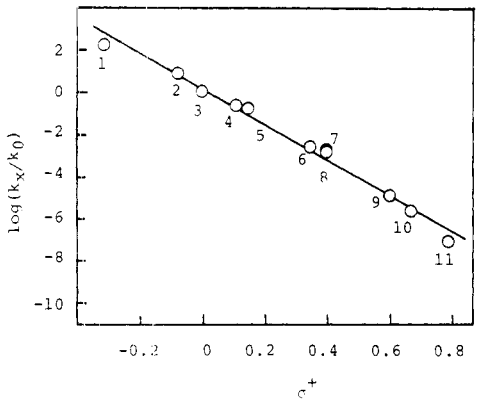

Figure 1. Relationship between the selected partial rate factors for nitration and σ^+: 1; *p*-Me, 2; *m*-Me, 3; H, 4; *p*-Cl, 5; *p*-Br, 6; *m*-F 7; *m*-Cl, 8; *m*-Br, 9; *m*-SO_2Me, 10; *m*-NO_2, 11; *p*-NO_2.

($PhNO_2 \cdot H_2O$ or $PhNO_2 \cdot H_2O \cdot H_2SO_4$), which is mainly due to the increase in the concentration of $PhNO_2 \cdot H_2SO_4$.

As far as methyl phenyl sulfone was concerned, it was assumed in a previous paper[5] that the change in isomer proportion with acidity was due to a hydrogen-bonded complex. The contrast of isomer proportion in nitromethane with those in sulfuric acid[5] supports this assumption. However, we cannot give a more detailed discussion except to say that free methyl phenyl sulfone is not important in the nitration in sulfuric acid, because it is too complicated to determine what are the species undergoing nitration by the same treatment as that for nitrobenzene.

Hammett Relationship for the Nitration of Nitrobenzene and Methyl Phenyl Sulfone. As pointed out earlier, the prf's of nitrobenzene and methyl phenyl sulfone for the nitration in aqueous sulfuric acid were lower than expected.[4,5] It can be explained in terms of the above discussion.

If we use the selected prf's for nitration, a good Hammett relationship is obtained as shown in Figure 1 (ρ = −8.5, n = 11, r = 0.99). The prf's used for nitrobenzene and methyl phenyl sulfone were calculated from the values listed in Table II. For the relative rate of toluene, the value of 79 was adopted. It was obtained by Ridd et al.[22] as the intrinsic one by comparing the relative rate for nitration with that for bromination. Other prf's come from the report of Coombes et al.[4] A better linearity of the points on σ^+ plots may be due to the fact that the species undergoing nitration for these substrates are kinetically free substrates, and the rates are not influenced by the solvation under the experimental conditions used. Supposing this speculation is right, the observed ortho isomers (11.1% and 10.8% yields) are the results of the nitration of "free" nitrobenzene and methyl phenyl sulfone.

Registry No. Nitrobenzene, 98-95-3; methyl phenyl sulfone, 3112-85-4; nitronium hexafluorophosphate, 19200-21-6.

(22) R. Danieli, A. Ricci, H. M. Gillow, and J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2*, 1477 (1974).

Sesterterpenes from *Spongia idia*

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Received March 31, 1980

The sponge *Spongia idia* (=*Leiosella idia*) from Pt. Loma, San Diego, contained both linear and pentacyclic sesterterpenes. The linear sesterterpenes were identified as furospinulosin-1 (**1**) and idiadione (**2**). The pentacyclic sesterterpenes were heteronemin (**3**), 12-epideoxoscalarin (**4**), 12-deacetyl-12,18-diepiscalaradial (**5**), scalarafuran (**6**), and scalarolide (**7**). The structures of idiadione (**2**), scalarafuran (**6**), and scalarolide (**7**) were determined from spectral data and chemical interconversions. An ecological function for these molecules is proposed.

It has generally been assumed that the production of secondary metabolites by a marine sponge contributes to the survival of the sponge. We are investigating the hypothesis that certain sponge metabolites act to deter potential predators and/or prevent surface overgrowth. *Spongia idia* de Laubenfels (=*Leiosella idia*) was one of the most commonly encountered sponges in a sponge-dominated assemblage at an ecological study site off Pt. Loma, San Diego. *S. idia* did not appear to suffer predation, except by a specific dorid nudibranch, and its surface was rarely overgrown. We have therefore isolated and identified the major secondary metabolites from *S. idia* and have shown that some of these metabolites were active in bioassays employing adult and larval forms of common marine algae and invertebrates.

Sponges of the order Dictyoceratida, of which *Spongia idia* is an example, are known as a source of sesterterpenes, an otherwise rare group of terpenoids. Linear sesterterpenes have been isolated from various *Ircinia* species[1] while pentacyclic sesterterpenes, often referred to as the scalarins, have been isolated from *Cacospongia scalaris*,[2] *C. mollior*,[3] *Spongia nitens*,[4] and *Heteronema erecta*.[5] In this paper, we report the unusual occurrence of both linear and pentacyclic sesterterpenes from *Spongia idia*.

The hexane-soluble material extracted from the lyophilized sponge was chromatographed on silica gel to obtain two linear sesterterpenes, furospinulosin-1 (**1**; 0.4% dry weight) and idiadione (**2**; 1.2% dry weight), and five pentacyclic sesterterpenes: heteronemin (**3**; 1.7% dry weight), 12-epideoxoscalarin (**4**; 0.7% dry weight), 12-deacetyl-12,18-diepiscalaradial (**5**; 0.2% dry weight), scalarafuran (**6**; 0.2% dry weight), and scalarolide (**7**; 0.3% dry weight) (see Chart I). Furospinulosin-1 (**1**),[1a] heteronemin

(1) (a) Cimino, G.; de Stefano, S.; Minale, L. *Tetrahedron* **1972**, *28*, 1315. (b) Minale, L.; Cimino, G.; de Stefano, S.; Sodano, G. *Fortschr. Chem. Org. Naturst.* **1976**, *33*, 1. (c) Faulkner, D. J. *Tetrahedron* **1977**, *33*, 1421.

(2) Fattorusso, E.; Magno, S.; Santacroce, C.; Sica, D. *Tetrahedron* **1972**, *28*, 5993.

(3) (a) Cimino, G.; de Stefano, S.; Minale, L. *Experientia* **1974**, *30*, 846. (b) Cafieri, F.; de Napoli, L.; Fattorusso, E.; *Tetrahedron Lett.* **1977**, 470. (c) Cimino, G.; Cafieri, F.; de Napoli, L.; Fattorusso, E. *Ibid.* **1978**, 2041.

(4) (a) Cimino, G.; de Stefano, S.; Minale, L.; Trevellone, E.; *J. Chem. Soc., Perkin Trans. 1* **1977**, 1587. (b) Cimino, G.; de Stefano, S.; di Luccia, A. *Experientia* **1979**, *35*, 1277.

(5) (a) Kazalauskas, R.; Murphy, P. T.; Quinn, R. J.; Wells, R. J. *Tetrahedron Lett.* **1976**, 2631. (b) Kashman, Y.; Rudi, A. *Tetrahedron* **1977**, *33*, 2997.

0022-3263/80/1945-4976$01.00/0

Chart I

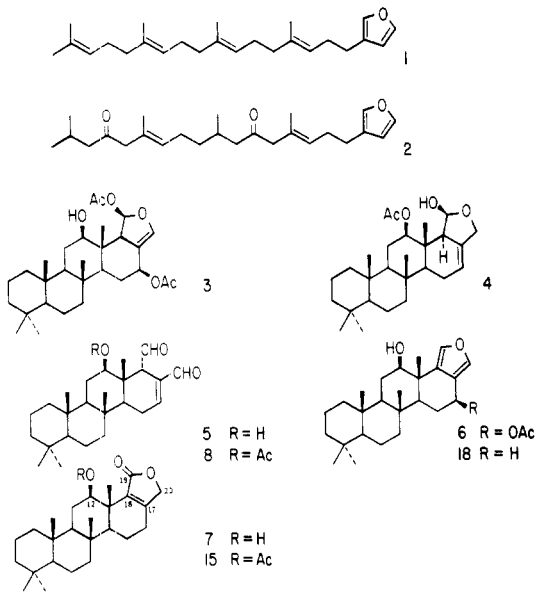
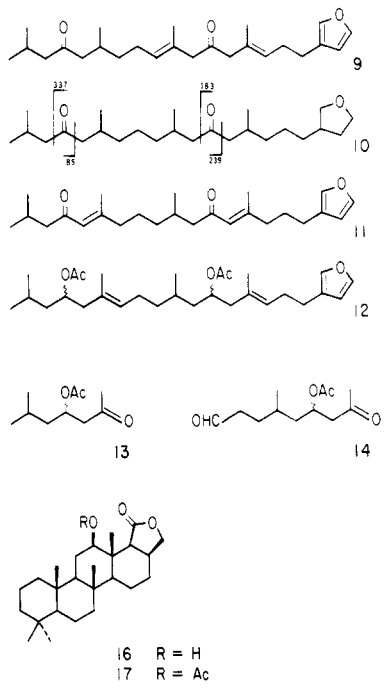


Chart II



(3),[5] and 12-epideoxoscalarin (4)[4a] were all identified from spectral data that were identical with literature values. 12-Deacetyl-12,18-diepiscalaradial (5) was converted into the known compound 12,18-diepiscalaradial (8)[4b] by treatment with acetic anhydride in pyridine. Scalarafuran (6) was recognized as having spectral data identical with those of a furan synthesized by controlled pyrolysis of heteronemin (3) at 220 °C.[5] We repeated the pyrolysis of heteronemin (3) to obtain a furan, identical in all respects with the furan from *S. idia* that we have named scalarafuran (6).

The major linear sesterterpene, idiadione (2), had the molecular formula $C_{25}H_{38}O_3$. The infrared spectrum contained a strong carbonyl band at 1710 cm^{-1} while the ^{13}C NMR spectrum contained two carbonyl signals at δ 209.0 (s) and 208.9 (s). The ^{13}C NMR signals at δ 142.4 (d), 138.6 (d), 124.3 (s), and 110.7 (d) indicated the presence of a β-substituted furan, and signals at δ 129.5 (s), 129.3 (d), 128.8 (s), and 128.7 (d) were assigned to two trisubstituted olefinic bonds. The ^1H NMR spectrum contained signals at δ 7.33 (br s, 1 H), 7.21 (br s, 1 H), and 6.27 (br s, 1 H), due to protons on a β-substituted furan, 5.29 (t, 1 H, J = 7 Hz) and 5.25 (t, 1 H, J = 7 Hz) due to the olefinic protons, 3.01 (br s, 4 H) assigned to two α-methylene groups in β,γ-unsaturated ketone moieties, 1.60 (s, 6 H) due to two vinyl methyl groups, and 0.89 (d, 6 H, J = 7 Hz) and 0.87 (d, 3 H, J = 7 Hz) assigned to an isopropyl group and a secondary methyl group, respectively. Assuming the regular isoprenoid skeleton, two structures **2** and **9** were compatible with these spectral data.

The positions of the ketone groups were confirmed by examination of the mass spectral fragmentation pattern of the tetrahydrofuran **10**, obtained by catalytic hydrogenation of idiadione (2). The structure **9** could be eliminated since treatment of idiadione (2) with sodium methoxide in methanol gave the bis(α,β-unsaturated ketone) **11** (see Chart II). The infrared spectrum of the diketone **11** contained only one carbonyl band at 1685 cm^{-1}. The ^1H NMR spectrum contained signals at δ 5.92 (br s, 2 H), 2.09 (s, 3 H), and 2.07 (s, 3 H) due to the α-protons and β-methyl groups on two α,β-unsaturated ketone moieties.

Reduction of idiadione (2) with sodium borohydride in ethanol, followed by acetylation of the product, gave a mixture of diastereoisomeric diacetates **12**. Ozonolysis of the mixture of diacetates **12** at −78 °C followed by hydrogenation of the ozonides over 10% palladium on charcoal at 0 °C gave the keto acetate **13** and a 1:1 mixture of the diastereoisomers of keto aldehyde **14**.[6] The keto acetate **13** (IR 1745, 1720 cm^{-1}) had the molecular formula $C_{10}H_{18}O_3$. The ^1H NMR spectrum contained signals at δ 2.09 (s, 3 H) and 1.96 (s, 3 H) due to the methyl ketone and acetate protons, at δ 0.93 (d, 6 H, J = 7 Hz) assigned to the terminal methyl groups, and an α-acetoxy proton signal at δ 5.16 (m, 1 H) coupled to methylene proton signals at δ 2.55 (dd, 1 H, J = 16, 6 Hz) and 2.48 (dd, 1 H, J = 16, 6 Hz). The keto aldehyde **14** had the molecular formula $C_{12}H_{20}O_4$. The ^1H NMR spectrum contained signals at δ 1.97 (s, 3 H), 2.09 (s, 3 H), 2.50 (dd, 1 H, J = 16, 6 Hz), 2.61 (dd, 1 H, J = 16, 6 Hz), and 5.17 (m, 1 H) due to a β-acetoxy methyl ketone moiety, an aldehyde proton signal at δ 9.71 (t, 1 H, J = 1 Hz) coupled to a signal at δ 2.39 (td, 2 H, J = 7, 1, 1 Hz), and a methyl signal at δ 0.94 (d, 3 H, J = 6 Hz). These data confirmed the position of the olefinic bonds in idiadione (2). The 6*E*,14*E* geometry of the olefinic bonds was determined by analysis of the chemical shift data for the methyl signals in the ^{13}C NMR spectrum of idiadione (2) [δ 22.3 (2), 19.4, *16.2*, *16.1*].

Scalarolide (**7**; mp >300 °C dec) had the molecular formula $C_{25}H_{38}O_3$, coincidentally isomeric with idiadione (2). However, the presence of five methyl signals at δ 0.81 (s, 3 H), 0.85 (s, 6 H), 0.89 (s, 3 H), and 1.13 (s, 3 H) in the ^1H NMR spectrum indicated that scalarolide (**7**) was related to the pentacyclic scalarins. The ^{13}C NMR spectrum contained signals at δ 175.9 (s) due to the lactone carbonyl, at δ 162.0 (s) and 135.8 (s) for the olefinic carbons at C-18 and C-17, respectively, and at δ 75.5 (d) and 72.0 (t), assigned to C-12 and a γ-carbon on the α,β-unsaturated γ-lactone ring. In the ^1H NMR spectrum, the axial proton at C-12 gave a signal at δ 3.67 (dd, 1 H, J = 11, 5 Hz) while the methylene protons in the lactone ring gave a signal at δ 4.69 (br s, 2 H). Assuming the scalarin skeleton, which seemed most likely from the ^{13}C NMR spectrum, we could

(6) We attempted to convert the diastereoisomeric mixture of keto aldehydes **14** into a single α,β-unsaturated ketone using mild bases but could not obtain a clean product due to reactions involving the aldehyde group.

place an equatorial hydroxyl at C-12 and an olefin at C-17(18) but could not, from the NMR spectra, determine whether the lactone carbonyl was at C-19 or C-20. However, the broad infrared bands at 3400 and 1715 cm^{-1} suggested an interaction between the C-12 hydroxyl and a C-19 lactone carbonyl.

The C-12 alcohol in scalarolide (**7**) was acetylated with great difficulty by using acetic anhydride containing *p*-toluenesulfonic acid. The infrared spectrum of the acetate **15** contained bands at 1755 and 1720 cm^{-1} for butenolide and acetate carbonyl groups. The ^1H NMR spectrum contained an acetate signal at δ 2.08 (s, 3 H), an α-acetoxy proton signal at δ 4.82 (dd, 1 H, J = 11, 5 Hz), and the butenolide methylene signal as an AB quartet at δ 4.57 (d, 1 H, J = 16.5 Hz) and 4.43 (d, 1 H, J = 16.5 Hz).

Hydrogenation of scalarolide (**7**) over 10% palladium on charcoal gave a γ-lactone, **16**, in which the lactone carbonyl band (IR 1745 cm^{-1}) was again abnormal. However, acetylation of the lactone **16** gave the corresponding γ-lactone **17**, with a normal γ-lactone band at 1780 cm^{-1} in the infrared spectrum. The ^1H NMR spectrum of the γ-lactone **16** contained a C-12 proton signal at δ 3.54 (dd, 1 H, J = 11, 5 Hz) together with signals at δ 2.47 (d, 1 H, J = 9 Hz, C-18), 2.68 (m, 1 H, C-17), 3.99 (t, 1 H, J = 9 Hz, C-20), and 4.28 (t, 1 H, J = 9 Hz, C-20), the assignments being confirmed by decoupling experiments. These data confirm that the lactone carbonyl must be at C-19.

Scalarolide (**7**) could be related to heteronemin (**3**) by the following reaction sequence. Reduction of scalarolide (**7**) with lithium aluminum hydride in tetrahydrofuran at 25 °C gave the furan **18**. The same furan **18** was prepared by hydrogenolysis of scalafuran (**6**), previously prepared from heteronemin (**3**). The ^1H NMR spectrum of the furan **18** contained signals at δ 7.39 (br s, 1 H) and 6.91 (br s, 1 H). When the reduction of scalarolide was repeated with lithium aluminum deuteride, the C-19 proton signal at δ 7.39 (cf. δ 7.41 in **6**) was missing from the deuterated product, confirming that the lactone carbonyl was at C-19.

Preliminary laboratory assays have revealed that sponge metabolites may indeed be important in preventing predation and overgrowth. Idiadione (**2**) and 12-deacetyl-12,18-diepiscalaradial (**5**) are both toxic to the sea star *Pisaster giganteus* at a concentration of 5 mg/L. Idiadione (**2**), heteronemin (**3**), and dialdehyde **5** all immobilize the larvae of the red abalone *Haliotis rufescens* at 1 mg/L in seawater. All the metabolites **1**–**5** are toxic to brine shrimp *Artemia* sp. at 10 mg/L while at the same concentration, heteronemin (**3**) is toxic to the gametes of the giant kelp *Macrocystis pyrifera*, idiadione (**2**) is toxic to the ectoproct *Membranipora membranacea*, and the dialdehyde **5** is toxic to the hydroid *Bougainvilla* sp.[7] The dorid nudibranch *Cadlina marginata* was the only predator observed to feed on *Spongia idia*. From the acetone extract of whole specimens of *C. marginata* we have isolated idiadione (**2**) together with some terpenoid furans and isonitriles that reflect the metabolites from other sponges in the nudibranch's diet.[8]

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. ^1H NMR spectra were recorded on a Varian HR-220 NMR spectrometer, and ^{13}C NMR 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 obtained from the mass spectrometry service at UCLA. 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, Extraction, and Chromtography. The sponge *Spongia idia* was collected by hand using SCUBA (−15 m) at Pt. Loma (San Diego, CA) in May 1979, immediately frozen, and then lyophilized. The sponge (33 g) was placed in a Soxhlet apparatus and exhaustively extracted with hexane (2 L), dichloromethane (2 L), and methanol (2 L). The hexane extract was evaporated to give a viscous oil (3.58 g, 11% dry weight) that was judged to contain the majority of secondary metabolites. The oil was preabsorbed onto silica gel and applied to a column of silica gel (300 g) that was eluted with solvents of increasing polarity from hexane through dichloromethane, ether, and ethyl acetate to obtain 12 major fractions. The fraction eluted with hexane contained furospinulosin-1 (**1**; 140 mg, 0.4% dry weight) which was further purified by LC on μ-Porasil. Fractions eluted with 10% ether in dichloromethane contained only idiadione (**2**; 353 mg, 1.2% dry weight). The fraction eluted with 25% ether in dichloromethane was rechromatographed on silica gel with 10% ether in hexane as eluant to obtain scalarafuran (**6**; 80 mg, 0.2% dry weight). The first fractions eluted with 1:1 ether/dichloromethane contained a mixture of heteronemin (**3**; 550 mg, 1.7% dry weight) and scalarolide (**7**; 96 mg, 0.3% dry weight) that could be separated by fractional crystallization from ether, a solvent in which scalarolide (**7**) was insoluble. The later fractions eluted with 1:1 ether/dichloromethane contained 12-deacetyl-12,18-diepiscalaradial (**5**; 70 mg, 0.2% dry weight), which crystallized from ether. The fractions eluted with ether contained 12-epideoxoscalarin (**4**; 230 mg, 0.7% dry weight). The spectral data for furospinulosin-1 (**1**), heteronemin (**3**), and 12-epideoxoscalarin (**4**) were identical with literature values.[1a,5,4a]

Idiadione (2): $[\alpha]_D$ −6.6° (*c* 2.6, $CHCl_3$); UV (MeOH) 211 nm (ϵ 27 300); IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (d, 3 H, J = 7 Hz), 0.89 (d, 6 H, J = 7 Hz), 1.60 (br s, 6 H), 3.01 (br s, 4 H), 5.25 (t, 1 H, J = 7 Hz), 5.29 (t, 1 H, J = 7 Hz), 6.27 (br s, 1 H), 7.21 (br s, 1 H), 7.33 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 209 (s), 208.9 (s), 142.4 (d), 138.6 (d), 129.5 (s), 129.3 (d), 128.8 (s), 128.7 (d), 124.3 (s), 110.7 (d), 54.2 (tt), 50.4 (t), 48.7 (t), 36.3 (t), 28.4 (d), 28.3 (t), 25.3 (t), 24.5 (t), 24.2 (d), 22.3 (2 q), 19.4 (q), 16.2 (q), 16.1 (q); high-resolution mass spectrum calcd for $C_{25}H_{38}O_3$ m/e 386.2821, found m/e 386.2795.

12-Deacetyl-12,18-diepiscalaradial (5): mp 216–218 °C; $[\alpha]_D$ −129° (*c* 1.2, $CHCl_3$); UV (MeOH) 230 nm (ϵ 12 500); IR ($CHCl_3$) 3450, 1715, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.83 (s, 6 H), 0.91 (s, 3 H), 3.61 (m, 1 H), 3.69 (br s, 1 H), 7.09 (br t, 1 H), 9.42 (s, 1 H), 9.89 (d, 1 H, J = 3 Hz); mass spectrum, m/e 386 (M^+).

Scalarafuran (6): mp 182 °C; $[\alpha]_D$ −19.8° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) 3500, 1730 cm^{-1}; ^1H NMR (CCl_4) δ 0.81 (s, 3 H), 0.83 (s, 3 H), 0.85 (s, 3 H), 0.90 (s, 3 H), 1.21 (s, 3 H), 2.03 (s, 3 H), 3.51 (br d, 1 H, J = 11 Hz), 5.60 (td, 1 H, J = 8.5,1.5 Hz), 7.14 (t, 1 H, J = 1.5 Hz), 7.41 (d, 1 H, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 171.0, 138.9, 137.2, 134.4, 120.8, 79.5, 68.0, 58.5, 56.5, 54.0, 42.8, 41.9, 41.5, 40.1, 39.7, 37.3 (2 C), 33.1 (2 C), 27.7, 24.5, 21.2, 18.7, 18.5, 18.0, 17.3, 16.1; mass spectrum, m/e 428 ($M^{+\cdot}$).

Scalarolide (7): mp >300 °C dec; $[\alpha]_D$ +24.9° (*c* 1.35, $CHCl_3$); UV (MeOH) 219 nm (ϵ 24 500); IR (KBr) 3460, 1715, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (s, 3 H), 0.85 (s, 6 H), 0.89 (s, 3 H), 1.13 (s, 3 H), 2.39 (m, 2 H), 3.67 (dd, 1 H, J = 11, 5 Hz), 4.69 (br s, 2 H), 5.94 (br s, OH); ^{13}C NMR ($CDCl_3$) δ 175.9 (s), 162.0 (s), 135.8 (s), 75.5 (d), 72.0 (t), 57.9 (d), 56.6 (d), 55.1 (d), 42.1 (s), 42.0 (t), 41.7 (t), 39.6 (t), 37.3 (s), 37.2 (s), 33.2 (q, s), 25.7 (t), 25.2 (t), 21.2 (q), 18.5 (t), 18.1 (t), 17.1 (t), 16.6 (q), 16.3 (q), 15.9 (q); high-resolution mass spectrum calcd for $C_{25}H_{38}O_3$ m/e 386.2821, found m/e 386.2847.

Acetylation of Dialdehyde 5. A solution of the dialdehyde **5** (5 mg, 0.013 mmol) and acetic anhydride (0.5 mL) in pyridine (1 mL) was stirred at 25 °C for 12 h. The reagents were evaporated under high vacuum. The residue was dissolved in dichloromethane, and the solution filtered through a short column of silica

(7) The bioassay results will be reported in full elsewhere.
(8) Wratten, S. J.; Walker, R. P.; Faulkner, D. J., unpublished data. Some of the compounds have not yet been identified.

gel to obtain 12,18-diepiscalaradial (**8**; 2 mg, 36% theroretical) with spectral data identical with those reported in the literature.[4b]

Pyrolysis of Heteronemin (3). Heteronemin (**3**; 32 mg, 0.07 mmol) was placed in a glass tube and sealed under vacuum. The tube was plunged into a heated oil bath at 220 °C. After 2 min the tube was removed, cooled to room temperature, and opened. Acetic acid had condensed in the neck of the tube. The product mixture was chromatographed by LC on μ-Porasil with 1% ether in dichloromethane as eluant to obtain at least six products. The major product was scalarafuran (**6**; 4.5 mg, 15% theoretical), identical in all respects with the natural compound.

Hydrogenation of Idiadione (2). A solution of idiadione (**2**; 30 mg, 0.08 mmol) in methanol (10 mL) containing 10% palladium on charcoal catalyst (2 mg) was stirred under an atmosphere of hydrogen for 12 h. The catalyst was removed by filtration and the solvent evaporated to obtain the tetrahydrofuran **10**: 16 mg (53% of theoretical); IR (film) 1710 cm^{-1}; ^1H NMR (CCl_4) δ 0.85 (d, 9 H, J = 7 Hz), 0.89 (d, 6 H, J = 7 Hz), 3.19 (t, 1 H, J = 7.5 Hz), 3.72 (m, 3 H); mass spectrum, m/e (relative intensity) 394 ($M^{+\cdot}$, 2), 337 (M − C_4H_9, 3), 295 (M − $C_6H_{11}O$, 20), 281 (M − $C_7H_{13}O$, 5), 254 (M − $C_9H_{16}O$, 4), 239 (M − $C_{10}H_{19}O$, 3), 197 ($C_{13}H_{25}O$ and $C_{12}H_{21}O_2$, 8), 183 ($C_{11}H_{19}O_2$, 4), 85 (84), 69 (92), 55 (100).

α,β-Unsaturated Ketone 11. A solution of idiadione (**2**; 62 mg, 0.16 mmol) in dry methanol (10 mL) containing sodium methoxide (~20 mg) was stirred for 3 days at room temperature. The reaction mixture was poured into water (50 mL), and the organic material was extracted with hexane (3 × 25 mL). The combined extracts were dried over sodium sulfate, and the solvent was evaporated to obtain an oil that was purified by LC on μ-Porasil with 10% ether in hexane as eluant to yield the α,β-unsaturated diketone **11**: 12 mg (20% of theoretical); IR (film) 1685 cm^{-1}; UV (MeOH) 243 nm (ε 16 700); ^1H NMR (CCl_4) δ 0.89 (d, 3 H, J = 7 Hz), 2.07 (s, 3 H), 2.09 (s, 3 H), 2.40 (t, 2 H, J = 7 Hz), 5.92 (br s, 2 H), 6.17 (br s, 1 H), 7.14 (br s, 1 H), 7.28 (br s, 1 H); mass spectrum, m/e 386 ($M^{+\cdot}$).

Reduction and Acetylation of Idiadione (2). Sodium borohydride (200 mg) was added to a solution of idiadione (**2**; 118 mg, 0.31 mmol) in ethanol (10 mL), and the solution was stirred at 25 °C for 30 min. Excess reagent was destroyed by addition of 5% hydrochloric acid (20 mL). The reaction product was extracted with dichloromethane (2 × 25 mL), and the combined extracts were dried over sodium sulfate. Evaporation of the solvent gave the diol (IR 3450 cm^{-1}) that was used without further purification. The diol was dissolved in a mixture of acetic anhydride (2 mL) and pyridine (4 mL), and the solution was stirred at 25 °C for 12 h. The reagents were evaporated under high vacuum, and the residue was dissolved in dichloromethane and then passed through a short column of silica gel to obtain the diacetate **12** (148 mg, quantitative) as a mixture of diastereoisomers: IR (film) 1735 cm^{-1}; ^1H NMR (CCl_4) δ 0.89 (d, 3 H, J = 7 Hz), 0.91 (d, 6 H, J = 7 Hz), 1.62 (br s, 6 H), 1.91 (s, 3 H), 1.92 (s, 3 H), 2.42 (t, 2 H, J = 7 Hz), 5.06 (m, 2 H), 6.17 (br s, 1 H), 7.12 (br s, 1 H), 7.25 (br s, 1 H); mass spectrum, m/e 474 (M^+).

Ozonolysis of Diacetate 12. A stream of ozone in oxygen was bubbled into a solution of the diacetate **12** (55 mg, 0.12 mmol) in ethyl acetate (25 mL) at −78 °C until a blue-colored solution resulted. Excess ozone was removed in a stream of nitrogen, and the solution was warmed to 0 °C. Palladium on charcoal catalyst (10%, 2 mg) was added, and the solution was stirred under an atmosphere of hydrogen at 0 °C for 12 h. The catalyst was removed by filtration and the solvent evaporated to yield a mixture of ketones. The mixture was separated by LC on μ-Porasil with 7% ether in dichloromethane as eluant to give the keto acetate **13** (11 mg, 50% theoretical) and a diastereoisomeric mixture (1:1) of keto aldehydes **14** (9 mg, 34% theoretical).

Keto Acetate 13: IR (film) 1745, 1720 cm^{-1}; ^1H NMR (CCl_4) δ 0.93 (d, 6 H, J = 7 Hz), 1.96 (s, 3 H), 2.09 (s, 3 H), 2.48 (dd, 1 H, J = 16, 6 Hz), 2.55 (dd, 1 H, J = 16, 6 Hz), 5.16 (m, 1 H); mass spectrum, m/e 186 ($M^{+\cdot}$).

Keto Aldehyde 14: IR (film) 1730 cm^{-1} (br); ^1H NMR (CCl_4) δ 0.94 (d, 3 H, J = 6 Hz), 1.97 (s, 3 H), 2.09 (s, 3 H), 2.40 (td, 2 H, J = 7, 7, 1 Hz), 2.50 (dd, 1 H, J = 16, 6 Hz), 2.61 (dd, 1 H, J = 16, 6 Hz), 5.17 (m, 1 H), 9.71 (br s, 1 H); mass spectrum, m/e 224 ($M^{+\cdot}$).

Acetylation of Scalarolide (7). A solution of scalarolide (**7**; 12 mg, 0.03 mmol), acetic anhydride (1 mL), and p-toluenesulfonic acid (2 mg) in methylene chloride (25 mL) was stirred at 25 °C for 18 h. The solvent and reagent were evaporated under vacuum, and the residue was partitioned between dichloromethane (3 × 25 mL) and water (10 mL). The combined dichloromethane extracts were dried over sodium sulfate, and the solvent was removed to yield an oil that was purified by LC on μ-Porasil with 25% ether in dichloromethane as eluant to give the acetate **15**: 11 mg (83% theoretical); IR ($CHCl_3$) 1755, 1720 cm^{-1}; UV (MeOH) 218 nm (ε 24 500); ^1H NMR ($CDCl_3$) δ 0.81 (s, 3 H), 0.84 (s, 6 H), 0.91 (s, 3 H), 1.21 (s, 3 H), 2.08 (s, 3 H), 4.43 (d, 1 H, J = 16.5 Hz), 4.57 (d, 1 H, J = 16.5 Hz), 4.82 (dd, 1 H, J = 11, 5 Hz); mass spectrum, m/e 385 (M − 43), 368 (M − 60).

Hydrogenation of Scalarolide (7). A solution of scalarolide (**7**; 10 mg, 0.026 mmol) in methanol (10 mL) containing 10% palladium on charcoal catalyst (2 mg) was stirred under an atmosphere of hydrogen for 3 days. The catalyst was removed by filtration and the solvent evaporated to obtain the γ-lactone **16**: 10 mg (quantative); IR ($CHCl_3$) 3500, 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (s, 3 H), 0.84 (s, 6 H), 0.86 (s, 3 H), 1.01 (s, 3 H), 2.47 (d, 1 H, J = 9 Hz), 2.68 (m, 1 H), 3.54 (dd, 1 H, J = 11, 4 Hz), 3.99 (t, 1 H, J = 9 Hz), 4.28 (t, 1 H, J = 9 Hz), 4.36 (s, OH).

Acetylation of γ-Lactone 16. A solution of the γ-lactone **16** (10 mg, 0.026 mmol) in acetic anhydride (0.5 mL) and pyridine (1 mL) was stirred at 25 °C for 12 h. A workup in the manner described for the previous acetylation gave the acetoxy γ-lactone **17**: 10 mg (90% theoretical); IR ($CHCl_3$) 1780, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (s, 3 H), 0.82 (s, 3 H), 0.84 (s, 3 H), 0.89 (s, 3 H), 1.10 (s, 3 H), 2.04 (s, 3 H), 2.42 (d, 1 H, J = 8.5 Hz), 2.59 (m, 1 H), 3.84 (t, 1 H, J = 8.5 Hz), 4.09 (t, 1 H, J = 8.5 Hz), 4.84 (dd, 1 H, J = 11, 4 Hz); mass spectrum, m/e 370 (M − 60).

Furan 18. Method A. Lithium aluminum hydride (100 mg) was added to a solution of scalarolide (**7**; 14 mg, 0.036 mmol) in dry tetrahydrofuran (10 mL), and the reaction mixture was stirred under dry nitrogen at 25 °C for 1.5 h. Excess reagent was destroyed by dropwise addition of ethyl acetate, and the reaction products were partitioned between ether (3 × 25 mL) and 5% hydrochloric acid (25 mL). The combined ether extracts were dried over sodium sulfate, and the solvent was evaporated to obtain an oil that was purified by LC on μ-Porasil with 1% ether in dichloromethane as eluant to give the furan **18** (2 mg, 15% theoretical) as the major product: IR ($CHCl_3$) 3450 cm^{-1}; ^1H NMR (CCl_4) 0.81 (s, 3 H), 0.84 (s, 3 H), 0.85 (s, 3 H), 0.88 (s, 3 H), 1.14 (s, 3 H), 2.39 (m, 1 H), 2.67 (m, 1 H), 3.54 (m, 1 H), 6.91 (br s, 1 H), 7.39 (br s, 1 H); mass spectrum, m/e 370 ($M^{+\cdot}$).

Method B. A solution of scalarafuran (**6**; 5 mg, 0.012 mmol) in tetrahydrofuran (10 mL) containing 10% palladium on charcoal catalyst (2 mg) was stirred under an atmosphere of hydrogen at 25 °C for 35 min. The catalyst was removed by filtration and the solvent evaporated to obtain an oil containing two major products. The furan **18** (2 mg, 45% theoretical), spectroscopically identical with the previous sample, was purified by LC on μ-Porasil with 1% ether in dichloromethane as eluant.

Acknowledgment. It is a pleasure to acknowledge the advice and assistance provided by Dr. Paul K. Dayton. This research was funded by a grant from the Office of Sea Grant (R/MP-16, NOAA 04-8-M01-189).

Registry No. **1**, 35890-95-0; **2**, 75266-24-9; **3**, 62008-04-2; **4**, 75266-26-1; **5**, 75266-25-0; **6**, 62008-03-1; **7**, 75266-23-8; **8**, 72300-73-3; **10**, 75266-27-2; **11**, 75266-28-3; **12**, 75266-29-4; **13**, 75266-30-7; **14** (isomer 1), 75266-31-8; **14** (isomer 2), 75266-32-9; **15**, 75266-33-0; **16**, 75266-34-1; **17**, 75266-35-2; **18**, 75283-88-4.