22) It is possible that the brominated metabolites were produced by symbionts, such as cyanophytes, that are specific to a particular sponge but cannot live when the sponge occupies a shaded cryptic habitat.

s), 115.2 (s), 63.0 (m), 47.3 (q, 2 C), 25.9 (m); mass spectrum, *m/e* (relative intensity) 268, 266 (5), 188 (10), 58 (100); high-resolution mass spectrum, found *m/e* 266.0417, $C_{12}H_{15}N_2{}^{79}Br$ requires *m/e* 266.0419. Fractions eluted with 10% ether in hexane contained aureol (**6**; 400 mg, 1.67% dry weight), which was crystallized from hexane: mp 144–144.5 °C; $[\alpha]_D$ +65° (*c* 2.0, CCl_4); IR (CCl_4) 3300, 1490, 1450, 950 cm^{-1}; UV (MeOH) 299 nm (ε 3100), 216 (4600); (MeOH + OH^-) 302 nm (ε 2700), 227 (5000); ^1H NMR ($CDCl_3$) 0.78 (s, 3 H), 0.92 (s, 3 H), 1.06 (s, 3 H), 1.11 (d, 3 H, *J* = 7 Hz), 1.96 (d, 1 H, *J* = 16 Hz), 3.38 (d, 1 H, *J* = 16 Hz), 6.50 (br s, 1 H), 6.62 (m, 2 H); ^{13}C NMR ($CDCl_3$) 148.2 (s), 145.8 (s), 122.2 (s), 117.2 (d), 115.2 (d), 114.2 (d), 82.4 (s), 44.0 (d), 39.3 (d), 38.1 (s), 37.4 (t), 33.9 (t, s), 31.9 (q), 29.8 (q), 29.3 (t), 27.9 (t), 22.2 (t), 20.2 (q), 18.4 (t), 17.3 (q); high-resolution mass spectrum, found *m/e* 314.2241, $C_{21}H_{30}O_2$ requires *m/e* 314.2246.

8-Epichromazonarol (20) and Bromoindole 27. The crude extract of *S. aurea* [77-062] (1.0 g) was preadsorbed onto silica gel and chromatographed on a column (65 cm × 3 cm diameter) of silica gel with 10% ether in hexane as eluant to obtain 8-epichromazonarol (**20**) as a white solid (391 mg, 2.2% dry weight) that was recrystallized from aqueous methanol: mp 132–134 °C; $[\alpha]_D$ −2° (*c* 1.0, CCl_4); IR (CCl_4) 3400 cm^{-1}; UV (MeOH) 300 nm (ε 3100), 210 (16200); (MeOH + OH^-) 305 nm (ε 3200); ^1H NMR ($CDCl_3$) δ 0.72 (s, 3 H), 0.82 (s, 3 H), 0.90 (s, 3 H), 1.16 (s, 3 H), 2.72 (d, 1 H, *J* = 17 Hz), 2.89 (dd, 1 H, *J* = 17, 7 Hz), 4.75 (br s, 1 H, OH), 6.57 (m, 3 H); ^1H NMR (C_6D_6) δ 0.79 (s, 3 H), 0.87 (s, 3 H), 0.88 (s, 3 H), 1.06 (s, 3 H), 2.50 (d, 1 H, *J* = 17 Hz), 2.68 (dd, 1 H, *J* = 17, 7 Hz), 4.13 (br s, 1 H, OH), 6.36 (br d, 1 H, *J* = 8 Hz), 6.46 (br s, 1 H), 6.84 (d, 1 H, *J* = 8 Hz); ^{13}C NMR (C_6D_6) δ 148.5 (s), 148.2 (s), 123.3 (s), 117.3 (d), 114.7 (d), 113.8 (d), 75.2 (s), 55.1 (d), 49.4 (d), 41.7 (t), 40.5 (t), 39.9 (t), 38.1 (s), 33.5 (q), 33.0 (s), 27.0 (q), 22.7 (t), 21.7 (q), 18.3 (t), 18.1 (t), 16.1 (q); mass spectrum, *m/e* (relative intensity) 314 (45), 299 (10), 191 (100), 176 (35), 161 (55); high-resolution mass spectrum, found *m/e* 314.2250, $C_{21}H_{30}O_2$ requires *m/e* 314.2246. The bromoindole **27** precipitated from the aqueous phase that had been standing for several days at room temperature: yield 102 mg (0.16% dry weight); mp >300 °C dec; IR ($CHCl_3$) 3500–3100, 1670, 1600 cm^{-1}; UV (MeOH) 360 nm (ε 13400); ^1H NMR (Me_2SO-d_6) δ 6.72 (s, 1 H), 7.26 (d, 1 H, *J* = 8 Hz), 7.63 (s, 1 H), 7.77 (d, 1 H, *J* = 8 Hz), 8.16 (s, 1 H); mass spectrum, *m/e* (relative intensity) 307, 305 (90), 236, 234 (40), 210, 208 (20), 155 (100), 128 (50); high-resolution mass spectrum, found *m/e* 306.9804, $C_{12}H_8{}^{81}BrO_2N_3$ requires *m/e* 306.9799.

Chromatography of *S. echina* [79-019]. The crude extract (3.1 g) was chromatographed on a column (55 cm × 3 cm diameter) of silica gel with eluants of increasing polarity from hexane through ether and ethyl acetate to 20% methanol in ethyl acetate. Material eluted with 5% ether in hexane was rechromatographed on silica gel to obtain the phenol **25** (90 mg, 0.04% dry weight) as an oil: $[\alpha]^{20}_D$ + 3.3° (*c* 0.6, CCl_4); IR (CCl_4) 3600, 1620, 1500, 1465, 1055 cm^{-1}; UV (MeOH) 293 nm (ε 2900), 212 (15000); (MeOH + OH^-) 309 nm (ε 3000); ^1H NMR ($CDCl_3$) δ 0.95 (d, 3 H, *J* = 7 Hz), 1.03 (s, 3 H), 1.63 (br s, 3 H), 1.72 (br s, 3 H), 3.35 (d, 2 H, *J* = 7 Hz), 3.74 (s, 3 H), 3.84 (s, 3 H), 5.32 (br t, 1 H, *J* = 7 Hz), 5.39 (br t, 1 H, *J* = 7 Hz), 6.30 (d, 1 H, *J* = 3 Hz), 6.35 (d, 1 H, *J* = 3 Hz); ^{13}C NMR (C_6D_6) δ 153.6 (s), 147.4 (s), 147.2 (s), 139.4 (s), 138.2 (s), 137.4 (s), 123.1 (d), 122.6 (d), 105.9 (d), 97.5 (d), 55.3 (q, 2 C), 39.9 (s), 38.1 (d), 36.3 (t), 35.1 (t), 28.8 (t), 27.9 (t), 26.6 (q), 24.4 (t), 19.8 (q), 16.3 (q), 16.1 (q); high-resolution mass spectrum, found *m/e* 358.2542, $C_{23}H_{34}O_3$ requires *m/e* 358.2539. Fractions eluted with ethyl acetate gave 5,6-dibromo-*N,N*-dimethyltryptamine (**3**; 2.2 g, 0.88% dry weight) identical in all respects with material isolated previously.

***N,N*-Dimethyltryptamine (5).** A solution of the dibromoindole **3** (15 mg, 0.04 mmol) in anhydrous methanol (3 mL) containing 10% palladized charcoal (5 mg) was stirred under an atmosphere of hydrogen for 18 h. The catalyst was removed by filtration and the solvent evaporated to obtain *N,N*-dimethyltryptamine (**5**) in quantitative yield: mp 42–45 °C (lit.[7] mp 44.6–46.8 °C).

The same procedure was applied to the bromoindole **4** to also afford *N,N*-dimethyltryptamine (**5**) in quantitative yield.

Aureol Acetate 7. A solution of aureol (**6**; 25 mg, 0.08 mmol) in acetic anhydride (1 mL) and pyridine (2 mL) was allowed to stand at room temperature for 18 h. The solvents were removed in vacuo, and the residue was partitioned between ether (2 × 10 mL) and water (10 mL). The ether extracts were dried over sodium sulfate, and the solvent was evaporated to obtain the acetate **7** (26 mg, 92% of theoretical yield) as an oil: IR ($CHCl_3$) 1760, 1490, 1360, 960 cm^{-1}; UV (MeOH) 279 nm (ε 3000), 225 (7000), 202 (12500); ^1H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.91 (s, 3 H), 1.06 (s, 3 H), 1.10 (d, 3 H, *J* = 7 Hz), 1.99 (d, 1 H, *J* = 16 Hz), 2.25 (s, 3 H), 3.42 (d, 1 H, *J* = 16 Hz), 6.72 (m, 3 H); ^{13}C NMR (C_6D_6) 172.6, 149.6, 146.0, 122.1, 122.0, 120.3, 117.2, 82.9, 44.4, 39.5, 38.1, 37.5, 34.2, 34.0, 32.0, 30.1, 29.6, 28.0, 22.4, 20.6, 20.1, 18.7, 17.4; high-resolution mass spectrum, found *m/e* 356.2352, $C_{23}H_{32}O_3$ requires *m/e* 356.2351.

Bromoaureol Acetate 8. A solution of bromine in carbon tetrachloride was added dropwise to a solution of aureol (**6**; 30 mg, 0.1 mmol) in carbon tetrachloride (5 mL) until the red-brown color remained for 30 min. Excess bromine and hydrogen bromide were removed in a stream of nitrogen, and the solvent was removed. The residue was dissolved in acetic anhydride (0.5 mL) and pyridine (1.0 mL), and the solution was kept at room temperature for 18 h. The solvent was evaporated and the residue partitioned between ether (2 × 10 mL) and water (10 mL). The ether extract was dried over sodium sulfate and the solvent evaporated to obtain the acetate **8** (40 mg, 96% of theoretical yield) which was crystallized from acetone/water: mp 146–146.5 °C; IR (CCl_4) 1755 cm^{-1}; UV (MeOH) 310 nm (ε 7000), 231 (10000); ^1H NMR ($CDCl_3$) 0.78 (s, 3 H), 0.91 (s, 3 H), 1.01 (s, 3 H), 1.11 (d, 3 H, *J* = 7 Hz), 2.19 (d, 1 H, *J* = 15 Hz), 2.32 (s, 3 H), 3.16 (br d, 1 H, *J* = 15 Hz), 6.72 (d, 1 H, *J* = 7 Hz), 6.89 (d, 1 H, *J* = 7 Hz); high-resolution mass spectrum, found *m/e* 436.1477, $C_{23}H_{31}{}^{81}BrO_3$ requires *m/e* 436.1457.

Diacetate 9. Boron trifluoride etherate (1 drop) was added to a solution of aureol (**6**; 30 mg, 0.1 mmol) in acetic anhydride (3 mL), and the mixture was stirred at room temperature for 3 h. The product was poured into water (10 mL) and extracted with ether (20 mL). The ether extract was washed with water (3 × 50 mL) and dried over sodium sulfate, and the solvent was evaporated to yield the diacetate **9** (32 mg) as an oil: IR (CCl_4) 1755 cm^{-1}; UV (MeOH) 265 nm (ε 1100), 257 (1300); ^1H NMR ($CDCl_3$) δ 0.78 (d, 3 H, *J* = 7 Hz), 0.93 (s, 3 H), 0.99 (s, 3 H), 1.00 (s, 3 H), 2.24 (s, 3 H), 2.32 (s, 3 H), 2.62 (s, 2 H), 6.91 (dd, 1 H, *J* = 8, 2 Hz), 7.01 (d, 1 H, *J* = 8 Hz), 7.18 (d, 1 H, *J* = 2 Hz); ^{13}C NMR (C_6D_6) δ 168.4 (2 C), 146.4, 146.1, 137.4, 133.5, 132.9, 124.0, 123.2, 119.8, 42.0, 40.1, 35.2, 34.7, 34.1, 28.4, 28.2, 27.3, 26.6, 24.4, 22.4, 20.3 (3 C), 16.4; high-resolution mass spectrum, found *m/e* 356.2320, $C_{23}H_{32}O_3$ ($M^+ - CH_2CO$) requires *m/e* 356.2351.

Hydroquinone 10. Lithium aluminum hydride (20 mg) was added to a solution of the diacetate (30 mg, 0.09 mmol) in dry ether (5 mL), and the solution was stirred at room temperature for 20 min. Excess reagent was destroyed by dropwise addition of water (**Caution**!) followed by 1 N hydrochloric acid (several drops). The ether layer was separated, washed with water (5 mL), and dried over sodium sulfate, and the solvent was evaporated to obtain an oil. The oil was chromatographed on a preparative silica gel TLC plate with 1:1 ether–hexane as eluant to obtain the hydroquinone **10** (14 mg, 59% of theoretical yield): IR (CCl_4) 3400 cm^{-1}; UV (MeOH) 299 nm (ε 5000), 220 (5000); ^1H NMR ($CDCl_3$) 0.84 (d, 3 H, *J* = 7 Hz), 0.98 (s, 3 H), 0.99 (s, 3 H), 1.04 (s, 3 H), 2.49 (d, 1 H, *J* = 15 Hz), 2.94 (d, 1 H, *J* = 15 Hz), 4.38 (OH), 4.90 (OH), 6.55 (dd, 1 H, *J* = 8, 3 Hz), 6.66 (d, 1 H, *J* = 3 Hz), 6.68 (d, 1 H, *J* = 8 Hz).

Dimethyl Ether 11. Dimethyl sulfate (20 mg) was added to a solution of the hydroquinone **10** (20 mg, 0.07 mmol) in dry acetone (8 mL) containing potassium carbonate (5 mg), and the mixture was heated under reflux for 36 h. The solvent was evaporated and the residue partitioned between ether (20 mL) and 20% aqueous ammonia (10 mL). The ether extracts were washed with water (20 mL) and dried over sodium sulfate, and the solvent was evaporated to obtain the dimethyl ether **11** (18 mg, 83% of theoretical yield) which was crystallized from hexane: mp 73–73.5 °C; UV (MeOH) 301 nm (ε 4500), 222 (5500); ^1H NMR ($CDCl_3$) 0.78 (d, 3 H, *J* = 7 Hz), 0.92 (s, 3 H), 0.99 (s, 3 H), 1.00 (s, 3 H), 2.02 (m, 4 H), 2.61 (d, 1 H, *J* = 15 Hz), 2.92 (d, 1 H, *J* = 15 Hz), 3.72 (s, 3 H), 3.74 (s, 3 H), 6.66 (dd, 1 H, *J* = 9, 3 Hz), 6.75 (d, 1 H, *J* = 9 Hz), 6.85 (d, 1 H, *J* = 3 Hz); high-resolution mass spectrum, found *m/e* 342.2535, $C_{23}H_{34}O_2$ requires *m/e* 342.2559.

Dimethyl Ether of Zonarol. Zonarol[23] (316 mg, 1.0 mmol) was added to a solution of dimethyl sulfate (190 mg, 1.5 mmol) in acetone (15 mL) containing anhydrous potassium carbonate (1 g). The mixture was heated under reflux for 4 h and cooled, and the acetone was evaporated. The residue was partitioned between ether (30 mL) and water (30 mL). The ether layer was washed with water (2 × 10 mL) and dried over sodium sulfate, and the solvent was evaporated to obtain the dimethyl ether **17** (320 mg, 98% of theoretical yield): ^{1}H NMR ($CDCl_3$) δ 0.81 (s, 3 H), 0.84 (s, 3 H), 0.89 (s, 3 H), 2.75 (d, 2 H, J = 8 Hz), 3.74 (s, 3 H), 3.80 (s, 3 H), 4.61 (br s, 1 H), 4.74 (br s, 1 H), 6.62 (dd, 1 H, J = 8, 3 Hz), 6.74 (d, 1 H, J = 3 Hz), 6.75 (d, 1 H, J = 8 Hz); mass spectrum, m/e 342.

Epoxides 18 and 19. *meta*-Chloroperbenzoic acid (50 mg, 0.28 mmol) was added to a solution of the dimethyl ether **17** (86 mg, 0.25 mmol) in dichloromethane (7 mL), and the mixture was stirred at room temperature for 1 h. The solution was washed with saturated sodium bicarbonate solution (3 × 5 mL) and dried over sodium sulfate, and the solvent was evaporated to yield a mixture of epoxides **18** and **19**. The epoxides were separated by LC on μ-Porasil with 8% ether in hexane as eluant; the minor epoxide **19** had a shorter retention time.

Epoxide 18: 65 mg (72% of theoretical yield); ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 3 H), 0.87 (s, 3 H), 0.92 (s, 3 H), 2.56 (m, 2 H), 2.84 (m, 1 H), 3.75 (s, 3 H), 3.77 (s, 3 H), 6.62 (dd, 1 H, J = 8, 3 Hz), 6.72 (d, 1 H, J = 8 Hz), 6.80 (d, 1 H, J = 3 Hz).

Epoxide 19: 22 mg (24% of theoretical yield); ^{1}H NMR ($CDCl_3$) δ 0.89 (s, 3 H), 0.92 (s, 3 H), 1.02 (s, 3 H), 2.14 (d, 1 H, J = 4 Hz), 2.34 (m, 2 H), 2.58 (d, 1 H, J = 4 Hz), 3.77 (s, 6 H), 6.64 (dd, 1 H, J = 8, 3 Hz), 6.74 (d, 1 H, J = 8 Hz), 6.75 (d, 1 H, J = 3 Hz).

Alcohols 14 and 15. Lithium aluminum hydride (20 mg) was added to a solution of the epoxide **18** (40 mg, 0.11 mmol) in dry ether (10 mL), and the reaction mixture was heated under reflux for 20 min. Hydrochloric acid (5%) was added dropwise to the cooled solution (**Caution!**) to destroy excess reagent. The ether layer was separated and dried over sodium sulfate, and the solvent was evaporated to obtain alcohol **14** (40 mg, quantitative); ^{1}H NMR ($CDCl_3$) δ 0.80 (s, 3 H), 0.85 (s, 3 H), 0.90 (s, 3 H), 1.28 (s, 3 H), 2.54 (dd, 1 H, J = 15, 4 Hz), 2.89 (dd, 1 H, J = 15, 6 Hz), 3.75 (s, 3 H), 3.82 (s, 3 H), 6.66 (dd, 1 H, J = 8, 3 Hz), 6.78 (d, 1 H, J = 8 Hz), 6.83 (d, 1 H, J = 3 Hz); ^{13}C NMR (Table I); high-resolution mass spectrum, found m/e 360.2634, $C_{23}H_{36}O_3$ requires m/e 360.2664.

Under the same reaction conditions, epoxide **19** (16 mg, 0.045 mmol) was reduced to alcohol **15** (16 mg, quantitative): ^{1}H NMR ($CDCl_3$) δ 0.86 (s, 3 H), 0.89 (s, 3 H), 0.90 (s, 3 H), 1.07 (s, 3 H), 2.52 (br d, 1 H, J = 15 Hz), 2.97 (dd, 1 H, J = 15, 7 Hz), 3.77 (s, 3 H), 3.80 (s, 3 H), 6.65 (dd, 1 H, J = 8, 3 Hz), 6.75 (d, 1 H, J = 8 Hz), 6.82 (d, 1 H, J = 3 Hz); ^{13}C NMR (Table I); high-resolution mass spectrum, found m/e 360.2665, $C_{23}H_{36}O_3$ requires m/e 360.2664.

8-Epichromazonarol Acetate 22. 8-Epichromazonarol (20 mg, 0.06 mmol) was dissolved in acetic anhydride (1 mL) and pyridine (2 mL), and the solution was stirred at room temperature for 16 h. The solvents were evaporated to obtain the monoacetate **22** (22 mg, 98% of theoretical yield) as a pale green oil: IR (CCl_4) 1760, 1140 cm^{-1}; UV (MeOH) 287 nm (ϵ 4400), 212 (17 600); ^{1}H NMR ($CDCl_3$) δ 0.70 (s, 3 H), 0.82 (s, 3 H), 0.88 (s, 3 H), 1.16 (s, 3 H), 2.25 (s, 3 H), 2.72 (d, 1 H, J = 17 Hz), 2.93 (dd, 1 H, J = 17, 7 Hz), 6.72 (s, 1 H), 6.77 (m, 2 H); mass spectrum, m/e (relative intensity) 356 (70), 341 (5), 314 (100), 191 (55), 175 (15), 161 (30); high-resolution mass spectrum, found m/e 356.2341, $C_{23}H_{32}O_3$ requires m/e 356.2351.

8-Epichromazonarol Methyl Ether 23. 8-Epichromazonarol (20 mg, 0.06 mmol) and methyl iodide (2 mL) were added to a suspension of potassium carbonate (15 mg) in dry acetone (10 mL), and the mixture was boiled under reflux for 16 h. The cooled product was poured into water (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with water and dried over sodium sulfate, and the solvent was evaporated to obtain the methyl ether **23** (18 mg, 87% of theoretical yield) as an oil: IR ($CHCl_3$) 1140, 1120, 1040 cm^{-1}; UV (MeOH) 300 nm (ϵ 3900), 210 (19 000); ^{1}H NMR ($CDCl_3$) 0.73 (s, 3 H), 0.84 (s, 3 H), 0.91 (s, 3 H), 1.18 (s, 3 H), 2.75 (d, 1 H, J = 17 Hz), 2.93 (dd, 1 H, J = 17, 7 Hz), 3.77 (s, 3 H), 6.61 (s, 1 H), 6.68 (s, 2 H); mass spectrum, m/e (relative intensity) 328 (100), 313 (5), 191 (35), 175 (25), 137 (35); high-resolution mass spectrum, found m/e 328.2417, $C_{22}H_{32}O_2$ requires 328.2402.

Treatment of 8-Epichromazonarol (20) with Boron Tribromide. Boron tribromide (75 mg) in dry dichloromethane (10 mL) was added dropwise to a cooled solution of 8-epichromazonarol (**20**; 50 mg, 0.16 mmol) in dry dichloromethane (15 mL), and the reaction mixture was stirred at −78 °C for 30 min and at 25 °C for 18 h. The solution was poured into water (20 mL) and the organic phase separated. The aqueous phase was extracted with ether (2 × 20 mL), the combined organic extracts were dried over sodium sulfate, and the solvent was evaporated to obtain a glass (49 mg). The glass was chromatographed on a column (30 cm × 1.5 cm diameter) of silica gel with 30% ether in hexane as eluant to obtain three fractions: an unidentified mixture of at least three compounds, a 2:1 mixture of 8-epichromazonarol (**20**) and chromazonarol (**21**) (22 mg, 44% of theoretical yield), and the hydroquinone **24** (9 mg, 18% of theoretical yield). The 2:1 mixture of chromazonarols was compared with chromazonarol (**21**) and 8-epichromazonarol (**20**) by gas chromatography on a 6 ft × 2 mm column of 3% SP 2250 on 100–120 mesh Supelcoport at 230 °C; the retention time of 8-epichromazonarol was 11 min and that of chromazonarol was 18.4 min. The hydroquinone **24** was obtained as an oil: IR ($CHCl_3$) 3600, 1660, 1150 cm^{-1}; UV (MeOH) 295 nm (ϵ 3600), 210 (21 000); ^{1}H NMR ($CDCl_3$) 0.84 (s, 3 H), 0.90 (s, 3 H), 1.00 (s, 3 H), 1.54 (s, 3 H), 3.32 (br s, 2 H), 4.38 (s, 1 H, OH), 4.88 (s, 1 H, OH), 6.59 (m, 3 H); mass spectrum, m/e (relative intensity) 314 (20), 297 (10), 191 (100), 176 (20), 161 (35); high-resolution mass spectrum, found m/e 314.2248, $C_{21}H_{30}O_2$ requires m/e 314.2246.

Acetylation of Phenol 25. A solution of the phenol **25** (2 mg) in acetic anhydride (0.25 mL) and pyridine (0.5 mL) was allowed to stand for 4 h. The solvent was evaporated to obtain an acetate (2 mg): IR (CCl_4) 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 3 H, J = 7 Hz), 1.02 (s, 3 H), 1.62 (br s, 3 H), 1.68 (br s, 3 H), 2.29 (s, 3 H), 3.19 (d, 2 H, J = 7 Hz), 3.77 (s, 3 H), 3.79 (s, 3 H), 5.21 (br t, 1 H, J = 7 Hz), 5.39 (br t, 1 H, J = 7 Hz), 6.32 (d, 1 H, J = 2 Hz), 6.38 (d, 1 H, J = 2 Hz); mass spectrum, m/e 400 (M^+).

Single-Crystal X-ray Analysis. A platelike crystal with dimensions 0.4 × 0.4 × 0.15 mm was chosen for further work. Preliminary X-ray photographs showed monoclinic symmetry and accurate cell constants, as determined by a least-squares fit of 15 diffractometer-measured 2θ values, were a = 8.545 (3), b = 10.639 (5), and c = 11.994 (5) Å and β = 100.42 (3)°. Systematic extinctions ($0k0$ absent if $k = 2n + 1$), crystal density (1.35 g cm^{-3}), and the presence of chirality were uniquely accommodated by space group $P2_1$ with two molecules of $C_{23}H_{31}BrO_3$ per unit cell. All unique diffraction maxima with $2\theta \leq 50°$ were collected on a computer-controlled four-circle diffractometer using graphite monochromated Mo Kα (0.710 69 Å) radiation and a variable-speed ω-scan technique. Of the 2002 reflections surveyed in this fashion, 1817 (91%) were judged observed [$|F_o| \geq 3\sigma(F)$] after correcting for Lorentz, polarization, and background effects.[24] No crystal decomposition was detected by periodically monitoring check reflections.

A phasing model was achieved by standard heavy-atom procedures. The deconvolution of the Patterson synthesis gave a trial Br position. The false mirror symmetry of the resulting Br-phased electron density synthesis was broken by carefully selecting a connected eight-atom fragment and using this fragment plus the Br to recompute an electron density synthesis. Continuation of this procedure eventually gave all 27 nonhydrogen atoms in the asymmetric unit. Block-diagonal least-squares refinements of positional and isotropic thermal parameters were

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followed by the calculation of a difference electron density synthesis which revealed most of the hydrogen atom positions. Full-matrix least-squares refinements in which the positional and anisotropic thermal parameters of the nonhydrogen atoms were varied and the anomalous contribution of the Br (2.6 electrons) was included have converged to a standard crystallographic residual of 0.063 for the structure and 0.071 for its enantiomer. (See supplementary material for additional crystallographic details.)

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Registry No. 3, 72853-80-6; 4, 17274-65-6; 5, 61-50-7; 6, 72853-81-7; 7, 72853-82-8; 8, 72853-83-9; 9, 72853-84-0; 10, 72853-85-1; 11, 72853-86-2; 12, 72853-87-3; 14, 69809-39-8; 15, 72866-02-5; 16, 39707-54-5; 17, 69880-60-0; 18, 69809-38-7; 19, 72903-64-1; 20, 72937-17-8; 21, 57291-88-0; 22, 72903-65-2; 23, 72853-88-4; 24, 72853-89-5; 25, 72853-90-8; 25 acetate, 72853-91-9; 27, 72853-92-0.

Supplementary Material Available: Positional and thermal parameters (Table 1), bond distances (Table 2), and bond angles (Table 3) (5 pages). Ordering information is given on any current masthead page.

Tulirinol, an Antifeedant Sesquiterpene Lactone for the Gypsy Moth Larvae from *Liriodendron tulipifera*

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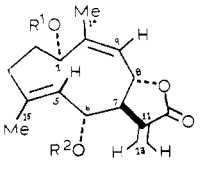
The isolation and structure determination of tulirinol (1), an antifeedant for the gypsy moth larvae from the leaves of *Liriodendron tulipifera* L., are reported. Tulirinol is the first recognized *trans*-4,*cis*-9-cyclodecadiene sesquiterpene, details of which are given for its characterization by spectral methods including X-ray crystallography. The absolute stereochemistry was determined by the Horeau partial resolution method. Tatridin A was identified as deacetyltulirinol (5).

The leaves of *Liriodendron tulipifera* L. (Magnoliaceae), commonly known as the tulip poplar, gave an ethanolic extract that inhibited the feeding of gypsy moth larvae, *Lymantria dispar* L.[2] Systematic fractionation of the extract has already yielded three feeding-deterrent sesquiterpene lactones: lipiferolide, epitulipinolide diepoxide,[3] and peroxyferolide.[4] This report is on the isolation and characterization of a fourth antifeedant, tulirinol (1), by spectral and chemical methods, including X-ray crystallography.

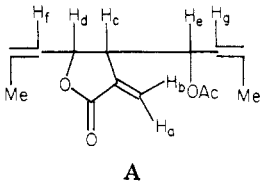
Tulirinol (1), mp 204–6 °C, was isolated by extensive



1; R^1 = H, R^2 = Ac
2; R^1 = R^2 = Ac
5; R^1 = R^2 = H
6; R^1 = PhCH(Et)CO, R^2 = Ac

chromatography of a partition fraction by monitoring biological activity at each stage of purification.[5] The molecular formula, $C_{17}H_{22}O_5$, was established by elemental analysis and mass spectrometry. The IR spectrum showed absorptions for hydroxyl, two carbonyls, a lactone (1768 cm^{-1}), and an ester (1738 cm^{-1}), while the UV spectrum had a low-wavelength peak at λ_{max} 208 nm (log ϵ 4.33) typical of an α-methylene γ-lactone. The ^1H NMR spectrum was most informative, exhibiting two weakly split olefinic methyl peaks at δ 1.81 and 1.91, and a three-proton singlet at δ 2.05 assignable to an acetate methyl. At low field, a pair of doublets with additional fine splitting (J = 0.6 Hz) were located at δ 5.72 (J = 3.1 Hz) and 6.07 (J = 3.4 Hz), which are characteristic of γ-lactone α-methylene protons.

Double-resonance experiments allowed for the ordering of all functional groups except the hydroxyl. Irradiation at either of the two exocyclic olefinic proton frequencies caused collapse of the geminal coupling (0.6 Hz) in the other and a change in a multiplet at δ 3.08 (H_c) from a triple triplet to a split triplet. These protons, H_a, H_b, and H_c, could be arranged as in A. Irradiation at δ 3.08 col-



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(5) Tulirinol showed a significant feeding inhibitory activity.[2] At concentrations of 50 and 250 μg/mL feeding was 69 and 53%, respectively.

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