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Three New Rearranged Spongian Diterpenes from *Chromodoris macfarlandi*: Reappraisal of the Structures of Dendrillolides A and B

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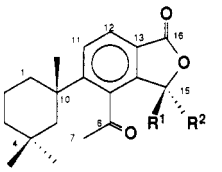
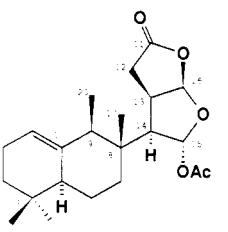
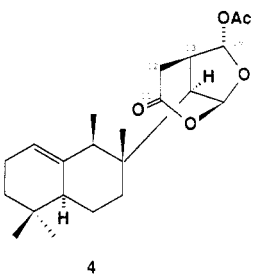
Chromodoris macfarlandi collected at Scripps Canyon, La Jolla, was found to contain three new diterpene acetates. The structure of macfarlandin C (3) was determined by a single-crystal X-ray diffraction analysis. The structures of macfarlandin D (4) and macfarlandin E (5) were elucidated from spectral data. Comparison of the spectral data of macfarlandin D (4) with those of dendrillolide A indicates that the proposed structure for the latter compound is incorrect.

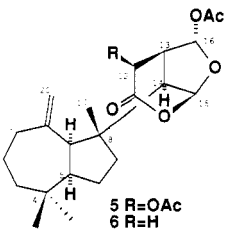
We recently reported[1] the isolation and structure elucidation of two new aromatic spongian-related norditerpenes, macfarlandins A (1) and B (2), from the acetone extract of *Chromodoris macfarlandi*, a dorid nudibranch which inhabits the coastal waters of California. It was shown that these compounds are closely related to aplysulphurin,[2] a metabolite of an Australian sponge *Aplysilla* (= *Darwinella*) *sulphurea*. We now report three new rearranged diterpene acetates from *C. macfarlandi*, macfarlandins C (3), D (4), and E (5). Comparison of the spectral data of dendrillolides A (6) and B (7)[3] with those of norrisolide (8)[4] and macfarlandins C (3) and D (4) reveals that the proposed structure of dendrillolide A is incorrect and raises doubts about the proposed structure of dendrillolide B.

The more polar fraction obtained from chromatography of the dichloromethane soluble portion of the acetone extract of *C. macfarlandi* was separated by LC on Partisil (3:2 ether/hexanes) to afford, in order of elution, macfarlandins E (5), C (3), and D (4). Macfarlandin C (3), mp 195–196 °C, is a diterpene acetate of molecular formula $C_{22}H_{32}O_5$. The molecular formula was derived from the ^{13}C NMR spectrum coupled with the exact mass of the fragment ion at m/z 316.2041 ($C_{20}H_{28}O_3$, M − AcOH). Infrared bands at 1798 and 1748 cm^{-1} were assigned to a γ-lactone and an ester, respectively. The ^1H NMR spectrum contained a six-proton spin system (Table I) that was consistent with either A, a substructure found in norrisolide (8), or B, a substructure assigned to dendrillolide A (6). We were presented with a dilemma because the proton coupling constants were almost identical with those of dendrillolide A (6) while the infrared spectrum required a γ-lactone. The remaining $C_{14}H_{28}$ portion of macfarlandin C (3) is bicyclic and contains a trisubstituted olefinic bond [^{13}C NMR δ 140.2 (s), 118.3 (d)]. The ^1H NMR spectrum contained four methyl signals at δ 0.82 (s, 3 H), 0.84 (s, 3 H), 0.88 (s, 3 H), and 1.01 (d, 3 H, J = 7 Hz). The methyl doublet was coupled to an allylic proton signal at δ 1.90 (br q, 1 H, J = 7 Hz) that was in turn allylically coupled to an olefinic proton signal at 5.32 (br t, 1 H, J = 4 Hz). In a key NOEDS experiment (Table









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0022-3263/86/1951-4564$01.50/0

Table I. Comparison of Selected Spectral Data for Macfarlandin C (3), Macfarlandin D (4), Macfarlandin E (5), Norrisolide (8), and Dendrillolide A (6)

	macfarlandin C (3)	macfarlandin D (4)	macfarlandin E (5)	norrisolide (8)	dendrillolide A (6)
IR (cm^{-1})	1798, 1748	1752	1770, 1760, 1755	1800, 1760	1785, 1740
$[\alpha]_D^{26}$ ($CHCl_3$)	−29°	+169°	−29°	+16°	+84°
^1H NMR, H at C no.					
12	2.56, dd, 17.3, 9 2.74, dd, 17.3, 10.4	3.12, dd, 20, 6.2 2.64, d, 20	5.80, d, 5.0	2.55, d, 2H, 7	2.21, dd, 17.5, 9.3 2.45, dd, 17.5, 10.1
13	3.04, m, 10.4, 9, 6.6, 4	2.62, m, 6.2, 3.1, 1.2	2.87, ddd, 5.0, 3.8, 0.8	3.36, m, 9.5, 7, 7, 6	2.80, m, 10.1, 9.3, 6.5, 4.1
14	2.81, dd, 6.6, 6.6	2.45, dd, 3.1, 3.1	2.67, dd, 3.8, 2.5	3.07, dd, 9.3, 3.5	2.48, dd, 6.5, 6.2
15	6.52, d, 6.6	5.75, dd, 3.1, 1.2	5.73, dd, 2.5, 0.8	6.44, d, 3.5	6.39, d, 6.2
16	6.04, d, 4	6.13, s	6.49, s	6.14, d, 6	5.82, d, 4.1

[a] ($CDCl_3$, except dendrillolide A (1% $C_6D_6/CDCl_3$)) chemical shift (δ), multiplicity, coupling constants (Hz).

Table II. Observed H–C–C–H Torsional Angles (deg) for Norrisolide (8) and Macfarlandin C (3)

torsional angle	norrisolide (8)	macfarlandin C (3)
H14–C14–C15–H15	−103	−164
H14–C14–C13–H13	0	57
H13–C13–C16–H16	−12	−35
H13–C13–C12–H12a	17	20
H13–C13–C12–H12b	136	154

Table III. C–C–C–C Torsional Angles[a] (deg)

torsional angle	norrisolide (8)	macfarlandin C (3)	ideal envelope
C15–C14–C13–C16	2 [1]	37 [36]	0
C14–C13–C16–O3	−21 [−23]	−30 [−31]	−20
C13–C16–O3–C15	36 [39]	9 [12]	35
C16–O3–C15–C14	−35 [−39]	13 [12]	−35
O3–C15–C14–C13	20 [22]	−31 [−30]	20

[a] Values in brackets were obtained from an energy minimization at the MM2 level (see text).

IV), irradiation of the CH_3-20 signal caused a 15% enhancement of H-1, an observation that requires the stereochemistry shown.

In order to fully define the relative stereochemistry of macfarlandin C (3) and to solve the aforementioned dilemma, a single-crystal X-ray diffraction experiment was performed. Figure 1 is a computer-generated drawing of the final X-ray model of macfarlandin C (3). Surprisingly, the substituted dioxabicyclo[3.3.0]octane ring system in 3 was identical with that of norrisolide (8), including relative stereochemistry, despite the differences in the ^1H NMR coupling constant data. In general, all bond distances and angles agree well with accepted values. The conformation of the octalin portion is unexceptional, but the conformation of the 2,8-dioxabicyclo[3.3.0]octane is interesting in the sense that it differs strikingly from that observed in the norrisolide structure. Table II contains all of the H–C–C–H torsional angles, which are consistent with the observed coupling constants. These differences arise because the five-membered rings involving C13, C14, C15, C16, and O3 have different conformations in the two structures. There are two simple (ideal) conformations for five-membered rings called the "envelope" or C_m conformation and the "skew" or C_2 conformation. In the C_m conformation four atoms are in a plane, and the fourth atom is out of the plane. In terms of internal ring dihedral angles, one angle is ideally zero, the angles next to this are plus and minus the same amount, and the last two angles are plus and minus a somewhat larger amount. The atom opposite the zero degree torsional angle is called the flap. As can be seen from the listing in Table III, norrisolide (8) fits this description very well. The ring would be described as having the envelope conformation with oxygen being the flap. The case for macfarlandin C (3) is quite different. The ring has the twofold or skew conformation.

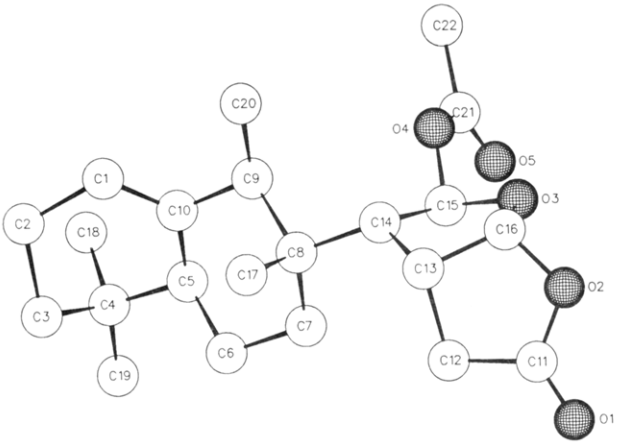
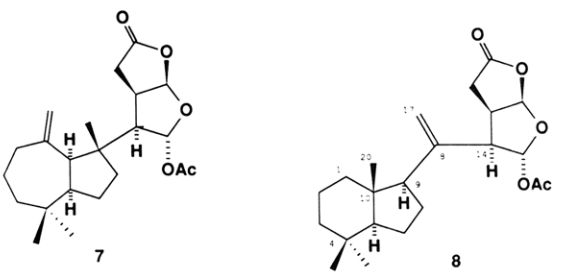


Figure 1. Computer-generated perspective drawing of the final X-ray model of macfarlandin C (3). Hydrogens are omitted for clarity and the absolute configuration drawn is an arbitrary choice.



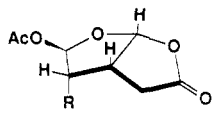
The twofold axis runs through the C13–C14 bond and O3. Starting with the torsional angles about O3, they occur in pairs with the same sign, i.e., two angles of roughly 10°, two angles of −30°, and a final large angle of −37°. Whether these angles, observed in the solid-state structure, would persist in solution was briefly investigated with molecular mechanics calculations. The values in brackets in Table III were obtained from an energy minimization at the MM2 level. The starting geometry for these calculations was that of the X-ray structure. The excellent agreement between the observed and the calculated values indicated that the X-ray structure of macfarlandin C (3) represents at least a local energy minimum in the MM2 approximation. Further work to investigate whether these geometries are global minima and to understand the origin of these conformational preferences is underway. No doubt the hybridization of C8 and the nature of the $C_{14}H_{23}$ substituent are particularly important factors for determining the conformation and resulting coupling constants in the bicyclic lactone acetal groups of 3, 6, and 8. It is prescient to note, however, the limitations of stereochemical and conformational analysis of five-membered ring systems based solely on a simple Karplus type analysis of vicinal coupling constants, the absolute values of which are often small and highly dependent on conformation and

Table IV. Selected Nuclear Overhauser Enhancement Data for Macfarlandin C (3), Macfarlandin D (4), and Macfarlandin E (5)

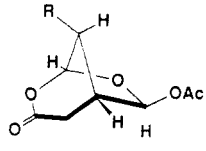
irradiated signal	enhanced signals (% enhancement)		
	3	4	5
H-9	H-15 (9)		H-5 (8), H-12 (4) H-15 (12), H-20 *Z* (12)
H-13	H-16 (19)		
H-14			H-13 (7), H-15 (8) H-20 *Z* (2)
H-15	H-9 (6)	H-14 (7), H-9 (7)	
H-16	H-13 (11), H-14 (5)	H-13 + H-12 endo (11)	H-13 (3)
CH_3-17			H-12 (10), H-13 (20) H-14 (9)
CH_3-18			H-9 (2)
CH_3-20	H-1 (10), H-9 (15) H-14 (6)	H-1 (18), H-9 (13) H-13 (8), H-14 (15)	
H-20 *E*			H-1α (4), H-20 *Z* (17)
H-20 *Z*			H-9 (6), H-13 (1) H-14 (2), H-12 (1) H-20 *E* (23)

substituent effects.

Macfarlandin D (**4**) was obtained as very fine needles, mp 190–191 °C, from ether/hexane. The ^{13}C NMR spectrum, together with an exact mass measurement [*m/z* 316.2041 (M – AcOH)] indicated that macfarlandins C and D were isomers. Furthermore, the ^1H and ^{13}C NMR data indicated that both compounds contained the same bicyclic $C_{14}H_{23}$ substituent. However, the spectral data clearly indicated that macfarlandin D contained substructure B.



A



B

The infrared band at 1752 cm^{-1} was assigned to a combination of the acetate and δ-lactone groups. Further evidence for fragment B is provided by analysis of coupling constants and by intramolecular nuclear Overhauser enhancements (Table IV). In particular, the long-range W-coupling observed between H-15 and H-13 in macfarlandin D (**4**), which is absent in the three dioxabicyclo-[3.3.0]octane compounds **3**, **6** and **7**, is typical of coplanar bridgehead protons in similar bicyclic ring systems. Diagnostic NOE's measured in the ^1H NMR spectrum of **4** included an 11% enhancement of H-13 and H-12(ax) upon irradiation of H-16(ax), which establishes an exo configuration for the acetoxyl group. Other inter-ring NOE's from the C-9 methyl to H-13 (8%) and H-14 (15%) and from H-15 to H-9 (7%) are consistent with the relative configuration shown for C-14. Examination of a Dreiding model indicated that these NOE's could not be simultaneously observed if **4** had the epimeric C-14 configuration. The complete ^{13}C NMR assignments of macfarlandin D (**4**) (Table V) were obtained from 2-D carbon–proton correlation experiments,[5] both for direct couplings (J = 135 Hz) and for long-range couplings (J = 10 Hz).

Table V. ^{13}C NMR Data [50 MHz, $CDCl_3$,[d] Chemical Shift (δ), Multiplicity] for Macfarlandins C (3), D (4), and E (5) and Dendrillolide A (6)

C no.	3	4	5	6
1	118.3 d	118.4 d	28.3 t[a]	28.7 t[c]
2	23.0 t	29.9 t	38.3 t[b]	38.7 t[b]
3	32.6 t	32.7 t	37.5 t[b]	37.7 t[b]
4	31.2 s	31.1 s	45.4 s	46.7 s
5	49.0 d	48.9 d	54.2 d	54.9 d[a]
6	25.2 t	25.0 t	27.0 t[a]	27.1 t
7	35.4 t	36.4 t	40.0 t[b]	37.7 t[b]
8	39.6 s	39.0 s	30.1 s	36.0 s
9	44.4 d	46.8 d	57.7 d	55.7 d[a]
10	140.2 s	140.1 s	152.5 s	153.7 s
11	175.3 s	167.8 s	165.8 s	175.2 s
12	30.2 t	34.0 t	65.8 d	28.8 t[c]
13	42.1 d	38.0 d	54.2 d	41.9 d
14	51.7 d	48.0 d	51.8 d	54.5 d[a]
15	104.8 d	100.3 d	101.2 d	105.0 d
16	96.0 d	101.5 d	96.0 d	97.1 d
17	18.9 q	17.8 q	24.5 q	24.1 q
18	26.8 q[a]	26.5 q[a]	26.0 q	25.8 q
19	27.6 q[a]	27.6 q[a]	34.2 q	34.5 q
20	11.6 q	12.3 q	115.2 t	113.3 t
OAc	21.1 q	21.0 q	21.1 q, 20.6 q	20.7 q
	169.7 s	169.5 s	169. 3 2s	169.1 s

[a–c] Assignments may be interchanged within a column. [d] The ^{13}C NMR spectrum of **6** was recorded in C_6D_6[3] and the assignments for **4** and **5** were made on the basis of separate ^1H–^{13}C 2D NMR shift correlation experiments.[5] Assignments for **3** and **6** were made by analogy with **4** and **5**, respectively.

Macfarlandin E (**5**), previously obtained as a metabolite of *C. norrisi*,[6] gave a molecular formula of $C_{24}H_{34}O_7$ from high resolution mass measurement (M – AcOH, *m/z* 374.2097). Comparison of the ^1H NMR data for the C-12 to C-16 portion of macfarlandin E (**5**) with those of **3**, **4**, **6**, and **8** indicated the presence of a bicyclo[3.2.1] ring system (substructure B) with an additional acetoxyl group at C-12. The long-range W-coupling between H-13 and H-15 (0.8 Hz) and a nuclear Overhauser enhancement of H-13, but not H-12, on irradiation of H-16 (Table IV) were the key elements in assigning the structure and stereochemistry of this portion of the molecule. The infrared spectrum shows an anomalously high frequency δ-lactone band at 1770 cm^{-1} shifted to higher frequency by the electronegative α-acetoxy group.[7] Comparison of the ^1H and ^{13}C NMR data of macfarlandin E (**5**) with those of dendrillolide A (**6**) suggested that the $C_{14}H_{23}$ portion of both molecules was identical. The stereochemistry of the $C_{14}H_{23}$ portion of macfarlandin E (**5**) was confirmed by a series of NOEDS experiments (Table IV). The nuclear Overhauser enhancements observed on irradiation of H-9 are only possible if the allylic proton H-9 is cis to H-5 and C-14.

The structures proposed for dendrillolides A (**6**) and B (**7**) must be reexamined in the light of the data reported above. We had proposed that dendrillolide B (**7**) contained substructure A, on the basis of comparison of ^1H NMR data with those of norrisolide, and that dendrillolide A (**6**) therefore contained the alternative substructure B. It is now apparent that the differences in the relevant ^1H NMR data of **6** and **7** (Table I) are due to subtle differences in the geometry of substructure A, and that the structure proposed for dendrillolide A (**6**) is definitely incorrect.

(5) 2D ^{13}C–^1H correlation experiments were carried out on a Bruker WP2 OOSY NMR spectrometer with standard Bruker software. Typically, ^{13}C FID's were collected with 2K data points and an adjusted spectral width giving 6–10 Hz/point in F_2. 256 FID's were collected with an adjusted increment size and one order of zero filling to give 2–4 Hz/point in F_1. Sine bell multiplication was applied in T_2 and Gaussian multiplication in T_1. The fixed delays were optimized for one-bond couplings of J = 135 Hz or for long-range couplings of J = 10 Hz.

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Although the structure assigned to dendrillolide B (**7**) is not necessarily incorrect, dendrillolides A and B cannot have the same structure, and it will therefore be necessary to reassign their structures using either NOE studies or, preferably, single-crystal X-ray diffraction analyses.

The macfarlandins are presumed to be sponge metabolites obtained by *Chromodoris macfarlandi* from a dietary source. To date we have not been able to locate the sponge(s) upon which the nudibranch feeds. Examination of the organic extracts of seven individual animals showed marked variation in diterpene composition. Macfarlandins A (**1**) and B (**2**) were always found together in roughly the same ratio (^{1}H NMR integration of peak areas) but the ratio of **1** and **2** to macfarlandins C (**3**), D (**4**), and E (**5**) varied greatly. Macfarlandins C–E were found in all nudibranchs but macfarlandins A and B were absent in some individuals. This suggests that *C. macfarlandi* consumes at least two different aplysillid sponges,[8] one of which contains the aromatic norditerpenes **1** and **2** while the other contains **3**, **4**, and **5**.

Macfarlandin D (**4**) showed antimicrobial activity against *B. subtilis* in the disk assay system at 10 μg per disk. Macfarlandin E (**5**) was marginally active against *Vibrio anguillarum* and *Beneckea harveyi* (100 μg per disk) while macfarlandin C (**3**) was inactive against all bacteria tested.

Experimental Section

Extraction and Chromatography. The dichloromethane-soluble material from an acetone extract of 22 specimens of *C. macfarlandi* was separated by flash chromatography as described previously.[1] Selected fractions were purified by LC on Partisil using 3:2 ether–hexane as eluant to obtain, in order of elution, macfarlandin E (**5**, 0.45 mg/animal), macfarlandin C (**3**, 0.40 mg/animal), and macfarlandin D (**4**, 0.50 mg/animal).

Macfarlandin C (3): needles from ether/hexane, mp 195–196 °C; $[\alpha]_D$ −29.1° (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 1798, 1748 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (s, 3 H), 0.84 (s, 3 H), 1.01 (d, 3 H, *J* = 7 Hz), 1.16 (dt, 1 H, *J* = 13.0, 4.6 Hz), 1.36 (ddd, 1 H, *J* = 13, 7.5, 6.9 Hz), 1.90 (bq, 1 H, *J* = 7 Hz), 2.05 (m, 2 H, $W_{1/2}$ = 18 Hz), 2.10 (s, 3 H), 2.56 (dd, 1 H, *J* = 17.3, 9 Hz), 2.74 (dd, *J* = 17.3, 10.4 Hz), 2.81 (t, 1 H, *J* = 6.6 Hz), 3.04 (m, 1 H, *J* = 10.9, 9, 6.6, 4 Hz), 5.32 (br t, 1 H, *J* = 4 Hz), 6.04 (d, 1 H, *J* = 4 Hz), 6.52 (d, 1 H, *J* = 6.6 Hz); NOEDS, see Table IV; ^{13}C NMR, see Table V; EIMS, *m/z* (relative intensity) 316 (M − AcOH, 3), 191 (24), 190 (100), 179 (55), 175 (26), 161 (12), 151 (14), 137 (66), 135 (15), 134 (19), 133 (11), 122 (19), 121 (14), 119 (20); HRMS, found 316.2040, $C_{20}H_{28}O_3$ requires 316.2039.

Macfarlandin D (4): needles from ether/hexanes; mp 190–191 °C; $[\alpha]_D$ −169° (c 1.2, $CHCl_3$); IR ($CHCl_3$) 1752 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.84 (s, 3 H), 0.87 (s, 3 H), 0.88 (s, 3 H), 1.04 (d, 3 H, *J* = 6.8 Hz), 1.16 (dt, 1 H, *J* = 12.6, 4.8 Hz), 1.36 (ddd, 1 H, *J* = 12.6, 7, 6.9 Hz), 2.04 (m, 2 H, $W_{1/2}$ = 18 Hz), 2.10 (s, 3 H), 2.22 (bq, 1 H, *J* = 6.8 Hz), 2.45 (t, 1 H, *J* = 3.1 Hz), 2.62 (m, 1 H, *J* = 6.2, 3.1, 1.2 Hz), 2.64 (d, 1 H, *J* = 20 Hz), 3.12 (dd, 1 H, *J* = 20, 6.2 Hz), 5.33 (bt, 1 H, *J* = 4 Hz), 5.75 (dd, 1 H, *J* = 3.1, 1.2 Hz), 6.13 (s, 1 H); NOEDS, see Table IV; ^{13}C NMR ($CDCl_3$), see Table V; EIMS, *m/z* (relative intensity) 316 (M − AcOH, 21), 273 (11), 239 (43), 190 (70), 179 (100); HRMS, found *m/z* 316.2041, $C_{20}H_{28}O_3$ requires 316.2039.

Macfarlandin E (5): glass, $[\alpha]_D$ −29° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 1770, 1760, 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.95 (s, 3 H), 1.00 (s, 3 H), 1.08 (s, 3 H), 2.11 (s, 3 H), 2.21 (s, 3 H), 2.43 (bdd, 1 H, *J* = 12, 5 Hz), 2.67 (dd, 1 H, *J* = 3.8, 2.5 Hz), 2.74 (d, 1 H, *J* = 9 Hz), 2.87 (ddd, 1 H, *J* = 5, 3.8, 0.8 Hz), 4.68 (d, 1 H, *J* = 1.8 Hz), 4.89 (d, 1 H, *J* = 1.8 Hz), 5.73 (dd, 1 H, *J* = 2.5, 0.8 Hz), 5.80 (d, 1 H, *J* = 5.0 Hz), 6.49 (s, 1 H); NOEDS see Table IV; ^{13}C NMR ($CDCl_3$) see Table V; EIMS, *m/z* (relative intensity) 374 (M − AcOH, 12).

Single-Crystal X-ray Diffraction Analysis of Macfarlandin C (3). Preliminary X-ray photographs displayed orthorhombic symmetry. Accurate lattice constants of *a* = 6.642 (1), *b* = 13.012 (3), and *c* = 24.811 (3) Å were determined from a least-squares fitting of 15 moderate 2θ values (35° ≤ 2θ ≤ 45°); and systematic extinctions, crystal density, and optical activity were uniquely accommodated by space group $P2_12_12_1$ with one molecule of $C_{22}H_{32}O_5$ forming the asymmetric unit. All unique diffraction maxima with 2θ ≤ 114° were collected on a computer-controlled four-circle diffractometer using graphite monochromated Cu Kᾱ radiation (1.54178 Å) and variable speed, 1° ω scans. Of the 1696 reflections measured in this way, 1029 (61%) were judged observed ($F_o \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[9] The structure was solved uneventfully by using direct methods and block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.076 for the observed reflections. Additional crystallographic data are available and are described in the paragraph entitled supplementary material available at the end of this paper.

Diterpene Composition of Individual Nudibranchs. Seven specimens of *C. macfarlandi* were separately soaked in acetone (5–10 ml) for 24 h. The acetone extracts were concentrated and the residues partitioned between dichloromethane and water. The dichloromethane layers were dried, evaporated, and redissolved in deuteriochloroform and examined by ^{1}H NMR spectroscopy. The relative compositions of **3**, **4**, and **5** in the extracts were assayed by comparing the intensities of characteristic peaks in the spectra.

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Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances, interatomic angles, and torsional angles for **3** (6 pages). Ordering information is given on any current masthead page.

(8) Many members of the family Aplysillidae produce diterpenes related to or derived from the spongian diterpenes. Bergquist, P. R.; Karuso, P. 3rd International Conference on the Biology of Sponges, Woods Hold, MA, November 1985.

(9) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P. T. Buerskens et al., University of Nijmegen, Netherlands, 1981; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.