at the 17-position after attachment to the phosphazene ring. By contrast, changes in the chemical shifts for the resonances of aromatic ^{13}C nuclei for steroid VI were detected following reaction of the sodium salt of VI with $(NPCl_2)_3$. ^{13}C NMR spectroscopy (together with mass spectrometry) was also used to confirm the identity of the unreacted steroids VI, VII, and XIV isolated from the reaction products. This confirmed the absence of side reactions. No mass spectral or ^{13}C NMR spectral changes occurred after XVII had been treated with liquid methylamine (for 72 h).

Acknowledgment. This work was supported by the Public Health Service through Grant No. 5R01HL11418-09.

Registry No. III, 940-71-6; IV (HOR = VI), 74026-89-4; IV (HOR = VII), 75267-32-2; IV (HOR = VIII), 75267-33-3; IV (HOR = XIV), 75267-34-4; V (HOR = VI), 74026-90-7; V (HOR = VII), 74026-91-8; V (HOR = VIII), 74026-95-2; V (HOR = IX), 75267-35-5; V (HOR = X), 74026-93-0; V (HOR = XIV), 75283-90-8; V (HOR = XV), 75267-37-7; VI, 53-63-4; VI sodium salt, 74026-88-3; VII, 53-16-7; VII sodium salt, 74040-94-1; VIII, 50-28-2; VIII sodium salt, 17181-19-0; IX, 57-63-6; IX sodium salt, 75267-38-8; X, 57-88-5; XI, 17608-41-2; XII sodium salt, 75267-39-9; XIII sodium salt, 75267-40-2; XIV, 1035-77-4; XIV sodium salt, 74026-92-9; XVI, 1624-62-0; XVII, 72-33-3; XIX (HOR = IX), 75267-41-3; XIX (HOR = X), 75267-42-4; XIX (HOR = XI), 75267-43-5; XX (HOR = VII), 75267-44-6; XXI (HOR = VII), 75330-94-8; XXII (HOR = VII), 75299-11-5; XXIII (HOR = VII), 75363-53-0; XXIV (HOR = VII), 75283-91-9; XXV (HOR = VII), 75331-70-3; XXVI (HOR = VII), 75267-45-7; XXVII (HOR = VII), 75267-46-8; $N_3P_3Cl_5(OCH_2CF_3)$, 13053-90-2; $N_3P_3Cl_5(OC_6H_5)$, 3028-10-2; $N_3P_3Cl_5(OC_6H_4Br\text{-}p)$, 3887-16-9; $N_3P_3Cl_5(OH)$, 75267-47-9; $N_3P_3Cl_5(ONa)$, 75283-92-0; $N_3P_3Cl_4(OCH_2CF_3)_2$, 75267-48-0; $N_3P_3Cl_4(OH)_2$, 75267-49-1; $N_3P_3Cl_4(ONa)_2$, 75267-50-4; $N_3P_3Cl_3(OCH_2CF_3)_3$, 75330-95-9; $N_3P_3Cl_2(OCH_2CF_3)_4$, 75267-51-5; $N_3P_3Cl(OCH_2CF_3)_5$, 55975-53-6; $N_3P_3Cl(OC_6H_5)_5$, 5032-39-3; $[NP(OCH_2CF_3)_2]_3$, 1065-05-0; $[NP(OC_6H_5)_2]_3$, 1184-10-7; $[NP(NHCH_3)_2]_3$, 1635-63-8; $N_3P_3(NHCH_3)_5(OCH_2CF_3)$, 75283-93-1; $N_3P_3(NHCH_3)_5(OH)$, 75267-52-6; $N_3P_3(NHCH_3)_5(ONa)$, 75267-53-7; $N_3P_3(NHCH_3)_4(OH)$, 75267-54-8; $N_3P_3(NHCH_3)_4(ONa)_2$, 75267-55-9.

Ichthyotoxic and Cytotoxic Metabolites of the Tropical Brown Alga *Stypopodium zonale* (Lamouroux) Papenfuss[1]

William H. Gerwick and William Fenical*

Institute of Marine Resources, Scripps Institution of Oceanography, La Jolla, California 92093

Received May 12, 1980

Seven new natural products, stypoldione, stypotriol, stypodiol, epistypodiol, epitaondiol, 2-(geranylgeranyl)-5-methyl-1,4-benzohydroquinone, and 2-(geranylgeranyl)-5-methyl-1,4-benzoquinone, and two previously reported metabolites, taondiol and atomaric acid, have been isolated from the Caribbean brown alga *Stypopodium zonale*. Taondiol was obtained as the enantiomer of that previously reported. The structures of the new compounds were based upon the previously described X-ray structure of stypoldione and upon detailed ^{13}C and ^1H NMR analyses. Nearly all the compounds isolated showed toxic or strong narcotic effects upon the reef-dwelling fish, *Eupomacentrus leucostictus*, and stypoldione was found to be an extremely potent inhibitor of synchronous cell division in a fertilized sea urchin egg assay.

In the course of our investigations of the chemical defense strategies of tropical marine algae, we are continuing to explore the natural products chemistry and subsequent chemical ecology of brown seaweeds of the family Dictyotaceae (Dictyotales). One such example in this family is the brown alga *Stypopodium zonale* (Lamouroux) Papenfuss, which is found to grow luxuriantly in the Western Caribbean Sea where herbivorous invertebrates and fishes are particularly abundant.[2] In an earlier communication, we reported the structures of two ichthyotoxic metabolites, stypoldione and stypotriol, isolated from *S. zonale*.[3] In this complete report of our investigations of this alga, we describe the structures of several new biologically active compounds and amplify upon our initial findings.

Stypopodium zonale was initially chosen for study based on observations that when the freshly collected plant was placed in a well-aerated aquarium, the alga was found to excrete rust-colored substances which proved to be toxic to the Caribbean herbivorous fish *Eupomacentrus leucostictus*. During the course of 1 week, with daily changes of the aquarium water, the plants continued to excrete ichthyotoxic substances with no visible degeneration of the plants themselves. Diethyl ether extraction of the water yielded a complex mixture of UV-absorbing compounds, the major component of which was the bright red *o*-quinone, stypoldione (1). Stypoldione in seawater, at 1.0 μg/mL, induced the same toxic symptoms as the algae-treated water.

The chloroform–methanol extract of the fresh alga proved even more toxic than pure 1, suggesting that a more potent intracellular toxin was present. Indeed, when algal extracts were rapidly chromatographed in the field, a white solid, stypotriol (2), was obtained, which rapidly began turning pink and then red. The hydroquinone 2 was substantially more toxic than 1 (LD $\simeq$ 0.2 μg/mL), but as indicated by the color change, it is rapidly air oxidized to stypoldione such that precise concentrations in seawater cannot be produced.[4] Hence, the major toxic metabolite of *S. zonale* is the *o*-hydroquinone 2, which when excreted, is rapidly air oxidized to the *o*-quinone 1. The structures of 1 and 2 were communicated earlier[3] based upon a conclusive X-ray analysis of 1. Complete analysis of the extract has now resulted in the isolation of compounds 2 and 4–10 (Chart I), and several of these compounds contribute to the observed overall ichthyotoxicity of *S. zonale*. Contrary to our earlier report, the alga does contain taondiol (9),[5] as well as atomaric acid (10);[6] however, the

(1) Inshore Marine Shallow Water Ecosystem Project Contribution no. 60.

(2) Ogden, J. D.; Lobel, P. S. *Environ. Biol. Fishes* **1978**, *3*(1), 49.

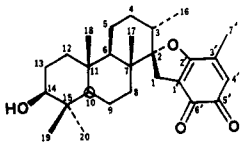
(3) Gerwick, W. H.; Fenical, W.; Fritsch, N.; Clardy, J. *Tetrahedron Lett.* **1979**, 145.

(4) The details of this fish toxicity bioassay were recently summarized, see: Sun, H. H.; Fenical, W. *Tetrahedron Lett.* **1979**, 685.

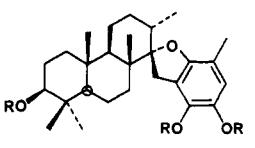
(5) González, A. G.; Darias, J.; Martín, J. D. *Tetrahedron Lett.* **1971**, 2729.

0022-3263/81/1946-0022$01.00/0

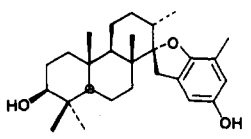
Chart I



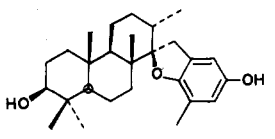
1



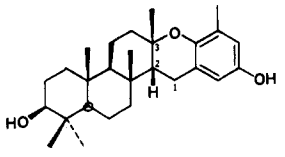
2 R = H
3 R = Ac



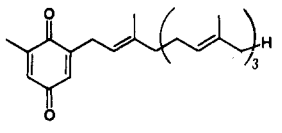
4



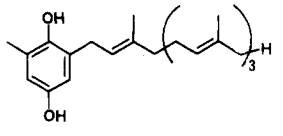
5



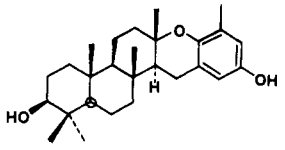
6



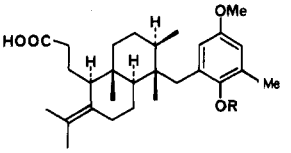
7



8



9



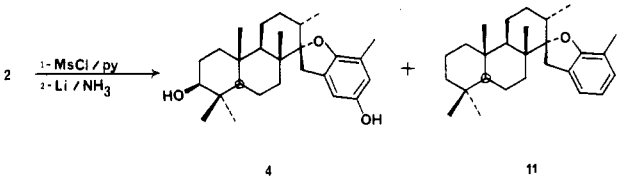
10, R = H
13, R = Ac

former diol was isolated as the enantiomer of that which occurs in *Taonia atomaria*.[5]

Freshly collected *S. zonale*[7] (Carrie Bow Cay, Belize, 1978) was stored in ethanol for transport and subsequently repeatedly extracted with chloroform/methanol. Fractionation of the extract by silica gel column chromatography, followed by purification of fractions by silica gel preparative high-performance LC yielded **1**, **2**, and **4**–**10**. When a small portion of the extract was acetylated (Ac_2O/py/25 °C) prior to column chromatography, only **3** was obtained, confirming that **1** is an artifact of the isolation process.

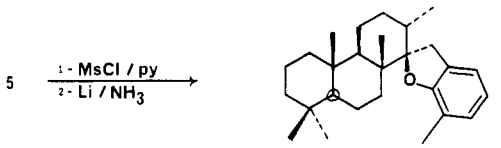
Stypoldione (**1**), $[\alpha]_D$ −65.1°, formed bright red crystals from diethyl ether and was found to compose 6% of the extract after lengthy isolation procedures. Treatment with $Na_2S_2O_4$[8] smoothly converted **1** to stypotriol, which could be stabilized by storage under argon. Acetylation of stypotriol yielded the triacetate **3**, which was identical with

Scheme I



4 11

Scheme II



12

that obtained via fractionation of the acetylated crude extract. The structures of **1** and **2**, as reported earlier with relative stereochemistry only, provided the foundation for the subsequent assignments of several new metabolites, particularly **4**–**6**. The ^1H and ^{13}C NMR features of several of these new compounds are tabulated in Tables I and II.

Stypodiol (**4**), $[\alpha]_D$ −3.1° (*c* 0.98, $CHCl_3$), a new compound, was found to compose 0.05% of the extract. The diol analyzed for $C_{27}H_{40}O_3$ by high-resolution mass spectrometry, and acetylation yielded a diacetate, all of which illustrated that **4** contained one less hydroxyl functionality in comparison with stypotriol. The secondary (equatorial) alcohol at C-14 was intact as noted by the shift in the ^1H NMR spectra of a double doublet methine proton at δ 3.26 in the alcohol to δ 4.55 in the acetate. Further, two aromatic protons, observed as broadened bands at δ 6.43 and 6.39 in the alcohol, shifted to a broadened two-proton band at δ 6.65 in the acetate. This shift strongly suggested both protons to be ortho to a phenol hydroxyl group, hence placing meta protons at C-4′ and C-6′. Consideration of the ^1H and ^{13}C NMR data for **4** (Tables I and II) led to its assignment as the C-6′ deoxy derivative of stypotriol; however, secure information to fix the stereochemistry of this metabolite was lacking. For conclusive establishment of the structure of **4**, stypotriol (**2**) was converted to stypodiol (Scheme I). Treatment of **2** with methanesulfonyl chloride in pyridine gave a trimesylate derivative, which was reduced with lithium in ammonia[9] without further purification. From the resulting complex mixture, stypodiol, $[\alpha]_D$ −3.6° (*c* 0.52, $CHCl_3$), and the aromatic ether **11** were obtained. The comparable rotation of **4**, produced from **2**, indicated that stypodiol has the same absolute stereochemistry as stypotriol.

A closely related compound, epistypodiol (**5**), was isolated from fractions also containing **4**. The diol showed $[\alpha]_D$ −4.5° (*c* 1.35, $CHCl_3$) and also analyzed for $C_{27}H_{40}O_3$ by high-resolution mass spectrometry. Acetylation gave a diacetate, the spectral features of which were analogous to those of **4**. In this case, a double doublet alcohol methine proton shifted from δ 3.22 to 4.55, again confirming the C-14 hydroxyl to be present. The highly comparable ^1H and ^{13}C NMR data (Tables I and II) suggested that **5** was an epimer of **4**. Specifically, significantly different shifts were observed for the C-1 protons in the ^1H NMR spectrum.

Also, a shift of a singlet methyl group of δ 1.15 was observed, and this methyl was assigned as C-17. Hence, the NMR data suggested that **5** was the C-2 epimer (spiro

(6) González, A. G.; Darias, J.; Martín, J. D.; Norte, M *Tetrahedron Lett.* **1974**, 3951.
(7) Voucher specimens of this alga are on deposit at the National Herbarium, Smithsonian Institution, Washington, D.C.
(8) Reynolds, G. A.; Van Allan, J. A. "Organic Syntheses"; Wiley: New York 1963; Collect. Vol. IV, p 15.
(9) Kenner, G. W.; Williams, N. R. *J. Chem. Soc.* **1955**, 522.

Table I. Selected 220-MHz ^{1}H NMR Data for Several *S. zonale* Metabolites

H(s) at C no.	1[a]	2[b]	4[b]	5[b]	6[b]	9[b]
1	2.90 (1 H, d, J = 16),	3.18 (1 H, d, J = 16),	3.18 (1 H, d, J = 16),	3.07 (1 H, d, J = 17),	2.68 (1 H, dd, J = 15, 14)	2.62 (2 H, m)
	2.59 (1 H, d, J = 16)	2.76 (1 H, d, J = 16)	2.74 (1 H, d, J = 16)	2.90 (1 H, d, J = 17)	2.47 (1 H, dd, J = 15, 5)	
14	3.11 (1 H, dd, J = 10, 4)	3.24 (1 H, dd, J = 10, 4)	3.23 (1 H, dd, J = 10, 4)	3.21 (1 H, dd, J = 10, 4)	3.29 (1 H, dd, J = 10, 4)	3.18 (1 H, dd, J = 10, 4)
17–20	0.97 (3 H, s),	0.97 (3 H, s),	0.93 (3 H, s),	1.15 (3 H, s),	1.19 (3 H, s),	1.05 (3 H, s),
	0.96 (3 H, s),	0.92 (3 H, s),	0.93 (3 H, s),	0.93 (3 H, s),	1.00 (3 H, s),	0.99 (3 H, s),
	0.85 (3 H, s),	0.85 (3 H, s),	0.85 (3 H, s),	0.87 (3 H, s),	0.92 (3 H, s),	0.95 (3 H, s),
	0.73 (3 H, s)	0.76 (3 H, s)	0.76 (3 H, s)	0.81 (3 H, s)	0.80 (3 H, s)	0.79 (3 H, s)
16	0.74 (3 H, d, J = 6)	0.68 (3 H, d, J = 6)	0.67 (3 H, d, J = 6)	0.73 (3 H, d, J = 6)	1.22 (3 H, s)	1.11 (3 H, s)
4′/6′	5.99 (1 H, m, J = 1)	6.44 (1 H, s)	6.43 (1 H, m),	6.45 (1 H, m),	6.45 (1 H, m, J = 2),	6.57 (1 H, m, J = 2),
			6.39 (1 H, m)	6.52 (1 H, m)	6.38 (1 H, m, J = 2)	6.43 (1 H, m, J = 2)
7′	2.14 (3 H, d, J = 1)	2.10 (3 H, s)	2.16 (3 H, d, J = 1)	2.13 (3 H, d, J = 1)	2.08 (3 H, s)	2.15 (3 H, d, J = 1)

[a] Recorded in CCl_4 with internal Me_4Si as standard. [b] Recorded in $CDCl_3$ with internal Me_4Si as standard.

Table II. ^{13}C NMR Data for Several *S. zonale* Metabolites

1[a]	4[c]	5[a]	6[c]	9[b]	13[d]
182.7 (s)	153.2	153.3 (s)	151.3 (s)	150.6	180.7 (s)
174.5 (s)	152.1	150.2 (s)	144.7 (s)	145.2	168.2 (s)
170.3 (s)	127.4	127.3 (s)	126.7 (s)	126.8	157.1 (s)
143.2 (s)	118.3	118.4 (s)	122.8 (s)	123.0	143.4 (s)
128.7 (d)	116.2	116.1 (d)	116.8 (d)	116.2	133.4 (s)
114.5 (s)	109.5	109.3 (d)	113.9 (d)	113.7	133.3 (s)
103.8 (s)	94.7	96.2 (s)	78.8 (d)	79.0	131.3 (s)
78.7 (d)	77.9	79.0 (d)	76.7 (s)	76.6	123.5 (s)
55.3 (d)	55.5	55.7 (d)	49.1 (d)	55.7	114.6 (d)
51.6 (d)	51.7	53.0 (d)	48.3 (d)	54.8	113.6 (d)
42.5 (s)	42.7	43.9 (s)	45.8 (d)	46.5	54.9 (q)
38.8 (d)	39.4	39.1 (s)	40.7 (t)	42.1	53.6 (d)
38.4 (s)	38.8	39.1 (t)	39.8 (s)	39.9	42.3 (d)
37.1 (t)	37.3	37.1 (s)	37.3 (s)	39.8	40.7 (s)
37.1 (s)	37.3	35.5 (q)	35.2 (s)	37.6	39.2 (s)
33.0 (t)	35.5	33.4 (t)	32.4 (t)	36.8	36.9 (t)
30.9 (t)	33.2	32.0 (t)	31.3 (t)	33.9	35.9 (d)
30.5 (t)	31.5	31.0 (t)	30.0 (t)	23.5	33.2 (s)
28.0 (q)	28.5	28.3 (q)	29.9 (t)	22.6	25.7 (t)
27.3 (t)	28.2	27.6 (t)	28.3 (q)	21.1	25.2 (t)
20.2 (t)	20.6	20.5	25.1 (q)	20.9	24.1 (t)
17.7	18.2	18.0	23.6 (t)	20.6	22.8 (t)
17.0	17.3	16.6 (q)	22.0 (q)	19.9	20.8
16.8	16.6	16.1 (q)	17.5 (q)	18.0	20.8
16.3	16.2	15.7 (t)	17.3 (q)	16.6	20.5
15.4	16.0	15.6 (q)	17.0 (q)	16.3	20.5
15.4 (q)	15.7	15.1 (q)	16.6 (t)	16.0	20.1
					18.1
					17.2
					15.8 (q)

[a] In $CDCl_3$. [b] In acetone-d_6. [c] In pyridine-d_5. [d] In benzene-d_6.

carbon) of stypodiol. Epistypodiol was reduced (Scheme II), using the ester reduction method already applied to stypotriol, to gain insight into this problem. From the resulting mixture the aromatic ether **12** was isolated, which was highly comparable but not identical with **11**. Again the ^{1}H NMR features for **12** indicated that it was the C-2 epimer of **11**.

No chemical methods were found to relate epistypodiol to **1** or **2**. However, it seems most reasonable, considering the probable biosynthesis of these compounds, to consider the site of epimerization at either C-2 or C-3. Epimerization of C-3 would yield an axial methyl group. Considering the δ gauche effects of the substituents at C-2, this methyl group would be predicted[10] to shift to between 12.1 and 14.3 ppm in the ^{13}C NMR spectrum. By single frequency decoupling techniques, the C-16 methyl group (a three-proton doublet at δ 0.73 in the ^{1}H NMR spectrum) was located at 15.6 ppm, a position in close agreement with the known equatorial methyl group in **1** and **4**, discounting the possible epimerization at C-3. Hence, C-2 must be the site of epimerization, and this proposal is supported by the aforementioned shift in the C-17 methyl. In stypodiol and stypotriol, the C-17 methyl is oriented trans-diaxial to the spiro oxygen. However, in epimer **5**, the oxygen is equatorial and induces a downfield shift (δ 0.95 → 1.15) via a gauche interaction.

Epitaondiol (**6**) was also isolated from *S. zonale*, but only from collections of the alga from deeper waters (−20 m). The diol crystallized from diethyl ether, mp 149–152 °C, and analyzed for $C_{27}H_{40}O_3$ by high-resolution mass spectrometry. The ^{1}H and ^{13}C NMR features of **6** were highly comparable to those obtained from authentic taondiol (**9**), but they were not identical, hence suggesting the compound to be epimeric to taondiol. As in the stypodiol–

(10) Crews, P.; Kho-Wiseman, E. *Tetrahedron Lett.* **1978**, 2483.

epistypodiol case, the most likely sites of epimerization are C-2 or C-3, or both. The simple C-3 epimer was discounted by direct comparison with the authentic epimer, since this compound had been earlier synthesized via base treatment of taondiol.[11] Assignment of **6** as the C-2 epimer of taondiol resulted from a complete analysis of the ^1H NMR features for this compound by conformational analyses using molecular models. The C-1 methylene protons in **6** were observed as an ABX pattern at δ 2.68 and 2.47, with a geminal coupling constant of 15 Hz. Additional couplings of 5 and 14 Hz were observed in these patterns, reflecting the coupling with the C-2 methine proton. With the Karplus equation as a guide, calculated dihedral angles of 0° or 180° (14 Hz) and 60° of 120° (5 Hz) must exist between these six-membered-ring protons. These data are best fit by the C-2 epimer (dihedral angles of 164, 44°) of taondiol. This isomer would consist of a cis-fused ether ring with an axial methyl at C-3 and an equatorial proton at C-2. The bis epimer at C-2 and C-3 was considered unlikely since the adjacent C-ring would be forced to exist in a boat conformation. If this conformation was present, however, base treatment would be expected to readily epimerize C-3, as observed in taondiol, in this case yielding a more stable C-ring conformer. Under the conditions which readily epimerize taondiol,[11] **6** failed to epimerize, hence reinforcing our proposed assignment.

The linear, mixed biosynthetic apparent precursors, **7** and **8**, were also isolated as 2% each of the extract. The quinone **7** analyzed for $C_{27}H_{38}O_2$ by high-resolution mass spectrometry, and from its infrared ($\nu_{C=O}$ 1610 cm^{-1}), ultraviolet (λ_{max} 250 nm, ϵ 2160), and NMR features (see the Experimental Section) was readily assigned as 2-(geranylgeranyl)-5-methyl-1,4-benzoquinone. Comparison of the spectral data from **7** with that from the authentic quinone, obtained via synthesis,[12] proved them to be identical. The corresponding hydroquinone (**8**) yielded a crystalline diacetate upon acetylation (Ac_2O/py/25 °C), mp 115–116 °C, and air oxidation smoothly converted **8** to the quinone **7**.

Isolated along with the new metabolites described above were the previously reported compounds taondiol (**9**) and atomaric acid (**10**). Confirmation of the structure assignments was made by comparison of these metabolites with authentic samples kindly provided by Dr. J. D. Martín.[5,6] In addition to the favorable comparison of **10** with authentic material, the phenol was acetylated to yield the corresponding acetate **13**. The acetate had more favorable solubility characteristics and its ^{13}C NMR features are reported in Table II. Taondiol, as isolated from *Taonia atomaria*, showed $[\alpha]_D$ −76° (*c* 0.30, $CHCl_3$). The metabolite we isolated showed $[\alpha]_D$ +49.6° (*c* 0.59, $CHCl_3$), hence our material, while apparently partially racemized, is enantiomeric to that from *T. atomaria*.

The compounds produced by *S. zonale* all show pronounced deleterious effects against the herbivorous fish *Eupomacentrus leucostictus*.[4] Stypoldione, stypotriol, and epistypodiol (**1**, **2**, and **5**) are toxic at the 1.0-, 0.2-, and 10-μg/mL levels, respectively. While not toxic, stypodiol (**4**) induces an intense hyperactivity and is perhaps in part responsible for the "escape" behavior observed when fishes encounter the algae in an enclosed aquarium. The linear precursors **7** and **8** and taondiol and atomaric acid (**9**, **10**) produce distinct lethargic behavior and narcosis at 10-μg/mL levels. The extracellular toxin stypoldione (**1**) is an effective inhibitor of synchronous cell division in the fertilized sea urchin egg assay (*Strongylocentrotus purpuratus* Stimpson), ED_{50} = 1.1 μg/mL, and appears to inhibit cleavage via inhibition of tubulin polymerization.[13] Several cytotoxins useful as anticancer drugs (colchicine for example) act via this mechanism of inhibition.

The production of toxic and narcotic substances by *S. zonale* would appear to contribute greatly to the survival of this plant in the predator-rich areas in which it abounds. The fish involved in the assay experiments with these compounds is an abundant herbivore inhabiting similar spatial domains as *S. zonale*, but the fish has never been observed to feed on the alga.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer and ultraviolet spectra were recorded on a Perkin-Elmer Model 124 double-beam spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter, using a 10-cm microcell. ^1H NMR spectra were recorded on Varian HR-220 and T-60 NMR spectrometers, chemical shifts are reported relative to Me_4Si (δ 0), and coupling constants are given in hertz. ^{13}C NMR spectra were recorded on Varian CFT-20 and JEOL FX-100 spectrometers. Low-resolution mass spectra were obtained from a Hewlett-Packard 5930-A mass spectrometer and high-resolution mass spectra were supplied by the Department of Chemistry, University of California, Los Angeles. Melting points were determined on a Fisher-Johns melting apparatus and are reported uncorrected. All solvents used were distilled from glass prior to use.

Collection and Isolation. *Stypopodium zonale* was collected in April 1977, by hand, using SCUBA (−3 to −20 m), near Carrie Bow Cay, Belize. The collection was stored in eight black 2-quart bottles in isopropyl alcohol, and within 1 month, the IPA was decanted, the algae were homogenized, and the algal cake was Soxhlet extracted with $CHCl_3$/MeOH (2:1). The $CHCl_3$/MeOH was removed in vacuo and the residue partitioned between saturated brine (1 L) and $CHCl_3$ (4 × 1 L). The $CHCl_3$ extract was dried over $MgSO_4$ and the solvent evaporated to yield 134 g of a brown tar (dry weight of extracted alga 1.4 kg). Crude extract (20 g) was applied to a column (6.5 × 100 cm) of Davison Grade 62 silica gel and fractions were eluted with solvents of increasing polarity (2,2,4-trimethylpentane (TMP)/dichloromethane/ethyl acetate). Nonpolar fractions (2% to 10% CH_2Cl_2 in TMP) were further purified by high-performance LC (μ-Porasil, 50 cm, 3% EtOAc in TMP) to obtain the quinone **7** (2.0%) and hydroquinone **8** (2.0%). Atomaric acid (**10**) tailed severely on silica chromatography and appeared in many of the mid-polarity fractions. Preparative thick-layer chromatography gave a band of nearly pure **10**, which was further purified by high-performance LC (μ-Porasil, 50 cm, 30% EtOAc/TMP). A complex mixture of compounds including **4**, **5**, and **9** was eluted in the same fraction (100% CH_2Cl_2) and was easily separated by using high-performance LC (μ-Porasil, 50 cm, 20% EtOAc/TMP) to yield **4** (0.05%), **5** (0.5%), and **9** (0.05%). Stypoldione (**1**) was eluted from the silica column (10% EtOAc/CH_2Cl_2) in nearly pure form. After concentration, **1** crystallized from diethyl ether. Stypotriol (**2**) was obtained from a pipet column in the field, using partially hydrated Davison Grade 62 silica gel with diethyl ether/benzene (1:1) as the eluant, and was also crystalline upon concentration. In a separate experiment, a small collection of a deep water "form" of *S. zonale* was processed as above. Another new compound, isotaondiol (**6**), was obtained and purified as described above.

Acetylations. All acetylations were conducted in a similar manner. The natural product (5–15 mg) was combined with excess pyridine (ca. 2 mL) and acetic anhydride (ca. 2 mL) with stirring at room temperature. After 16–24 h, ice and then water were added and the mixture was extracted with diethyl ether (3 × 25 mL). The combined Et_2O extracts were washed first with 5% HCl (3 × 25 mL) and next with saturated $NaHCO_3$ solution (3

(11) González, A. G.; Alvarez, M. A.; Darias, J.; Martín, J. D. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2637.

(12) We thank Dr. T. Kato for providing spectral data on synthetic 2-(geranylgeranyl)-6-methyl-1,4-benzoquinone. For the details of the synthesis of this quinone, see: Kumanireng, A. S.; Kato, T.; Kitahara, Y. *Chem. Lett.* **1973**, 1045.

(13) Jacobs, R. S.; White, S.; Wilson, L. *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, in press.

× 25 mL). The ether solution was dried over anhydrous $MgSO_4$ and reduced in vacuo to yield the acetylated products.

Stypoldione (1). Stypoldione crystallized from ether into large red rombuses. Repeated recrystallization gave 1 in 6% yield of the crude extract: mp 170 °C dec; $[\alpha]_D$ −65.1° (*c* 0.461, $CHCl_3$); IR ($CHCl_3$) $\nu_{C=O}$ 1675, 1650 cm^{-1}; UV λ_{max} (MeOH) 475, 270 nm (ϵ 882, 2470); high-resolution mass spectrum (70 eV), *m/e* 428.2924 (M^+ + 2; 0.3 mamu deviation, $C_{27}H_{40}O_4$, 30.8%), 412.2994 ($C_{27}H_{40}O_3$, 27.3%), 257.2282 ($C_{19}H_{29}$, 100%), 191.0737 ($C_{11}H_{11}O_3$, 37.8%), 175.1481 ($C_{13}H_{19}$, 35%), 175.073€ ($C_{11}H_{11}O_2$, 28.7%), 135.1184 ($C_{10}H_{15}$, 77%), 107.0864 (C_8H_{11}, 66.5%).

Stypotriol (2). In addition to the isolation of **2** by rapid chromatography in the field, small amounts of stypotriol (0.01%) were recovered from the large-scale column chromatography of the crude $CHCl_3$/MeOH extract. Stypotriol gave $[\alpha]_D$ −10.0° (*c* 0.82, $CHCl_3$); IR ($CHCl_3$) 3500 cm^{-1}; UV λ_{max} (MeOH) 291 nm (ϵ 2990); low-resolution mass spectrum (70 eV, 150 °C), *m/e* 428 (M^+, $C_{27}H_{40}O_4$).

Triacetate 3. Acetylation of the crude extract followed by fractionation on silica gel or direct acetylation of stypotriol as described above gave the crystalline triacetate in high yield: mp 248–250 °C; IR ($CHCl_3$) 2950, 1775, 1730, 1370, 1245, 1205 cm^{-1}; low-resolution mass spectrum (70 eV, 200 °C), *m/e* 554 (5), 512 (17), 470 (4), 256 (3), 149 (21), 43 (100); ^1H NMR (220 MHz, CCl_4) δ 650 (1 H, m), 4.47 (1 H, dd, *J* = 10, 4 Hz), 3.06 (1 H, d, *J* = 17.5 Hz), 2.58 (1 H, d, *J* = 17.5 Hz), 2.15 (3 H, br s), 2.11 (6 H, s), 1.92 (3 H, s), 1.03 (3 H, s), 0.97 (3 H, s), 0.89 (6 H, s), 0.81 (3 H, d, *J* = 6 Hz).

Reduction of Stypoldione (1) to 2. To a stirred solution of 1 (15 mg) in 10 mL of EtOH was added 20 mL of an aqueous solution of $Na_2S_2O_4$[8] (40 mg). The red solution immediately decolorized, and after 1 min 50 mL of 5% HCl was added and the solution was extracted with Et_2O (3 × 50 mL). The combined Et_2O phases were washed with saturated $NaHCO_3$, dried over anhydrous $MgSO_4$, and reduced in vacuo to yield a gummy white solid (15 mg, 99%). The solid was stable for long periods when kept under argon or hydrogen but immediately began to turn pink in air.

Stypodiol (4). The diol **4** was separated from several related metabolites by using high-performance LC (μ-Porasil, 50 cm, 20% EtOAc/TMP) and was isolated as an air-unstable white solid. Compound **4**: 0.05% of the crude extract; $[\alpha]_D$ −3.06° (*c* 0.98, $CHCl_3$); IR ($CHCl_3$) 3400, 1475, 1225, 1020 cm^{-1}; UV λ_{max} (MeOH) 305 (ϵ 2020); high-resolution mass spectrum (70 eV), *m/e* 412.2993 (M^+; 1.6 mamu deviation, $C_{27}H_{40}O_3$, 100%), 257.2272 ($C_{19}H_{29}$, 85%), 175.0763 ($C_{11}H_{11}O_2$, 35%), 137.0607 ($C_8H_9O_2$, 60%), 135.1171 ($C_{10}H_{15}$, 45%), 109.0990 (C_8H_{13}, 59%), 95.0850 (C_7H_{11}, 58%), 81.0712 (C_6H_9, 44%). **Diacetate**: IR ($CHCl_3$) 1770, 1730 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) δ 6.42 (2 H, s), 4.57 (1 H, dd, *J* = 10, 4), 3.84 (1 H, d, *J* = 16), 2.84 (1 H, d, *J* = 16), 2.24 (3 H, s), 2.19 (3 H, d, *J* = 1.0), 2.05 (3 H, s), 1.2–1.9 (15 H, m), 0.94 (3 H, s), 0.89 (6 H, s), 0.83 (3 H, s), 0.67 (3 H, d, *J* = 6).

Epistypodiol (5). The diol **5** was isolated as an oil (0.05%) from column fractions by high-performance LC (μ-Porasil, 50 cm, 20% EtOAc/TMP): $[\alpha]_D$ −4.5° (*c* 1.35, $CHCl_3$); IR ($CHCl_3$) 3350, 2950, 1475, 1375, 1270, 1225 cm^{-1}; UV λ_{max} (MeOH) 230, 304 (ϵ 6250, 5650); high-resolution mass spectrum (70 eV), *m/e* 412.2993 (M^+; 1.5 mamu deviation, $C_{27}H_{40}O_3$, 79%), 257.2249 ($C_{19}H_{29}$, 100%), 175.0748 ($C_{11}H_{11}O_2$, 56%), 135.0799 ($C_9H_{11}O_1$, 42%), 121.1030 (C_9H_{13}, 48%), 109.1003 (C_8H_{13}, 37%), 95.0845 (C_7H_{11}, 56%), 81.0694 (C_6H_9, 55%). **Diacetate**: IR ($CHCl_3$) 2950, 1740, 1720, 1460, 1370, 1250 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) δ 6.66 (1 H, d, *J* = 1.5), 6.58 (1 H, d, *J* = 1.5), 4.49 (1 H, dd, *J* = 10, 4), 3.16 (1 H, d, *J* = 17), 3.00 (1 H, d, *J* = 17), 2.24 (3 H, s), 2.15 (3 H, d, *J* = 1.0), 2.04 (3 H, s), 1.2–1.8 (15 H, m), 1.16 (3 H, s), 0.89 (3 H, s), 0.84 (3 H, s), 0.82 (3 H, s), 0.72 (3 H, d, *J* = 6.5).

Epitaondiol (6). Compound **6** was isolated from a separate collection of *Stypopodium zonale* from Carrie Bow Cay made in deeper water (−20 m) and purified by preparative silica column high-performance LC (16 mm × 50 cm), using 40% EtOAc/TMP as the eluting solvent. The diol crystallized as colorless needles from diethyl ether (mp 149–152 °C) and showed $[\alpha]_D$ +43.1° (*c* 1.03, $CHCl_3$): IR ($CHCl_3$) 3500, 1610, 1460, 1375, 1140, 1015 cm^{-1}; UV λ_{max} (MeOH) 292 nm (ϵ 3950); high-resolution mass spectrum (70 eV, 180 °C), *m/e* 412.2986 (M^+; 0.8 mamu deviation, $C_{27}H_{40}O_3$, 79%), 257.2283 ($C_{19}H_{29}$, 100%), 175.0761 ($C_{11}H_{11}O_2$, 47%), 135.1173 ($C_{10}H_{15}$, 47%), 121.1017 (C_9H_{13}, 48%), 109.1020 (C_8H_{13}, 50%), 95.0866 (C_7H_{11}, 41%), 93.0707 (C_7H_9, 38%), 81.0708 (C_6H_9, 45%).

2-(Geranylgeranyl)-6-methyl-1,4-benzoquinone (7). The quinone **7** was isolated (2.0% extract) as a light yellow mobile oil, and final purification was achieved by high-performance LC (μ-Porasil, 50 cm, 3% EtOAc/TMP). For **7**: IR ($CHCl_3$) 2950, 1610, 1500, 1440 cm^{-1}; UV λ_{max} (MeOH) 254 (ϵ 2160); high-resolution mass spectrum (70 eV), *m/e* 394.2879 (M^+; 0.7 mamu deviation, $C_{27}H_{38}O_2$, 10.9%), 190.0979 ($C_{12}H_{14}O_2$, 9.0%), 176.0821 ($C_{11}H_{12}O_2$, 17.2%), 175.0764 ($C_{11}H_{11}O_2$, 100%), 137.0600 ($C_8H_9O_2$, 21.1%), 135.1170 ($C_{10}H_{15}$, 14.1%), 121.0995 (C_9H_{13}, 10.3%), 93.0708 (C_7H_9, 13.3%), 81.0719 (C_6H_9, 42.2%); ^1H NMR (220 MHz, CCl_4) δ 6.48 (1 H, d, *J* = 2.5), 6.36 (1 H, d, *J* = 2.5), 5.15 (1 H, t, *J* = 6), 5.06 (3 H, m), 3.09 (2 H, d, *J* = 7), 2.06 (3 H, d, *J* = 2.5), 1.89–2.15 (12 H, m), 1.64 (6 H, s), 1.59 (9 H, s); ^{13}C NMR ($CDCl_3$) 187.9 (s), 187.9 (s), 148.5 (s), 145.9 (s), 139.9 (s), 135.4 (s), 134.9 (s), 133.2 (d), 132.3 (d), 131.2 (s), 124.5 (d), 124.3 (d), 123.9 (d), 118.1 (d), 39.7 (t), 39.7 (t), 39.7 (t), 29.7 (q), 27.6 (t), 26.8 (t), 26.6 (t), 26.5 (t), 25.7 (q), 17.7 (q), 16.0 (q), 16.0 (q), 16.0 (q).

2-(Geranylgeranyl)-6-methyl-1,4-benzohydroquinone (8). The hydroquinone **8** was isolated as a colorless mobile oil (2% extract) and purified by high-performance LC (μ-Porasil, 50 cm, 3% EtOAc/TMP). For **8**: IR 3400 cm^{-1}; UV λ_{max} (MeOH) 287 nm (ϵ 2950); low-resolution mass spectrum (70 eV), *m/e* 396 (0.1), 279 (0.3), 189 (2.6), 175 (6.1), 149 (15.3), 137 (14.3), 93 (25), 91 (21), 81 (41), 69 (100), 55 (56), 43 (70), 41 (91); ^1H NMR (220 MHz, CCl_4) 6.34 (1 H, d, *J* = 3.0), 6.26 (1 H, d, *J* = 3.0), 5.25 (1 H, t, *J* = 6), 5.03 (3 H, m), 4.48 (1 H, D_2O exchangeable), 4.29 (1 H, D_2O exchangeable), 3.20 (2 H, d, *J* = 7), 2.12 (3 H, s), 1.80–2.12 (12 H, m), 1.76 (3 H, s), 1.65 (3 H, s), 1.57 (9 H, s). **Diacetate**: mp 105–106 °C; IR ($CHCl_3$) 2950, 1750, 1440, 1360, 1160 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) δ 6.71 (1 H, d, *J* = 3.0), 6.64 (1 H, d, *J* = 3.0), 5.18 (1 H, dd, *J* = 6, 6), 5.03 (3 H, m), 3.12 (2 H, d, *J* = 7), 2.27 (3 H, s), 2.23 (3 H, s), 2.14 (3 H, s), 1.85–2.14 (12 H, m), 1.68 (6 H, s), 1.59 (9 H, s).

Synthesis of Stypodiol (4) and Ether 11 from Stypotriol (2). Stypotriol (**2**; 73 mg, 0.17 mmol) formed by reduction of **1** with $Na_2S_2O_4$ (see above) was dissolved in pyridine (8 mL) and cooled to 0 °C under an argon atmosphere. A 1:1 mixture of methanesulfonyl chloride (excess) and benzene (10 mL) was cautiously added dropwise over a 0.5-h period to the stirred solution. The reaction was allowed to run 18 h and to warm to 25 °C. Water was slowly added to quench the reaction, and the mixture was extracted with Et_2O (5 × 50 mL). The Et_2O extract was washed with water (3 × 50 mL), 5% HCl (3 × 50 mL), and saturated $NaHCO_3$ solution (3 × 50 mL) and subsequently dried over anhydrous $MgSO_4$. The filtered solution was reduced in vacuo to yield 68.5 mg (0.1 mmol) of a solid material which was homogeneous by TLC (62% yield). The trimesylate showed the following spectral features: IR (CCl_4) 1375, 1240, 1210, 1180, 1165 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 3.20 (3 H, s), 3.05 (3 H, s), 2.90 (3 H, s). Without further purification, the trimesylate was reduced with Li/NH_3. A solution, at −78 °C under argon, containing 40 mL of NH_3, 10 mL of diethyl ether, and 175 mg (0.652 mmol, 6 equiv) of finely pounded, cut, and washed (pentane) Li was prepared by dissolving the Li wire over a 30-min period. To the resultant blue solution was carefully added 68.5 mg (0.106 mmol) of stypotriol trimesylate in diethyl ether (10 mL), and the reaction was maintained at −78 °C for 80 min, at which time excess NH_4Cl was slowly and cautiously added. Dilution with diethyl ether and evaporation of the ammonia was followed by a water wash (2 × 100 mL); the Et_2O phase was then dried over anhydrous $MgSO_4$ and reduced in vacuo. Analysis of the crude reaction mixture by TLC indicated several products were formed, and these were separated by preparative TLC. A nonpolar UV-absorbing compound was isolated in low yield (4 mg, 0.0105 mmol, 10% yield) and shown to be the aryl ether **11**: ^1H NMR (220 MHz, $CDCl_3$) δ 6.87 (2 H, d, *J* = 7.5), 6.65 (1 H, dd, *J* = 7.5, 7.5), 3.25 (1 H, d, *J* = 16), 2.79 (1 H, d, *J* = 16), 2.23 (3 H, s), 1.0–1.8 (17 H, m), 0.95 (3 H, s), 0.85 (3 H, s), 0.79 (6 H, s), 0.67 (3 H, d, *J* = 6); low-resolution mass spectrum, *m/e* 380 (M^+, 8.5), 259 (4), 191 (4), 157 (7), 149 (16), 145 (18), 121 (10), 91 (18), 55 (62), 43 (88), 41 (98), 28 (100). A second more polar product was isolated in modest yield (5.2 mg, 0.0125 mmol, 12% yield) and shown to be identical

with stypodiol (4) by TLC and ^1H NMR (220 MHz). The synthetic product showed $[\alpha]_D$ -3.65° (c 0.52, $CHCl_3$).

Synthesis of Ether 12 from Epistypodiol (5). To a stirred solution of pyridine (5 mL, 0 °C) containing 56 mg (0.135 mm) of 4 was added 10 mL of a 1:1 solution of benzene and methanesulfonyl chloride (excess) dropwise over 0.5 h. After being warmed to 25 °C (12 h), the reaction mixture was quenched with ice and water and extracted with Et_2O (3 × 50 mL). The combined Et_2O phases were washed with water (3 × 50 mL), 5% HCl (3 × 50 mL), and saturated $NaHCO_3$ solution (3 × 50 mL) and dried over anhydrous $MgSO_4$. The Et_2O was removed in vacuo to yield 51.9 mg (0.103 mmol, 77% yield) of an oil which was homogeneous by TLC. The dimesylate was the sole product retrieved and its formation confirmed by the following spectral features: IR (CCl_4) 1370, 1340, 1230, 1180 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 3.13 (3 H, s), 3.03 (3 H, s). Without further purification, the dimesylate was reduced to the ether 12. A solution containing 20 mL of NH_3, 5 mL of Et_2O (-78 °C, under argon), and 55.5 mg (0.206 mmol, 2 equiv) of pounded, cut, and washed (pentane) Li was produced by dissolving the Li over a 30-min period. To the resultant blue solution was carefully added 51.9 mg (0.103 mmol) of epistypodiol dimesylate in Et_2O (7 mL) and the reaction was allowed to proceed for 90 min at -78 °C. The reaction was quenched by careful addition of excess NH_4Cl and diluted with Et_2O, and the NH_3 solution allowed to evaporate overnight. The Et_2O solution was washed with water (2 × 75 mL), dried over anhydrous $MgSO_4$ and reduced in vacuo to yield a mixture of products as analyzed by TLC. The least polar component was recovered by preparative TLC (6 mg, 0.016 mmol, 15.5% yield) and determined to be the desired aryl ether (12): ^1H NMR (220 MHz, $CDCl_3$) δ 6.95 (1 H, dd, J = 7, 1.0 Hz), 6.86 (1 H, dd, J = 7, 1.0 Hz), 6.66 (1 H, dd, J = 7, 7), 3.17 (1 H, d, J = 17), 2.97 (1 H, d, J = 17), 2.17 (3 H, d, J = 1), 1.2-1.8 (17 H, m), 1.17 (3 H, s), 0.86 (3 H, s), 0.79 (6 H, s), 0.72 (3 H, d, J = 7); low-resolution mass spectrum, m/e 380 (M^+, 9), 256 (6), 191 (5), 159 (7), 149 (3), 145 (7), 121 (16), 91 (20), 55 (65), 43 (85), 41 (100).

Base Treatment of Epitaondiol (6). Epitaondiol (6, 102.9 mg) was refluxed in 5% KOH in MeOH for 4 h. The MeOH was removed in vacuo and the residue was taken up in Et_2O. The Et_2O phase was washed with 5% HCl (3 × 50 mL) and finally with saturated $NaHCO_3$. The Et_2O mix was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo to yield only starting material as determined by TLC and ^1H NMR analysis.

Air Oxidation of Hydroquinone 8. Filtered air was continuously bubbled through a room-temperature CH_2Cl_2 solution of the hydroquinone 8 for 24 h. CH_2Cl_2 was periodically replenished. Removal of the solvent in vacuo gave a two-component mixture which by high-performance LC (μ-Porasil, 50 cm, CH_2Cl_2) separated into starting material and a less polar component, identified as 7 by comparison with the natural product.

Acknowledgment. We thank Drs. Klaus Rützler and Jim Norris, Smithsonian Institution, for the kind invitation to participate in the IMSWE tropical reef research program, supported in part by a grant from Exxon Corporation, in Belize and for advice and guidance with the biological aspects of our research. We thank Dr. J. D. Martin for providing authentic samples of taondiol and atomaric acid and Dr. P. Crews for providing several ^{13}C NMR spectra. This research is a result of financial support from NOAA, Department of Commerce, Office of Sea Grant, under Grant No. 04-7-158-44121.

Registry No. 1, 71103-05-4; 2, 71106-25-7; 2 trimesylate, 75558-33-7; 3, 71103-04-3; 4, 75657-53-3; 4 diacetate, 75578-63-1; 5, 75578-65-3; 5 diacetate, 75657-52-2; 5 dimesylate, 75578-64-2; 6, 75598-52-6; 7, 57576-82-6; 8, 57576-81-5; 8 diacetate, 75558-34-8; 9, 34274-99-2; 10, 55907-34-1; 11, 75558-35-9; 12, 75598-51-5; 13, 75558-36-0.

Photochemistry of Aliphatic Imides. Synthesis of Azetidine-2,4-diones via Photochemical Isomerization of Succinimides and *N*-Formyl-*N*-methyl α,β-Unsaturated Amides[1]

Kazuhiro Maruyama,* Takeshi Ishitoku, and Yasuo Kubo

Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606, Japan

Received June 2, 1980

Photochemical reactions of alkyl-substituted succinimides and *N*-formyl-*N*-methyl α,β-unsaturated amides were studied. Photolysis of succinimide 1 gave azetidine-2,4-dione 2 together with a small amount of 3. The photoinduced ring-contraction reaction is explained in terms of a two-photon mechanism. Similarly, several other succinimide derivatives photochemically gave the corresponding azetidine-2,4-diones. In addition, the photochemical cyclization of 3 to 2 was extended to the synthesis of azetidine-2,4-diones from *N*-formyl-*N*-methyl α,β-unsaturated amides.

In recent years considerable interest has been shown in the photochemistry of alicyclic imides. A number of studies have revealed that alicyclic imides photochemically behave similarly to simple carbonyl compounds, i.e., ketones and aldehydes. For example, the Paterno–Büchi reaction,[2] hydrogen abstraction,[3] and α cleavage[4] have been investigated. In regard to the α-cleavage reaction of imides, however, only a few reports have been published, and the scope and generality of the reaction have not been thoroughly investigated. Recently we have reported in preliminary form evidence that succinimides undergo the α-cleavage reaction to give azetidine-2,4-diones.[5] In this paper we describe the details of the reaction as well as the photochemical cyclization of *N*-formyl-*N*-methyl α,β-unsaturated amides.[6] The reaction provides a new and general synthetic method for the synthesis of alkyl-substituted azetidine-2,4-diones. The previously reported

(1) This work is supported in a part by a grant from the Ministry of Education, Science, and Culture (No. 347017).

(2) (a) Maruyama, K.; Kubo, Y. *J. Org. Chem.* **1977**, *42*, 3215. (b) Maruyama, K.; Ogawa, T.; Kubo, Y. *Chem. Lett.* **1978**, 1107. (c) Kanaoka, Y.; Yoshida, K.; Hatanaka, Y. *J. Org. Chem.* **1979**, *44*, 664.

(3) (a) Kanaoka, Y.; Hatanaka, Y. *J. Org. Chem.* **1976**, *41*, 400. (b) Kanaoka, Y.; Okajima, H.; Hatanaka, Y. *Heterocycles* **1977**, *8*, 339. (c) Nakai, H.; Sato, Y.; Mizoguchi, T.; Yamazaki, M.; Kanaoka, Y. *Ibid.* **1977**, *8*, 345.

(4) (a) Gandhi, R. P.; Singh, M.; Sharma, T. D.; Mukherji, S. M. *Tetrahedron Lett.* **1973**, 675. (b) Scharf, G.; Fuchs, B. *J. Chem. Soc., Chem. Commun.* **1975**, 244. (c) Schtyser, J. A.; DeSchryver, F. C. *Tetrahedron* **1976**, *32*, 251.

(5) (a) Maruyama, K.; Ishitoku, T.; Kubo, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3671. (b) Kanaoka et al. independently published an analogous report on α cleavage of cyclic imides: Kanaoka, Y.; Okajima, H.; Hatanaka, Y. *J. Org. Chem.* **1979**, *44*, 1749.

(6) A preliminary report of this work has appeared previously: Maruyama, K.; Ishitoku, T.; Kubo, Y. *Chem. Lett.* **1980**, 265.

0022-3263/81/1946-0027$01.00/0