descriptions are provided for each method.

Method A. A solution of $NaBH(OAc)_3$ was prepared by dissolving $NaBH_4$ pellets (25 mmol, 945 mg, 4 pellets) in glacial acetic acid (35 mL) with ice-bath cooling such that the temperature was maintained between 15 and 20 °C. To this was added β-ionone tosylhydrazone[1b] (3.60 g, 10 mmol) and the mixture was stirred at ambient temperature for 1 h followed by 2.5 h at 70 °C. The solution was then poured into crushed ice, made basic with aqueous NaOH, and extracted with three portions of pentane. The pentane solution was dried and concentrated on a rotary evaporator and the residue was carefully distilled at reduced pressure (Kugelrohr apparatus) to obtain 1.66 g (87%) of diene product, identical in all respects with an authentic sample.[1b]

Method B. To a stirred slurry of 6-undecanone tosylhydrazone (5.08 g, 15 mmol) in 50 mL of glacial acetic acid was added $NaBH_4$ pellets (ca. 5.67 g, 150 mmol, 24 pellets) at such a rate that foaming was not a problem (ca. 1 h). The solution was stirred at room temperature for 1 h and then at 70 °C for 1.5 h and worked up as in method A. Distillation at reduced pressure (Kugelrohr apparatus) yielded 1.96 g of undecane, identical with an authentic sample.

Method C. See Table I, footnote *a*.

Method D. A partial solution of β-ionone tosylhydrazone (1.80 g, 5 mmol) in 10 mL of CH_3COOD was prepared by warming for a few minutes under an N_2 atmosphere. To this was added a solution of $NaBD(OAc)_3$ prepared by carefully adding $NaBD_4$ (523 mg, 12.5 mmol) to CH_3COOD (10 mL). The solution was stirred at room temperature for 1 h followed by 1.5 h at 70 °C. Workup as before afforded 0.77 g (81%) of 4-(2-methylcyclohexenyl)-2-butene-*2,4-d*, which showed 95 ± 5% d_2 incorporation by NMR.

Method E. Similar to method D; solutions of $NaBD_4$ (1.046 g, 25 mmol) and propyl phenyl ketone tosylhydrazone (1.58 g, 5 mmol) were each prepared in 10 mL of CH_3COOD. The combined solution was stirred at room temperature for 1 h and at 70 °C for 4 h and worked up as before to give 0.48 g (72%) of 1-phenylbutane-*1,1-d*$_2$. Analysis by NMR indicated 95 ± 5% d_2.

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Registry No.—$NaBH_4$, 16940-66-2; HOAc, 64-19-7; $NaBD_4$, 15681-89-7; CH_3COOD, 758-12-3.

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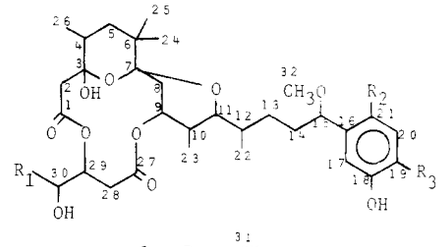
Communications

Toxins from Blue–Green Algae:[1] Structures of Oscillatoxin A and Three Related Bromine-Containing Toxins

Summary: Oscillatoxin A, a major toxic metabolite of a mixture of *Oscillatoria nigroviridis* and *Schizothrix calcicola* from Enewetak, has been identified from high-frequency ^1H and ^{13}C NMR studies as 31-nordebromoaplysiatoxin. Three minor bromine-containing toxic compounds from this algal mixture, viz., 21-bromooscillatoxin A, 19,21-dibromooscillatoxin A, and 19-bromoaplysiatoxin, have also been identified.

Sir: At one time a cyanophyte was suspected to be the primary causative organism of ciguatera, a disease associated with outbreaks of fish poisoning in the tropical and subtropical Pacific. While examining possible sources of the toxin in ciguateric fish of the Gilbert Islands, Banner found that two lipid-soluble toxins were present in *Schizothrix calcicola* from the atoll of Marakei, but neither toxin was characterized and both proved to be nonciguateric.[2]

In a previous communication[3] we reported the isolation of debromoaplysiatoxin (DAT, **1**) from a mixture of predominately two cyanophytes belonging to the Oscillatoriaceae tentatively identified as *Oscillatoria nigroviridis* and *Schizothrix calcicola*. We have now isolated from this algal mixture a second major toxic[4] component which we have named oscillatoxin A (OT-A, **2**) along with small amounts of 21-



1 $R_1 = CH_3$, $R_2 = R_3 = H$

2 $R_1 = R_2 = R_3 = H$

3 $R_1 = R_3 = H$, $R_2 = Br$

4 $R_1 = H$, $R_2 = R_3 = Br$

5 $R_1 = CH_3$, $R_2 = R_3 = Br$

bromo- and 19,21-dibromooscillatoxin A (**3** and **4**) and 19-bromoaplysiatoxin (**5**). DAT and OT-A may be identical with or related to the two lipid-soluble toxins that Banner had detected in *S. calcicola* from Marakei.

Frozen *O. nigroviridis-S. calcicola* (8 kg wet weight) collected from the seaward reef flat of Enewetak Island was homogenized and extracted with a mixture of methylene chloride and methanol (1:2 by volume). Water was added to the filtrate and the methylene chloride layer was washed repeatedly with water, dried over anhydrous sodium sulfate, and evaporated

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Table I. Proton NMR Data for Oscillatoxin A (OT-A) in Acetone-d_6

δ, ppm[a]	No. of protons	Assignment[b]	Multiplicity, J (Hz)
8.25[c]	1	OH on 18	br s
7.13	1	20	t, $J_{19,20} = J_{20,21} = 7.5$
6.93	1	17	dd, $J_{17,19} = 2$, $J_{17,21} = 1$
6.84	1	21	dt, $J_{20,21} = 7.5$, $J_{17,21} = J_{19,21} = 1$
6.72	1	19	ddd, $J_{19,20} = 7.5$, $J_{17,19} = 2$, $J_{19,21} = 1$
5.22	1	29	m
5.21	1	9	m
4.34[c]	1	OH on 3	d, $J_{OH(3),4} = 2$[d]
4.14[c]	1	OH on 30	t, $J_{OH(30),30} = J_{OH(30),30'} = 6.5$
3.99	1	15	t, $J_{14,15} = J_{14',15} = 6.5$
3.92	1	11	dd, $J_{10,11} = 10.5$[e], $J_{11,12} = 2.5$
3.69	1	30	m[f]
3.67	1	30′	m[g]
3.17	3	OCH_3	s
2.96	1	28	m
2.93	1	28′	m
2.74	1	2	d, $J_{2,2'} = -13$
2.72	1	8 (eq)	dd, $J_{8,8'} = -14.5$, $J_{8,9} = 3$[h]
2.53	1	2′	d, $J_{2,2'} = -13$
1.95	1	14	tt, $J_{14,14'} = -13$, $J_{13,14} = 13$, $J_{13',14} = J_{14,15} = 6.5$
1.84	1	4	m
1.72	1	8′ (ax)	dd, $J_{8,8'} = -14.5$, $J_{8',9} = 3.5$[i]
1.70	1	10	m
1.62	1	5 (ax)	t, $J_{5,5'} = -13$, $J_{4,5} = 13$[e]
1.60	1	14′	dtd, $J_{14,14'} = -13$, $J_{13',14'} = J_{14',15} = 6.5$, $J_{13,14'} = 2$
1.53	1	12	m
1.40	1	13	m
1.32	1	13′	m
1.06	1	5′ (eq)	dd, $J_{5,5'} = -13$, $J_{4,5'} = 4$
0.86	3	26	d, $J_{4,26} = 7$
0.84	3	25	s
0.81	3	24	s
0.80	3	22	d, $J_{12,22} = 7$
0.73	3	23	d, $J_{10,23} = 7$

[a] Relative to $(CH_3)_4Si$ (δ = 0) and solvent peak (δ 2.06) as internal standards. [b] Based on extensive spin–spin decoupling experiments at 360 MHz. [c] Disappears on addition of D_2O. [d] W coupling. [e] Trans diaxial coupling. [f] Becomes dd on addition of D_2O ($J_{30,30'} = -10$, $J_{29,30} = 3$). [g] Becomes dd on addition of D_2O ($J_{30,30'} = -10$, $J_{29,30'} = 3$). [h] Diequatorial coupling. [i] Axial–equatorial coupling.

to give the crude extract (14.5 g). Column chromatography of this extract on Florisil yielded two toxic fractions. The first toxic fraction (1.3 g), eluted with hexane/chloroform (1:1), was separated further by column chromatography on silica gel H (TLC grade) and gel filtration on Sephadex LH-20 with chloroform/methanol (1:1) to produce 467 mg of nearly pure DAT (**1**) and 33.4 mg of a mixture of **2**, **3**, **4**, and **5**. LC of the latter mixture on Porasil A using chloroform/acetonitrile (85:15) yielded 6.5 mg of pure **5** and 15 mg of a mixture of **3** and **4**. The second toxic fraction (0.77 g), eluted from the Florisil column with chloroform, contained OT-A (**2**) as the major component. Gel filtration on Sephadex LH-20 using chloroform/methanol (1:1) followed by LC on Porasil A using chloroform/acetonitrile (85:15) gave pure **2**.

Comparison of the ^1H and ^{13}C NMR spectral data of OT-A and DAT suggested to us that OT-A was 31-nordebromoaplysiatoxin. The 360-MHz ^1H NMR spectrum of OT-A in acetone-d_6 (Table I) lacked a doublet at δ 1.14 for a methyl group on C-30 and it showed two 1 H signals at δ 3.67 and 3.69 for nonequivalent methylene protons on C-30 rather than one signal at 4.05 ppm for a methine proton on C-30. Also the signal for the hydroxyl proton on C-30, a doublet at δ 4.23 for DAT, appeared as a triplet (disappeared on the addition of D_2O) at δ 4.14 for OT-A. The remainder of the OT-A spectrum was identical with that of DAT. Aside from the difference at C-30, extensive proton spin–spin decoupling experiments verified that the rest of the OT-A structure, including relative stereochemistry (C-29 uncertain), was the same as that proposed for DAT.[5] The ^{13}C NMR spectrum of OT-A contained 31 signals, one less peak than the ^{13}C NMR spectrum of DAT (Table II). All but three of the OT-A carbon signals (C-28, C-29, C-30) resonated within 0.4 ppm of the corresponding signals for DAT. The OT-A signals for C-28, C-29, and C-30 showed chemical-shift differences from the DAT signals, +2.48, −1.40, and −3.89 ppm, respectively, as expected for removing the methyl substituent from C-30. In the off-resonance spectrum the C-30 signal was a triplet at δ 62.40 for OT-A, whereas it was a doublet at δ 66.29 for DAT. The very close correspondence between the chemical shifts of the remaining carbon signals for OT-A and DAT again showed that the two toxins have the same relative stereochemistry at C-3, C-4, C-7, C-9, C-10, C-11, C-12, and C-15.

Electron impact (EI) mass spectrometry failed to show a molecular ion for OT-A, but like the aplysiatoxins[5] did show a fragment ion peak due to the loss of water from the molecular ion. A high-resolution mass measurement (Found: (560.30084. Calcd for $C_{31}H_{44}O_9$: 560.29854) confirmed the

Table II. Carbon-13 NMR Data for Debromoaplysiatoxin (DAT) and Oscillatoxin A (OT-A) in Acetone-d_6

Chemical shift[a]			Chemical shift[a]		
DAT	OT-A	Assignment[b]	DAT	OT-A	Assignment[b]
169.56 (s)	169.28 (s)	1 or 27	46.11 (t)	46.18 (t)	
168.37 (s)	168.73 (s)	1 or 27	40.34 (t)	40.39 (t)	5
157.48 (s)	157.54 (s)	18	38.16 (s)	38.28 (s)	6
145.07 (s)	145.07 (s)	16	35.30 (t)	35.29 (t)	
128.97 (d)	128.98 (d)	20	34.87 (d)	34.86 (d)	
118.53 (d)	118.55 (d)	21	34.60 (d)	34.73 (d)	
114.16 (d)	114.18 (d)	19	33.89 (t)	36.37 (t)	28
113.84 (d)	113.92 (d)	17	33.41 (d)	33.48 (d)	
100.00 (s)	100.23 (s)	3 or 7	32.84 (t)	32.89 (t)	
97.98 (s)	98.22 (s)	3 or 7	30.41 (t)	30.45 (t)	13
85.03 (d)	85.06 (d)	11	26.02 (q)	26.08 (q)	25
73.44 (d)	72.04 (d)	29	22.81 (q)	22.85 (q)	24
72.46 (d)	72.59 (d)	9	16.96 (q)		31
68.99 (d)	69.17 (d)	15	15.74 (q)	15.75 (q)	26
66.29 (d)	62.40 (t)	30	12.80 (q)	12.82 (q)	22
55.82 (q)	55.85 (q)	32	12.27 (q)	12.32 (q)	23

[a] In ppm using acetone-d_6 (δ 29.20) as an internal reference. [b] Proton correlations are based on detailed single-frequency off-resonance decoupling experiments at 90 MHz.

elemental composition of this fragment ion.

The sign and magnitude of the optical rotations of OT-A, $[\alpha]^{25}_D$ + 67 ± 10° (EtOH, *c* 0.12), and DAT, $[\alpha]^{25}_D$ + 60.6 ° (EtOH, *c* 0.66), suggested that the two compounds have the same absolute configuration (C-29 uncertain).

Structures **3**, **4**, and **5** were deduced on the basis of low- (100 MHz) and high-frequency (360 MHz) proton magnetic resonance studies. The ^{1}H NMR spectra of the compounds assigned structures **3** and **4** differed from the ^{1}H NMR spectrum of OT-A primarily in the aromatic region. An AMX pattern at δ 6.82 (dd, 1 H, *J* = 8.0, 2.0 Hz), 7.05 (d, 1 H, *J* = 2.0 Hz), and 7.44 (d, 1 H, *J* = 8.0 Hz) was consistent with a 3,4-disubstituted phenol moiety in **3**. The ^{1}H NMR spectrum of **4** contained only two singlets (δ 7.22 and 7.64) in the aromatic region, in agreement with a 2,4,5-trisubstituted phenol system. The ^{1}H NMR spectrum of **5** showed a doublet at δ 1.11, indicating the presence of a methyl group on C-30, and it exhibited only two aromatic proton signals at δ 7.21 (s) and 7.63 (s). Again, the EI mass spectra of **3**, **4**, and **5** did not exhibit molecular ions, but characteristic M − H_2O peaks were observed and high-resolution measurements confirmed their elemental compositions.[6]

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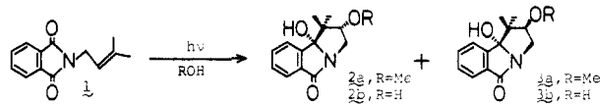
Photochemical Cyclization of *N*-2-Alkenyl- and *N*-3-Alkenylphthalimides

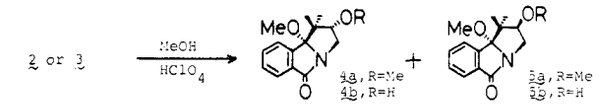
Summary: Photolysis of *N*-(3-methyl-2-butenyl)phthalimide (**1**) in methanol gave cyclic compounds **2a** and **3a** probably via successive processes; intramolecular electron transfer (**1** → **19**), polar addition of methanol (**19** → **20**), and cyclization of diradical (**20** → **2a** + **3a**).

Sir: It is well known that *N*-alkylated phthalimides undergo photochemical hydrogen abstraction reactions.[1] However, as far as we know, no examples of photochemical reactions of phthalimides with monoolefins have been published.[2] We now wish to report the first examples of photochemical reactions of phthalimides with monoolefins, in particular the intramolecular photochemical reactions of *N*-2-alkenyl- and *N*-3-alkenylphthalimides.

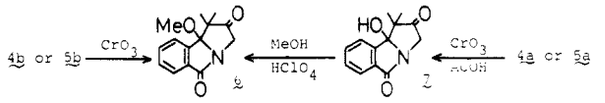
For example, a solution of *N*-(3-methyl-2-butenyl)-phthalimide (**1**) (5 mM) in methanol was irradiated under N_2



with a 300-W high-pressure Hg-arc lamp (Eikosha PIH-300) through quartz for about 5 h.[3] At this stage, the starting material had almost disappeared. After workup, two products were obtained. The structure and stereochemistry of the isomeric products ($C_{14}H_{17}NO_3$, mass *m/e* 247, elemental analyses) **2a** (41%, mp 98–99 °C) and **3a** (41%, mp 200–201 °C) were assigned as the following. **2a:** IR (KBr) 3400 (OH), 1685 cm^{-1} (amide); ^{1}H NMR ($CDCl_3$) δ 0.42 (s, 3 H, Me), 1.42 (s, 3 H, Me), 3.48 (s, 3 H, OMe), 3.5–3.9 (m, 3 H), 4.51 (s, 1 H, OH), 7.3–7.9 (m, 4 H). **3a:** IR (KBr) 3250 (OH), 1680 cm^{-1} (amide); ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 3 H, Me), 1.40 (s, 3 H, Me), 3.07 (s, 1 H, OH), 3.27 and 3.62 (two dd, 2 H, NCH_2), 3.43 (s, 3 H, OMe), 4.37 (t, 1 H, methine), 7.3–7.8 (m, 4 H). The products **2a** and **3a** were resistant to acetylation by acetic anhydride–pyridine and to chromic acid oxidation, but they were converted to an equilibrium mixture of methyl ethers, **4a** (mp 89–90 °C)/**5a** (mp 98–99 °C) = 3:1, probably via a

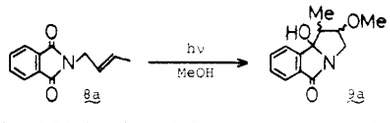


common stable tertiary carbonium ion, on treatment with a trace amount of acid ($HClO_4$) in methanol. Diols **2b** (mp 172–174 °C) and **3b** (mp 178–181 °C), which were obtained by photolysis of **1** in water–acetonitrile (v/v 1:8) in a yield of 70% (**2b**/**3b** = 1:1), were converted to an equilibrium mixture of monomethyl ethers **4b** (oil)/**5b** (oil) = 3:1 by a similar procedure. The secondary alcohol **4b** was easily oxidized to ketone **6** (50%, mp 108–110 °C) by Jones oxidation. The ketone **6** was



also obtained by the reverse manipulation; i.e., initial oxidation of **4a** accompanied by hydrolysis to **7** (72%, mp 200–202 °C) followed by methylation to give **6**. ^{1}H NMR spectra of **2a** and **3a** showed the presence of two kinds of *C*-methyl groups. The anisotropic shielding effect of the phenyl ring is probably responsible for the higher chemical shift of one of the two methyl groups. Similarly in **2–7** one of the two methyl groups had its ^{1}H NMR signals at δ 0.28–0.50. The stereochemistry of **2–5** was assigned on the basis of their ^{1}H NMR spectra. Thus, for the isomers **2** or **4**, the higher field shift of the methine protons compared to those of the corresponding isomers **3** or **5** (for example, **3a** − **2a** = 0.5, **3b** − **2b** = 0.58 ppm HCOMe) is explicable in terms of the same anisotropic effect seen for the methyl groups. Further support for these structures will be shown in connection with other photoproducts (vide infra). Photolysis (10 h) of **1** in acetonitrile resulted in recovery of the starting material.

Irradiation of *N*-(2-butenyl)phthalimide (**8a**) in methanol gave the corresponding products **9a** (mixture, 75%), but *N*-allylphthalimide (**8b**) afforded no corresponding products on photolysis in methanol.



Photolysis of *N*-(3-phenyl-2-propenyl)phthalimide (**10**) in methanol gave **11** (68%, mp 162–164 °C) and **12** (17%, mp