261.0344), 234.0249 ($C_{14}H_6N_2S$ requires 234.0246); EIMS m/z (38), 261 (42), 234 (14), 190 (16), 117 (13), 69 (18), 58 (100).

Kuanoniamine B (3): yellow amorphous powder from chloroform; mp >300 °C; UV (MeOH) λ_{max} 204 (log ϵ 4.24), 240 (4.32), 264 (4.18), 294 sh (3.89), 344 (3.87), 360 (3.87), 450 nm (3.44); UV ($MeOH_2^+$) λ_{max} 204 (log ϵ 4.17), 238 (4.21), 270 (4.08), 306 (4.27), 344 (3.65), 360 (3.73), 530 nm (3.41); IR (solution in chloroform) 3620, 1640, 1450, 1220, 1110, 1040 cm^{-1}; HREIMS m/z 402.1520 ($C_{23}H_{22}N_4OS$ requires 402.1526); EIMS m/z 402 (19), 314 (20), 301 (21), 289 (72), 261 (78), 234 (23), 190 (22).

Kuanoniamine C (4): yellow amorphous powder from chloroform; mp >300 °C; UV (MeOH) λ_{max} 206 (log ϵ 4.24), 240 (4.32), 264 (4.20), 294 sh (3.90), 344 (3.88), 359 (3.86), 450 nm (3.30). UV ($MeOH_2^+$) λ_{max} 206 (log ϵ 4.16), 240 (4.22), 270 (4.07), 306 (4.27), 360 (3.75), 526 nm (3.40); IR (solution in chloroform) 3580, 3150, 1645, 1590, 1370, 1310, 1140 cm^{-1}; HREIMS m/z 374.1270 ($C_{21}H_{18}N_4OS$ requires 374.1339), 289.0311 ($C_{16}H_7N_3OS$ requires 289.0313); EIMS m/z 374 (5%), 370 (10), 313 (15), 299 (46), 289 (52), 278 (47), 261 (61), 234 (11), 190 (13), 169 (12), 149 (49), 86 (77), 69 (100).

Kuanoniamine D (5): yellow amorphous powder from chloroform; mp >300 °C; UV (MeOH) λ_{max} 206 (log ϵ 4.24), 240 (4.32), 264 (4.20), 344 (3.88), 358 (3.87), 452 nm (3.38); UV ($MeOH_2^+$) λ_{max} 206 (log ϵ 4.15), 240 (4.22), 270 (4.07), 306 (4.27), 360 (3.75), 526 (3.39); IR (solution in chloroform) 3610, 3000, 2940, 2840, 1640, 1590, 1460, 1240, 1210, 1100, 1060, 1000 cm^{-1}; HREIMS m/z 360.1007 ($C_{20}H_{16}N_4OS$ requires 360.1045), 288.0590 ($C_{17}H_{10}N_3S$ requires 288.0595); EIMS m/z 360 (40), 356 (18), 314 (26), 301 (31), 299 (30), 288 (100).

Benzothiazole (Aldrich) HMBC spectrum (Figure 2) was measured at 500 MHz. Long-range couplings are optimized for J = 10 Hz. Final data set 2K × 1K.

Acknowledgment. We thank Drs. P. Karuso and A. Poiner for collecting the animals, W. Yoshida for performing HMBC experiments on benzothiazole, and F. Caplan for performing the cytotoxicity tests. This research was supported by the National Science Foundation and the Univeristy of Hawaii Sea Grant College Program under Grant NA81AA-D-0070 from NOAA, Office of Sea Grant, U.S. Department of Commerce.

Isonitriles from the Blue-Green Alga *Scytonema mirabile*

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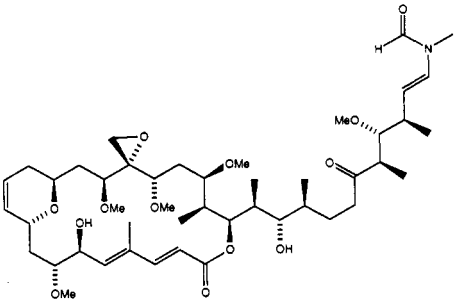
An aerial form of *Scytonema mirabile* (Dillwyn) Bornet, designated strain number BY-8-1, has been found to contain six novel isonitriles, viz. mirabilene isonitriles A-F (**7-12**), which are mildly cytotoxic and antimicrobial. The gross structures of **7-12** were determined by detailed spectral analysis. The relative and absolute stereochemistry of **7-12** were solved by chemical degradation and direct comparison of degradation products with synthetic samples; mirabilene-A isonitrile (**7**), for example, was degraded to methyl (3*R*,5*R*,7*S*,9*S*)-3,5,7,9-tetramethoxy-10-oxoundecanal (**15**) and isopropyl (*S*)-3-trifluoroacetamidobutyrate (**14**), which indicated that the absolute configurations of C-4, C-6, C-8, C-10, and C-16 in **7** were all *S*.

The major cytotoxic, fungicidal agent in the cultured terrestrial blue-green alga *Scytonema mirabile* (isolate BY-8-1) is tolytoxin (**1**).[1] Polymethoxyalkenes **2-3**, which are related to **4-6** from another tolytoxin-producing cyanophyte *Tolypothrix conglutinata* var. *colorata*,[2] are also present in *S. mirabile*.[3] Upon examining the extract of *S. mirabile*, another member of the Scytonemataceae, for other cytotoxins and fungicides, a new group of isonitriles was found, viz. the mirabilene isonitriles **7-12**, which are mildly cytotoxic and antimicrobial and obviously related to compounds **2** and **3**.[4] Hitherto isonitriles (e.g. hapalindoles) had been found only in blue-green algae belonging to the Stigonemataceae.[5,6] In this paper we describe the total structures of the mirabilene isonitriles.



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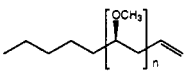

2 n = 5

3 n = 6

4 n = 8

5 n = 9

6 n = 10

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(2) Mynderse, J. S.; Moore, R. E. *Phytochemistry* **1979**, *18*, 1181.

(3) Mori, Y.; Kohchi, Y.; Suzuki, M.; Carmeli, S.; Moore, R. E.; Patterson, G. M. L. Manuscript in preparation.

(4) The mirabilene isonitriles are cytotoxic to LoVo (a human colon adenocarcinoma cell line) at 5 μg/mL and KB (a human nasopharyngeal carcinoma cell line) at 1-10 μg/mL (**7** being the most active). None of the compounds, however, exhibit selective cytotoxicity toward murine or human solid tumor cell lines over L1210 leukemia in the Corbett assay [Corbett, T. H.; Polin, L.; Wozniak, A. J.; Bissery, M.; LoRusso, P. M.; Valeriote, F. A.; Baker, L. H. *Proc. Am. Assoc. Cancer Res.* **1988**, *29*, 533] or toward leukemia cell lines over CFU-GM (a normal bone marrow cell line) in the Valeriote assay. All of the mirabilene isonitriles exhibited weak antimicrobial activity (zones of 10-15 mm with 10 μg/disc) against Gram-positive bacteria and filamentous fungi (*Aspergillus oryzae* and *Penicillium notatum*). The details of the bioactivity data will be reported elsewhere.

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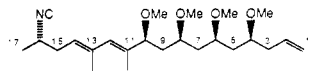
0022-3263/90/1955-4431$02.50/0

Table I. ^1H and ^{13}C NMR Data of Mirabilene-A Isonitrile (7)

H no.	δ_H mult	J (Hz)	C no.	δ_C mult	HMBC correlations
1*Z*	5.08 ddt	17.0, 2.5, 1.2	1	117.02 t	3,3′
1*E*	5.05 ddt	10.0, 2.0, 1.2			
2	5.86 ddt	17.0, 10.0, 7.0	2	135.21 d	1*E*,1*Z*,3,3′,4
3,3′	2.26 dddd	7.0, 5.4, 2.5, 1.2	3	38.20 t	1*E*,1*Z*,2,4,5,5′
4	3.33 ddt	7.4, 5.0, 5.4	4	77.50 d	2,3,3′,4-OMe,5,5′,6
4-OMe	3.14 s		4-OMe	56.19 q	4
5	1.62 ddd	5.0, 6.5, −14.0	5	38.02 t	3,3′,6,7,7′
5′	1.92 ddd	5.4, 7.4, −14.0			
6	3.53 dddd	5.0, 5.4, 6.5, 7.0	6	75.42 d	4,5,5′,6-OMe,7,7′,8
6-OMe	3.18 s		6-OMe	55.94 q	6
7	1.71 ddd	5.0, 6.2, −14.1	7	38.20 t	5,5′,6,8,9,9′
7′	1.97 ddd	5.8, 7.0, −14.1			
8	3.50 dddd	5.4, 5.8, 6.2, 7.0	8	75.72 d	6,7,7′,8-OMe,9,9′,10
8-OMe	3.22 s		8-OMe	56.00 q	8
9	1.84 ddd	5.4, 6.6, −14.0	9	38.56 t	7,7′,8,10
9′	2.13 ddd	6.6, 7.0, −14.0			
10	3.82 t	6.6	10	84.95 d	8,9,9′,10-OMe,12
10-OMe	3.12 s		10-OMe	55.70 q	10
			11	135.95 s	9,9′,10,11-Me
11-Me	1.84 d	1.2	11-Me	12.50 q	10,12
12	5.94 brs		12	131.78 d	10,11-Me,13-Me,14
			13	136.21 s	13-Me,15,15′
13-Me	1.58 d	0.8	13-Me	17.34 q	12,14
14	5.28 dt	1.2, 7.4	14	123.87 d	12,13-Me,15,15′,16
15	1.90 m		15	35.46 t	14,16,17
15′	2.01 ddd	6.6, 7.4, −14.1			
16	2.98 brdq	6.6, 6.6	16	49.88 dt	15,15′,17
17	0.84 dt	6.6, 2.0	17	21.00 q	15,15′,16
			NC	158.29 st	16

Isolation and Characterization. *S. mirabile* BY-8-1 was isolated from an algal sample collected on Mt. Tantalus, Oahu, HI. The alga was mass cultured in the laboratory and the freeze-dried cyanophyte was extracted with 7:3 EtOH/water. The extract was subjected to rapid chromatography on RP-18 and the fractions that were eluted with 9:1 MeOH/water and MeOH were further fractionated by MPLC on silica gel to give a crude mixture of **2**, **3**, and **7**–**12**. Separation of this mixture was achieved



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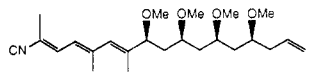

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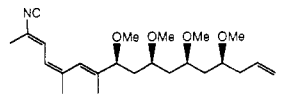

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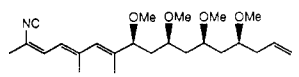

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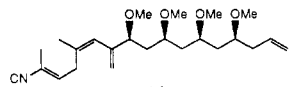

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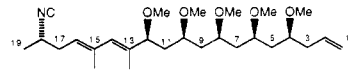

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by HPLC on RP-18, from which the compounds were eluted by 3:1 MeOH/water in the following order: mirabilene-A isonitrile (**7**), mirabilene-E isonitrile (**11**), mirabilene-F isonitrile (**12**), mirabilene-D isonitrile (**10**), mirabilene-B isonitrile (**8**), mirabilene-C isonitrile (**9**), 4,6,8,10,12-pentamethoxy-1-heptadecene (**2**), and 4,6,8,10,12,14-hexamethoxy-1-nonadecene (**3**).

The IR spectra of the mirabilene isonitriles exhibited a strong C–O stretching band at 1100 cm^{-1} and a single sharp isonitrile stretching absorption that was at 2145–2150 cm^{-1} for compounds **7** and **12** (non conjugated isonitrile) and 2110–2115 cm^{-1} for compounds **8**–**11** (conjugated isonitrile). The FAB mass spectra exhibited protonated molecular ion peaks at m/z 408 for mirabilene-A isonitrile ($C_{24}H_{41}NO_4$), m/z 406 for mirabilene isonitriles B–E ($C_{24}H_{39}NO_4$), and m/z 466 for mirabilene-F isonitrile ($C_{27}H_{47}NO_5$).

Gross Structure Determination. Analysis of the 500-MHz ^1H and 125-MHz ^{13}C NMR spectra of mirabilene-A isonitrile (**7**) immediately suggested the presence of a secondary isonitrile group. The C-16 signal (49.9 ppm) was coupled to the isonitrile nitrogen (3.7 Hz) as was the signal at 158.3 ppm (3.7 Hz) for the isonitrile carbon; both carbon signals were broad 1:1:1 triplets. The H-16 signal (2.98 ppm) was a broad 1:5:10:10:5:1 hextet and the broadness indicated that H-16 was coupled to the isonitrile nitrogen by about 1 Hz. Finally the H_3-17 signal (0.84 ppm) was a sharp doublet of 1:1:1 triplets (6.6, 2.0 Hz), the latter splitting showing that the methyl protons were also coupled to the isonitrile nitrogen.

In mirabilene-A isonitrile the presence of four consecutive methoxyethylene units where the methoxy groups were isotactic, similar to the arrangement in compounds **2**–**6**, was evident from the magnetically nonequivalent methylene proton signals (see Table I).[2] Terminal double bond signals, similar to the ones for compounds **2**–**6**, were also present in the NMR spectrum. The remaining signals could be assigned to a 1,3-dimethyl tetrasubstituted diene moiety and an allylic methylene (H_2-15). Homonuclear COSY and heteronuclear HMQC[7] and HMBC[8] experi-

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Table II. NOEs Observed for Mirabilene Isonitriles

	7	8	9	10	11	12	
H irr	NOE (%)	NOE (%)	NOE (%)	NOE (%)	NOE (%)	H irr	NOE (%)
10	9,9′, 10-OME, 12 (14.5)	9′ (2.3), 12 (15.2)	10-OMe, 12 (11.4)	9′ (3.0), 10-OMe, 12 (13.6)	11 (6.0), 12 (2.0)	12	12-OMe, 14 (16.4)
11-CH_2 (*Z*)					10 (6.5), 11-*E* (25.0)		
11-CH_2 (*E*)					11-Z (28.0), 14, 14′ (5), 15 (3.0)		
11-Me	9′ (3.0), 14 (2.5)	9 (15.0), 9′ (3.8), 13-Me (7)	10-OMe, 10 (0.5), 15 (2.0)	14 (7.5)		13-Me	11-*Z* (2), 11-*E* (3), 14 (2.5)
12	10 (15.0), 13-Me (1), 14 (2.7)	10 (14.6), 13-Me (3)	10 (9.3), 13-Me (2), 15 (4.6)	10 (13.5), 13-Me (2), 14 (6.7)	10 (2.0), 13-Me (7)	14	12 (7.2), 15-Me (1), 16 (2.7)
13-Me	12 (1.5)	11-Me (3), 12 (3.5), 15 (14.1)	12 (1.8), 14 (4.8)	12 (3.5), 15 (13.0)	12 (4.0), 15 (1.0)	15-Me	14 (1.8)
14	11-Me (2), 12 (2.1), 15 (1.5), 15′ (2.0), 16 (3.0)	11-Me (2), 15 (1.8), 17 (5.5)	13-Me (5), 17 (6.7)	11-Me (3), 12 (5.2), 15 (2.1)		16	13-Me (1), 18 (3.8)
15		13-Me (10), 14 (1.8)	11-Me (3), 12 (3.5)	13-Me (8), 14 (2.0), 17 (4.0)	14 (2.5), 14′ (2.5), 11′ (1.5)		
16	14 (3.0), 17 (2.1)					18	16 (3.0), 19 (1.5)
17	16 (4)	14 (11.2)	14 (5.0)	15 (10.5)		19	18 (3.5)

ments allowed us to propose the gross structure of mirabilene-A isonitrile as **7**. The NOEs between H-10 and H-12 and between H-12 and H-14 established the configuration of the diene moiety as 11*E*,13*E*. Moreover, the magnitudes of the NOEs between H-12 and H-14, between H-12 and 13-Me, and between H-14 and 11-Me suggested that the diene existed in two rapidly interconverting conformations, one of which was cisoid and the other transoid (see Table II). The difference NOE experiment also confirmed the assignments of H-1*E* and H-1*Z* (positive NOE between H-1*E* and H-2 and negative NOE between H-1*Z* and H-2) and the four methoxy groups (NOE between the protons of a methoxyl group and the methine bearing the methoxyl group).

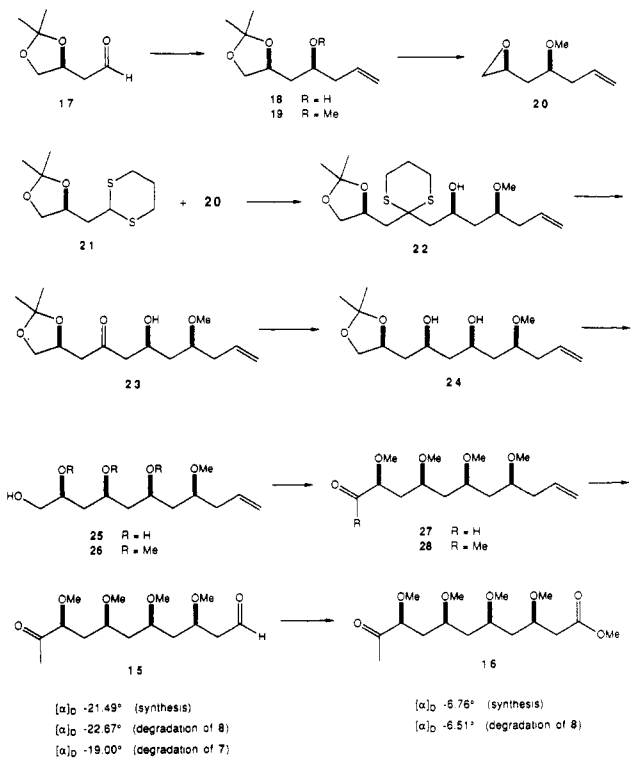
Mirabilene isonitriles B–D (**8–10**) were found to be geometric isomers of 15,16-didehydromirabilene-A isonitrile. Each compound had the molecular formula $C_{24}H_{39}NO_4$ and exhibited the same proton and carbon NMR signals that differed only in chemical shift. The carbon signal for C-16, however, could not be seen for any of the three compounds, even when the ^{13}C NMR spectrum was determined with a long recycling delay. The chemical shift of C-16 (120.3–121.0 ppm) was assigned from the HMBC spectrum, which showed a cross peak to the H_3-17 signal; cross peaks were also observed from C-16 to H-14 and H-15 in the HMBC spectrum of mirabilene B isonitrile. Failure to observe the C-16 signal was attributed to the splitting by the neighboring ^{14}N and the long T_1. The chemical shifts of the proton and carbon signals for the C-1 to C-10 segment in compounds **8–10** (also **11**) were found to be almost identical with those of compound **7**. The proton and carbon NMR signals for the remaining portions of compounds **8–10** could be assigned only by the heteronuclear correlations that appeared in the HMQC and HMBC experiments. The stereochemistry of the triene functionalities in **8–10** was deduced from difference NOE experiments. A 11*E*,13*E* configuration was assigned to compound **8** as it displayed the same pattern of NOEs as was shown by compound **7** for this portion of the molecule (see Table II). The NOEs between H-14 and H-15, H-14 and Me-17, and 13-Me and H-15 established the 15*E* configuration. The NOE values (see Table II), however, suggested that the C12–C13 bond was predominantly cisoid and the C14–C15 bond was predominantly transoid. Appreciable NOEs between H-10 and H-12, H-12 and H-15, 13-Me and H-14, H-14 and Me-17, and 11-Me and H-15 allowed us to assign the 11*E*,13*Z*,15*E* configuration to compound **9**. In this case the NOE values suggested that the C12–C13 and C14–C15 bonds were both predominantly transoid. Compound **10** showed the same NOEs as compounds **7** and **8** for the C11–C12 and C13–C14 double bonds and an NOE was observed between H-15 and Me-17, which established the configuration to be 11*E*,13*E*,15*Z*. The NOE values between 11-Me and H-14, H-12 and 13-Me, 13-Me and H-15, and H-14 and H-15 (see Table II) suggested that the C12–C13 and C14–C15 bonds were both predominantly transoid.

Mirabilene-E isonitrile (**11**), although having the same molecular formula as compounds **8–10**, $C_{24}H_{39}NO_4$, exhibited a different signal pattern in the ^1H NMR spectrum. The C-1 to C-10 segment was shown to be identical with that of compounds **7–10** by homonuclear COSY and heteronuclear HMQC and HMBC experiments. The 2D experiments also established the gross structure of the remaining part of the molecule. The proton assignments for the terminal methylene on C11 and the establishment of the configurations of the C12–C13 and C15–C16 double bonds as 12*Z*,15*E* were determined by difference NOE experiments (see Table II).

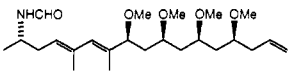
Mirabilene-F isonitrile (**12**) exhibited ^1H and ^{13}C NMR spectra that were comparable to those for mirabilene-A isonitrile (**7**). Except for small chemical shifts differences and some additional signals suggesting one more -CH-$(OCH_3)CH_2$- unit for **12**, the NMR spectra of **7** and **12** were essentially identical. The difference was shown by the mass spectrum, which gave a molecular ion at m/z 566 corresponding to the molecular formula $C_{27}H_{47}NO_5$. Similar NMR arguments as were used for compound **7** were used to arrive at the gross structure and relative stereochemistry of mirabilene-F isonitrile (see Tables I and II).

Stereochemistry. Treatment of mirabilene-A isonitrile (**7**) with formic acid in tetrahydrofuran afforded the corresponding formamide **13**. Lemieux oxidation of **13** followed by Fischer esterification of the resulting *N*-formylamino acid with 2-propanol and acylation of the amino group with trifluoroacetic anhydride gave isopropyl

Scheme I



(*S*)-3-trifluoroacetamidobutyrate (**14**) as determined by gas chromatography on a chiral column. This meant that the absolute configuration of C-16 in **7** had to be also *S*.



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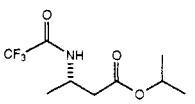

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Ozonolysis of **7** or mirabilene-B isonitrile (**8**) led to levorotatory, isotactic 10-keto-3,5,7,9-tetramethoxyundecanal (**15**), which was identical in all respects, spectrally and optically, with the synthetic 3*R*,5*R*,7*S*,9*S* isomer (Scheme I). Oxidation of **15** from **8** with potassium permanganate followed by esterification of the resulting acid with diazomethane afforded the levorotatory keto ester **16**, which was identical with the synthetic 3*R*,5*R*,7*S*,9*S* compound. This meant that the absolute configurations of the four methoxyl-bearing methines in **7** and **8** were all *S*.

Synthesis of **15** and **16** was achieved as follows: Treatment of aldehyde **17**, prepared from (*S*)-(−)-butane-1,2,4-triol, with allylmagnesium bromide gave, after separation by flash chromatography, syn alcohol **18**, which was then methylated to give **19** in 44% yield. Routine synthetic operations converted the acetonide **19** to oxirane **20** in 65% overall yield. Extention of the isotactic 1,3-polymethoxy chain was achieved by using our previously described method.[9] Coupling of **20** with the anion generated from the chiral dithiane **21** gave **22** (87%) and deprotection of the dithioacetal group afforded the β-hydroxy ketone **23** in 92% yield. A highly syn-stereoselective reduction of **23** was carried out by using lithium aluminum hydride–lithium iodide in ether at −100 °C (syn/anti = 96:4) to give syn diol **24**, obtained in 85% yield after flash chromatography.

Acid treatment of **24** gave **25** (92%), which was transformed to the tetramethoxy derivative **26** in three steps (58% overall yield). Swern oxidation of **26** to the aldehyde **27** followed by the addition of methylmagnesium iodide and Swern oxidation of the resulting alcohol gave the keto olefin **28** in 73% overall yield. Finally Lemieux–Johnson oxidation of **28** yielded the keto aldehyde **15** (73%), $[\alpha]^{25}_D$ −21.49°, the structure of which was confirmed by ^1H and ^{13}C NMR and mass spectroscopy. Oxidation of **28** with potassium permanganate in the presence of excess sodium periodate followed by esterification with diazomethane gave the keto ester **16**, $[\alpha]^{25}_D$ −6.76°, in 67% yield.

Mirabilene isonitriles C–F presumably have the relative and absolute stereochemistry depicted by **9–12**. Since mirabilene isonitriles A and F exhibit similar optical rotations and CD spectra, the two compounds most probably have the same stereochemistry.

Experimental Section

Spectral Analysis and General Procedures. ^1H NMR chemical shifts are referenced in benzene-d_6 to the residual benzene signal (7.15 ppm) and in chloroform-*d* to TMS (0 ppm); ^{13}C chemical shifts are referenced in benzene-d_6 and chloroform-*d* to the solvent signals (128 and 77 ppm, respectively). Homonuclear ^1H connectivities were determined by using the COSY experiment. Homonuclear ^1H NOEs were obtained by difference NOE experiments using a 3-s irradiation period. Heteronuclear ^1H–^{13}C connectivities were determined by HMQC and HMBC experiments.[7,8] IR spectra were measured in dichloromethane unless otherwise noted. UV and CD spectra were recorded in MeOH at 25 °C. Optical rotations were determined in chloroform at 25 °C. Analytical HPLC was carried out by using a diode array UV detector linked to a computer.

In workup of reaction mixtures, extracts were generally washed with brine and dried over $MgSO_4$ before the solvent was evaporated.

Culture Conditions. An aerial form of *Scytonema mirabile* (Dillwyn) Bornet, designated strain number BY-8-1, was isolated from an algal sample collected from a shingled roof of an abandoned home on the slopes of Mt. Tantalus, Oahu, HI. Clonal cultures were prepared by repeated subculture on solidified media. The alga was cultured in 20-L glass bottles containing a modified inorganic medium, designated A_3M_7.[5] Prior to autoclaving, the pH of the medium was adjusted to 7.0 with sodium hydroxide. Cultures were illuminated continuously at an incident intensity of 300 μeinstein m^{-2} s^{-1} from banks of cool-white fluorescent tubes and aerated at a rate of 1 L/min with a mixture of 0.5% CO_2 in air and incubated at a temperature of 24 ± 1 °C. After 30–45 days the alga was harvested by filtration. Yields of lyophilized cells averaged 0.125 g/L of culture.

Isolation. Freeze-dried alga (82 g) was extracted with 3 × 3-L portions of a 7:3 EtOH/water solution (24 h for each). The total extract (38.4 g) was flash chromatographed on a RP-18 column (30 mL, YMC-GEL, ODS 120A). The chromatogram was developed with 100 mL of each of the following solvents: H_2O, 1:1, 3:1, and 9:1 MeOH/H_2O mixtures, MeOH, MeCN, and ethyl acetate. Seven fractions (100 mL) were collected.

Fraction 3 (3:1 MeOH/H_2O) was subjected to gel filtration on Sephadex LH-20 (150 mL of dry gel) using 1:1 dichloromethane/MeOH. Tolytoxin emerged from the column in the 200–275-mL fraction and was further purified on a preparative HPLC column (YMC AM-343-5 ODS, 120A, 20 × 300 mm) using 3:1 MeOH/water as the eluant (6 mL/min). The separation was monitored by UV at 254 nm. Tolytoxin had a retention time of 54 min.

The fourth and fifth fractions from the RP-18 column were rechromatographed on a silica gel (EM Science Kieselgel 60, 230–400 mesh) MPLC column (2.5 × 30 cm) equipped with a UV detector to monitor the separation at 254 nm. The column was eluted first with 2:8 hexane/ethyl acetate (1.5 L) and then with

(9) (a) Mori, Y.; Takeuchi, A.; Kageyama, H.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5423. (b) Mori, Y.; Kuhara, H.; Takeuchi, A.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419.

ethyl acetate (1 L). The first 300 mL of effluent was discarded, but the next 200 mL contained a mixture of the mirabilene isonitriles (412 mg). The mixture was injected (~50 mg per injection) onto a preparative HPLC column (Alltech, Econosil C-18, 10 μm, 22 × 250 mm) and eluted with 3:1 MeOH/water (5 mL/min). Compounds were eluted from the column in the following order: mirabilene-A isonitrile (**7**, 34 min), mirabilene-E isonitrile (**11**, 37 min), mirabilene-F isonitrile (**12**, 43 min), mirabilene-D isonitrile (**10**, 45 min), mirabilene-B isonitrile (**8**, 46 min), mirabilene-C isonitrile (**9**, 49 min), 4,6,8,10,12-pentamethoxy-1-heptadecene (**2**, 51.5 min), and 4,6,8,10,12,14-hexamethoxy-1-nonadecene (**3**, 54 min). Each compound was repurified on a semipreparative RP-18 column (Alltech, Econosil 10 μm, 10 × 250 mm), using a 3:1 MeOH/water solution (2 mL/min) as the eluant.

Mirabilene-A isonitrile (7): $[\alpha]_D$ +2.40° (*c* 1.0); CD $[\theta]_{230}$ +9000 (broad peak); UV 233.2 nm (ε 11900); IR 2980, 2935, 2830, 2150, 1670, 1460, 1370, 1190, 1100(st), 1025, 925 cm^{-1}; for NMR data see Table I; FAB MS (glycerol) *m/z* 446 $(M + K)^+$, 430 $(M + Na)^+$, 413 $(M + K - MeOH)^+$, 408 $(M + H)^+$, 397 $(M + Na - MeOH)^+$, 375 $(M - MeOH)^+$, 344 $(M + H - 2MeOH)^+$, 312 $(M + H - 3MeOH)^+$; high-resolution FAB MS, 408.31270 $(M + H)^+$ calcd for $C_{24}H_{42}NO_4$, mmu error −1.3; high-resolution EI MS 407.30450 $(M)^+$ calcd for $C_{24}H_{41}NO_4$, mmu error −0.9.

Mirabilene-B isonitrile (8): $[\alpha]_D$ +40.95° (*c* 1.4); CD $[\theta]_{225}$ −3000, $[\theta]_{280}$ +6000, $[\theta]_{304}$ +7950; UV 205 nm (ε 6450), 217 (5800), 290.6 (24700), 303.3 (26100), 319.1 (17000); IR 2980, 2935, 2830, 2110, 1650, 1450, 1380, 1200, 1105 (st), 1035, 965 cm^{-1}; ^1H NMR (500 MHz, benzene-d_6) δ 5.07 (br d, J = 17.1 Hz, H-1Z), 5.05 (br d, *J* = 11.1 Hz, H-1*E*), 5.86 (ddt, *J* = 17.1, 11.1, and 6.5 Hz, H-2), 2.26 (br dd, *J* = 5.7 and 6.5 Hz, H-3 and H-3′), 3.32 (ddt, *J* = 4.8, 7.9, and 5.7 Hz, H-4), 3.13 (s, OMe on C-4), 1.61 (ddd, *J* = 4.8, 7.0, and −14.0 Hz, H-5), 1.91 (ddd, *J* = 5.7, 7.9, and −14.0 Hz, H-5′), 3.54 (dddd, *J* = 5.3, 5.7, 7.0, and 7.4 *Hz*, H-6), 3.15 (s, OMe on C-6), 1.71 (ddd, *J* = 5.3, 6.6, and −14.0 Hz, H-7), 1.97 (ddd, *J* = 5.7, 7.4, and −14.0 Hz, H-7′), 3.49 (ddt, J = 6.6, 7.0, and 5.7 Hz, H-8), 3.19 (s, OMe on C-8), 1.80 (ddd, *J* = 5.7, 6.6, and −14.0 Hz, H-9), 2.10 (dt, *J* = −14.0 and 7.0 Hz, H-9′), 3.81 (br dd, *J* = 6.6 and 7.0 Hz, H-10), 3.10 (s, OMe on C-10), 1.74 (d, *J* = 0.9 Hz, 11-Me), 5.95 (br s, H-12), 1.56 (br s, 13-Me), 5.87 (br d, *J* = 11.9 Hz, H-14), 6.39 (br d, *J* = 11.9 Hz, H-15), 1.46 (br s, H_3-17); ^{13}C NMR (125 MHz, benzene-d_6) δ (multiplicity, carbon position, HMBC correlations) 117.08 (t, C-1, H-3,3′), 135.08 (d, C-2, H-1*E*,1*Z*,3,3′,4), 38.14 (t, C-3, H-1*E*,1*Z*,2,5,5′), 77.45 (d, C-4, H-3,3′,4-OMe,5,5′,6), 56.14 (q, 4-OMe, H-4), 37.94 (t, C-5, H-3,3′,4,6), 75.54 (d, C-6, H-4,5,5′,6-OMe,8), 55.83 (q, 6-OMe, H-6), 38.04 (t, C-7, H-5,5′,6,8,9,9′), 75.61 (d, C-8, H-6,7,7′,8-OMe,9,9′,10), 55.91 (q, 8-OMe, H-8), 38.50 (t, C-9, H-6,7,7′,8), 85.11 (d, C-10, H-8,9,9′,10-OMe,12), 55.80 (q, 10-OMe, H-10), 138.68 (s, C-11, H-9,9′,10,11-Me,12), 13.05 (q, 11-Me, H-10,12), 131.62 (d, C-12, H-10,11-Me,13-Me,14), 139.51 (s, C-13, 11-Me,H-12,13-Me,15), 17.45 (q, 13-Me, H-12,14), 123.26 (d, C-14, H-12,13-Me), 126.46 (d, C-15, H-14,17), 120.96 (st [J_{CN} = 3.7 Hz], C-16, H-14,15,17), 16.60 (q, C-17, H-15), 165.85 (st [J_{CN} = 3.7 Hz], NC, not observed); FAB MS (glycerol) *m/z* 444 $(M + K)^+$, 428 $(M + Na)^+$, 406 $(M + H)^+$, 374 $(M + H - MeOH)^+$.

Mirabilene-C isonitrile (9): $[\alpha]_D$ −4.63° (*c* 0.36); CD $[\theta]_{212}$ +9600, $[\theta]_{280}$ +2000; UV 217.4 nm (ε 9200), 223.6 (8900), 263 (18300), 276.8 (22300), 319 (11200); IR 2980, 2935, 2830, 2110, 1650, 1440, 1375, 1190, 1100 (st), 920 cm^{-1}; ^1H NMR (500 MHz, benzene-d_6) δ 5.09 (br d, *J* = 16.9 Hz, H-1*Z*), 5.06 (br d, *J* = 10.7 Hz, H-1*E*), 5.89 (ddt, *J* = 16.9, 10.7, and 6.5 Hz, H-2), 2.28 (br dd, *J* = 5.1 and 6.5 Hz, H-3 and H-3′), 3.35 (ddt, *J* = 5.5, 7.1, and 5.1 Hz, H-4), 3.15 (s, OMe on C-4), 1.63 (ddd, *J* = 5.5, 6.3, and −14.2 Hz, H-5), 1.94 (ddd, *J* = 5.9, 7.1, and −14.2 Hz, H-5′), 3.56 (tt, *J* = 5.9 and 6.3 Hz, H-6), 3.19 (s, OMe on C-6), 1.71 (dt, *J* = −14.0 and 5.9 Hz, H-7), 1.99 (dt, *J* = −14.0 and 6.3 Hz, H-7′), 3.51 (ddt, *J* = 6.3, 6.7, and 5.9 Hz, H-8), 3.23 (s, OMe on C-8), 1.84 (ddd, *J* = 5.9, 6.3, and −13.8 Hz, H-9), 2.09 (dt, *J* = −13.8 and 6.7 Hz, H-9′), 3.82 (dd, *J* = 6.3 and 6.7 Hz, H-10), 3.09 (s, OMe on C-10), 1.56 (br s, 11-Me), 5.84 (s, H-12), 1.67 (br s, 13-Me), 5.64 (d, *J* = 11.7 Hz, H-14), 6.44 (d, *J* = 11.7 Hz, H-15), 1.48 (s, H_3-17); ^{13}C NMR (125 MHz, benzene-d_6) δ (multiplicity, carbon position, HMBC correlations) 117.07 (t, C-1, H-3,3′), 135.17 (d, C-2, H-1*E*,1*Z*,3,3′,4), 38.18 (t, C-3, H-1*E*,1*Z*,4,5,5′), 77.45 (d, C-4, H-3,3′,4-OMe,5,5′,6), 56.16 (q, 4-OMe, H-4), 37.90 (t, C-5, H-3,3′,4,6,7,7′), 75.46 (d, C-6, H-4,5,5′,6-OMe,7,7′,8), 55.83 (q, 6-OMe, H-6), 37.90 (t, C-7, H-5,6,8,9,9′), 75.65 (d, C-8, H-6,7,7′,8-OMe,9,9′,10), 56.00 (q, 8-OMe, H-8), 38.29 (t, C-9, H-7′,8,10), 84.05 (d, C-10, H-8,9,9′,10-OMe,11-Me,12), 55.78 (q, 10-OMe, H-10), 140.91 (s, C-11, H-9,9′,10,11-Me,12), 12.64 (q, 11-Me, H-10,12), 126.64 (d, C-12, H-10,11-Me,13-Me,14), 139.91 (s, C-13, H-12,13-Me,14,15), 24.48 (q, 13-Me, H-12,14), 120.96 (d, C-14, H-15,13-Me), 128.10 (d, C-15, H-17), 120.43 (st [J_{CN} = 3.7 Hz], C-16, H-17), 16.66 (q, C-17), 165.25 (st [J_{CN} = 3.7 Hz], NC, not observed); FAB MS (glycerol) *m/z* 444 $(M + K)^+$, 428 $(M + Na)^+$, 406 $(M + H)^+$, 374 $(M + H - MeOH)^+$, 342 $(M + H - 2MeOH)^+$, 310 $(M + H - 3MeOH)^+$, 278 $(M + H - 4MeOH)^+$; high-resolution FAB MS 406.29451 $(M + H)^+$, calcd for $C_{24}H_{40}NO_4$, mmu error 1.2.

Mirabilene-D isonitrile (10): CD $[\theta]_{215}$ +12200, $[\theta]_{292}$ +4000; UV 201.8 nm (ε 8500), 214.5 (7900), 292 (16900), 303 (17400); IR 2980, 2935, 2830, 2110, 1640, 1450, 1385, 1195, 1100 (st), 925 cm^{-1}; ^1H NMR (500 MHz, benzene-d_6) δ 5.09 (ddt, *J* = 17.2, 2.1, and 1.2 Hz, H-1*Z*), 5.05 (ddt, *J* = 10.0, 2.0, and 1.2 Hz, H-1*E*), 5.89 (ddt, *J* = 17.2, 10.0, and 7.1 Hz, H-2), 2.27 (dddd, *J* = 1.2, 2.1, 5.4, and 7.1 Hz, H-3 and H-3′), 3.33 (ddt, *J* = 5.0, 7.1, and 5.4 Hz, H-4), 3.15 (s, OMe on C-4), 1.62 (ddd, *J* = 5.0, 7.0, and −14.0 Hz, H-5), 1.93 (ddd, *J* = 5.7, 7.1, and −14.0 Hz, H-5′), 3.55 (dddd, *J* = 5.3, 5.7, 7.0, and 7.4 Hz, H-6), 3.20 (s, OMe on C-6), 1.70 (ddd, *J* = 5.3, 6.6, and −14.0 Hz, H-7), 1.97 (ddd, *J* = 5.7, 7.4, and −14.0 Hz, H-7′), 3.50 (ddt, *J* = 6.6, 7.0, and 5.7 Hz, H-8), 3.20 (s, OMe on C-8), 1.80 (ddd, *J* = 5.7, 6.6, and −14.0 Hz, H-9), 2.10 (dt, *J* = −14.0 and 7.0 Hz, H-9′), 3.83 (dd, *J* = 6.6 and 7.0 Hz, H-10), 3.08 (s, OMe on C-10), 1.89 (br s, 11-Me), 6.02 (br s, H-12), 1.67 (br s, 13-Me), 6.64 (d, *J* = 11.3 Hz, H-14), 5.84 (d, *J* = 11.3 Hz, H-15), 1.44 (s, H_3-17); ^{13}C NMR (125 MHz, benzene-d_6) δ (multiplicity, carbon position, HMBC correlations), 117.01 (t, C-1, H-3,3′), 135.20 (d, C-2, H-3,3′,4), 38.22 (t, C-3, H-1E,1Z,5,5′), 77.50 (d, C-4, H-3,3′,4-OMe,5,5′,6), 56.17 (q, 4-OMe, H-4), 37.99 (t, C-5, H-3,3′,7,7′), 75.80 (d, C-6, H-5,5′,6-OMe,8), 55.98 (q, 6-OMe, H-6), 38.15 (t, C-7, H-6,9,9′), 75.64 (d, C-8, H-6,7,7′,8-OMe,9,9′,10), 55.98 (q, 8-OMe, H-8), 38.50 (t, C-9, H-7,7′,10), 85.08 (d, C-10, H-8,9,9′,10-OMe,11-Me,12), 55.79 (q, 10-OMe, H-10), 139.31 (s, C-11, H-9,9′,11-Me), 13.18 (q, 11-Me, H-10,12), 131.38 (d, C-12, H-10,11-Me,13-Me,14), 138.20 (s, C-13, 13-Me), 17.95 (q, 13-Me, H-12,14), 124.33 (d, C-14, H-15,13-Me), 125.10 (d, C-15, H-17), 120.31 (st [J_{CN} = 3.7 Hz], C-16, H-17), 21.35 (q, C-17), 164.49 (st [J_{CN} = 3.7 Hz], NC, not observed); FAB MS (glycerol) *m/z* 444 $(M + K)^+$, 428 $(M + Na)^+$, 406 $(M + H)^+$.

Mirabilene-E isonitrile (11): CD $[\theta]_{215}$ −8000, $[\theta]_{235}$ −6000; UV 209 nm (ε 13700), 227 (9700), 241 (6200); IR 2980, 2935, 2830, 2115, 1645, 1460, 1380, 1190, 1100 (st), 920 cm^{-1}; ^1H NMR (500 MHz, benzene-d_6) δ 5.09 (ddt, *J* = 17.2, 2.1, and 1.1 Hz, H-1*Z*), 5.06 (ddt, *J* = 10.0, 1.2, and 0.8 Hz, H-1*E*), 5.87 (ddt, *J* = 17.2, 10.0, and 7.1 Hz, H-2), 2.28 (dddd, *J* = 1.2, 2.5, 5.1, and 7.1 Hz, H-3 and H-3′), 3.34 (ddt, *J* = 5.0, 7.5, and 5.1 Hz, H-4), 3.14 (s, OMe on C-4), 1.63 (ddd, *J* = 5.0, 7.4, and −14.0 Hz, H-5), 1.93 (ddd, *J* = 5.4, 7.5, and −14.0 Hz, H-5′), 3.55 (dddd, *J* = 5.0, 5.4, 6.7, and 7.4 Hz, H-6), 3.20 (s, OMe on C-6), 1.73 (ddd, *J* = 5.0, 5.9, and −14.0 Hz, H-7), 1.97 (ddd, *J* = 5.9, 6.7, and −14.0 Hz, H-7′), 3.51 (ddt, *J* = 5.7, 6.7, and 5.9 Hz, H-8), 3.15 (s, OMe on C-8), 1.78 (ddd, *J* = 5.7, 6.3, and −14.0 Hz, H-9), 2.10 (ddd, *J* = 6.7, 7.1, and −14.0 Hz, H-9′), 3.84 (dd, *J* = 6.3 and 7.1 Hz, H-10), 3.14 (s, OMe on C-10), 5.14 (d, *J* = 2.1 Hz, *Z* H in CH_2 on C-11), 4.80 (d, *J* = 1.2 Hz, *E* H in CH_2 on C-11), 5.82 (br s, H-12), 1.44 (br d, *J* = 1.2 Hz, Me on C-13), 2.61 (dd, *J* = 8.8 and −14.9 Hz, H-14), 2.64 (dd, *J* = 7.1 and −14.9 Hz, H-14′), 5.49 (dd, *J* = 8.8 and 7.1 Hz, H-15), 1.39 (br s, H_3-17); ^{13}C NMR (125 MHz, benzene-d_6) δ (multiplicity, carbon position, HMBC correlations) 117.06 (t, C-1, H-3,3′), 135.13 (d, C-2, H-1*Z*,3,3′,4), 38.15 (t, C-3, H-1*E*,1*Z*,2,5,5′), 77.49 (d, C-4, H-3,3′,4-OMe,5,5′,6), 56.16 (q, 4-OMe, H-4), 37.95 (t, C-5, H-3,3′,4,6,7′), 75.51 (d, C-6, H-4,5,5′,6-OMe,7,7′,8), 55.74 (q, 6-OMe, H-6), 38.15 (t, C-7, H-5,5′,6,8,9,9′), 75.45 (d, C-8, H-6,7,7′,8-OMe,9,9′,10), 55.95 (q, 8-OMe, H-8), 39.32 (t, C-9, H-7,7′,8,10), 82.79 (d, C-10, H-8,9,9′,10-OMe,11-CHH′), 56.00 (q, 10-OMe, H-10), 145.53 (s, C-11, H-9,9′,11,11′,13-Me,14,14′), 115.17 (t, C-11, H-10,12), 124.54 (d, C-12, H-10,11,11′), 136.75 (s, C-13, H-11,11′,12,13-Me,14,14′), 23.61 (q, 13-Me, H-12,14,14′), 31.30 (t, C-14, H-12,13-Me), 129.68 (d, C-15, H-14,14′,17), 123.15 (st [J_{CN} = 3.7 Hz], C-16, H-14,14′,15,17), 16.47 (q, C-17, H-15), 163.54 (st [J_{CN} = 3.7 Hz], NC, not observed); FAB MS (glycerol) *m/z* 444 $(M + K)^+$, 428 $(M + Na)^+$, 406 $(M + H)^+$, 374 $(M + H - MeOH)^+$; high-resolution FAB MS 406.29172 (M

+ H)$^+$, calcd for $C_{24}H_{40}NO_4$, mmu error 4.0.

Mirabilene-F isonitrile (12): $[\alpha]_D$ +1.29° (*c* 0.07); CD $[\theta]_{230}$ +5000 (broad peak); UV (MeOH) 233 nm (ε 9800); IR 2980, 2935, 2830, 2145, 1670, 1460, 1385, 1190, 1100 (st), 1020, 925 cm^{-1}; ^{1}H NMR (500 MHz, benzene-d_6) δ 5.10 (ddt, *J* = 17.1, 2.5, and 1.2 Hz, H-1Z), 5.06 (ddt, *J* = 10.0, 2.0, and 1.2 Hz, H-1*E*), 5.89 (ddt, *J* = 17.1, 10.0, and 7.0 Hz, H-2), 2.29 (dddd, *J* = 1.2, 2.5, 5.4, and 7.0 (H-3 and H-3′), 3.35 (ddt, *J* = 5.0, 7.0, and 5.4 Hz, H-4), 3.15 (s, OMe on C-4), 1.63 (ddd, *J* = 5.0, 7.0, and −14.0 Hz, H-5), 1.95 (ddd, *J* = 5.4, 7.1, and −14.0 Hz, H-5′), 3.57 (ddt, *J* = 7.0, 7.4, and 5.4 Hz, H-6), 3.20 (s, OMe on C-6), 1.71 (ddd, *J* = 5.4, 6.6, and −14.0 Hz, H-7), 1.99 (ddd, *J* = 5.7, 7.4, and −14.0 Hz, H-7′), 3.61 (dddd, *J* = 5.0, 5.7, 6.6, and 7.2 Hz, H-8), 3.26 (s, OMe on C-8), 1.79 (ddd, *J* = 5.0, 6.8, and −14.2 Hz, H-9), 2.03 (ddd, *J* = 5.9, 7.2, and −14.2 Hz, H-9′), 3.56 (dddd, *J* = 5.4, 5.9, 6.8, and 7.1 Hz, H-10), 3.24 (s, OMe on C-10), 1.88 (ddd, *J* = 5.4, 6.7, and −13.8 Hz, H-11), 2.18 (ddd, *J* = 6.7, 7.1, and −13.8 Hz, H-11′), 3.85 (t, *J* = 6.7 Hz, H-12), 3.14 (s, OMe on C-12), 1.84 (d, *J* = 1.2 Hz, Me on C-13), 5.96 (br s, H-14), 1.59 (br s, Me on C-15), 5.28 (br dd, *J* = 7.1 and 7.6 Hz, H-16), 1.86 (m, H-17), 1.98 (m, H-17′), 2.96 (ddq, *J* = 6.7, 7.1, and 7.3 Hz, H-18), 0.81 (dt, *J* = 7.3 and 2.1 Hz, H_3-19); ^{13}C NMR (125 MHz, benzene-d_6) δ (multiplicity, carbon position, HMBC correlations) 117.01 (t, C-1, H-3,3′), 135.21 (d, C-2, H-1Z,3,3′,4), 38.20 (t, C-3, H-1*E*,1Z,2,4,5,5′), 77.53 (d, C-4, H-3,3′,4-OMe,5,5′,6), 56.12 (q, 4-OMe, H-4), 38.00 (t, C-5, H-3,3′,6,7,7′), 75.55 (d, C-6, H-4,5,5′,6-OMe,7′,8), 55.98 (q, 6-OMe, H-6), 38.60 (t, C-7, H-5,5′,6,8,9,9′), 75.74 (d, C-8, H-6,7,7′,8-OMe,9,9′), 55.94 (q, 8-OMe, H-8), 38.30 (t, C-9, H-7,7′,10,11,11′), 75.72 (d, C-10, H-8,9,9′,10-OMe,11,11′,12), 56.01 (q, 10-OMe, H-10), 38.56 (t, C-11, H-9,9′10,12), 84.91 (d, C-12, H-10,11,11′,12-OMe,13-Me,14), 55.70 (q, 12-OMe, H-12), 136.19 (s, C-13, H-11,11′,12,13-Me), 12.54 (q, 13-Me, H-12,14), 131.63 (d, C-14, H-12,13-Me,15-Me,16), 136.19 (s, C-15, H-14,15-Me,16,17,17′), 17.33 (q, 15-Me, H-14,16), 123.81 (d, C-16, H-14,15-Me,17,17′,18), 35.46 (t, C-17, H-16,18,19), 49.80 (dt [J_{CN} = 3.7 Hz], C-18, H-16,17,17′,19), 20.95 (q, C-19, H-17,17′,18), 158.69 (st [J_{CN} = 3.7 Hz], NC, not observed); FAB MS (thioglycerol) *m/z* 504 (M + K)$^+$, 488 (M + Na)$^+$, 466 (M + H)$^+$, 434 (M + H − MeOH)$^+$, 402 (M + H − 2MeOH)$^+$; high-resolution FAB MS 466.34941 (M + H$^+$, calcd for $C_{27}H_{47}NO_5$, mmu error 3.9.

Conversion of Isonitrile 7 to Formamide 13. Mirabilene-A isonitrile (5.0 mg) was allowed to stand in a 1:1 mixture of formic acid and THF (1 mL) at room temperature for 30 min. The solvent was removed in vacuo to give a single product, **13**: ^{1}H NMR (300 MHz, benzene-d_6) δ 5.08 (ddt, *J* = 17.1, 2.5, and 1.2 Hz, H-1*Z*), 5.06 (ddt, *J* = 10.0, 2.0, and 1.2 Hz, H-1*E*), 5.89 (ddt, *J* = 17.1, 10.0, and 7.0 Hz, H-2), 2.28 (dddd, *J* = 1.2, 2.5, 5.4, and 7.0 (H-3 and H-3′), 3.35 (ddt, *J* = 5.0, 7.0, and 5.4 Hz, H-4), 3.15 (s, OMe on C-4), 1.63 (ddd, *J* = 5.0, 7.0, and −14.0 Hz, H-5), 1.96 (ddd, *J* = 5.4, 7.1, and −14.0 Hz, H-5′), 3.56 (ddt, *J* = 7.0, 7.4, and 5.4 Hz, H-6), 3.18 (s, OMe on C-6), 1.73 (ddd, *J* = 5.4, 6.6, and −14.0 Hz, H-7), 1.99 (ddd, *J* = 5.7, 7.4, and −14.0 Hz, H-7′), 3.54 (dddd, *J* = 5.0, 5.7, 6.6, and 7.2 Hz, H-8), 3.24 (s, OMe on C-8), 1.90 (ddd, *J* = 5.4, 6.7, and −13.8 Hz, H-9), 2.19 (ddd, *J* = 6.7, 7.1, and −13.8 Hz, H-9′), 3.87 (t, *J* = 6.7 Hz, H-10), 3.14 (s, OMe on C-10, 1.82 (d, *J* = 1.2 Hz, Me on C-11), 5.99 (br s, H-12), 1.68 (br s, Me on C-13), 5.32 (br dd, *J* = 7.1 and 7.6 Hz, H-14), 1.64 (m, H-15), 1.99 (m, H-15′), 4.09 (br ddq, *J* = 6.7, 7.1, and 6.3 Hz, H-16), 0.80 (d, *J* = 6.3 Hz, H_3-17), 7.12 (br s, NH on 16), 7.72 (br s, NCHO); ^{13}C NMR (75 MHz, acetone-d_6) δ (multiplicity, carbon position) 117.00 (t, C-1), 135.81 (d, C-2), 38.32 (t, C-3), 77.84 (d, C-4), 56.24 (q, 4-OMe), 38.25 (t, C-5), 75.88 (d, C-6), 55.95 (q, 6-OMe), 38.32 (t, C-7), 75.88 (d, C-8), 56.05 (q, 8-OMe), 38.73 (t, C-9), 85.38 (d, C-10), 55.63 (q, 10-OMe), 135.01 (s, C-11), 12.21 (q, 11-Me), 132.96 (d, C-12), 135.62 (s, C-13), 17.29 (q, 13-Me), 126.98 (d, C-14), 35.63 (t, C-15), 44.64 (d, C-16), 160.63 (d, 16-NHCHO), 20.49 (q, C-17).

Conversion of Formamide 13 to Isopropyl (*S*)-3-(Trifluoroacetamido)butyrate (14). Mirabilene-A formamide (0.5 mg) in acetone (0.1 mL) was reacted with excess aqueous $NaIO_4$ solution containing a small amount of $KMnO_4$ for 15 h at room temperature. Methanol was added and the mixture was allowed to stand until the permanganate color had discharged. The solvent was removed with a nitrogen stream and the residue was dissolved in 6 N HCl (0.3 mL) and heated at 100 °C for a few hours. 2-Propanol (0.7 mL) was added and the mixture was heated for 1 h and evaporated. The isopropyl 3-aminobutyrate was treated with 0.5 mL of 1:1 $(CF_3CO)_2O/CH_2Cl_2$ at 100 °C for 5 min, the excess reagent was evaporated with a stream of nitrogen, and the isopropyl 3-(trifluoroacetamido)butyrate was dissolved in 0.5 mL of CH_2Cl_2 for GCMS analysis on a 25 m × 0.25 mm Chirasil-Val column (Alltech). Using the following conditions, viz. column temperature 60 → 110 °C at 2°/min and a 12 psi head pressure (flow rate estimated to be about 0.6 mL), t_R for the D (*R*) and L (*S*) isomers of **14** are 14.6 and 15.1 min, respectively. The retention time for **14** from degradation of **13** was found to be 15.1 min.

Degradation of Mirabilene Isonitriles A (7) and B (8) to Keto Aldehyde 15 and Keto Ester 16. A solution of **8** (23 mg) in dichloromethane (5 mL) cooled in a dry ice/acetone bath (−78 °C) was treated with excess saturated ozone/CH_2Cl_2 solution. The reaction mixture was then allowed to warm to room temperature. After 2 h Me_2S (2 mL) was added and the mixture was allowed to stand overnight. After evaporation of the solvent the residual oil was chromatographed on a silica column with 7:3 EtOAc/hexane to give **15** (3.6 mg): $[\alpha]_D$ = −22.67° (*c* 0.06); ^{1}H NMR spectrum identical with that of synthetic **15**.

Similar treatment of **7** (10 mg) gave **15** (2 mg), $[\alpha]_D$ = −19.00° (*c* 0.2).

Keto aldehyde **15** (1.7 mg; from **8**) in 4:1 acetone/H_2O (0.5 mL) was reacted with $KMnO_4$ (2 mg) and the purple solution was stirred for 2 h at room temperature. The reaction mixture was made acidic with 1% HCl, the carboxylic acid was extracted with EtOAc and treated with ethereal diazomethane, and the resulting ester was purified by flash chromatography (45% EtOAc/hexane) to give **16** (1.0 mg), $[\alpha]_D$ −6.51° (*c* 0.08); ^{1}H NMR spectrum identical with that of synthetic **16**.

(2*S*,4*S*)-1,2-*O*-Isopropylidene-4-methoxy-6-heptene-1,2-diol (19). To a solution of allylmagnesium bromide (100 mmol) in ether (100 mL) at −20 °C was added dropwise a solution of aldehyde **17** (3.5 g, 24 mmol) in ether (20 mL). After being stirred at 0 °C for 1 h, the mixture was quenched with saturated aqueous NH_4Cl and extracted with ether, and the extract was purified by flash chromatography (3–10% acetone–CH_2Cl_2) to give **18** (1.97 g, 44%) and the 4*R* isomer of **18** (1.95 g, 44%). Compound **18**: bp 88 °C (7 mmHg, Kugelrohr distillation); $[\alpha]_D$ +13.3° (*c* 0.72); IR ($CHCl_3$) 3520, 1635, 1380, 1370 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 1.24 (3 H, s, Me), 1.31 (3 H, s, Me), 1.47 (1 H, dt, *J* = 14.2 and 9.1 Hz), 2.18 (2 H, m), 2.77 (1 H, d, *J* = 1.7 Hz, OH), 3.26 (1 H, t, *J* = 7.7 Hz), 3.72 (1 H, m), 3.73 (1 H, dd, *J* = 7.7 and 5.7 Hz), 3.94 (1 H, m), 5.02 (1 H, br d, *J* = 10.2 Hz), 5.03 (1 H, br d, *J* = 16.5 Hz), 5.84 (1 H, ddt, *J* = 16.5, 10.2, and 7.1 Hz). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.22; H, 9.96.

To a stirred solution of **18** (1.95 g, 10.5 mmol) in dry THF (50 mL) at 0 °C were added excess KH and MeI (4 mL). The reaction mixture was stirred for 1 h at room temperature under nitrogen. Excess KH was decomposed carefully by dropwise addition of MeOH and the oily product was separated by extraction with ether and purification by flash chromatography (6% acetone–CH_2Cl_2) to give **19** (2.07 g, 99%): bp 95 °C (10 mmHg, Kugelrohr distillation); $[\alpha]_D$ +35.9° (*c* 0.35); IR ($CHCl_3$) 1635, 1380, 1370, 1055, 920 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (3 H, s, Me), 1.41 (3 H, s, Me), 1.68 (1 H, ddd, *J* = 14.2, 6.6, and 5.6 Hz), 1.92 (1 H, dt, *J* = 14.2 and 6.4 Hz), 2.33 (2 H, br t, *J* = 6.4 Hz), 3.34 (3H, s, OMe), 3.55 (1 H, t, *J* = 7.8 Hz), 4.06 (1 H, dd, *J* = 8.1 and 5.9 Hz), 4.22 (1 H, quintet, *J* = 6.4 Hz), 5.09 (1 H, br d, *J* = 10.2 Hz, 5.10 (1 H, br d, *J* = 17.2 Hz), 5.81 (1 H, ddt, *J* = 17.2, 10.2, and 7.1 Hz). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.81; H, 10.22.

(2*S*,4*S*)-1,2-Epoxy-4-methoxy-6-heptene (20). To a solution of **19** (2.05 g, 10.2 mmol) in MeOH (40 mL) was added 5% HCl–MeOH (1 mL), and the solution was allowed to stand for 14 h at room temperature. After evaporation of the solvent the oily residue was purified by flash chromatography (80–100% EtOAc–hexane) to give a diol (1.57 g, 95%): $[\alpha]_D$ +72.7° (*c* 0.7); IR ($CHCl_3$) 3450, 1635, 1080, 918 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67 (2 H, m), 2.19 (1 H, t, *J* = 6.1 Hz, OH), 2.36 (2 H, m), 3.41 (3 H, s, OMe), 3.47 (1 H, dt, *J* = 11.2 and 5.4 Hz), 3.56 (2 H, m), 3.74 (1 H, s, OH), 3.90 (1 H, m), 5.10 (1 H, br d, 9.8 Hz), 5.11 (1 H, br d, *J* = 17.6 Hz), 5.77 (1 H, ddt, *J* = 17.6, 9.8, and 7.1 Hz).

The diol (1.56 g, 9.7 mmol) was dissolved in pyridine (15 mL) and *p*-toluenesulfonyl chloride (2.42 g, 12.6 mmol) was added at 0 °C. The reaction mixture was stirred at 0 °C for 4 h and the

product extracted out with ether and purified by flash chromatography (25% EtOAc–hexane) to give the tosylate (2.17 g, 71%).

To a stirred solution of the tosylate (2.15 g, 6.9 mmol) in ether (20 mL) and MeOH (4 mL) at 0 °C was added potassium *tert*-butoxide (920 mg, 8.2 mmol). The mixture was stirred at 0 °C for 2 h and the oily product was extracted from the mixture with pentane and distilled (bulb to bulb) to give the epoxide **20** (926 mg, 96%): bp 125 °C (30 mmHg); $[\alpha]_D$ +13.2° (*c* 0.46); IR ($CHCl_3$) 1635, 1230, 1080, 915 cm^{-1}; ^1H (400 MHz, $CDCl_3$) δ 1.72 (1 H, dt, J = 14.4 and 5.4 Hz), 1.77 (1 H, dt, J = 14.4 and 6.4 Hz), 2.36 (2 H, br t, J = 6.5 Hz), 2.48 (1 H, dd, J = 5.1 and 2.7 Hz), 2.77 (1 H, dd, J = 4.6 and 4.4 Hz), 3.03 (1 H, m), 3.37 (3 H, s, OMe), 3.41 (quintet, J = 5.9 Hz), 5.09 (1 H, br d, J = 10.3 Hz), 5.11 (1 H, br d, J = 17.1 Hz), 5.82 (1 H, ddt, J = 17.1, 10.3, and 7.1 Hz). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.82; H, 9.61.

(2*S*,6*S*,8*S*)-1,2-*O*-Isopropylidene-8-methoxy-4-(trimethylenedithio)-10-undecene-1,2,6-triol (22). To a stirred solution of 2-[(2*S*)-2,3-*O*-isopropylidene-2,3-dihydroxypropyl]-1,3-dithiane (**21**) (1.67 g, 7.1 mmol) in dry THF (20 mL) at −40 °C under nitrogen was added 1.6 M butyllithium in hexane (5 mL, 8 mmol). The solution was stirred at −30 °C for 2 h and then a solution of **20** (924 mg, 6.5 mmol) in dry THF (5 mL) was added. The reaction vessel was closed under a positive pressure of nitrogen and stored at −20 °C for 43 h. The reaction mixture was quenched with aqueous NH_4Cl and the product was extracted from the mixture with ether and flash chromatographed (15–20% EtOAc–hexane) to give **22** (2.05 g, 87%): $[\alpha]_D$ +25.22° (*c* 1.0); IR ($CHCl_3$) 3450, 1635, 1420, 1375, 1365, 1230, 1080, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3 H, s, Me), 1.39 (3 H, s, Me), 1.56 (1 H, ddd, J = 14.1, 4.6, and 2.9 Hz), 1.74 (1 H, ddd, J = 14.1, 9.5, and 8.3 Hz), 1.88–2.80 (3 H), 2.44–2.38 (5 H), 2.75–3.00 (4 H), 3.37 (3 H, s, OMe), 3.52 (1 H, m), 3.55 (1 H, t, J = 8.1 Hz), 3.82 (1 H, d, J = 1.2 Hz, OH), 4.13 (1 H, dd, J = 8.1 and 6.1 Hz), 4.15 (1 H, m), 4.40 (1 H, m), 5.09 (1 H, br d, J = 10.2 Hz), 5.10 (1 H, br d, J = 17.1 Hz), 5.80 (1 H, ddt, J = 17.1, 10.2, and 7.1 Hz); high-resolution EIMS 376.1752 (M^+), calcd for $C_{18}H_{32}O_4S_2$, mmu error 1.2.

(2*S*,6*S*,8*S*)-1,2-*O*-Isopropylidene-8-methoxy-4-oxo-10-undecene-1,2,6-triol (23). To a stirred solution of **22** (580 mg, 1.5 mmol) in 80% aqueous MeCN (60 mL) were added $CaCO_3$ (1.54 g, 15 mmol) and MeI (9.6 mL, 154 mmol). The mixture was stirred for 22 h at room temperature, diluted with ethyl acetate, and filtered through a short column of Celite. The filtrate was evaporated and the residue was purified by flash chromatography (30–40% EtOAc–hexane) to give **23** (403 mg, 92%): $[\alpha]_D$ −53.07° (*c* 0.6); IR ($CHCl_3$) 3540, 1700, 1375, 1365, 1220, 1075, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3 H, s, Me), 1.39 (3 H, s, Me), 1.62 (2 H, m), 2.31 (2 H, br t, J = 7.3 Hz), 2.52 (1 H, dd, J = 16.4 and 4.6 Hz), 2.62 (1 H, dd, J = 11.0 and 6.8 Hz), 2.66 (1 H, dd, J = 11.0 and 8.1 Hz), 3.37 (3 H, s, OMe), 3.52 (1 H, m), 3.53 (1 H, dd, J = 8.3 and 6.8 Hz), 3.74 (1 H, br s, OH), 4.17 (1 H, dd, J = 8.3 and 6.1 Hz), 4.23 (1 H, m), 4.46 (1 H, quintet, J = 6.4 Hz), 5.08 (1 H, br d, J = 9.8 Hz), 5.09 (1 H, br d, J = 17.6 Hz, 5.76 (1 H, ddt, J = 17.6, 9.8, and 7.1 Hz); CIMS (isobutane) m/z 287 (MH^+), 269 ($MH^+ - H_2O$).

(2*S*,4*S*,6*S*,8*S*)-1,2-*O*-Isopropylidene-8-methoxy-10-undecene-1,2,4,6-tetrol (24). To a stirred solution of **23** (610 mg, 2.13 mmol) and LiI (1.8 g, 12.3 mmol) in dry ether (60 mL) at −100 °C was added $LiAlH_4$ (0.78 g, 21 mmol). The reaction mixture was stirred for 1.5 h at −100 °C under nitrogen and then warmed gradually to −70 °C. Excess $LiAlH_4$ was decomposed by addition of EtOAc (5 mL) and 1 N NaOH. The mixture was then stirred at room temperature until the precipitates aggregated. The organic layer was separated and the aqueous portion was extracted with EtOAc. The combined extracts were evaporated and the residual oil purified by flash chromatography (10–15% acetone–CH_2Cl_2) to give **24** (518 mg, 85%): $[\alpha]_D$ +38.12° (*c* 1.0); IR ($CHCl_3$) 3460, 1618, 1425, 1380, 1370, 1190, 920 cm^{-1}; ^1H NMR (400 MHz, benzene-d_6) δ 1.31 (3 H, s, Me), 1.39 (3 H, s, Me), 1.28 (1 H, dt, J = 13.0 and 2.4 Hz), 1.34 (1 H, ddd, J = 14.4, 3.9 and 2.7 Hz), 1.45 (1 H, ddd, J = 14.4, 5.1 and 3.9 Hz), 1.63 (1 H, td, J = 9.8 and 2.4 Hz), 1.66 (1 H, td, J = 9.8 and 2.0 Hz), 1.78 (1 H, dt, J = 13.0 and 7.8 Hz), 2.12 (2 H, dd, J = 6.8 and 5.6 Hz), 2.96 (3 H, s, OMe), 3.22 (1 H, m), 3.46 (1 H, t, J = 7.8 Hz), 3.91 (1 H, dd, J = 8.1 and 5.9 Hz), 3.92 (1 H, m), 4.02 (1 H, m), 4.11 (1 H, br s, OH), 4.14 (1 H, br s, OH), 4.20 (1 H, tt, J = 7.6 and 5.6 Hz), 5.02 (1 H, br d, J = 17.0 Hz), 5.03 (1 H, br d, J = 10.3 Hz), 5.70 (1 H, ddt, J = 17.0, 10.3, and 7.1 Hz); CIMS (isobutane) m/z 289 (MH^+); high-resolution EIMS 273.1741 (M^+ − Me), calcd for $C_{14}H_{25}O_5$, mmu error 4.1.

(2*S*,4*S*,6*S*,8*S*)-2,4,6,8-Tetramethoxy-10-undecen-1-ol (26). A solution of **24** (1.13 g, 3.9 mmol) and *p*-toluenesulfonic acid (10 mg) was allowed to stand for 48 h at room temperature. After removal of the solvent the residue was purified by flash chromatography (6% MeOH–EtOAc) to give the tetrol **25** (895 mg, 92%): $[\alpha]_D$ +47.7° (*c* 0.86); IR ($CHCl_3$) 3440, 1630, 1425, 1080, 915, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.46–1.70 (6 H), 2.30 (2 H, m), 2.75 (1 H, br s, OH), 3.40 (3 H, s, OMe), 3.52 (2 H, m), 3.62 (1 H, br d, J = 8.6 Hz), 3.97 (1 H, m), 4.07 (1 H, m), 4.08 (1 H, br s, OH), 4.17 (1 H, br t, J = 9.8 Hz), 4.35 (1 H, br s, OH), 4.70 (1 H, br s, OH), 5.10 (2 H, m), 5.74 (1 H, ddt, J = 17.1, 9.8 and 7.3 Hz); CIMS (isobutane) m/z 249 (MH^+).

The tetrol **25** (840 mg, 3.4 mmol) and triphenylmethyl chloride (3.78 g, 13.5 mmol) were dissolved in pyridine (30 mL) and the solution was heated at 100 °C for 1 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (50–70% EtOAc–hexane) to give a trityl ether (1.33 g, 83%).

To a stirred solution of the trityl ether (1.33 g, 2.7 mmol) in dry THF (20 mL) were added MeI (5 mL) and excess KH at 0 °C, and the reaction mixture was stirred for 1 h at room temperature. Excess KH was decomposed by careful addition of water, the mixture was extracted with EtOAc, and the extract was flash chromatographed (15–20% EtOAc–hexane) to give a tetramethoxy compound (1.29 g, 90%).

To a solution of the tetramethoxy compound (1.29 g, 2.4 mmol) in MeOH (10 mL) was added 5% HCl–MeOH (1 mL). The mixture was stirred for 2 h at room temperature and the product was extracted from the mixture with EtOAc and flash chromatographed (60–90% EtOAc–hexane) to give **26** (551 mg, 78%): $[\alpha]_D$ +48.50° (*c* 0.63); IR ($CHCl_3$) 3450, 1635, 1090, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.58 (2 H, m), 1.76 (1 H, ddd, J = 14.7, 6.8, and 4.4 Hz), 1.82 (3 H, m), 2.31 (2 H, br t, J = 6.1 Hz), 3.30 (3 H, s, OMe), 3.31 (3 H, s, OMe), 3.34 (3 H, s, OMe), 3.39 (3 H, s, OMe), 3.30–3.50 (4 H), 3.55 (1 H, dd, J = 11.7 and 5.4 Hz), 3.70 (1 H, dd, J = 11.7 and 4.6 Hz), 5.09 (1 H, br d, J = 10.3 Hz), 5.10 (1 H, br d, J = 17.1 Hz), 5.81 (1 H, ddt, J = 17.1, 10.3, and 7.1 Hz); CIMS (isobutane) m/z 291 (MH^+), 259 (MH^+ − MeOH), 227 (MH^+ − 2MeOH), 195 (MH^+ − 3MeOH), 163 (MH^+ − 4MeOH).

(4*S*,6*S*,8*S*,10*S*)-4,6,8,10-Tetramethoxy-11-oxo-1-dodecene (28). To a stirred solution of oxalyl chloride (0.04 mL, 0.41 mmol) in dry CH_2Cl_2 (1 mL) was added dry DMSO (0.034 mL, 0.47 mmol) at −60 °C under nitrogen. After stirring for 10 min at −60 °C, a solution of **26** (92 mg, 0.32 mmol) in dry CH_2Cl_2 (1.5 mL) was added. The mixture was stirred for 15 min at −60 °C and then triethylamine (0.22 mL, 1.56 mmol) was added. The reaction mixture was warmed to room temperature and the product was extracted out with ether and flash chromatographed (40% EtOAc–hexane) to give aldehyde **27** (85 mg, 93%): $[\alpha]_D$ +26.78° (*c* 1.0); IR ($CHCl_3$) 1725, 1635, 1090, 925 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.54 (1 H, ddd, J = 14.3, 6.7, and 4.8 Hz), 1.59 (1 H, ddd, J = 14.3, 7.3, and 4.4 Hz), 1.78 (1 H, dt, J = 8.1 and 4.8 Hz), 1.82 (1 H, dt, J = 8.1 and 4.5 Hz), 1.91 (1 H, ddd, J = 14.7, 8.8, and 4.4 Hz), 2.03 (1 H, ddd, J = 14.7, 5.5, and 3.7 Hz), 2.29 (2 H, br t, J = 6.4 Hz), 3.23 (3 H, s, OMe), 3.28 (3 H, s, OMe), 3.32 (3 H, s, OMe), 3.43 (3 H, s, OMe), 3.31 (1 H, m), 3.39 (1 H, m), 3.50 (1 H, m), 3.70 (1 H, td, J = 5.1 and 1.1 Hz), 5.07 (1 H, br d, J = 10.3 Hz), 5.08 (1 H, br d, J = 17.2 Hz), 5.79 (1 H, ddt, J = 17.2, 10.3, and 7.0 Hz), 9.59 (1 H, d, J = 1.1 Hz); CIMS (isobutane) m/z 289 (MH^+), 257 (MH^+ − MeOH), 225 (MH^+ − 2MeOH), 193 (MH^+ − 3MeOH), 161 (MH^+ − 4MeOH).

To a solution of 1.0 M methylmagnesium iodide (4 mL) in dry ether (5 mL) at −30 °C was added a solution of **27** (100 mg, 0.35 mmol) in dry ether (2 mL). The mixture was stirred for 10 min and warmed to 0 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl and the crude product was extracted from the mixture with EtOAc. Flash chromatography (60% EtOAc–hexane) gave the pure alcohol (84 mg, 80%).

The alcohol (81 mg, 0.27 mmol) was oxidized to **28** (78 mg, 98%) by using the Swern conditions described above: $[\alpha]_D$ +16.14° (*c* 0.62); IR ($CHCl_3$) 1710, 1635, 1355, 1100, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.56 (1 H, ddd, J = 14.4, 7.1, and 5.0 Hz), 1.61

(1 H, ddd, J = 14.5, 6.4, and 4.7 Hz), 1.77 (1 H, ddd, J = 7.4, 5.4, and 3.0 Hz), 1.82 (1 H, ddd, J = 7.4, 5.7, and 3.7 Hz), 1.91 (1 H, br t, J = 5.7 Hz), 2.17 (3 H, s COMe), 3.24 (3 H, s, OMe), 3.30 (3 H, s, OMe), 3.34 (3 H, s, OMe), 3.36 (3 H, s, OMe), 3.37 (1 H, m), 3.44 (2 H, m), 3.71 (1 H, t, J = 5.7 Hz), 5.08 (1 H, br d, J = 10.4 Hz), 5.10 (1 H, br d, J = 16.8 Hz), 5.81 (1 H, ddt, J = 16.8, 10.4, and 7.1 Hz); CIMS (isobutane) m/z 303 (MH^+), 271 (MH^+ - MeOH), 239 (MH^+ - 2MeOH), 207 (MH^+ - 3MeOH), 175 (MH^+- 4MeOH).

(3*R*,5*R*,7*S*,9*S*)-3,5,7,9-Tetramethoxy-10-oxoundecanal (15). To a stirred solution of **28** (17 mg, 0.056 mmol) in dioxane (1.2 mL) and water (0.4 mL) was added OsO_4 (1 mg). After stirring for 30 min at room temperature, $NaIO_4$ (50 mg, 0.27 mmol) was added and the reaction mixture was stirred for 1.5 h. The product was extracted from the mixture with ether and flash chromatographed (70% EtOAc–hexane) to give keto aldehyde **15** (12.4 mg, 73%): $[\alpha]_D$ -21.49° (c 1.0); IR ($CHCl_3$) 1720, 1460, 1355, 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (1 H, dt, J = 14.3 and 5.5 Hz), 1.66 (1 H, dt, J = 14.3 and 5.5 Hz), 1.78–1.97 (4 H), 2.16 (3 H, s, COMe), 2.63 (2 H, dd, J = 5.9 and 2.2 Hz), 3.24 (3 H, s, OMe), 3.28 (3 H, s, OMe), 3.34 (3 H, s, OMe), 3.35 (3 H, s, OMe), 3.42 (2 H, m), 3.70 (1 H, t, J = 6.2 Hz), 3.84 (1 H, quintet, J = 6.2 Hz), 9.80 (1 H, t, J = 2.2 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 25.44, 35.94, 37.26, 37.78, 47.99, 56.07, 56.26, 56.67, 57.91, 73.51, 74.23, 74.69, 84.06, 201.21, 210.05; CIMS (isobutane) m/z 305 (MH^+), 273 (MH^+ - MeOH), 241 (MH^+ - 2MeOH), 209 (MH^+ - 3MeOH), 177 (MH^+ - 4MeOH).

Methyl (3*R*,5*R*,7*S*,9*S*)-3,5,7,9-Tetramethoxy-10-oxoundecanoate (16). To a solution of **28** (17.5 mg, 0.058 mmol) in dioxane (1.2 mL) and water (0.4 mL) were added $KMnO_4$ (2 mg) and $NaIO_4$ (62 mg), and the mixture was stirred for 2 h at room temperature. The reaction mixture was acidified with 1% HCl and the carboxylic acid extracted out with EtOAc. Treatment with ethereal diazomethane (2 mL) followed by flash chromatography (45% EtOAc–hexane) gave keto ester **16** (12.8 mg, 67%): $[\alpha]_D$ -6.76° (c 0.7); IR ($CHCl_3$) 1720, 1435, 1100 cm^{-1}; ^1H NMR (400 MHz, benzene-d_6) δ 1.64 (2 H, tt, J = 13.9 and 5.6 Hz), 1.84 (2 H, tt, J = 14.2 and 5.4 Hz), 1.93 (2 H, m), 1.94 (3 H, s, COMe), 2.41 (1 H, dd, J = 15.1 and 5.6 Hz), 2.54 (1 H, dd, J = 15.1 and 6.6 Hz), 3.05 (3 H, s, OMe), 3.11 (3 H, s, OMe), 3.12 (3 H, s, OMe), 3.16 (3 H, s, OMe), 3.35 (3 H, s, OMe), 3.46 (1 H, quintet, J = 5.6 Hz), 3.54 (1 H, quintet, J = 5.9 Hz), 3.60 (1 H, triplet, J = 5.9 Hz), 3.84 (1 H, quintet, J = 5.9 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 25.48, 36.05, 37.44, 37.88, 39.25, 51.64, 56.16, 56.29, 56.86, 57.93, 74.32, 74.86, 74.96, 84.16, 171.98, 210.08; CIMS (isobutane) m/z 335 (MH^+), 303 (MH^+ - MeOH), 271 (MH^+ - 2MeOH), 239 (MH^+ - 3MeOH), 207 (MH^+ - 4MeOH).

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Synthesis of Deuterium- and ^{15}N-Containing Pyrroline 1-Oxides: A Spin Trapping Study

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Our aim is to develop nitrone-based spin traps with improved sensitivity toward superoxide and hydroxyl radicals through isotopic substitution. Deuterated DMPO derivatives were prepared by either D_2O–NaOD or D_2O–DCl exchange reactions. The ^{15}N-substituted counterparts were synthesized starting with acetone-d_6 and (^{15}N)-hydroxylamine. These spin traps provide significantly enhanced sensitivity in the detection of superoxide and small carbon-centered free radicals.

In recent years reduced oxygen species, including superoxide and hydroxyl radical, have been studied intensively as these reactive intermediates appear to play an important role in mediating a variety of pathologic conditions. For example, it has been proposed that during ischemia/reperfusion injury, free radicals initiate events leading to cellular necrosis.[1,2] Yet, data in support of this hypothesis is largely indirect, coming from the observation that in vivo, free radical scavengers significantly ameliorate the injury.

Of the available methods for the detection of free radicals, only spin trapping offers the opportunity to simultaneously measure and distinguish among a variety of important biologically generated free radicals.[3-5] In this technique, a nitrone or nitroso compound reacts with a short-lived free radical to produce a nitroxide whose lifetime is considerably greater than that of the parent free radical.[6] The spin trap 5,5-dimethyl-1-pyrroline 1-oxide (DMPO, **8**) is most frequently used; however, this nitrone has several limitations. Its reaction with superoxide is rather slow, having a second-order rate constant of only 10 M^{-1} s^{-1}.[7] Its partition coefficient was found to be only

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