Oxidized Welwitindolinones from Terrestrial *Fischerella* spp.

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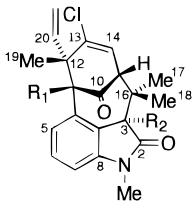
3-Hydroxy-*N*-methylwelwitindolinone C isonitrile (**3**), 3-hydroxy-*N*-methylwelwitindolinone C isothiocyanate (**4**), and the novel cyclic ether *N*-methylwelwitindolinone D isonitrile (**6**) are three new alkaloids from two terrestrial *Fischerella* spp. belonging to the Stigonemataceae. Photooxidation of *N*-methylwelwitindolinone C isonitrile (**1**) leads to isonitriles **3** and **6**. Isonitrile **3** is readily hydrated to 3-hydroxy-*N*-methylwelwitindolinone C formamide (**5**), an artifact produced during the isolation procedure.

Indole and indolinone alkaloids are commonly found in branched, filamentous blue-green algae (cyanobacteria) belonging to the Stigonemataceae.[1−9] For example, welwitindolinones, along with 12-*epi*-hapalindoles and 12-*epi*-fischerindoles, are present in *Hapalosiphon welwitschii* W. & G. S. West (UH isolate IC-52-3) and *Westiella intricata* Borzi (HT-29-1).[8] Herein we report the isolation of 3-hydroxywelwitindolinones and a related ether from terrestrial *Fischerella muscicola* (Thuret) Gomont (HG-39-5) and *Fischerella major* Gomont (HX-7-4).

The cyanophytes were mass cultured in the laboratory, and the extract[10] of each alga was subjected to successive gel filtration, normal-phase column chromatography, and reversed-phase HPLC. Eight alkaloids were isolated and identified on the basis of their spectral properties. Four of these were known natural products: welwitindolinone A isonitrile, *N*-methylwelwitindolinone C isonitrile (**1**), *N*-methylwelwitindolinone C isothiocyanate (**2**), and 12-*epi*-fischerindole I isonitrile. The remaining four were new alkaloids: 3-hydroxy-*N*-methylwelwitindolinone C isonitrile (**3**), 3-hydroxy-*N*-methylwelwitindolinone C isothiocyanate (**4**), 3-hydroxy-*N*-methylwelwitindolinone C formamide (**5**), and *N*-methylwelwitindolinone D isonitrile (**6**). The formamide **5**, however, appeared to be an artifact of **3** produced during the isolation procedure.



1	R_1 = NC	R_2 = H
2	R_1 = NCS	R_2 = H
3	R_1 = NC	R_2 = OH
4	R_1 = NCS	R_2 = OH
5	R_1 = NHCHO	R_2 = OH

Results and Discussion

Alkaloid **3** was isolated from *F. muscicola* HG-39-5 in 0.0016% yield and from *F. major* HX-7-4 in 0.0058% yield. Its EIMS displayed a 3:1 M^+ ion cluster at *m*/*z* 396/398 and a very strong fragment ion at *m*/*z* 361 for loss of a chlorine from the molecular ion. HREIMS established the molecular formula as $C_{22}H_{21}ClN_2O_3$. The IR and ^{13}C NMR spectra exhibited peaks [ν_{max} 2144 cm^{-1}; δ_C 164.3] that were characteristic of an isonitrile. Inspection of the ^1H and ^{13}C NMR data strongly suggested that **3** was *N*-methylwelwitindolinone C isonitrile (**1**) substituted at C-3 with a hydroxyl group. Apart from the absence of the H-3 signal and the presence of a broad signal for an exchangeable OH-proton (δ 2.65) and small differences in chemical shifts for the other signals, the ^1H NMR spectrum of **3** was similar in appearance to that of **1**, and this suggested that the relative stereochemistries of **1** and **3** were the same. Furthermore, the CD spectra of **1**,[11] which showed a positive peak at 260 nm ($\Delta\epsilon$ +8.3) and a negative peak at 235 nm ($\Delta\epsilon$ −32.0), and **3**, which showed a positive peak at 270 nm ($\Delta\epsilon$ +8.0) and a negative peak at 226 nm ($\Delta\epsilon$ −22.7), had similar shapes, and this suggested that the two analogues not only had identical relative stereochemistry, but identical absolute stereochemistry. The corresponding 3-*epi* analogues would probably have shown appreciably different ^1H NMR and CD spectra. Nevertheless, rigorous proof was obtained when it was found that photooxidation of **1** led to **3** and **6**.

Alkaloid **4** was isolated from *F. major* in 0.027% yield. Its EIMS showed a 3:1 M^+ ion cluster at *m*/*z* 428/430 and a fragment ion at *m*/*z* 393 for loss of a chlorine atom from the molecular ion. HREIMS gave the elemental composition $C_{22}H_{21}ClN_2O_3S$. Comparison of the ^1H and ^{13}C NMR spectra for **4** with those for **3** indicated that both alkaloids were identical in gross structure and relative stereochemistry and differed only in the nature of the group on C-11. The presence of a strong band at 2045 cm^{-1} in the IR spectrum and a signal at 141.2 ppm in the ^{13}C NMR spectrum established the presence of an isothiocyanate group. Analogue **4** obviously had to have an isothiocyanate group attached to C-11 instead of an isonitrile group. Because the CD spectra of **4**, which showed a positive peak at 270 nm ($\Delta\epsilon$ +7.1) and a negative peak at 227 nm ($\Delta\epsilon$ −15.9), and **3** were similar in shape, the absolute stereochemistries of these two compounds were identical.

Alkaloid **5** was isolated from *F. muscicola* HG-39-5 in <0.001% yield and from *F. major* HX-7-4 in 0.0033% yield. The FABMS showed a 3:1 MH^+ ion cluster at *m*/*z* 415/417 consistent with the molecular formula $C_{22}H_{23}ClN_2O_4$. The ^1H NMR spectrum showed that the alkaloid was a formamide, which proved to be identical with the hydration product of **3**. A close examination of the isolation procedure for **3** indicated that it was being slowly converted into **5**.

Alkaloid **6** was isolated from *F. major* in 0.004% yield. The DCIMS and positive ion FABMS both showed an intense MH^+ ion at *m*/*z* 377, and the EIMS exhibited a strong molecular ion at *m*/*z* 376. HREIMS indicated its elemental composition was $C_{22}H_{20}N_2O_4$. The absence of

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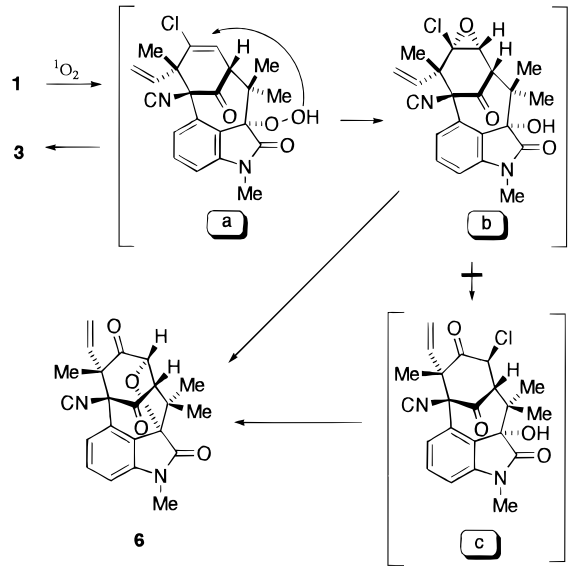
Scheme 1



chlorine in this alkaloid was at first surprising, as **6** could be generated by $^1O_2$-oxidation of **1**. Analysis of the ^1H and ^{13}C NMR spectra, which were typical of an *N*-methylwelwitindolinone, confirmed that there were 22 carbons and 20 hydrogens in the molecule. No evidence, however, could be found for the presence of an exchangeable proton in **6**, such as an OH group on C-3. The IR spectrum totally lacked absorption in the 3200−3700 cm^{-1} region; however, the ^{13}C chemical shift for C-3 (87 ppm), which was at a lower field than normally shown for an OH-bearing C-3, suggested that an ether-type oxygen was attached to C-3. Unlike **1** and **3**, however, **6** possessed another ketone group. HMBC correlations from H-14, H-15, and H_3-19 established C-13 as the second ketone carbonyl (δ_C 201.2) and C-14 as an oxygen-bearing methine (δ_H 4.92; $J_{H14,C14}$ = 158 Hz). Because three of the four oxygens in **6** belonged to carbonyls, the remaining oxygen had to be in an ether that connected C-3 and C-14. A coupling constant of 7.5 Hz between H-14 and H-15 was consistent with the dihedral angle of 28° between these two protons.[12] A NOE signal was completely absent between H_3-19 and H-14, and significant NOE signals could be seen from H_3-17 (but not from H_3-18) to both H-14 and H-15. H-14 was therefore oriented equatorially on the six-membered ring containing the two ketone groups. All of these data were consistent with the ether structure shown for **6**. IR (2138 cm^{-1}) and ^{13}C NMR (165.5 ppm) data indicated that **6** was an isonitrile. Alkaloid **6** had to have the same relative (e.g., at C-12) and absolute stereochemistry as **1** and **3**, because **3** and **6** were both produced by a photocatalyzed oxidation of **1**.

(3*S*)-Hydroperoxy (**a**), (13*S*,14*R*)-epoxy (**b**), and (14*S*)-chloro-13-oxo (**c**) intermediates may be involved in the formation of **6** from **1** (Scheme 1 and Figure 1 in Supporting Information). In the proposed pathway, **1** is first photocatalytically oxidized, most likely by a free-radical mechanism, to the hydroperoxide **a**. Simple reduction of **a** leads to **3**; however, an intramolecular epoxidation of the chloroalkene group by the hydroperoxy group of **a** leads to chloroepoxide **b**.[13] Cyclization of the 3-OH oxygen to C-14 of **b**, with concomitant opening of the epoxide ring, formation of the keto group on C-13, and loss of H^+ and Cl^-, results in **6**.[14] Alternatively, **6** could be forming by rearrangement of **b** to an α-chloroketone **c** prior to an intramolecular cyclization of the 3-OH oxygen onto C-14. The latter route, however, is a much less likely one inasmuch as chloroepoxides require relatively high temperatures to rearrange to α-chloroketones.[15,16]

Experimental Section

Spectral Analysis. NMR spectra were determined on a 11.75-T instrument operating at 500 MHz for ^1H and 125 MHz for ^{13}C. ^1H chemical shifts are referenced in $CDCl_3$ and CD_2Cl_2 to residual $CHCl_3$ (7.24 ppm) and $CHDCl_2$ (5.32 ppm); ^{13}C chemical shifts are referenced to the solvent ($CDCl_3$, 77.0 ppm; CD_2Cl_2, 52.8 ppm). Homonuclear connectivities were determined by using 2D double-quantum filtered COSY and 1D decoupling experiments. Homonuclear ^1H NOEs were obtained by difference NOE experiments using a 2-s irradiation period. One-bond heteronuclear $^1H-^{13}C$ connectivities were determined by 2D proton-detected HMQC experiments; two- and three-bond $^1H-^{13}C$ connectivities were determined by 2D proton-detected HMBC experiments. MS were determined in the EI (at UH), DCI, and FAB modes. UV spectra were measured in MeOH at 20 °C. Optical rotations were measured in CH_2Cl_2 and $CHCl_3$ at 20 °C or 25 °C at the sodium D line (589 nm).

Isolation and Cultivation of Algae. A nonaxenic, unialgal strain of *Fischerella muscicola* (Thuret) Gomont, designated UH strain HG-39-5, was isolated from an epilithic sample collected at Nau Madol, Pohnpei, Micronesia, and purified by repeated subculture on solidified media. The cyanophyte was cultured in autoclaved 20-L glass carboys containing an inorganic medium (modified BG-11) adjusted to pH 7.0 with MOPS. Cultures were continuously illuminated at an incident intensity of 80−100 μmol photos m^{-2} s^{-1} (photosynthetically active radiation) from banks of cool-white fluorescent tubes and vigorously aerated at a rate of 5 L/min with a mixture of 0.5% CO_2 in air at a temperature of 24 ± 1 °C. After 32 days the alga was harvested by filtration onto Whatman no. 4 paper. The yield of lyophilized cells was 0.51−0.71 g/L.

UH isolate HX-7-4, an epipelic cyanophyte identified as *Fischerella major* Gomont, was collected in March 1989, on the grounds of the Guindy campus of Madras University, Tamil Nadu, India. The cyanophyte was purified, and unialgal, nonaxenic mass cultures were grown in culture as described above. Incubation time ranged from 38 to 46 days. The yield of lyophilized cells was 0.24 to 0.47 g/L.

Isolation of Alkaloids from *Fischerella muscicola* HG-39-5. The freeze-dried alga (61.0 g) was extracted twice with 2.0 L of CH_2Cl_2−2-propanol (1:1) overnight. The extracts were combined and concentrated under reduced pressure to a green solid. This material was dissolved in MeOH and then applied to a Sephadex LH20−120 (Fluka, 30 cm × 2.3 cm diameter, flow rate 60 mL/h) equilibrated in MeOH. All fractions were analyzed by reversed-phase TLC and combined into three major fractions: (**A**) 339 mg, (**B**) 127 mg, and (**C**) 371 mg. Fraction **B** was further separated on an Econosil C_8 HPLC column (250 × 10 mm, Alltech) using 65% CH_3CN in H_2O as the mobile phase to give *N*-methylwelwitindolinone C isonitrile (**1**, 17 mg, ≥ 95% purity) and 3-hydroxy-*N*-methylwelwitindolinone C isonitrile (**3**, 1.0 mg), along with minor amount of 3-hydroxy-*N*-methylwelwitindolinone C formamide (**5**). Fraction **C** was separated on an Econosil C_{18} HPLC column (250 × 10 mm, Alltech) using 65% CH_3CN in H_2O to provide 12-*epi*-fischerindole I isonitrile (2.1 mg), welwitindolinone A isonitrile (3.7 mg), and *N*-methylwelwitindolinone C isothiocyanate (**2**, 1.3 mg).

Isolation of Alkaloids from *Fischerella major* HX-7-4. Lyophilized algae (40 g) was extracted twice with 1-L portions of CH_2Cl_2−2-propanol (1:1) overnight while stirring. The extracts were combined and evaporated under reduced pressure to give a green solid (2.9 g). The material was dissolved in MeOH, and the filtered solution was applied to a column of Sephadex LH20−120 (Fluka, 85 cm × 4.5 cm diameter, flow rate 7 mL/min) equilibrated in MeOH. The first 600 mL of MeOH were discarded, and five fractions were taken. Only fraction 4 (1075−1325 mL, 281 mg) contained indole-like compounds according to NMR. This fraction was further

Table 1. ^{1}H NMR Data (500 MHz) for Welwitindolinones **1**−**6**[a]

position	**1**	**2**	**3**[b]	**4**[b]	**5**[c]	**6**[d]
1(N)Me	3.16 s	3.15 s	3.15	3.15	3.11	3.19
3	3.75 s	3.75 s				
3-OH			2.65	not observed	not observed	
5	7.25 dd	7.18 dd	7.33 dd	7.21 dd	7.12 dd	7.29 dd
6	7.36 dd	7.33 dd	7.44 dd	7.41 dd	7.34 dd	7.45 dd
7	6.85 dd	6.83 d	6.89 dd	6.99 dd	6.82 dd	6.93 dd
14	6.24 d	6.23 d	6.40 d	6.36 d	5.95 d	4.92 d
15	3.25 d	3.28 d	3.18 d	3.22 d	3.12 d	3.57 d
17	1.67 s	1.67 s	1.71 s	1.70 s	1.63	1.55
18	0.78 s	0.79 s	0.81 s	0.75 s	0.99	0.80
19	1.53 s	1.47 s	1.55 s	1.46 s	1.32	1.39
20	5.35 m	5.32 m	5.49 dd	5.28 dd	6.55 dd	5.47 dd
21*E*	5.35 m	5.32 m	5.34 dd	5.60 d	5.65 d	5.36 dd
21*Z*	5.35 m	5.32 m	5.40 dd	5.57 d	5.43 d	5.43 dd
22(N)H					6.05 br d	
23					8.03 d	

[a] Spectra of **1**−**6** recorded in CD_2Cl_2. [b] *J*(H,H) in Hz for **3**: 5,6 = 8.4; 6,7 = 7.7; 5,7 = 0.9; 13,14 = 4.5; 20,21(*E*) = 10.5; 20,21(*Z*) = 17.0; (21*E*),21*Z*) = 1.0. The coupling constants for **4** are within ± 0.2 Hz of the values for **3**. [c] *J*(H,H) in Hz for **5**: 22,23 = 2.0; all other coupling constants for **5** are within ±0.2 Hz of the values for **3**. [d] *J*(H,H) in Hz for **6**: 5,6=8.3; 6,7=7.8; 5,7=0.7; 14,15=7.5; 20,21*E*=11.0; 20,21*Z*= 16.0; 21*E*,21*Z*=1.6. The following protons show significant NOE's: H_3-17 to H-14, H-15 and H-18; H_3-19 to H-21*Z*; H_3-18 to H-17.

Table 2. ^{13}C NMR Chemical Shifts and *^{1}H* HMBC Data (125 MHz) for Welwitindolinones **3**−**6**[a]

carbon	**3**	**4**	**5**	**6**
NMe	26.6	26.6	26.2	27.1
2	173.6; *NMe*	176.0; *NMe*	175; *NMe*	170; *NMe*
3	80.6; *15,17,18*	81.4; *17,18*	79; *17,18*	87; *14,15,17,18*
4	128.4; *6*	131.6; *6,7*	134; *6*	126.9; *6*
5	126.2	126.8; *6*	122.8; *7*	124.0
6	130.8	131.0	129.5	131.4
7	110.0	110.6; *5,6,NMe*	108.9; *5*	110.5
8	145.5; *6,NMe*	146.3; *6,NMe*	145; *6,NMe*	144.4; *6,NMe*
9	126.4; *5,7*	127.9; *5,7*	126.5; *7*	126.5; *5,7*
10	193.6; *14,15*	197.8; *14,15*	200; *14*	192.8; *14,15*
11	82.0; *5,15,19*	85.4; *5,15,19,20*	71.5; *5,15,19,23*	81; *5,15,19*
12	55.5; *14,19,20,21E*	57.8;*14,19,20,21EZ*	54; *14,19,21EZ*	61.5; *14,19*
13	133.3; *14,19*	133.0; *14,15,19,20*	135; *14,15,19,20*	201.2; *14,15,19*
14	126.0; *15*	127.2; *15*	126.2; *15*	79.7
15	61.0; *15*	62.1; *14,17,18*	60; *17,18*	62.1; *17,18*
16	42.8; 15,17,18	43.1; *15,17,18*	43; *15,17,18*	54; *15,17,18*
17	22.8; *15,18*	23.2; *18*	24.1; *15,18*	25.0; *15,18*
18	21.2; *15,17*	21.7; *15,17*	23.4; *17*	19.7; *17*
19	22.1; *20*	21.8	21.3; *20*	20.2
20	137.1; *19,21EZ*	139.7; *19,21*	139.3; *19,21*	133.1; *19,21*
21	118.4; *20*	117.4	117.9	120.6
23	164.3	141.2	161.3; *NH*	165

[a] Spectra recorded in CD_2Cl_2.

separated by column chromatography (Si gel, 45 cm × 2.5 cm diameter) with CH_2Cl_2−isooctane (10:1) to give pure *N*-methylwelwitindolinone C isothiocyanate (**2**, 35 mg). The more polar fractions were combined (180 mg) and separated by reversed-phase HPLC (Econosil C_8, 250 × 10 mm column, 10 μm, 2:3 CH_3CN-H_2O, flow rate 1 mL/min). Eight fractions were taken. Two of them, 23.0<t_R<27.6 min and 27.6<t_R<32.4 min, contained pure *N*-methyl-welwitindolinone C isonitrile (**1**, 20.7 mg) and 3-hydroxy-*N*-methylwelwitindolinone C isothiocyanate (**4**, 10.6 mg), respectively. Fractions eluting at 9.8<t_R<11.6 and 14.8<t_R<17.2 min gave pure 3-hydroxy-*N*-methylwelwitindolinone C formamide (**5**, 1.3 mg) and 3-hydroxy-*N*-methylwelwitindolinone C isonitrile (**3**, 2.3 mg), respectively, after further HPLC (Econosil C_8, 250 × 4.6 mm column, 5 μm, CH_3CN-H_2O 2:3 for **5** and CH_3CN-H_2O (1:1) for **3**, flow rate 1 mL/min). Another fraction, 11.6<t_R<14.8 min, gave pure *N*-methylwelwitindolinone D isonitrile (**6**, 1.6 mg) after further HPLC (Ultracarb, 250 × 10 mm, CH_3CN-H_2O 1:1, flow rate 2.5 mL/min).

3-Hydroxy-*N*-methylwelwitindolinone C isonitrile (3): $[\alpha]_D$ −103° (*c* 0.4, CH_2Cl_2); UV (MeOH) λ_{max} (ϵ) 220 (43 300), 266 (13 200), 301 (3600) nm; CD (MeOH) λ ($\Delta\epsilon$) 226 (−22.7), 270 (+8.0) nm; IR (CH_2Cl_2) ν_{max} 3600, 2919, 2144 (s, NC), 1725 (s), 1602, 1584, and 1355 cm^{-1}; ^{1}H NMR (C_6D_6) δ (multiplicity, *J* in Hz; assignment) 7.43 (d, 8.4; H-5), 6.79 (t, 8.1; H-6), 5.95 (d, 7.6; H-7), 5.91 (d, 4.4; H-14), 5.46 (dd, 10.7/17.3; H-20), 5.20 (d, 17.3; H-21*Z*), 5.09 (d, 10.5; H-21*E*), 2.61 (d, 4.4; H-15), 2.45 (s; NMe), 1.52 (s; H_3-17), 1.38 (s; H_3-19), 0.60 (s; H_3-18); ^{1}H NMR (CD_2Cl_2), see Table 1; ^{13}C NMR (CD_2Cl_2), see Table 2; EIMS *m/z* 396/398 (3:1 M^+ ion cluster), 381/383 (3:1 $[M - Me]^+$ cluster), 361 ($[M - Cl]^+$); HREIMS *m/z* 396.1228 (calcd for $C_{22}H_{21}ClN_2O_3$, 396.1241).

3-Hydroxy-*N*-methylwelwitindolinone C isothiocyanate (4): $[\alpha]_D$ −290° (*c* 2.6, CD_2Cl_2); UV (MeOH) λ_{max} (ϵ) 208 (31 100), 212 (26 500), 259 (5680) nm; CD (MeOH) λ ($\Delta\epsilon$) 227 (−15.9), 270 (+7.1) nm; IR (neat) ν_{max} 3401, 2045, 1712, 1609, 1584, 1456 cm^{-1}; ^{1}H NMR (CD_2Cl_2), see Table 1; ^{13}C NMR (CD_2Cl_2), see Table 2; EIMS *m/z* 428/430 (3:1 M^+ ion cluster, 13/4), 393 ($[M - Cl]^+$, 15), 283 (56), 257 (15), 200 (17), 127 (42), 91 (48), 83 (100); HREIMS *m/z* 428.0949 (calcd for $C_{22}H_{21}ClN_2O_3S$, 428.0962).

3-Hydroxy-*N*-methylwelwitindolinone C formamide (5): 3:1 mixture of *Z:E* conformers; CD (MeOH) λ ($\Delta\epsilon$) 230 (−12.6), 267 (+5.2) nm; IR (CH_2Cl_2) ν_{max} 3272, 3049, 2931, 2860, 1719 (s), 1684 (s), 1608, 1590, 1490, 1460, and 1261 cm^{-1}; ^{1}H NMR (CD_2Cl_2), see Table 1; ^{13}C NMR (CD_2Cl_2), see Table 2; HREIMS *m/z* 396.1247 ($M^+ - H_2O$; calcd for $C_{22}H_{21}{}^{35}ClN_2O_3$, 396.1241); HRFABMS (glycerine) *m/z* 415.1445 (MH^+; calcd for $C_{22}H_{24}{}^{35}ClN_2O_4$, 415.1425).

***N*-Methylwelwitindolinone D isonitrile (6):** $[\alpha]_D$ −30° (CH_2Cl_2, c 0.37); UV (MeOH) λ_{max} nm (ϵ) 207 (3910), 213 (3390), 267 (824); IR (neat) ν_{max} 2934, 2138, 1732, 1608, 1590, 1463,

1366, 1345, 1192, 1040, 1016, 955 cm^{-1}; ^1H NMR (CD_2Cl_2), see Table 1; ^{13}C NMR (CD_2Cl_2), see Table 2; DCIMS (NH_3) and FABMS (MeOH/glycerol) *m/z* 377 (MH^+); EIMS *m/z* 376 (M^+, 55), 361 (38), 333 (46), 305 (43), 279 (25), 265 (28), 251 (90), 223 (46), 222 (44), 83 (100); HREIMS *m/z* 376.1430 (calcd for $C_{22}H_{20}N_2O_4$, 376.1423).

Photooxidation of 1 to 3 and 6. A solution of **1** (25 mg, 66 μmol) in MeOH containing a trace amount of rose bengal was vigorously aerated with pure oxygen and continuously irradiated with a 90-W bulb for 4 days. The solvent was evaporated with a stream of nitrogen and the residue chromatographed on a 20 cm × 20 cm thin-layer silica plate (Whatman, 250 μm), developing the chromatogram three times with CH_2Cl_2−isooctane (7:3). Two major zones were collected from the plate, and the one with the higher R_f corresponded to recovered starting material (12.5 mg). The lower R_f fraction was rechromatographed on the thin-layer silica plate, developing the chromatogram three times with CH_2Cl_2−isooctane (3:2). The faster moving band yielded 1.3 mg of **3**. The slower moving band gave 0.8 mg of **6**. The semisynthetic **3** and **6** were identical in all respects, including optical properties, with the natural products.

Hydration of 3 to 5. A stirred solution of **3** (2 mg) in 300 μL of THF was treated with 2.5 N HCl (200 μL) at 0 °C and then allowed to warm to room temperature. After 12 h the mixture was neutralized with 2.5 N NaOH and extracted with CH_2Cl_2. The dried extract was subjected to reversed-phase HPLC (Phenomenex Ultracarb 5 ODS 30, 20 × 10 mm, 2.0 mL/min) with MeCN−H_2O (3:2) to give 1 mg of **5**, which was identical in all respects with the **5** isolated from the cyanobacterial extract.

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Supporting Information Available: Figure 1: molecular modeling of the proposed pathway for the photooxidation of **1** via intermediates **a**−**d** to **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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