Dactyloquinones A and B, New Sesquiterpenoid Quinones from the Okinawan Marine Sponge *Dactylospongia elegans*

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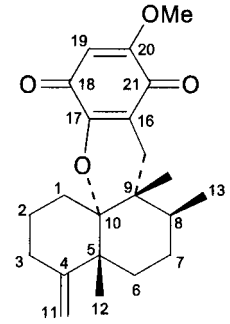
Structurally unique new sesquiterpenoid quinones dactyloquinone A (**1**) and B (**2**), each possessing a dihydropyran moiety, were isolated from an Okinawan sponge *Dactylospongia elegans*, along with known sesquiterpenoid quinones. The structures of these compounds were determined by spectroscopic analysis.

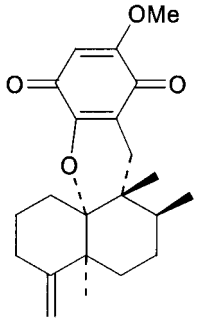
Numerous sesquiterpenoid quinones and hydroquinones have been isolated from various species of marine sponges,[1] and the sesquiterpene moiety frequently has a drimane skeleton, as in zonarol (**3**),[2] or a 4,9-friedodrimane skeleton, as in avarol (**4**).[3,4] Other types of rearranged drimanes, which have linear (farnesane) and monocyclic (cyclofarnesane) skeletons, have also been observed.[5] In drimane and 4,9-friedodrimane-type sesquiterpenoid quinones, the sesquiterpene skeleton in most cases is connected to the 1,4-benzoquinone functionality only at C-11, via carbon−carbon bonding. Bonding to C-11 and carbon−oxygen bonding of C-8 or C-10 to hydroxy-1,4-benzoquinone have also been noted to form dihydropyran rings, as in the case of cyclospongiaquinone-1 (**5**)[6] and smenoqualone (**6**).[7] The latter dihydropyran-containing compounds are limited in number, and no 4,9-friedodrimane-type compound containing a dihydropyran moiety has been reported to date.

Many sesquiterpenoid quinones and hydroquinones are of considerable interest from the standpoint of biological activities such as antimicrobial,[8] antileukemic,[9] immunomodulation,[10] and anti-HIV activities.[11]

During the course of investigation on chemical constituents of Okinawan marine invertebrates,[12] structurally unique new sesquiterpenoid quinones, dactyloquinones A (**1**) and B (**2**), were isolated from the Okinawan sponge *Dactylospongia elegans*. These compounds are the first examples of dihydropyran-containing 4,9-friedodrimane-type sesquiterpenoid quinones. Their isolation and structure elucidation are presented in the following.



dactyloquinone A (**1**)



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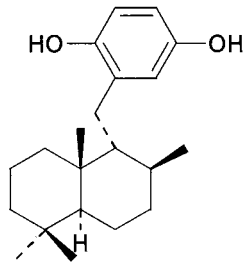
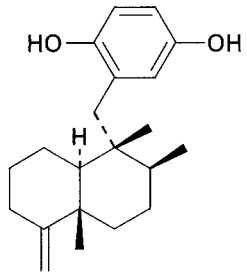
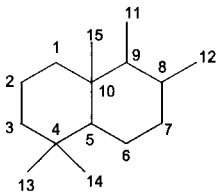


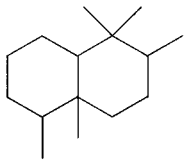
zonarol (**3**)



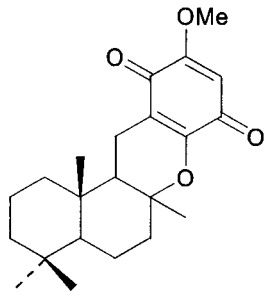
avarol (**4**)



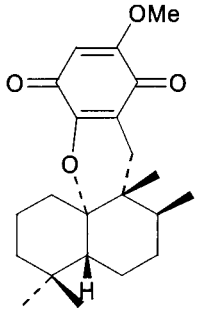
drimane skeleton



4,9-friedodrimane skeleton



cyclospongiaquinone-1 (**5**)



smenoqualone (**6**)

Results and Discussion

Sponge specimens of *D. elegans* (wet wt 2.5 kg), from the coral reef of Ishigaki Island, Okinawa, Japan, obtained in November 2000, were extracted with MeOH and then acetone. The combined extracts (97.3 g) were partitioned between H_2O and AcOEt and then $CHCl_3$. The AcOEt-soluble portion (10.7 g) was purified to give the sesquiterpenoid quinones dactyloquinones A (**1**) and B (**2**) along with ilimaquinone,[13] 5-epiilimaquinone,[14] smenospongine,[15] smenospondiol,[16] cyclospongiaquinone-1 (**5**),[6] and pelorol.[17]

Dactyloquinone A (**1**) was found to have molecular formula $C_{22}H_{28}O_4$ based on high-resolution mass measurement. The presence of a 1,4-benzoquinone chromophore was suggested by IR absorption at 1663 and 1644 cm^{-1} and UV absorption at λ_{max} 279, 285, and 396 nm. The ^{13}C NMR and DEPT spectra revealed 22 carbons and indicated the

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Table 1. NMR Data for **1** and **2**

	1		**2**	
no.	^{13}C NMR[a]	^{1}H NMR[b]	^{13}C NMR[a]	^{1}H NMR[b]
1	25.0 (CH_2)	1.57 (1H, m) 1.90 (1H, dt, 4.7, 14.0)	29.1 (CH_2)	1.88 (2H, m)
2	22.1 (CH_2)	1.51 (2H, m)	23.2 (CH_2)	1.75 (1H, m) 1.83 (1H, m)
3	31.4 (CH_2)	2.22 (1H, br d, 13.8) 2.38 (1H, br t, 13.8)	30.0 (CH_2)	2.20 (1H, br dd, 4.8, 14.0) 2.60 (1H, m)
4	155.0 (C)		152.9 (C)	
5	43.8 (C)		44.4 (C)	
6	31.0 (CH_2)	1.35 (1H, m) 2.09 (1H, dt, 5.6, 13.0)	32.6 (CH_2)	1.79 (1H, m) 1.95 (1H, m)
7	26.8 (CH_2)	1.49 (2H, m)	26.9 (CH_2)	1.28 (1H, m) 1.62 (1H, m)
8	32.6 (CH)	1.44 (1H, m)	33.8 (CH)	1.44 (1H, m)
9	37.4 (C)		38.8 (C)	
10	89.1 (C)		88.0 (C)	
11	106.0 (CH_2)	4.69 (1H, s) 4.79 (1H, s)	107.5 (CH_2)	4.80 (1H, s) 4.90 (1H, s)
12	23.9 (CH_3)	1.27 (3H, s)	27.6 (CH_3)	1.37 (3H, s)
13	16.2 (CH_3)	0.81 (3H, d, 6.6)	16.2 (CH_3)	0.76 (3H, d, 6.8)
14	19.1 (CH_3)	1.01 (3H, s)	19.9 (CH_3)	1.12 (3H, s)
15	28.4 (CH_2)	2.03 (1H, d, 19.1) 2.51 (1H, d, 19.1)	28.1 (CH_2)	2.11 (1H, d, 19.0) 2.64 (1H, d, 19.0)
16	115.4 (C)		114.1 (C)	
17	152.3 (C)		152.6 (C)	
18	181.0 (C)		181.1 (C)	
19	104.9 (CH)	5.70 (1H, s)	104.7 (CH)	5.72 (1H, s)
20	159.3 (C)		159.4 (C)	
21	181.3 (C)		181.6 (C)	
20-OMe	56.3 (CH_3)	3.79 (3H, s)	56.3 (CH_3)	3.80 (3H,s)

[a] 125 MHz $CDCl_3$. [b] 500 MHz, $CDCl_3$.

presence of four methyls, six sp^3 methylenes, one sp^2 methylene, one sp^3 methine, one sp^2 methine, three sp^3 quaternary carbons, and six sp^2 quaternary carbons (Table 1). ^{1}H and ^{13}C NMR correlations were evident from the HMQC spectrum. ^{1}H and ^{13}C NMR indicated a dialkoxy-1,4-benzoquinone moiety [δ_H 3.79 (3H, s), 5.70 (1H, s), δ_C 104.9 (CH), 115.4 (C), 152.3 (C), 159.3 (C), 181.0 (C), 181.3 (C)], an oxygenated sp^3 quaternary carbon [δ_C 89.1 (C)], and an *exo*-methylene [δ_H 4.69 (1H, s), 4.79 (1H, s), δ_C 106.0 (CH_2), 155.0 (C)]. COSY cross-peaks indicated the following partial structures: C-1 to C-3 and C-6 to C-8, C-13. These structures and the dialkoxy-1,4-benzoquinone moiety were connected to each other through quaternary carbons, as indicated by the following HMBC spectrum correlations: H-11/C-3, C-5; Me-12/C-4, C-6, C-10; Me-13/C-9; Me-14/C-8, C-10, C-15; H-15/C-8, C-10, C-14, C-16, C-17, C-21; and H-19/C-17, C-18, C-20, C-21. It was thus evident that the 4,9-friedodrimane skeleton was connected to a dialkoxy-1,4-benzoquinone. The presence of a dihydropyran moiety was clearly indicated by the absence of absorption of hydroxyl groups in the IR spectrum and absence of any effect on the UV spectrum upon addition of base. The planar structure of **1** was thus determined. The relative configuration of **1** was elucidated from the following NOESY correlations: H-1 (δ_H 1.90)/Me-12, Me-14; H-1 (δ_H 1.57)/H-15 (δ_H 2.03); Me-13/Me-14, H-15 (δ_H 2.51) (Figure 1). The structure of **1** was thus determined.

Dactyloquinone B (**2**) was found to have molecular formula $C_{22}H_{28}O_4$ based on high-resolution mass measurement, and a dialkoxy-1,4-benzoquinone chromophore was demonstrated by IR and UV absorptions. Its planar structure was found consistent with **1** based on ^{1}H and ^{13}C NMR spectra and two-dimensional NMR (COSY, HMQC, and HMBC) data. The ^{13}C NMR spectrum of **2** was closely related to those of **1**, except for the C-1, C-4, and Me-12 positions, thus suggesting **2** to be the stereoisomer of **1** at the C-5 position. The relative configuration of **2** was elucidated from the following NOESY correlations: H-2 (δ_H 1.75)/H-3 (δ_H 2.60); H-2 (δ_H 1.83)/Me-14; H-3 (δ_H 2.60)/Me-12; H-6 (δ_H 1.79)/H-8, Me-12; Me-13/Me-14 (Figure 2). The structure of **2** could thus be determined from these findings.

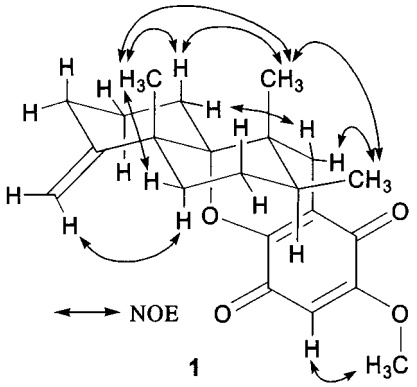

Figure 1. Selected NOE correlations of **1**.

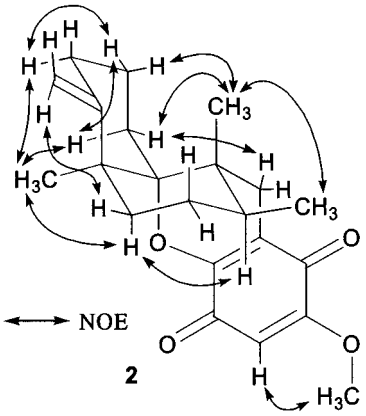

Figure 2. Selected NOE correlations of **2**.

Dactyloquinones A (**1**) and B (**2**) are the first examples of 4,9-friedodrimane-type sesquiterpenoid quinones each containing a dihydropyran moiety constructed with ether linkages between C-10 and C-17. These compounds are of interest for their biogenetic pathways.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-360 polarimeter. IR spectra were recorded with a JASCO FT-IR/620 spectrometer, and UV spectra with a JASCO V-550 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DRX-500 spectrometer. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad). EIMS were obtained with a Thermo Quest TSQ 700 spectrometer, and a high-resolution EIMS (HREIMS) spectrum was obtained using a VG Auto Spec E spectrometer. Flash column chromatography was carried out on Kanto Chemical silica gel 60N (spherical, neutral) 40−50 μm or ODS Wakogel LP-40 C-18. HPLC separations were performed using a YMC-Pack R&D ODS (250 × 20 mm) column and a UV detector (254 nm).

Animal Material. Sponge specimens (dark brown thin encrustations) were obtained from the coral reef of Ishigaki Island, Okinawa, Japan, at a depth of 5 m by hand using scuba, in November 2000.

The sponge specimen was *Dactylospongia elegans* (Thiele, 1899), class Demospongiae, order Dictyoceratida, family Thorectidae. A voucher specimen has been deposited at University of Amsterdam (ZMA POR. 16688), and another is maintained at Tokyo University of Pharmacy and Life Science (S-00-7).

Extraction and Isolation. Wet specimens (2.5 kg) were cut into small pieces and extracted with MeOH (12.5 L × 3) and then acetone (7.0 L × 2). The combined extracts were concentrated and partitioned between AcOEt (2.5 L × 4) and water (2.0 L) to give an AcOEt-soluble portion (10.7 g).

The AcOEt-soluble portion was chromatographed on Si gel using a hexane−AcOEt (3:1) to AcOEt gradient and MeOH as eluent to produce fractions 1 (1.3 g), 2 (2.5 g), and 3 (5.9 g). Fraction 2 was subjected to flash Si gel column chromatography (elution with hexane−AcOEt (3:1 to 5:3)) to give fractions 2-1, 2-2, and 2-3. Fraction 2-2 was gel-filtered on Sephadex LH-20 with $CHCl_3$−MeOH (1:1) and subjected to repeated flash ODS column chromatography with MeOH−water (8:1) to provide ilimaquinone (369.7 mg). On fraction 2-3, repeated flash Si gel column chromatography (elution with hexane−AcOEt (5:3)) was conducted to give fractions 2-3-1, 2-3-2, and 2-3-3. Fraction 2-3-1 was subjected to repeated flash ODS column chromatography (elution with MeOH−acetone (3:1) and acetone−water (4:1)) and ODS−HPLC (elution with MeOH−water (6:1 to 4:1)) to give dactyloquinone A (**1**) (9.6 mg), 5-epiilimaquinone (15.8 mg), and a mixture of cyclospongiaquinone-1 and dactyloquinone B (**2**). A mixture of cyclospongiaquinone-1 and dactyloquinone B (**2**) was subjected to PTLC (hexane−AcOEt (2:1)) to give cyclospongiaquinone-1 (0.7 mg) and dactyloquinone B (**2**) (1.0 mg). Fraction 2-3-2 was subjected to repeated flash Si gel column chromatography (elution with $CHCl_3$−MeOH (19:1) and hexane−AcOEt (2:1)) to produce smenospondiol (11.0 mg), pelorol (106.0 mg), and smenospongine (11.8 mg).

Dactyloquinone A (1): pale yellow powder; mp 183−185 °C; $[\alpha]^{26}_D$ −28.3° (*c* 0.6, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 279 (4.2), 285 (4.2), 396 (3.3) nm; IR (KBr) ν_{max} 2939, 1663, 1644 cm^{-1}; ^{1}H NMR and ^{13}C NMR, see Table 1; HMBC correlation (H/C) H-1/C-9, C-10; H-11/C-3, C-5; Me-12/C-4, C-6, C-10; Me-13/C-9; Me-14/C-8, C-10, C-15; H-15/C-8, C-10, C-14, C-17, C-21; H-19/C-17, C-21; 20-OMe/C-20; EIMS *m*/*z* 356 [M$^+$] (100), 341 (26), 189 (29), 175 (46), 167 (62), 139 (54), 91 (58); HREIMS *m*/*z* 356.2006 (calcd for $C_{22}H_{28}O_4$, 356.1988).

Dactyloquinone B (2): pale yellow powder; mp 178−180 °C; $[\alpha]^{26}_D$ −33.1° (*c* 1.5, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 278 (4.2), 287 (4.2), 398 (2.1) nm; IR (KBr) ν_{max} 2937, 1662, 1644 cm^{-1}; ^{1}H NMR and ^{13}C NMR, see Table 1; HMBC correlation (H/C) H-1/C-9, C-10; H-11/C-3, C-5; Me-12/C-4, C-6, C-10; Me-13/C-9; Me-14/C-8, C-10, C-15; H-15/C-8, C-10, C-14, C-17, C-21; H-19/C-17, C-21; 20-OMe/C-20; EIMS *m*/*z* 356 [M$^+$] (100), 328 (30), 189 (28), 175 (64), 167 (40), 139 (42), 91 (29); HREIMS *m*/*z* 356.1990 (calcd for $C_{22}H_{28}O_4$, 356.1988).

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Supporting Information Available: Copies of 1D and 2D NMR spectra of dactyloquinone A (**1**) and B (**2**). This material is available free of charge via the Internet at http://pubs.acs.org.

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