HPO_4 in ca. 16 mL of MeOH (dried over molecular sieves) was added 2.52 g of 6% sodium amalgam at −4 °C, and then the reaction mixture was allowed to warm to ambient temperature. The progress of the reduction was followed by TLC (15:75 hexanes/CH_2Cl_2). After the mixture was stirred for 6.5 h, 698 mg (4.92 mmol) of anhydrous Na_2HPO_4 and 1.90 g of 6% of sodium amalgam was added to the mixture at 25 °C to complete the reaction. After stirring for an additional 2.5 h, the reaction mixture was poured into 20 mL of cold saturated NH_4Cl solution and extracted with 4 × 20 mL of pentane and dried over $MgSO_4$. The solvent was removed carefully by distillation at atmospheric pressure to leave 272 mg (80% purity) of crude oil containing some solvent. The oil was chromatographed by using gradient elution (pentane and then 50:50 pentane/CH_2Cl_2) to give 164 mg (65%) of (+)-**1**. Enantiomeric excess of (+)-**1** was determined by means of a chiral shift experiment[13] [(+)-**1**/Eu(hfc)$_3$ = 0.15] to be greater than 99% ee: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.51–1.65 (m, 3 H), 1.60 (s, 3 H), 1.68 (s, 3 H), 1.96–2.11 (m, 2 H), 5.07 (dd, 1 H, J = 1.9, 11.2 Hz), 5.08–5.17 (m, 1 H), 5.21 (dd, 1 H, J = 1.9, 16.9 Hz), 5.91 (dd, 1 H, J = 11.2, 16.9 Hz).

2-Acryloyl-1,3-oxathiane 10. (a) 2-(1-Hydroxyallyl)-1,3-oxathiane 11. To a solution of 4.07 g (20.3 mmol) of 1,3-oxathiane in ca. 50 mL of dry THF was added 15.2 mL (24.4 mmol, 1.2 equiv) of *n*-BuLi solution (1.6 M in hexanes) at −78 °C. After being stirred for 30 min at −78 °C the reaction mixture was allowed to warm for 30 min and then recooled to −78 °C. A solution of 1.37 g (24.4 mmol) of freshly distilled acrolein in ca. 40 mL of dry THF was added dropwise to the solution of lithio-1,3-oxathiane **2** at −78 °C. After being stirred for 4 h at −78 °C, the reaction mixture was poured into 40 mL of cold saturated NH_4Cl solution. The aqueous layer was extracted with 4 × 30 mL ether; the combined organic layer was washed with brine and dried over $MgSO_4$. Concentration of the solvent gave 5.75 g of alcohol **11** as a yellow oil. This material was used for the next oxidation reaction without further purifications.

(b) 2-Acryloyl-1,3-oxathiane 10. To a solution of 2.16 mL of dimethyl sulfoxide in ca. 40 mL of dry CH_2Cl_2 was added dropwise 4.30 mL of trifluoroacetic anhydride in 20 mL of dry CH_2Cl_2 at −78 °C over 1 h. The resulting white suspension was stirred for 30 min at −78 °C, and then 5.75 g of alcohol **11** in ca. 50 mL of dry CH_2Cl_2 was added slowly over 50 min. After being stirred for 1.5 h at −78 °C, the reaction mixture was quenched with 8.0 mL of dry triethylamine, allowed to warm, and then poured into 150 mL of cold 10% HCl solution. The aqueous layer was extracted with 3 × 50 mL of CH_2Cl_2, and the combined organic layer was washed with 50 mL of water and dried over $MgSO_4$. Removal of the solvent gave 7.70 g of crude ketone **10** as a yellow oil, which was purified by flash chromatography to yield 3.34 (13.1 mmol, 65% based on 1,3-oxathiane **2**) of pure ketone **10** as crystalline material. Recrystallization from hexanes provided an analytical sample: mp 56–57 °C; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3 H, J = 8.3 Hz), 1.30 (s, 3 H), 1.49 (s, 3 H), 3.48 (dt, 1 H, J = 4.4, 10.4 Hz), 5.64 (s, 1 H), 5.82 (dd, 1 H, J = 1.8, 10.4 Hz), 6.46 (dd, 1 H, J = 1.9, 17.5 Hz), 6.78 (dd, 1 H, J = 10.4, 17.5 Hz); ^{13}C NMR ($CDCl_3$) δ 21.67, 22.16, 23.64, 28.95, 30.67, 34.17, 41.10, 43.71, 49.91, 76.56, 81.51, 129.88, 130.63, 192.51; IR ($CHCl_3$) 3020, 2960, 2920, 2865, 1705, 1615, 1455, 1400, 1385, 1366, 1300, 1188, 1145, 1115, 1082, 1060, 1000, 975, 962, 906 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72. Found: C, 65.81; H, 8.86.

Oxathianecarbinol (*S*)-4. A mixture of 1.185 g (4.66 mmol) of acryloyl-1,3-oxathiane **10** and 1.40 (5.37 mmol) of magnesium bromide etherate in ca. 60 mL of dry THF was refluxed to obtain a clear solution and then was cooled to −78 °C. To the above solution was rapidly added 8.1 mL of methylmagnesium bromide solution (2.9 M in THF) at −78 °C. After the mixture was stirred for 2 h at −78 °C, 20 mL of saturated NH_4Cl solution was added to the reaction mixture. The aqueous layer was extracted with 3 × 30 mL of ether, and the combined organic layer was washed with 40 mL of brine and dried over $MgSO_4$. Concentration of the solvent at reduced pressure gave 1.39 g of crude oil (*S*)-**4**, 94% de (by ^{1}H NMR). This material was purified by flash chromatography (10:90 EtOAc/hexanes) to provide 1.09 g (4.04 mmol), 87%) of (*S*)-**4** as a colorless oil, 94% de by ^{1}H NMR: ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3 H, J = 6.5 Hz), 1.27 (s, 3 H), 1.33 (s, 3 H), 1.41 (s, 3 H), 2.73 (br s, 1 H), 3.38 (dt, 1 H, J = 4.3, 10.4 Hz), 4.83 (s, 1 H), 5.17 (dd, 1 H, J = 1.4, 10.7 Hz), 5.38 (dd, 1 H, J = 1.4, 17.2 Hz), 6.00 (dd, 1 H, J = 10.7, 17.2 Hz); ^{13}C NMR (acetone-d_6) δ 22.41, 23.19, 24.49, 29.94, 30.44, 32.02, 35.46, 42.53, 43.20, 51.72, 74.65, 78.00, 86.69, 112.79, 143.35.

(*S*)-(−)-2-Methyl-3-butene-1,2-diol [(*S*)-(−)-6a]. The oxathianecarbinol (*S*)-**4** was treated with NCS, $AgNO_3$, and 2,6-lutidine as described for (*R*)-(+)-**6a**. Workup and continuous extraction as before followed by flash chromatography gave diol (*S*)-(−)-**6a** (61% yield), and the sultine[6] (99% yield): ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 3 H), 3.40, 3.50 (AB q, 2 H, J = 10.3 Hz), 3.50 (br s, 2 H), 5.12 (dd, 1 H, J = 2.0, 12.0 Hz), 5.30 (dd, 1 H, J = 2.0, 17.4 Hz), 5.91 (dd, 1 H, J = 12.0, 17.4 Hz).

(*S*)-(−)-2-Methyl-2-hydroxybuten-1-yl *p*-Toluenesulfonate [(*S*)-(−)-6b]. The tosylate (*S*)-(−)-**6b** was prepared from diol (*S*)-(−)-**6a** as described above for the enantiomer in 61% yield (purified by flash chromatography): mp 37–41 °C; $[\alpha]^{20}_D$ −12.22° (*c* 2.97, $CHCl_3$). This material was further purified by recrystallization from ether–hexanes to give (*S*)-(−)-**6b** in 49% yield: mp 43–44 °C; $[\alpha]^{20}_D$ −14.01° (*c* 3.26, $CHCl_3$). The enantiomeric purity of (*S*)-(−)-**6b** was determined by means of a chiral shift experiment [(*S*)-(−)-**6b**/Eu(hfc)$_3$ = 0.29] to be 94% ee: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 2.46 (s, 3 H), 3.89 (s, 2 H), 5.17 (dd, 1 H, J = 0.96, 10.7 Hz), 5.32 (dd, 1 H, J = 0.96, 17.3 Hz), 5.81 (dd, 1 H, J = 10.7, 17.3 Hz), 7.38 (d, 2 H, J = 8.48 Hz), 7.79 (d, 2 H, J = 8.48 Hz).

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Aromatic Norditerpenes from the Nudibranch *Chromodoris macfarlandi*

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Dorid nudibranchs are shell-less marine molluscs that are believed to have acquired a chemical defense against predation that compensates for the loss of the shell.[1] Members of the genus *Chromodoris* feed on sponges, from which they obtain their defensive chemicals.[2] In this paper, we report the isolation of two aromatic norditerpenes, macfarlandin A (**1**) and macfarlandin B (**2**) from *Chromodoris macfarlandi* (see Chart I). The macfarlandins **1** and **2** are closely related to the diterpene aplysulphurin (**3**), a metabolite of the sponge *Aplysilla sulphurea*.[3]

Twenty-two specimens of *Chromodoris macfarlandi* were collected by hand at a depth of approximately −30 m in Scripps Canyon, La Jolla. The dichloromethane-soluble material from an acetone extract of the animals contained a mixture of terpenoid compounds from which two aromatic norditerpenes, macfarlandin A (**1**), mp 183–184 °C, and macfarlandin B (**2**), a glass, were obtained.

It was immediately apparent that the macfarlandins were closely related isomers. Both compounds gave almost identical mass spectral data: the highest peak in the electron impact mass spectra at m/z 343.1545 for **1** and m/z 343.1523 for **2** corresponded to an $[M - CH_3]^+$ ion but the chemical ionization mass spectra both contained $[M + H]^+$ peaks at m/z 359, indicating the molecular formula $C_{21}H_{26}O_5$. The ^{13}C NMR spectrum of macfarlandin A (**1**)

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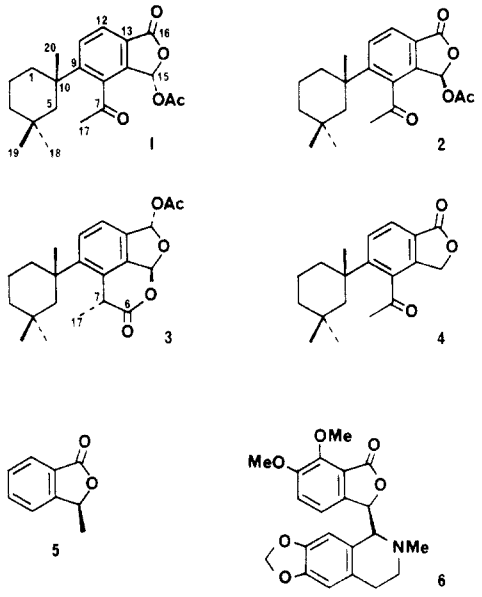
0022-3263/86/1951-2601$01.50/0

Table I. Selected ^1H NMR Data for Macfarlandin A (1), Macfarlandin B (2), and Aplysulphurin (3)

H at C	δ (mult, integration, coupling constant)		
	1[a]	2[a]	3[b]
5	2.07 (d, 1 H, 13)	1.83 (d, 1 H, 14)	1.98 (d, 1 H, 14)
	1.48 (d, 1 H, 13)	1.52 (d, 1 H, 14)	1.54 (d, 1 H, 14)
7			4.40 (q, 1 H, 7)
11		7.86 (d, 1 H, 8.3)	7.52 (d, 1 H, 8.2)
	7.84 (s, 2 H)		
12		7.80 (d, 1 H, 8.3)	7.36 (d, 1 H, 8.2)
15	7.37 (s, 1 H)	7.43 (s, 1 H)	7.01 (d, 1 H, 1.9)
16			7.27 (d, 1 H, 1.9)
17	2.60 (s, 3 H)	2.62 (s, 3 H)	1.76 (d, 3 H, 7)
18	0.44 (s, 3 H)	0.55 (s, 3 H)	0.52 (s, 3 H)
19	0.94 (s, 3 H)	0.95 (s, 3 H)	0.97 (s, 3 H)
20	1.37 (s, 3 H)	1.38 (s, 3 H)	1.23 (s, 3 H)
OAc	2.15 (s, 3 H)	2.16 (s, 3 H)	2.17 (s, 3 H)

[a] 360 MHz ($CDCl_3$). [b] 400 MHz ($CDCl_3$) (ref 3).

Chart I



contained 21 signals including a ketone carbonyl signal at δ 203.4 (s), two ester carbonyl signals at δ 168.5 (s) and 167.0 (s), six olefinic signals at δ 152.7 (s), 140.8 (s), 137.6 (s), 132.4 (d), 125.2 (d), and 124.3 (s), and an acetal carbon signal at δ 91.4 (d). The ^1H NMR signal at δ 7.84 (br, s, 2 H) could be resolved into an AB quartet (J = 8 Hz) by using resolution enhancement and was assigned to ortho protons on an aromatic ring. The ^1H NMR signals at δ 7.37 (s, 1 H) and 2.60 (s, 3 H) were assigned to a benzylic acetal proton and an aryl methyl ketone, respectively. The UV bands at 216 (ε 17 200) and 246 nm (ε 15 800) suggested an aromatic system, and the infrared band at 1702 cm^{-1} is typical of an aryl ketone. A search of the marine natural product literature revealed that a similar 1,2,3,4-tetrasubstituted aromatic ring system existed in aplysulphurin (**3**), a diterpene acetate from *Aplysilla sulphurea*.[3]

The ^1H and ^{13}C NMR data for macfarlandins A (**1**) and B (**2**) were compared with those of aplysulphurin (**3**) (see Tables I and II). The presence of an identical ring A moiety in all three compounds was indicated by the similarity of the chemical shifts for the relevant ^{13}C and ^1H signals, particularly the unusually high-field methyl signal assigned to CH_3-18[4] and the AB quartets due to the isolated methylene group at C-5 in the ^1H NMR spectra. A

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Table II. ^{13}C NMR Data for Macfarlandin A (1), Macfarlandin B (2), and Aplysulphurin (3)[a]

C	δ (no. of attached H)		
	1[b]	2[b]	3[c]
1	37.8 (2)	39.0[d] (2)	38.6[d] (2)
2	19.9 (2)	19.5 (2)	19.1 (2)
3	39.4 (2)	39.5[d] (2)	39.4[d] (2)
4	31.8 (0)	31.7 (0)	31.7 (0)
5	52.4 (2)	50.7 (2)	50.9 (2)
6			170.7 (0)
7	203.4 (0)	203.4 (0)	41.6 (1)
8	140.8[d] (0)	140.8 (0)	131.9 (0)
9	152.7 (0)	154.1 (0)	148.7 (0)
10	41.1 (0)	40.9 (0)	38.9 (0)
11	125.2 (1)	125.8 (1)	129.2 (1)
12	132.4 (1)	130.8 (1)	122.3 (1)
13	124.3 (0)	124.3 (0)	133.3 (0)
14	137.6[d] (0)	138.6 (0)	137.8 (0)
15	91.4 (1)	91.2 (1)	100.3 (1)
16	168.5 (0)	168.9 (1)	101.9 (1)
17	33.9 (3)	33.1[e] (3)	17.3 (3)
18	28.9 (3)	29.0 (3)	27.5 (3)
19	32.2 (3)	31.6[e] (3)	32.5[e] (3)
20	33.2 (3)	33.3[e] (3)	32.7[e] (3)
OAc	20.6 (3)	20.5 (3)	20.8 (3)
	167.0 (0)	166.9 (0)	169.6 (0)

[a] Some signals of **3** have been reassigned to conform with assignments made on the basis of a 2D ^{13}C–^1H correlation experiment on **1**. [b] 50 MHz ($CDCl_3$). [c] 100 MHz ($CDCl_3$) (ref 3). [d,e] Signals may be interchanged within a column.

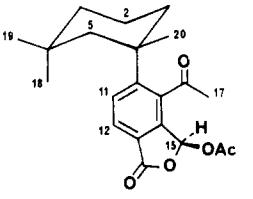

Figure 1. A perspective drawing of macfarlandin A (**1**).

strong broad band in the infrared spectrum at 1787 cm^{-1} could be assigned to the combination of the two carbonyl groups in a γ-acetoxyphthalide moiety that also gave rise to the ^1H NMR signals at δ 7.37 (s, 1 H) and 2.15 (s, 3 H) in **1** and 7.43 (s, 1 H), and 2.16 (s, 3 H) in **2** and ^{13}C NMR signals at δ 168.5 (s), 167.0 (s), 91.4 (d) and 20.6 (q) in **1** and at δ 168.9 (s), 167.0 (s), 91.2 (d), and 20.6 (q) in **2**. Assuming that the macfarlandins were closely related to aplysulphurin, it seems reasonable to propose that the methyl ketone was at C-8 with the lactone ring at C-13 and C-14. The regiochemistry about the aromatic ring in **1** (see Figure 1) and **2** was defined by NOEDS experiments. In particular, irradiation of the 17-methyl signal resulted in enhancement of the 15-acetal proton signal and a smaller

Table III. Selected Nuclear Overhauser Enhancement Data

irradiated proton	observed NOE's (%)[a] 1	2
H-11,12	H-5α (4)	H-5α (~3)
H_3-17	H-15 (13), H_3-20 (1.7)	H-15 (8.1), H_3-20 (1.8), H-5α (7)
H_3-18	H-11,12 (2), H-5α (2)	H-5α (4.5)
H_3-20	H_3-17 (1.2)	H_3-17 (1.3)

[a] NOE's are less than the theoretical maxima. Irradiations were carried out at subsaturating rf power on undegassed samples.

enhancement of the 20-methyl signal. Other significant enhancements are listed in Table III.

Both macfarlandins A (1) and B (2) were reduced to the same desacetoxy derivative 4 by catalytic hydrogenolysis in the presence of acetic acid and are therefore epimers at C-15. The ^{1}H NMR spectrum of the desacetoxy derivative 4 contained signals at δ 5.14 (d, 1 H, J = 15.3 Hz) and 5.19 (d, 1 H, J = 15.3 Hz) due to the benzylic protons at C-15.

The absolute configurations at C-15 in 1 and 2 were established by analysis of their CD spectra. The CD spectra of 1 and 2 are essentially opposite in appearance, indicating a large contribution from the C-15 substituent to the observed dichroism.[5] Macfarlandin A (1) exhibited a positive Cotton effect at 260 nm (ΔE +2.5), assigned to the n → π* transition of the phthalide group,[6] while macfarlandin B (2) showed a negative Cotton effect at 252 nm (ΔE −6.1). (*S*)-3-Methylphthalide (**5**)[7] and L-α-hydrastine (**6**)[8] gave ORD curves implying negative Cotton effects at ~260 nm. We have therefore assigned the 15*S* configuration to macfarlandin A (1) and the 15*R* configuration to macfarlandin B (2). The C-10 configuration in both compounds is assumed to be the same as that found for the spongian derivative isoagatholactone.[9]

The numbering system employed implies that the macfarlandins 1 and 2 are related to spongian diterpenes[10] by cleavage of the 5,6-bond, migration of the C-17 methyl group from C-8 to C-7, and loss of C-6, presumably by oxidation and decarboxylation.

Macfarlandin A (1) inhibited the growth of *Bacillus subtilis* at 10 μg/disc but macfarlandin B (2) was active against both *B. subtilis* and *S. aureus* at 10 μg/disc, noted by using the standard disc–assay procedure.

Although we have not been able to locate a sponge source for the macfarlandins, it is highly probable that *Chromodoris macfarlandi* obtains these metabolites from a Dendroceratid sponge, some of which are thin encrusting species that are extremely difficult to locate and collect. The macfarlandins may be considered as protected 1,4-dicarbonyl compounds that, together with furans and isonitrile–isothiocyanate pairs, are preferentially concentrated from sponge sources by nudibranchs to serve as defensive chemicals.[1] The macfarlandins are the first aromatic norditerpenes to be described from marine sources.

Experimental Section

Collection, Extraction, and Chromatography. Twenty-two specimens of *Chromodoris macfarlandi* were collected by hand by using SCUBA (−30 m) in Scripps Canyon, La Jolla, CA (August–October, 1984) and were soaked in acetone at 5 °C for 2–3 weeks. The solvent was decanted and new acetone added and again decanted after 2 days. The combined extracts were evaporated, and the aqueous residue was extracted with dichloromethane (3 × 25 mL). The combined organic extracts were dried over sodium sulfate and filtered, and the solvent was evaporated to obtain an orange oil (ca. 200 mg). The oil was filtered through a plug of TLC grade silica gel using 1:1 ether/hexane as eluant to obtain a yellow oil (159 mg). The oil was dissolved in a small volume of 60% ether in hexane, and the solution was cooled to 0 °C for 18 h to obtain crystals of macfarlandin A (1, 16.5 mg). The mother liquors were chromatographed by LC on Partisil using first 2:1 ether/hexane and then 9:11 ether/hexane as eluants to obtain additional macfarlandin A (1), macfarlandin B (2, 10.3 mg, 0.47 mg/animal), and four additional diterpenes. The samples of macfarlandin A were combined and recrystallized from ether/hexane to obtain colorless prisms (22.8 mg, 1 mg/animal).

Macfarlandin A (1): mp 183–184 °C; $[\alpha]_D$ +189° (*c* 0.65, $CHCl_3$); IR ($CHCl_3$) 3050, 1787, 1702, 1593 cm^{-1}; UV (MeOH) 216 nm (ε 17 200), 246 (15 800); ^{1}H NMR ($CDCl_3$), see Table I; ^{13}C NMR ($CDCl_3$), see Table II; CD (MeOH), 219 (ΔE −30.5), 260 (ΔE +2.5), 308 nm (ΔE +2.8); EIMS, *m/z* (relative intensity) 343 (5), 299 (12), 298 (18), 284 (27), 283 (100); CIMS (NH_3), *m/z* (relative intensity) 376 (100, M + NH_4^+), 359 (22, M + H^+), 317 (24), 301 (32); HRMS, *m/z* 343.1545, $C_{20}H_{23}O_5$ (M − CH_3)$^+$ requires 343.1546.

Macfarlandin B (2): glass; $[\alpha]_D$ −128° (*c* 0.99, $CHCl_3$); IR ($CHCl_3$) 3030, 1790, 1700 cm^{-1}; UV (MeOH) 209 nm (ε 18 400), 245 (12 000); ^{1}H NMR ($CDCl_3$), see Table I; ^{13}C NMR ($CDCl_3$), see Table II; CD (MeOH), 217 nm (ΔE +8.8), 252 (ΔE −6.1), 282 (ΔE −6.3), 302 (ΔE −4.4); EIMS, *m/z* (relative intensity) 343 (3), 284 (24), 283 (100), 213 (23); CIMS, *m/z* (relative intensity) 376 (100), 359 (20), HRMS, *m/z* 343.1523, $C_{20}H_{23}O_5$ (M − CH_3)$^+$ requires 343.1546.

Hydrogenolysis of Macfarlandin A (1). A solution of macfarlandin A (1, 6.2 mg, 0.017 mmol) in ethyl acetate (1.0 mL) containing 10% palladium on charcoal catalyst (9 mg) and acetic acid (2 drops) was stirred under an atmosphere of hydrogen for a total of 34 h. The catalyst was removed by filtration and the solvent evaporated to obtain an oil that was chromatographed by LC on Partisil using 1:1 ether/hexane as eluant to obtain recovered starting material (1.6 mg, 26% recovery) and the desacetoxy derivative 4 (2.5 mg, 56% yield) as an oil: IR ($CHCl_3$) 1768, 1700, 1595 cm^{-1}; UV (MeOH) 242 nm (ε 9800); ^{1}H NMR ($CDCl_3$) δ 7.83 (d, 1 H, J = 8.3 Hz), 7.72 (d, 1 H, J = 8.3 Hz), 5.19 (d, 1 H, J = 16 Hz), 5.14 (d, 1 H, J = 16 Hz), 2.61 (s, 3 H), 1.98 (br d, 1 H, J = 14 Hz), 1.48 (d, 1 H, J = 14 Hz), 1.35 (s, 3 H), 0.94 (s, 3 H), 0.49 (s, 3 H); CD (MeOH), 214 nm (ΔE −3.8), 256 (ΔE +0.9), 304 (ΔE +1.7); EIMS, *m/z* (relative intensity) 285 (M − CH_3), 267 (12), 215 (32), 211 (13), 201 (14).

Hydrogenolysis of Macfarlandin B (2). A solution of macfarlandin B (2, 3.7 mg) in ethyl acetate (1 mL) containing 10% palladium on charcoal catalyst (7 mg) and acetic acid (3 drops) was hydrogenated according to the procedure above to obtain the desacetoxy derivative 4 (1.9 mg, 62% yield) that had the same ^{1}H NMR spectrum and LC retention time as the product of hydrogenation of macfarlandin A (1).

Acknowledgment. We thank Dr. Valerie Paul and John O'Sullivan for collecting the nudibranchs, Joseph Taulane for assistance in obtaining the CD data, and Mary Kay Harper for antimicrobial data. The use of the 200-MHz NMR spectrometer at the Research School of Chemistry, Canberra, for some of the ^{13}C NMR measurements is gratefully acknowledged. This research was supported by a grant from the National Institutes of Health (AI-11969) and an instrument grant from the National Science Foundation (CHE84-14054).

(5) The very large Cotton effects observed at ~220 nm in 1 and 2 are opposite in sign to the respective maxima at ~260 nm and probably reflect inherently disymmetric chromophoric interactions of the acetate carbonyl and phthalide moieties. This effect is absent in the desacetoxy derivative 4.

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