Sesquiterpenoid Aminoquinones from the Marine Sponge *Dysidea* sp.

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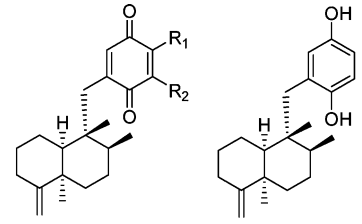
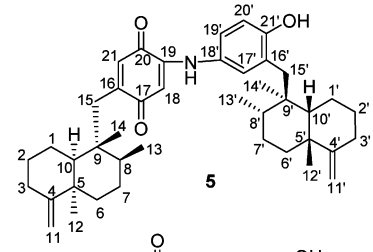
Received January 16, 2010

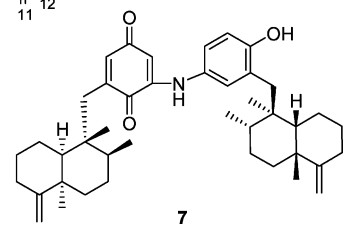
Four new sesquiterpenoid arenarone derivatives, 18-aminoarenarone (**1**), 19-aminoarenarone (**2**), 18-methylaminoarenarone (**3**), and 19-methylaminoarenarone (**4**), and the new dimeric popolohuanone F (**5**), a derivative of 19-aminoarenarone (**2**) and arenarol (**6**), have been isolated from the Australian marine sponge *Dysidea* sp. together with the known compounds arenarol (**6**) and popolohuanone A (**7**). The structures of the new compounds **1**−**5** were established from extensive NMR spectroscopic data. Popolohuanones A (**7**) and F (**5**) and arenarol (**6**) showed DPPH radical scavenging activity with IC_{50} values of 35, 35, and 19 μM, respectively.

A variety of compounds having a quinone or hydroquinone moiety attached to a sesquiterpenoid skeleton have been isolated from marine sponges.[1,2] The sesquiterpenoid moieties of these compounds commonly contain the *trans*- or *cis*-4,9-friedodrim-4(11)-ene or the *trans*- or *cis*-4,9-friedodrim-3-ene skeletons.[3] The cytotoxic sesquiterpenoids arenarol and arenarone isolated from the marine sponge *Dysidea arenaria*[4] are the parent compounds of sponge metabolites possessing the *cis*-4,9-friedodrim-4(11)-ene skeletons. Sesquiterpenoid quinones and hydroquinones have attracted much interest due to their biological properties, such as antitumor, antimicrobial, anti-HIV, antioxidant, and others.[5]

In the course of our search for antioxidants from marine organisms we investigated the $CHCl_3$ extract of an Australian marine sponge *Dysidea* sp. (order Dictyoceratida, family Dysideidae), which showed a strong antioxidant effect in scavenging the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH). Bioassay-guided fractionation of the $CHCl_3$ extract led to the isolation of the inactive compounds **1**−**4** and the active DPPH scavenging compounds **5**−**7**. Compounds **1**−**5** were new sesquiterpenoid quinones. Compounds **6** and **7** were the known metabolites arenarol (**6**)[4] and popolohuanone A (**7**).[6] The known compounds were identified by comparison of their spectroscopic data with published values. In this paper we describe the isolation and structural elucidation of the new natural compounds **1**−**5**.







Compound **1** has the molecular formula $C_{21}H_{29}NO_2$ as determined by HREIMS and ^{13}C NMR data (Table 1). The ^{13}C NMR and DEPT spectra revealed 21 carbons and indicated the presence of three methyls, seven methylenes, four methines, and seven quaternary carbons. The UV (283 nm), IR (1671, 1640, 1595 cm^{-1}), and ^{13}C NMR spectra (δ 183.7 and 186.7) indicated the presence of a 1,4-benzoquinone moiety in **1**. Moreover, the IR spectrum contained the bands of an amino group (3514, 3397 cm^{-1}). The bathochromic shift of the absorption maximum of the quinoid chromophore in the UV spectrum of **1** (283 nm versus 245 nm in arenarone[4]) indicated an amino group on the quinoid moiety. The upfield shifts of the quinoid proton (δ 5.73) in the ^1H NMR spectrum and the corresponding sp^2 methine carbon (δ 101.8) in the ^{13}C NMR spectrum of **1** were due to an *ortho*-situated amino group.[7] The ^1H NMR *meta*-coupling pattern of the quinone ring protons of **1** (H-19, d, $J = 2.7$ Hz; H-21, d, $J = 2.7$ Hz) clearly indicates the C-18 position of the amino group appended to the quinone ring (Table 2). This was supported by the HMBC correlations from H-21 to C-15, C-17, and C-19 and from H-19 to C-17 and C-21.

The ^1H and ^{13}C NMR spectra (Tables 1 and 2) and the fragment ion at *m/z* 191.1795 (calcd for $C_{14}H_{23}$, 191.1799) in the mass spectrum of **1** showed the presence of a rearranged drimane skeleton in **1**. The ^1H and ^{13}C NMR shifts of a sesquiterpene moiety in **1** matched the ^1H and ^{13}C NMR values for the sesquiterpene quinones arenarone,[4] (+)-5-*epi*-ilimaquinone,[8] (+)-5-*epi*-smenospongine,[9] and other metabolites bearing the *cis*-4,9-friedodrim-4(11)-ene skeleton.[3,8−10] An NOE between H-10 (δ 1.12) and H_3-12 protons (δ 1.06) in the NOESY spectrum justified the *cis* fusion of the decalin system in **1**. Moreover, H-10 (δ 1.12) gave cross-peaks with H_2-15 (δ 2.62 and 2.39), indicating the α-orientation of H-10, Me-12, and C-15. The decalin system and quinone ring were suggested to be connected between C-9 and C-16 through C-15 on the basis of HMBC correlations of H_2-15 to C-9, C-10, C-16, and C-21. Detailed NMR spectroscopic analysis (HSQC, $^1H-^1H$-COSY, and HMBC) and comparison with 18-aminoavarone[11] allowed the assignment of all the proton and carbon values of **1**. Thus the structure of **1** was determined as 18-aminoarenarone.

The molecular formula of **2** determined by HREIMS, $C_{21}H_{29}NO_2$, was the same as that of **1**, indicating that the two compounds are isomers. Signals of the terpenoid substructure in the ^1H and ^{13}C NMR spectra of **2** (Tables 1 and 2) fully coincided with those of **1**, clearly indicating the presence of the same *cis*-4,9-friedodrim-

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10.1021/np1000285
Published on Web 03/15/2010

Table 1. ^{13}C NMR (δ_C, mult.) Data for Compounds **1**−**5** (125 MHz, $CDCl_3$)

no.	1	2	3	4	5		no.
1	21.8, CH_2	21.9, CH_2	21.8, CH_2	21.9, CH_2	21.9, CH_2	22.5, CH_2	1′
2	24.5, CH_2	24.6, CH_2	24.6, CH_2	24.6, CH_2	24.6, CH_2	24.8, CH_2	2′
3	31.7, CH_2	31.8, CH_2	31.7, CH_2	31.8, CH_2	31.8, CH_2	31.7, CH_2	3′
4	153.1, C	153.3, C	153.2, C	153.3, C	153.3, C	153.3, C	4′
5	39.3, C	39.5, C	39.4, C	39.5, C	39.5, C	39.3, C	5′
6	37.8, CH_2	37.9, CH_2	37.8, CH_2	37.9, CH_2	37.9, CH_2	37.7, CH_2	6′
7	27.4, CH_2	27.5, CH_2	27.4, CH_2	27.5, CH_2	27.5, CH_2	27.4, CH_2	7′
8	38.2, CH	38.6, CH	38.2, CH	38.6, CH	38.6, CH	37.6, CH	8′
9	44.1, C	45.0, C	44.0, C	45.1, C	45.2, C	43.6, C	9′
10	47.2, CH	47.8, CH	47.2, CH	47.8, CH	47.9, CH	46.5, CH	10′
11	106.1, CH_2	106.0, CH_2	106.0, CH_2	105.9, CH_2	105.9, CH_2	106.0, CH_2	11′
12	32.9, CH_3	33.0, CH_3	32.9, CH_3	32.9, CH_3	32.9, CH_3	33.0, CH_3	12′
13	17.2, CH_3	17.3, CH_3	17.2, CH_3	17.3, CH_3	17.3, CH_3	17.9, CH_3	13′
14	19.1, CH_3	19.1, CH_3	19.1, CH_3	19.1, CH_3	19.0, CH_3	19.1, CH_3	14′
15	34.9, CH_2	35.7, CH_2	34.9, CH_2	35.8, CH_2	35.7, CH_2	37.5, CH_2	15′
16	142.7, C	150.4, C	142.1, C	151.4, C	151.2, C	126.7, C	16′
17	183.7, C	186.1, C	183.7, C	185.1, C	185.8, C	127.7, CH	17′
18	147.1, C	102.9, CH	147.8, C	98.3, CH	100.2, CH	129.6, C	18′
19	101.8, CH	146.0, C	97.6, CH	147.0, C	143.5, C	122.1, CH	19′
20	186.7, C	183.8, C	185.5, C	183.5, C	183.9, C	116.4, CH	20′
21	138.5, CH	131.8, CH	139.5, CH	131.4, CH	131.5, CH	152.6, C	21′
22			29.1, CH_3	28.9, CH_3			

Table 2. ^1H NMR and HMBC Data for Compounds **1**−**4** (500 MHz, $CDCl_3$)

	1		2		3		4	
no.	δ_H (J in Hz)	HMBC[a]	δ_H (J in Hz)	HMBC[a]	δ_H (J in Hz)	HMBC[a]	δ_H (J in Hz)	HMBC[a]
1	1.99, m	2, 3, 5, 9, 10	2.00, m	2, 3, 5, 9, 10	1.99, m	2, 3, 5, 9, 10	2.04, m	2, 3, 5, 9, 10
	1.81, m		1.81, m		1.81, m		1.78, m	
2	1.81, m	1, 3, 4, 10	1.81, m	1, 3, 4, 10	1.81, m	1, 3, 4, 10	1.78, m	1, 3, 4, 10
	1.68, m		1.68, m		1.68, m		1.67, m	
3	2.45, m	1, 2, 4, 5, 11	2.45, m	1, 2, 4, 5, 11	2.45, m	1, 2, 4, 5, 11	2.46, m	1, 2, 4, 5, 11
	2.14, m		2.14, m		2.13, m		2.13, m	
6	2.05, m	4, 5, 7, 8, 10	2.05, m	4, 5, 7, 8, 10	2.05, m	4, 5, 7, 8, 10	2.04, m	4, 5, 7, 8, 10
	1.12, m		1.12, m		1.10, m		1.11, m	
7	1.55, m	5, 6, 8, 9, 13	1.56, m	5, 6, 8, 9, 13	1.54, m	5, 6, 8, 9, 13	1.54, m	5, 6, 8, 9, 13
	1.25, m		1.25, m		1.25, m		1.24, m	
8	1.25, m	6, 9, 10, 14, 15	1.25, m	6, 9, 10, 14, 15	1.28, m	6, 9, 10, 14, 15	1.24, m	6, 9, 10, 14, 15
10	1.12, m	1, 2, 5, 8, 9, 14, 15	1.13, m	1, 2, 5, 8, 9, 14, 15	1.14, m	1, 2, 5, 8, 9, 14, 15	1.12, m	1, 2, 5, 8, 9, 14, 15
11	4.72, s	3, 4, 5	4.72, s	3, 4, 5	4.72, s	3, 4, 5	4.72, s	3, 4, 5
	4.70, s		4.70, s		4.70, s		4.70, s	
12	1.06, s	4, 5, 6, 10	1.07, s	4, 5, 6, 10	1.06, s	4, 5, 6, 10	1.07, s	4, 5, 6, 10
13	0.89, d (6.5)	7, 8, 9	0.90, d (6.5)	7, 8, 9	0.89, d (6.5)	7, 8, 9	0.90, d (6.5)	7, 8, 9
14	0.91, s	8, 9, 10, 15	0.92, s	8, 9, 10, 15	0.91, s	8, 9, 10, 15	0.92, s	8, 9, 10, 15
15	2.62, d (13.4)	8, 9, 10, 16, 17, 21	2.68, d (13.6)	8, 9, 10, 16, 17, 21	2.60, d (14)	8, 9, 10, 16, 17, 21	2.71, d (13.6)	8, 9, 10, 16, 17, 21
	2.39, d (13.4)		2.39, d (13.6)		2.39, d (14)		2.41, d (13.6)	
18			5.72, s	16, 19, 20			5.44, s	16, 19, 20
19	5.73, d (2.7)	17, 18, 21			5.42, d (2.3)	17, 18, 21		
21	6.37, d (2.7)	15, 16, 17, 19	6.40, s	15, 16, 17, 19	6.39, d (2.3)	15, 16, 17, 19	6.38, s	15, 16, 17, 19
22					2.85, d (5.8)	18	2.84, d (5.4)	19
NH_2	5.02, br s		4.82, br s					
NH					5.68, br d		5.55, br d	

[a] HMBC correlations, optimized for 5 Hz, are from proton(s) stated to the indicated carbon.

4(11)-ene skeleton found in **1**. The only difference between **1** and **2** was the position of the amino group. In the ^1H NMR spectrum of **2** two quinoid protons showed singlets indicating their *para* orientation. The position of the amino group at C-19 was supported by HMBC correlations from H-21 to C-15, C-17, and C-19 and from H-18 to C-16 and C-20. Full ^1H and ^{13}C NMR assignments were readily obtained from HSQC and HMBC correlations and by comparison with **1**. Thus the structure of **2** was determined as 19-aminoarenarone.

A HREIMS measurement of the molecular ion of **3** (*m*/*z* 341.2350) suggested the molecular formula $C_{22}H_{31}NO_2$. The ^{13}C NMR and DEPT spectra indicated the presence of four methyls, seven methylenes, four methines, and seven quaternary carbons (Table 1). These data suggested the difference between **3** and **1** was a single methyl group. Comparison of the ^1H and ^{13}C NMR data of **3** (Tables 1 and 2) with those of **1** showed strong structural similarities between the two molecules and suggested that **3** was a methylamino analogue of **1**. In addition to the signals confirming the terpenoid part, the ^1H NMR spectrum of **3** (Table 2) contained *meta*-coupled proton signals reminiscent of a quinone ring and a doublet signal from protons of an *N*-methyl group (δ 2.85) coupled with a broad signal from one exchangeable proton at δ 5.68, as shown by the $^1H-^1H$-COSY spectrum. The key HMBC correlation from the protons of the *N*-Me group (δ 2.85) to the carbon atom of the quinone ring at δ 147.8 positioned the methylamino group at C-18. Full ^1H and ^{13}C NMR assignments were readily obtained from HSQC and HMBC correlations and by comparison with **1** and 18-methylaminoavarone.[12] Thus the structure of **3** was determined as 18-methylaminoarenarone.

The molecular formula of compound **4** determined by HREIMS, $C_{22}H_{31}NO_2$, was the same as that of **3**, indicating that the two compounds were isomers. The only difference between **4** and **3** was the position of a methylamino group. In the ^1H NMR spectrum of **4** two quinoid protons showed singlets indicating their *para*

orientation (Table 2). The position of the methylamino group at C-19 was supported by HMBC correlations from H-21 to C-15, C-17, and C-19, from H-18 to C-16 and C-20, and from H_3-22 to C-19. Thus the structure of **4** was determined to be 19-methylaminoarenarone.

Compound **5**, named popolohuanone F, was obtained as a noncrystalline violet solid, and the molecular formula was established to be $C_{42}H_{57}NO_3$ by HREIMS data. The HREIMS data and the ^{1}H and ^{13}C NMR spectra suggested that **5** was a dimeric sesquiterpenoid quinone related to popolohuanone A (**7**) from a *Dysidea* sp. sponge.[6] The ^{1}H NMR spectrum of **5** showed signals due to two secondary methyls (δ 0.91 and 0.99), four tertiary methyls (δ 1.07, 1.06, 0.93, and 0.92), and a multiplet of four exomethylene protons (δ 4.72). These data suggested the presence of two trimethyl decalin moieties, each with one exomethylene group. Indeed, comparison of two sets of signals in the ^{1}H NMR and ^{13}C NMR spectra of **5** with those for **1**−**4** and **7**[6] suggested the identity of their terpenoid parts. Moreover, the signals of the terpenoid and quinoid moieties of one-half of the molecule **5** fully coincided with signals of **2** in the ^{1}H and ^{13}C NMR spectra. The presence of a 2,5-disubstituted 1,4-benzoquinone as in **2** was evident from two singlet quinoid protons in the ^{1}H NMR spectrum (δ 6.47 and 5.95). Key HMBC correlations from H-18 (δ 5.95) to C-16 (δ 151.2), from H-21 (δ 6.47) to C-19 (δ 143.5), and from N*H* (δ 7.06) to C-18 (δ 100.2) supported the position of the amino group at C-19. Signals belonging to the second half of **5** in the ^{1}H and ^{13}C NMR spectra coincided with those of one-half of popolohuanone A (**7**)[6] bearing a 2,4-disubstituted phenol moiety. The presence of the same phenol moiety in **5** was evident from the coupling pattern of aromatic protons (δ 6.95 dd, J = 8.5, 2.7 Hz, δ 6.93 d, J = 2.7 Hz, δ 6.76 d, J = 8.5 Hz) in the ^{1}H NMR spectrum. Key HMBC correlations from N*H* (δ 7.06) to C-17′ (δ 127.7) and C-19′ (δ 122.1) and from O*H* (δ 4.97) to C-20′ (δ 116.4), C-16′ (δ 126.7), and C-21′ (δ 152.6) supported the substitution pattern in the phenol moiety. The relative configuration of the decalin moieties in popolohuanone F (**5**) was justified on the basis of NOESY correlations. Analyses of the cross-peaks of the first decalin moiety in the NOESY spectrum of **5** showed that H-10 (δ 1.17) gave cross-peaks with H_3-12 (δ 1.06) and H_2-15 (δ 2.75 and 2.39), indicating the α-orientation of H-10, Me-12, and C-15. Cross-peaks between H-10′ (δ 1.35) and both H_3-12′ (δ 1.07) and H_2-15′ (δ 2.73 and 2.57) of the second decalin part of **5** revealed the α-orientation of H-10′, Me-12′, and C-15′, while cross-peaks between H_3-13′ (δ 0.99) and H_3-14′ (δ 0.92) indicated that Me-13′ and Me-14′ were β-oriented. Thus, the structure of popolohuanone F was elucidated to be **5**. Thereby, popolohuanone F (**5**) and popolohuanone A (**7**) are the third pair of isomers isolated from this marine sponge.

Popolohuanone F (**5**) and popolohuanone A (**7**) exhibited moderate potencies, with IC_{50} values of 35 μM in scavenging the DPPH free radical, while arenarol (**6**) showed potent antioxidant activity with an IC_{50} of 19 μM, comparable with that of Trolox (IC_{50} 16 μM). Compounds **1**−**5** at a concentration of 100 μg/mL were inactive against *Staphylococcus aureus*, *Candida albicans*, and *Escherichia coli* and did not show cytotoxic activity against mouse Ehrlich carcinoma cells.

Popolohuanone F adds to the series of dimeric popolohuanones A,[6] B,[6] C,[13] D,[13] and E[14] isolated from *Dysidea* sponges. A condensation reaction between 18-aminoarenarone (**1**) or 19-aminoarenarone (**2**) and arenarol (**6**) provides a simple explanation for the formation of the popolohuanones A (**7**) and F (**5**), respectively. 18-Aminoarenarone (**1**) and 19-aminoarenarone (**2**) are the first examples of natural aminoquinones being possible biosynthetic precursors of the dimeric popolohuanones A (**7**) and F (**5**).

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a Perkin-Elmer 343 polarimeter. UV spectra were recorded on an UV-mini 1240 spectrophotometer (Shimadzu). IR spectra were recorded on a Bruker Vector-22 FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE DRX-500 NMR spectrometer at 500 and 125 MHz, respectively. Chemical shifts were referenced to the solvent peak ($CDCl_3$, δ 7.26 for ^{1}H and δ 77.0 for ^{13}C). HMBC spectra were optimized for 5 Hz coupling. HREIMS were performed on an AMD-604 S mass spectrometer (Intectra, Germany). Sorbfil plates coated with silica gel (Sorbpolimer, Krasnodar, Russia) were used for TLC; Sephadex LH-20 (Pharmacia Fine Chemicals) and silica gel (Sorbpolimer, Krasnodar, Russia) were used for column chromatography. All solvents were distilled prior to use.

Animal Material. The sponge *Dysidea* sp. was collected by scuba diving at Scott Reef, Northwest Australia (14°05′88 S, 121°44′51 E), at a depth of 15 m in November of 1990 during the 12th scientific cruise of R/V *Academik Oparin*. A voucher specimen (PIBOC O12-225) is kept in the collection of the Pacific Institute of Bioorganic Chemistry, Vladivostok, Russia. Taxonomic identification was provided by one of the authors (V.B.K.).

The sponge has an elongated massive and branching flattened form up to 15 cm. The sponge was violet with pink to tan in color alive and dirty violet when dry. The surface is coarsely conulose, and the conules are about 5 mm high and 7−10 mm apart. The texture is soft, elastic but slightly dry because of the greatly reduced endosomal content, and easily torn. The surface is armored with a thin layer of fine sand and spicule fragments. The sparse reticulum of the choanosomal skeleton consists of laminated fibers (200 μm) that are fully axially cored by inorganic material with abundant fibrofasciculate (up to 1 mm in diameter). The secondary fiber skeleton is not well developed. Despite intensive taxonomic examination, it was not possible to identify the sponge to the species level. This sponge is closest in appearance to the description of *Dysidea* sp.1[13] and *D. frondosa* (Bergquist, 1995).[15]

Extraction and Isolation. The freeze-dried sponge (80 g) was extracted with $CHCl_3$ (300 mL × 3) at room temperature, and the solvent was concentrated under reduced pressure. The $CHCl_3$ extract was chromatographed on a silica gel column in *n*-hexane−acetone (7:1). Fractionation was guided by spraying of TLC plates with an EtOH solution of DPPH. The first, light pink fraction gave inactive compound **4**. The second, bright pink fraction afforded inactive compound **3**. The third, colorless fraction gave active compound **6**. The fourth, violet fraction yielded a mixture of active compounds **5** and **7**. The fifth, red-orange fraction gave inactive compound **2**. The sixth, red-orange fraction gave inactive compound **1**. TLC separation of the mixture of **5** and **7** on Sorbfil plates in $CHCl_3$ afforded compounds **5** and **7**. All compounds were further purified on a Sephadex LH-20 column in $CHCl_3$−MeOH (9:1) to yield **1** (6 mg, 0.0075% to the sponge dry weight), **2** (3.8 mg, 0.0048%), **3** (4 mg, 0.005%), **4** (2.1 mg, 0.0026%), **5** (3.9 mg, 0.0049%), **6** (4 mg, 0.005%), and **7** (8.3 mg, 0.01%).

18-Aminoarenarone (1): amorphous, red solid; $[\alpha]^{20}_D$ +69.7 (*c* 0.13, $CHCl_3$); UV−vis (EtOH) λ_{max} (log ε) 214 (4.20), 283 (3.85), 483 (3.27) nm; IR ($CHCl_3$) ν_{max} 3514, 3397, 2932, 2866, 1671, 1640, 1595, 1521 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; HREIMS *m*/*z* 327.2189 [M$^+$] (calcd for $C_{21}H_{29}NO_2$, 327.2198).

19-Aminoarenarone (2): amorphous, red solid; $[\alpha]^{20}_D$ +64.4 (*c* 0.23, $CHCl_3$); UV−vis (EtOH) λ_{max} (log ε) 207 (4.08), 284 (3.59), 482 (2.95) nm; IR ($CHCl_3$) ν_{max} 3510, 3403, 2933, 2869, 1672, 1636, 1588, 1515 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; HREIMS *m*/*z* 327.2194 [M$^+$] (calcd for $C_{21}H_{29}NO_2$, 327.2198).

18-Methylaminoarenarone (3): red oil; $[\alpha]^{20}_D$ +41 (*c* 0.48, $CHCl_3$); UV−vis (EtOH) λ_{max} (log ε) 220 (4.24), 284 (3.86), 487 (3.38) nm; IR ($CHCl_3$) ν_{max} 3408, 2933, 2869, 1671, 1636, 1514 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; HREIMS *m*/*z* 341.2350 [M$^+$] (calcd for $C_{22}H_{31}NO_2$, 341.2352).

19-Methylaminoarenarone (4): red oil; $[\alpha]^{20}_D$ +40 (*c* 0.26, $CHCl_3$); UV−vis (EtOH) λ_{max} (log ε) 207 (4.08), 286 (3.67), 483 (3.10) nm; IR ($CHCl_3$) ν_{max} 3408, 2931, 2857, 1665, 1630, 1592, 1517 cm^{-1}; ^{1}H and ^{13}C NMR data see Tables 1 and 2; HREIMS *m*/*z* 341.2348 [M$^+$] (calcd for $C_{22}H_{31}NO_2$, 341.2352).

Popolohuanone F (5): amorphous, violet solid; UV−vis (EtOH) λ_{max} (log ε) 234 (4.62), 269 (4.17), 531 (3.51) nm; IR ($CHCl_3$) ν_{max} 3600, 3370, 2930, 2868, 1663, 1630, 1589, 1508 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) [HMBC, optimized for 5 Hz] δ 7.06 (1H, br s, N*H*) [18, 20, 17′, 18′, 19′], 6.47 (1H, s, H-21) [15, 16, 17, 19], 5.95 (1H, s, H-18) [16, 19, 20], 6.95 (1H, dd, J = 8.5, 2.7 Hz, H-19′) [17′,18′, 21′], 6.93 (1H, d, J = 2.7 Hz, H-17′) [18′, 19′, 21′], 6.76 (1H, d, J = 8.5 Hz, H-20′) [16′, 18′, 21′], 4.97 (1H, br s, O*H*) [16′, 20′, 21′], 2.75

and 2.39 (each 1H, d, $J = 13.5$ Hz, CH_2-15) [8, 9, 10, 16, 17, 21], 2.73 and 2.57 (each 1H, d, $J = 14.4$ Hz, CH_2-15′) [8′, 9′, 10′, 16′, 17′, 21′], 2.05 and 2.00 (each 2H, m, CH_2-1, 1′) [2, 3, 5, 9, 10, 2′, 3′, 5′, 9′, 10′], 1.82 and 1.70 (each 2H, m, CH_2-2, 2′) [1, 3, 4, 10, 1′, 3′ 4′, 10′], 2.46 and 2.13 (each 2H, m, CH_2-3, 3′) [1, 2, 4, 5, 11, 1′, 2′, 4′, 5′, 11′], 2.06 and 1.15 (each 2H, m, CH_2-6, 6′) [4, 5, 7, 8, 10, 4′, 5′, 7′, 8′, 10′], 1.56 and 1.26 (each 2H, m, CH_2-7, 7′) [5, 6, 8, 9, 13, 5′, 6′, 8′, 9′, 13′], 1.37 (1H, m, H-8) [6, 9, 10, 14, 15], 1.43 (1H, m, H-8′) [6′, 9′, 10′, 14′, 15′], 1.17 (1H, m, H-10) [1, 2, 5, 8, 9, 14, 15], 1.35 (1H, m, H-10′) [1′, 2′, 5′, 8′, 9′, 14′, 15′], 4.72 (4H, m, CH_2-11, 11′) [3, 4, 5, 3′, 4′, 5′], 1.06 (3H, s, CH_3-12) [4, 5, 6, 10], 1.07 (3H, s, CH_3-12′) [4′, 5′, 6′, 10′], 0.91 (3H, d, $J = 6.5$ Hz, CH_3-13) [7, 8, 9], 0.99 (3H, d, $J = 6.5$ Hz, CH_3-13′) [7′, 8′, 9′], 0.93 (3H, s, CH_3-14) [8, 9, 10, 15], 0.92 (3H, s, CH_3-14′) [8′, 9′, 10′, 15′]; ^{13}C NMR data see Table 1; HREIMS *m*/*z* 623.4342 [M$^+$] (calcd for $C_{42}H_{57}NO_3$, 623.4339). The strongly colored solution did not allow a measurement of the $[\alpha]_D$, even after dilution.

Arenarol (6): $[\alpha]^{20}_D$ +18.7 (*c* 0.16, $CHCl_3$); lit. $[\alpha]^{20}_D$ +19 (*c* 0.1, $CHCl_3$).[4] MS and NMR data matched those previously reported.

DPPH Radical Scavenging Assay. The assay used was adapted from the published method.[16] Free-radical scavenging activity was performed in EtOH, at different concentrations (5, 10, 20, 50, and 100 μM). Solutions of compounds were prepared and adjusted to 2 mL total volume with 0.7 mL of DPPH−EtOH solution (6 mg/50 mL; 0.1 mM final concentration). The absorbance at 517 nm was determined after 30 min, and the percent free-radical inhibition was calculated as follows: Inhibition (%) $= 100 - [(A_{sample} - A_{compound})/A_{control} \times 100]$, where A_{sample} is the absorbance of a reaction mixture, $A_{compound}$ is the absorbance at 517 nm of a test compound at test concentrations, and $A_{control}$ is the absorbance of the 0.1 mM DPPH solution. A correction for sample absorbance at 517 nm is necessary due to the highly colored nature of the compounds. The percentage of inhibition was plotted to obtain the IC_{50} value. Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) was used as positive control standard. The IC_{50} value denotes the concentration of compound required to scavenge 50% DPPH free radical.

Acknowledgment. The authors are grateful to O. P. Moiseyenko for mass spectra measurements. This research was supported by a FEBRAS grant (09-III-C-05-145) and the program "Molecular and Cell Biology" of the Presidium of the Russian Academy of Sciences.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **1**−**5**; a photograph of the marine sponge *Dysidea* sp. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Faulkner, D. J. *Nat. Prod. Rep.* **2002**, *19*, 1–48, and previous reviews in this series.
(2) Blunt, J. W.; Copp, B. R.; Hu, W.-P.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2009**, *26*, 170–244, and previous reviews in this series.
(3) Salmoun, M.; Devijver, C.; Daloze, D.; Breakman, J. C.; Gomez, R.; de Kluijver, M.; Van Soest, R. W. M. *J. Nat. Prod.* **2000**, *63*, 452–456.
(4) Schmitz, F. J.; Lakshmi, V.; Powell, D. R.; van der Helm, D. *J. Org. Chem.* **1984**, *49*, 241–244.
(5) Sladić, D.; Gasic, M. J. *Molecules* **2006**, *11*, 1–33.
(6) Rodriguez, A. D.; Yoshida, W. Y.; Scheuer, P. J. *Tetrahedron* **1990**, *46*, 8025–8030.
(7) Kondracki, M.-L.; Guyot, M. *Tetrahedron Lett.* **1987**, *28*, 5815–5818.
(8) Rodríguez, J.; Quiñoá, E.; Riguera, R.; Peters, B. M.; Abrell, L. M.; Crews, P. *Tetrahedron* **1992**, *32*, 6667–6680.
(9) Kwak, J. H.; Schmitz, F. J.; Kelly, M. *J. Nat. Prod.* **2000**, *63*, 1153–1156.
(10) Aoki, S.; Kong, D.; Matsui, K.; Rachmat, R.; Kobayashi, M. *Chem. Pharm. Bull.* **2004**, *52*, 935–937.
(11) Diaz-Marrero, A. R.; Austin, P.; Van Soest, R.; Matainaho, T.; Roskelley, C. D.; Roberge, M.; Andersen, R. J. *Org. Lett.* **2006**, *8*, 3749–3752.
(12) Cimino, G.; De Rosa, S.; Cariello, L.; Zanetti, L. *Experientia* **1982**, *38*, 896.
(13) Alvi, K. A.; Diaz, M. C.; Crews, P.; Slate, D. L.; Lee, R. H.; Moretti, R. *J. Org. Chem.* **1992**, *57*, 6604–6607.
(14) Carney, J. R.; Scheuer, P. J. *Tetrahedron Lett.* **1993**, *34*, 3727–3730.
(15) Bergquist, P. R. *Mem. Queensl. Mus.* **1995**, *38*, 1–51.
(16) Pejin, B.; Iodice, C.; Tommonaro, G.; De Rosa, S. *J. Nat. Prod.* **2008**, *71*, 1850–1853.

NP1000285