New Sesquiterpene/Quinones from Two Sponges of the Genus *Hyrtios*

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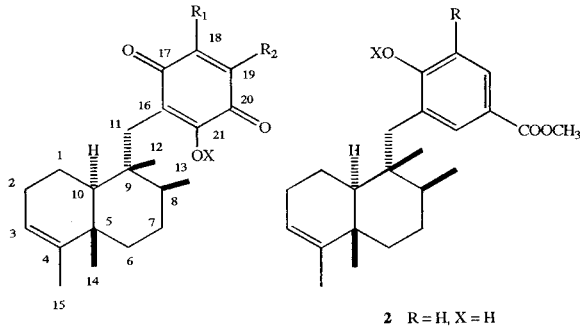
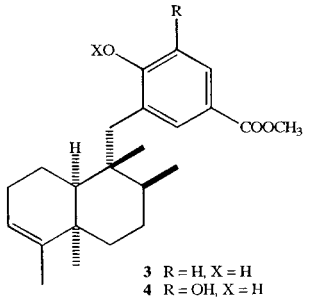
Two sponges of the genus *Hyrtios* have been found to contain new sesquiterpene/quinones identified by detailed spectroscopic analysis. Four new compounds with a 4,9-friedodrim-3-ene skeleton [hyrtiophenol (**2**), 5-epihyrtiophenol (**3**), 18-hydroxy-5-epihyrtiophenol (**4**), and 18-hydroxyhyrtiophenol (**5**)] were isolated from *Hyrtios* sp. (Seychelles Islands) along with isospongiaquinone (**1**). Moreover, the new compound 21-hydroxy-19-methoxyarenarone (**8**), which bears the 4,9-friedodrim-4(15)-ene skeleton, was isolated from *Hyrtios tubulatus* (Curaçao) along with arenarol (**6**) and 5-epiilimaquinone (**7**). Assignment of the ^{13}C NMR signals of four types of 4,9-friedodrimene skeletons found in sponges is presented.

In our screening for biologically active and taxonomically significant metabolites from sponges, the CH_2Cl_2 soluble fraction of the MeOH extract of two sponges of the genus *Hyrtios* (Thorectidae, Dictyoceratida) were found to contain sesquiterpene/quinones, a still expanding group of C15−C6 metabolites with potentially interesting medicinal applications. A paper reviewing this class of marine secondary metabolites has been published recently by Capon.[1] It comprises compounds of mixed biogenetic origin possessing a sesquiterpene unit with a quinone, a quinol, or a related analogue. Five of these merosesquiterpenes, bearing the 4,9-friedodrim-3-ene skeleton, were isolated from a specimen of *Hyrtios* sp. collected off Mahe (Seychelles) including isospongiaquinone (**1**)[2] and four new compounds, which we have named hyrtiophenol (**2**), 5-epihyrtiophenol (**3**), 18-hydroxy-5-epihyrtiophenol (**4**), and 18-hydroxyhyrtiophenol (**5**). Moreover, three merosesquiterpenes, bearing the isomeric 4,9-friedodrim-4(15)-ene skeleton, were isolated from a sample of *Hyrtios tubulatus* collected off Curaçao, including arenarol (**6**),[3] 5-epiilimaquinone (**7**),[4] and a new quinone named 21-hydroxy-19-methoxyarenarone (**8**). In this paper we report the structural characterization of the five new compounds.

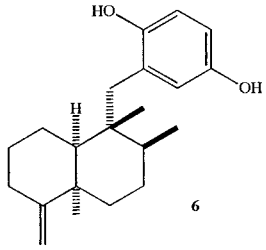


1 $R_1 = OCH_3$, $R_2 = H$, X = H
13 $R_1 = H$, $R_2 = OCH_3$, X = H
15 $R_1 = OCH_3$, $R_2 = H$, X = Ac

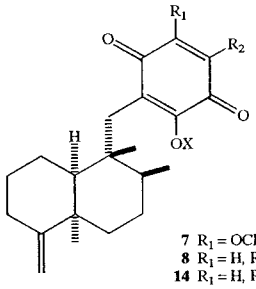
2 R = H, X = H
5 R = OH, X = H
9 R = H, X = Ac
12 R = OAc, X = Ac



3 R = H, X = H
4 R = OH, X = H
10 R = H, X = Ac
11 R = OAc, X = Ac



6



7 $R_1 = OCH_3$, $R_2 = H$, X = H
8 $R_1 = H$, $R_2 = OCH_3$, X = H
14 $R_1 = H$, $R_2 = OCH_3$, X = Ac

Results and Discussion

Compound **1**, the major compound of *Hyrtios* sp. (3.7% of the MeOH extract) had the molecular formula $C_{22}H_{30}O_4$ (M^+ at *m/z* 358.2151 by HREIMS, calcd 358.2144). The analysis of its spectroscopic data and a detailed 1D and 2D NMR study at 600 MHz (COSY, HMQC, HMBC, NOE difference experiments) led to the assignments reported in Tables 1 and 2 and led to the conclusion that its structure was identical to that of isospongiaquinone, a sesquiterpene/quinone isolated in 1978 from the Australian sponge *Stelospongia conulata* by Kazlauskas et al.[2] But, the assignment of the ^{13}C NMR signals reported for isospongiaquinone showed significant differences from that of compound **1** (Table 2, entries 1a and 1c). Indeed, in 16 out of the 22 carbon atoms a difference of 0.6 ± 0.2 ppm is systematically observed. It probably corresponds to a slight variation of calibration between the two spectra. But, in the six remaining carbon atoms the $\Delta\delta$ is greater or smaller than this value. As our assignments agreed with those proposed for several other sesquiterpene/quinones possessing the 4,9-friedodrim-3-ene skeleton (Figure 1), we had to admit that the assignments proposed by Kazlauskas et al.[2] for the carbon atoms C-1, C-5, C-9, C-13, C-14, and C-15 of isospongiaquinone were questionable and must be revised as reported in entry 1b of Table 2. This being

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Table 1. ^{1}H NMR Data of Isospongiaquinone (**1**), Hyrtiophenol (**2**), 5-Epihyrtiophenol (**3**), and 21-Hydroxy-19-methoxyarenarone (**8**) [600 MHz, $CDCl_3$, δ, J in Hz]

position	**1**	**2**	**3**	**8**
H_2C-1	1.40, m	1.61, m	2.10, m	2.08, m
	1.97, m	2.03, m	2.16, m	1.83, m
H_2C-2	1.82, m	2.08, m	2.10, m	1.72, m
	1.93, m	2.22, m	2.22, m	1.64, m
HC-3	5.06, bs	5.14, bs	5.33, bs	2.40, m
				2.08, m
H_2C-6	0.96 (ax), m	1.34 (ax), m	0.77 (ax), ddd,	1.99, m
	1.57 (eq), ddd,	1.56 (eq), ddd,	13.0, 13.0, 3.0	1.09, m
	13.0, 3.0, 3.0	13.0, 3.0, 3.0	1.84 (eq), ddd,	
			13.0, 3.0, 3.0	
H_2C-7	1.25, m	1.31, m	1.08, m	1.22, m
	1.28, m	1.36, m	1.25, m	1.47, m
HC-8	1.17, m	0.90, m	1.36, m	1.20, m
HC-10	0.95, bd, 12.0	1.18, bd, 12.0	1.22, m	1.22, m
H_2C-11	2.42, d, 14.0	2.69, d, 14.0	2.59, d, 14.0	2.47, d, 13.0
	2.55, d, 14.0	2.68, d, 13.0	2.81, d, 14.0	2.57, d, 13.0
	AB system	AB system	AB system	AB system
H_3C-12	0.77, s	0.87, s	0.96, s	0.86, s
H_3C-13	0.90, d, 6.0	1.02, d, 6.0	0.99, d, 7.0	0.89, d, 6.5
H_3C-14	0.94, s	1.01, s	0.90, s	1.04, s
H_3C-15	1.47, bs	1.49, bs	1.64, bs	4.65, bs
				4.68, bs
H_3C-O	3.79, s	3.86, s	3.87, s	3.80, s
HC-18		6.75, d, 8.5	6.77, d, 8.5	5.82, s
HC-19	5.77, s	7.75, dd, 8.5, 2.5	7.77, dd, 8.5, 2.5	
HC-21		7.79, d, 2.5	7.81, d, 2.5	

Table 2. ^{13}C NMR Data of Isospongiaquinone (**1**), Hyrtiophenol (**2**), 5-Epihyrtiophenol (**3**), 18-Hydroxy-5-epihyrtiophenol (**4**), Arenarol (**6**), and 21-Hydroxy-19-methoxyarenarone (**8**) [150.87 MHz, $CDCl_3$]

carbon	**1**[a]	**1**[b]	**1**[c]	**2**	**3**	**4**	**6**	**8**
C-1	*17.7*	19.9	20.6	20.6	19.8	19.7	23.2	23.2
C-2	27.1	27.1	27.8	26.8	25.0	25.0	25.6	25.6
C-3	121.0	121.0	121.6	121.3	124.3	124.3	32.6	32.6
C-4	143.9	143.9	144.7	144.8	139.9	140.0	155.3	154.1
C-5	*43.1*	38.6	39.2	39.0	37.7	37.7	40.0	40.2
C-6	36.1	36.1	36.7	36.7	37.8	37.8	38.1*[d]	38.5
C-7	28.1	28.1	28.6	28.4	29.5	29.5	28.2	28.6
C-8	38.1	38.1	38.6	36.5	37.6	37.6	38.2*	40.6
C-9	*38.6*	43.1	43.8	42.4	43.9	43.9	44.2	46.3
C-10	48.2	48.2	48.6	46.3	44.9	44.9	47.1	49.6
C-11	32.5	32.5	33.0	37.9	38.2	38.1	38.3*	33.8
C-12	17.3	17.3	18.0	18.3	17.3	17.3	19.8	19.2
C-13	*18.1*	17.7	18.4	18.4	18.4	18.4	18.6	19.0
C-14	*19.9*	20.2	20.9	20.7	32.9	33.0	33.6	33.8
C-15	*20.2*	18.1	18.9	18.8	20.4	20.5	106.5	106.4
C-16	117.8	117.8	118.3	125.7	125.9	126.2	127.2	121.6
C-17	182.4	182.4	183.0	159.6	159.5	149.2	149.4	188.0
C-18	161.8	161.8	162.5	116.0	116.0	143.1	117.0	109.6
C-19	102.0	102.0	102.7	130.0	129.9	114.6	114.5	156.3
C-20	182.0	182.0	182.8	122.7	122.7	121.3	154.1	179.2
C-21	153.4	153.4	154.0	135.9	135.8	128.1	120.0	152.1
C-22	56.8	56.8	57.5	167.8	167.9	168.2		57.0
C-23				52.5	52.5	52.8		

[a] ^{13}C NMR values reported by Kazlauskas et al.[2] [b] Corrected assignments. [c] This work. [d] *These values may be interchanged.

accepted, the ^{13}C NMR spectrum of compound **1** corresponds closely to that of isospongiaquinone, indicating that they are indeed identical. Moreover, it is worth mentioning that when comparing the ^{13}C NMR assignments proposed in the literature for different compounds having in common the *trans*-4,9-friedodrim-3-ene skeleton, it appeared that some confusion exists about the assignments of the quaternary carbon atoms C-5 and C-9. These atoms typically absorb around δ 38.4 and 42.5 (Figure 1). The corresponding signals have been assigned without discrimination to one or the other of these two atoms (see for example refs 2 and 5−8). In this work, we observed in the HMBC spectra of compound **1** clear correlations between the H_2-11 signals and the signals at δ 38.6 (C-8), 48.6 (C-10), 18.0 (C-12), 118.3 (C-16), 153.4 (C-21), and 43.8. Therefore the last signal can be attributed without ambiguity to C-9. No correlation was found between H_2-11 and the signal at δ 39.2. Moreover, the singlet at δ 0.98 attributable to H_3-14 was clearly correlated with signals at δ 144.7 (C-4), 36.7 (C-6), 48.6 (C-10), and 39.2. This last signal can thus be attributed with certainty to C-5. These assigments may be extended to any compound in the series.

From the same sponge, four further minor compounds [hyrtiophenol (**2**), 5-epihyrtiophenol (**3**), 18-hydroxy-5-epihyrtiophenol (**4**), and 18-hydroxyhyrtiophenol (**5**)], incorporating the rearranged drimane skeleton 4,9-friedodrim-3-ene coupled to a methyl benzoate moiety of varying oxidation level, were isolated besides isospongiaquinone (**1**).

Hyrtiophenol (**2**) possessed the molecular formula $C_{23}H_{32}O_3$, as shown by HREIMS (M^+ at m/z 356.2356, calcd 356.2351). The NMR spectral data revealed two substructures consisting of a sesquiterpene and a trisubstituted benzene moiety. The NMR ^{13}C and ^{1}H chemical shifts corresponding to the sesquiterpene substructure (Tables 1 and 2) indicated among others the presence of a secondary methyl, two tertiary methyls, and a trisubstituted double bond bearing one further methyl group. Such a pattern, together with the presence in the mass spectrum of an intense fragment ion at m/z 191.1803 ($C_{14}H_{23}$, calcd 191.1800), is reminescent of the 4,9-friedodrim-3-ene skeleton. The assignment of all hydrogen and carbon signals of **2** was performed by 1D and 2D NMR experiments at 600 MHz (^{1}H, ^{13}C, ^{1}H/^{1}H COSY, HMQC, HMBC). Comparison of the NMR data (Tables 1 and 2) with those of **1** clearly showed that both compounds possessed the same *trans*-4,9-friedodrim-3-ene skeleton, the only significant differences being the replacement of the signals of the aromatic moiety of **1** (C-16 to C-22) with those of a *p*-hydroxybenzoate unit. The presence of the latter was strengthened by comparison between measured and calculated proton chemical shifts[9] as well as by comparison with the NMR data reported by Rodriguez et al. for the aromatic part of dactylosponol.[10] These observations together with the other spectral properties were consistent

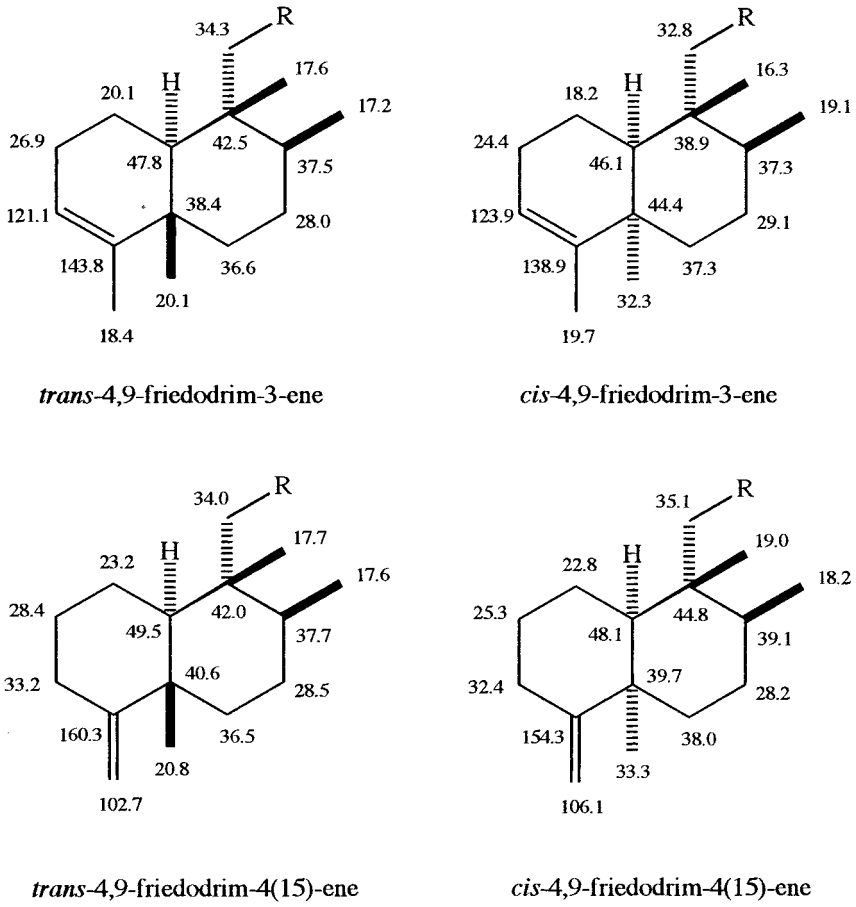

Figure 1. Calculated mean δ ^{13}C for four different 4,9-friedodrimene skeletons found in sponges.

with hyrtiophenol being assigned structure **2**. As expected, acetylation of **2** afforded the monoacetate **9**.

The molecular formula ($C_{23}H_{32}O_3$) determined for **3** by HREIMS indicated that it is isomeric with hyrtiophenol (**2**). Furthermore, the close similarity between the mass spectra fragmentations and the ^{13}C NMR data (Table 2) of **3** and **2** suggested that they were stereoisomers. The only significant variation was the difference of chemical shift of the methyl located at the ring junction (δ H_3C-14, 20.7 for **2** and 32.9 for **3**). This difference is consistent with a *cis* ring junction in **3** rather than a *trans* as in **2**.[11] It follows that compound **3** is 5-epihyrtiophenol. This structure hypothesis was supported by a detailed 2D NMR study (^1H/^1H COSY, HMQC, HMBC) that allowed the assignment of all the ^1H and ^{13}C signals (Tables 1 and 2) as well as by acetylation that afforded the monoacetate **10**.

The ^1H and ^{13}C NMR data of compound **4** (Table 2 and Experimental Section) as well as the presence in its EIMS spectrum of the diagnostic fragment ion at *m/z* 191 suggested the presence of a sesquiterpenic moiety identical with that of 5-epihyrtiophenol (**3**). IR bands at 3339 and 1680 cm^{-1} indicated the presence in the aromatic part of hydroxyl and conjugated ester groups, respectively. Acetylation of **4** with acetic anhydride−pyridine yielded diacetyl compound **11** (M^+ at *m/z* 456 compatible with the molecular formula $C_{27}H_{36}O_6$), indicating the presence of an additional hydroxyl group on the aromatic moiety. Since *meta*-coupling was observed between the two aromatic proton signals of both **4** and **11**, the presence of a 1,3,4,5-tetrasubstituted benzene ring could be deduced. Moreover, the UV spectrum and the ^1H and ^{13}C NMR signals corresponding to the aromatic part of **4** were comparable to those reported for smenodiol[10] and dictyoceratin-A.[12] This led us to conclude that compound **4** is 18-hydroxy-5-epihyrtiophenol.

The UV spectrum and part of the ^1H NMR signals of compound **5** closely resembled those attributable to the aromatic moiety of compound **4**, while the remaining signals resembled those attributable to the sesquiterpenic moiety of compound **2**. These data indicated that **5** is the epimer at C-5 of compound **4**. Acetylation of **5** afforded the diacetylated compound **12**.

Three further sesquiterpene/quinones were isolated from a sample of *H. tubulatus* collected at Curaçao. Indeed, the CH_2Cl_2 soluble fraction from the CH_3OH extract of the sponge yielded, after several successive chromatographies on silica gel, arenarol (**6**) and 5-epiilimaquinone (**7**), two already known sesquiterpene/quinones isolated from the Pacific sponge *Dysidea arenaria*,[3] and from the Pacific sponges *Fenestraspongia* sp.[4] and *Dactylospongia elegans*,[10] respectively. The third compound, **8**, is a new natural product.

The molecular formula determined for compound **8** by accurate mass measurement ($C_{22}H_{30}O_4$) confirmed it to be isomeric with 5-epiilimaquinone (**7**), and the spectral properties confirmed the presence of two substructures consisting of a sesquiterpene and a quinone moiety. The ^1H and ^{13}C NMR data corresponding to the sesquiterpenic part closely resembled those of arenarol (**6**), 5-epiilimaquinone (**7**), and other sesquiterpene/quinones bearing the *cis*-4,9-friedodrim-4(15)-ene skeleton (Figure 1). This established that all these compounds possessed the same sesquiterpenic moiety and that the relative stereochemistry about the ring junction in **8** was *cis* rather than *trans*. Moreover, from the comparison of the spectroscopic data attributable to the aromatic part of compound **8** with those

of 21-hydroxy-19-methoxyavarone (**13**),[2] it was evident that they shared the same *p*-quinone moiety. Compound **8** is thus 21-hydroxy-19-methoxyarenarone. As expected, it yielded monoacetate **14** on acetylation with the mixture pyridine/acetic anhydride.

During the accomplishment of this work we have compiled the ^{13}C NMR data of many sesquiterpene/quinones possessing the *cis*- or *trans*-4,9-friedodrim-4(15)-ene or the *cis*- or *trans*-4,9-friedodrim-3-ene skeletons, all of which are sesquiterpenic moieties often found in sponge secondary metabolites. When we compared the ^{13}C assignments deduced from the detailed 2D measurements we performed with those of the literature, we noted that several erroneous assignments had been reported. The case of isospongiaquinone is a good example of that problem. To clarify the situation, we reassigned, on the basis of our assignments and those in the literature that were based on reliable NMR measurements, the ^{13}C signals for several compounds of the four types of rearranged drimane sesquiterpenes. From the comparison of the data it appeared that the ^{13}C chemical shifts of the carbon atoms of the sesquiterpenic part are very little influenced by the nature of the substituent at C-11. This led us to calculate a mean chemical shift for all carbon atoms of each skeleton. The mean values thus obtained are reported in Figure 1. They can be used to quickly distinguish the four types of skeletons.

The major compound of both species of *Hyrtios* was found to be toxic against *Artemia* larvae. Thus, isospongiaquinone (**1**) had a LD_{50} of 2 mg/L, and 5-epiilimaquinone (**7**) had a LD_{50} of 4 mg/L.

This paper is the first report of *Hyrtios* species (Thorectidae, Dictyoceratida) of sesquiterpene/quinones related to the 4,9-friedodrimane skeleton. Until now, such derivatives had been reported[1,10,13] almost exclusively from Dictyoceratid sponges of the genera *Dysidea* (Dysideidae), *Fasciospongia* and *Smenospongia* (Thorectidae), and *Dactylospongia*, *Fenestraspongia*, *Hippospongia*, *Hyatella*, *Polyfibrospongia*, *Spongia*, and *Stelospongia* (Spongiidae). There is only one report of a 4,9-friedodrimane/quinone from a sponge of another order than the Dictyoceratida, namely, the isolation of siphonodictyoic acid as a minor compound from the burrowing sponge *Siphonodictyon coralliphagum* (Haplosclerida).[14] It seems thus that these compounds may be considered as potential markers for the three aforementioned Dictyoceratida families.

Experimental Section

General Experimental Procedures. HREIMS measurements were performed on a Micromass Autospec 3F instrument. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 600 and 150.87 MHz, respectively, using a Varian Unity 600 instrument. Some ^1H NMR spectra were recorded at 250 MHz on a Bruker WM 250 spectrometer using TMS as internal standard. The IR spectra were obtained on a Bruker IFS 25 instrument as a film on a NaCl disk, and the UV−vis spectra on a Philips PU 8700 spectrophotometer. The optical rotations were measured on a Perkin-Elmer 141 polarimeter (Hg-vapor lamp) in a 10 cm cell at room temperature. Thin-layer chromatography analyses (TLC) were performed on 0.25 mm Polygram silica gel SILG/UV_{254} precoated plates (Macherey Nagel), and column chromatographies over silica gel (MN Kieselgel 0.04−0.063 mm), using the flash technique. HPLC separations were performed on a Waters LCM1 plus apparatus coupled to a Waters 996 photodiode array detector, using a Waters Symmetry RP C18 column (4.6 × 250 mm; 5 μm).

Biological Material. *Hyrtios* sp. was collected by dredging off Mahé, 04°45′ S 55°33′ E, Seychelles, at a depth of 35−45 m (NIOP-E Cruise, stat. 738, December 24, 1992). The voucher, which is incorporated in the collections of the Zoological Museum of Amsterdam, reg. no. 10482, is a firm mass of 8 × 6 × 4 cm attached to a piece of dead coral. The surface is densely and entirely encrusted by shell debris and sand obscuring any surface characteristics. The color was beige-brown outside, but orange inside. A few slightly raised thick-walled oscules of less than 5 mm in diameter occur on one side. The interior is fleshy, but likewise with high content of shell debris and sand. The skeleton consists of a densely and irregularly anastomosing system of debris-filled fibers, which appear laminated in places where the spongin is visible. Fibers are fenestrate-fasciculated, very irregular in outline, 120−250 μm in diameter. The asignment to the genus *Hyrtios* is tentative, based on the debris-filled fibers and firm consistency. No matching descriptions have appeared in the literature.

H. tubulatus was collected by scuba diving off the South coast of Curaçao, Netherlands Antilles, at a depth of 34.9 m. The voucher, which is incorporated in the collections of the Zoological Museum of Amsterdam, reg. no. 13673, is a spongy, compressible mass of tubes of 10 × 10 cm, individual tubes being 2−6 cm high and 2 cm in diameter. Each tube ends in a conspicuous oscule of about 1.5 cm diameter and surrounded by a 1 cm high membrane. The surface is strongly conulose, with conules 2−3 mm high, about 5 mm apart. The color is purplish gray alive, changing to dark gray-brown in methanol while staining it blackish brown. The skeleton consists of a loosely anastomosed system of debris-filled fibers, without clear distinction in primary and secondary fibers, 50−150 μm in diameter. The voucher was compared to the type specimen and found to be similar in all aspects.

Extraction, Isolation, and Spectral Properties. Samples of *Hyrtios* sp. (38 g dry weight) stored in EtOH were exhaustively extracted with MeOH. The MeOH extract was evaporated in vacuo and the residue (15.6 g) partitioned between water and CH_2Cl_2. The organic phase was evaporated to dryness in vacuo to obtain a gum (5.32 g). Part of this gum (2.37 g) was flash chromatographed over a Si gel column using as eluent hexane and increasing amounts of EtOAc. The fraction (370 mg) containing the major compound was further flash chromatographed over a Si gel column using CH_2Cl_2 with increasing amounts of MeOH. This led to isospongiaquinone (**1**; 256 mg; 3.7% of the MeOH extract), which was recrystallized from MeOH. The remaining fractions of the initial column chromatography were combined and flash chromatographed over a Si gel column with hexane/EtOAc (100:0 to 50:50). This afforded two UV positive fractions homogeneous by TLC but each showing two peaks by GC (OV1, 25 m). Further purification of these two fractions by HPLC (UV detection at 210 nm, eluent 90:10 MeOH/H_2O) afforded hyrtiophenol (**2**; 5 mg), 5-epihyrtiophenol (**3**; 3 mg), 18-hydroxy-5-epihyrtiophenol (**4**; 3 mg), and 18-hydroxyhyrtiophenol (**5**; 1 mg).

Specimens of *H. tubulatus* (30 g dry weight) stored in MeOH were exhaustively extracted with MeOH. The MeOH extract was evaporated in vacuo and the residue (11 g) partitioned between water and CH_2Cl_2. The organic phase was evaporated to dryness in vacuo to obtain a gum (2.30 g), which was chromatographed several times over Si gel columns using successively the following mixtures of solvents: toluene/EtOAc, hexane/acetone, and CH_2Cl_2/MeOH. This afforded arenarol (**6**; 3 mg), 5-epiilimaquinone (**7**; 25 mg), and 21-hydroxy-19-methoxyarenarone (**8**; 10 mg).

Isospongiaquinone (1): mp 95−98 °C; $[\alpha]^{20}_{579}$ +64.4° (*c* 0.27 $CHCl_3$); IR (film) 3341, 1652, 1645, 1609, 1243 cm^{-1}; UV (CH_3OH) λ_{max} 213 (9600), 288 nm (13485); UV (CH_3OH/NaOH) λ_{max} 210 (12850), 290 (8930), 526 nm (1650); ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HREIMS *m/z* 358.2151 [M^+] (12, calcd for $C_{22}H_{30}O_4$, 358.2144), 191.1803 (15, calcd for $C_{14}H_{23}$, 191.1800), 168.0423 (41, calcd for $C_8H_8O_4$, 168.0422), 121.1013 (12, calcd for C_9H_{13}, 121.1017), 107.0859 (30, calcd for C_8H_{11}, 107.0861), 95.0861 (100, calcd for C_7H_{11}, 95.0861).

Hyrtiophenol (2): amorphous solid; IR (film) 3311, 1678, 1296 cm^{-1}; UV (CH_3OH) λ_{max} 215 (12990), 262 nm (9250); UV (CH_3OH/NaOH) λ_{max} 210 (18100), 312 nm (14680); ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HREIMS *m/z* 356.2356 [M^+]

(0.2, calcd for $C_{23}H_{32}O_3$, 356.2351), 341.2113 (0.2, calcd for $C_{22}H_{29}O_3$, 341.2117), 325.2164 (2, calcd for $C_{22}H_{29}O_2$, 325.2167), 191.1807 (40, calcd for $C_{14}H_{23}$, 191.1800), 166.0622 (22, calcd for $C_9H_{10}O_3$, 166.0630), 121.1017 (13, calcd for C_9H_{13}, 121.1017), 107.0862 (30, calcd for C_8H_{11}, 107.0861), 95.0861 (100, calcd for C_7H_{11}, 95.0861).

5-Epihyrtiophenol (3): amorphous solid; IR (film) 3357, 1688, 1290 cm^{-1}; UV (CH_3OH) λ_{max} 216 (15075), 262 nm (9945); UV (CH_3OH/NaOH) λ_{max} 210 (19700), 311 nm (16880); ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m/z* 356 (0.3, M^+), 341 (0.6), 325 (7), 191 (90), 166 (52), 121 (37), 107 (43), 95 (100).

18-Hydroxy-5-epihyrtiophenol (4): amorphous solid; IR (film) 3339, 1680, 1303 cm^{-1}; UV (CH_3OH) λ_{max} 221 (17440), 269 (7460), 305 nm (3341, sh); UV (CH_3OH/NaOH) λ_{max} 210 (18520), 241 (13176), 284 (4310), 322 nm (6950); ^1H NMR (600 MHz) δ 7.49 (1H, d, 1.5), 7.45 (1H, d, 1.5), 5.32 (1H, bs), 3.87 (3H, s), 2.84 (1H, d, 14) and 2.60 (1H, d, 14) AB system, 1.64 (3H, bs), 0.98 (3H, d, 6), 0.95 (3H, s), 0.90 (3H, s); ^{13}C NMR, see Table 2.

18-Hydroxyhyrtiophenol (5): amorphous solid; IR (film) 3336, 1695, 1300 cm^{-1}; UV (CH_3OH) λ_{max} 220 (12500), 269 (5510), 305 nm (2580, sh); UV (CH_3OH/NaOH) λ_{max} 209 (12090), 241 (9040), 284 (3145), 322 nm (4805); ^1H NMR (600 MHz) δ 7.44 (1H, bs), 7.40 (1H, bs), 5.14 (1H, bs), 3.85 (3H, s), 2.71 (2H, bs, AB system), 1.49 (3H, bs), 1.02 (3H, d, 6), 1.01 (3H, s), 0.87 (3H, s).

Arenarol (6): amorphous solid; $[\alpha]^{20}_{579}$ +17° (*c* 0.23 CH_2Cl_2); MS and ^1H NMR spectra identical to those described by Schmitz et al.;[3] ^{13}C NMR, see Table 2.

5-Epiilimaquinone (7): amorphous solid; MS, ^1H NMR and ^{13}C NMR spectra identical to those described by Rodriguez et al.[10] and Carté et al.[4]

21-Hydroxy-19-methoxyarenarone (8): amorphous solid; IR (film) 3420, 1675, 1634, 1614, 1236, 1120 cm^{-1}; UV (CH_3OH) λ_{max} 293 (6520), 424 nm (240); ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HREIMS *m/z* 358.2146 [M^+] (2, calcd for $C_{22}H_{30}O_4$, 358.2144), 191.1799 (31, calcd for $C_{14}H_{23}$, 191.1800), 168.0423 (100, calcd for $C_8H_8O_4$, 168.0423), 95.0862 (95, calcd for C_7H_{11}, 95.0861).

Acetylation Reactions. Acetylation of **1** (5 mg) was performed at room temperature during 24 h, using a 1:1 mixture of Ac_2O and pyridine (1 mL). After addition of water (3 mL) and evaporation to dryness in vacuo the solid residue was purified by flash chromatography over a Si gel column using hexane with increasing amounts of EtOAc. This afforded isospongiaquinone acetate (**15**; 5 mg). Acetylation of compounds **2**−**5** and **8** were performed using the same general procedure.

Isospongiaquinone acetate (15): amorphous solid; IR (film) 1785, 1690, 1655, 1599 cm^{-1}; UV (hexane) λ_{max} 273 (12460); ^1H NMR (250 MHz) δ 5.89 (1H, s), 5.14 (1H, bs), 3.82 (3H, s), AB system at 2.65 (1H, d, 14) and 2.43 (1H, d, 14), 2.34 (3H, s), 1.53 (3H, bs), 0.99 (3H, s), 0.91 (3H, d, 6), 0.83 (3H, s); EIMS *m/z* 400 (1, M^+), 358 (6), 340 (19), 210 (22), 191 (27), 189 (30), 168 (61), 121 (27), 107 (48), 95 (100).

Hyrtiophenol acetate (9): amorphous solid; ^1H NMR (250 MHz) δ 7.91 (1H, dd, 8.5/2), 7.87 (1H, d, 2), 7.07 (1H, d, 8.5), 5.15 (1H, m), 3.89 (3H, s), 2.63 (2H, bs, AB system), 2.34 (3H, s), 1.54 (3H, bs), 1.02 (3H, s), 0.99 (3H, d, 6), 0.87 (3H, s); EIMS *m/z* 398 (0.25, M^+), 367 (2), 325 (1), 191 (47), 107 (45), 95 (100).

5-Epihyrtiophenol acetate (10): amorphous solid; ^1H NMR (250 MHz) δ 7.89 (2H, m), 7.08 (1H, d, 8.5), 5.34 (1H, m), 3.91 (3H, s), AB system at 2.75 (1H, d, 14) and 2.54 (1H, d, 14), 2.35 (3H, s), 1.64 (3H, bs), 0.97 (3H, d, 7), 0.95 (3H, s), 0.91 (3H, s); EIMS *m/z* 398 (0.4, M^+), 383 (0.6), 367 (1.6), 325 (2), 191 (75), 95 (100).

18-Hydroxy-5-epihyrtiophenol diacetate (11): amorphous solid; ^1H NMR (250 MHz) δ 7.82 (1H, d, 2.5), 7.75 (1H, d, 2.5), 5.32 (1H, m), 3.90 (3H, s), AB system at 2.76 (1H, d, 14) and 2.54 (1H, d, 14), 2.35 (3H, s), 2.28 (3H, s), 1.65 (3H, bs), 0.96 (3H, d, 7), 0.95 (3H, s), 0.92 (3H, s); EIMS *m/z* 456 (0.3, M^+), 441 (0.3), 425 (1.2), 383 (1.5), 191 (75), 95 (100).

18-Hydroxyhyrtiophenol diacetate (12): amorphous solid; ^1H NMR (250 MHz) δ 7.81 (1H, d, 2.5), 7.75 (1H, d, 2.5), 5.30 (1H, m), 3.88 (3H, s), 2.63 (2H, bs, AB system), 2.33 (3H, s), 2.28 (3H, s), 1.50 (3H, bs), 1.02 (3H, s), 0.97 (3H, d, 7), 0.86 (3H, s); EIMS *m/z* 456 (0.5, M^+), 425 (1.1), 383 (1.3), 191 (58), 95 (100).

21-Hydroxy-19-methoxyarenarone acetate (14): amorphous solid; IR (film) 1782, 1692, 1650, 1612, 1187 cm^{-1}; ^1H NMR (250 MHz) δ 5.94 (1H, s), 4.71 (1H, bs), 4.68 (3H, bs), 3.83 (3H, s), AB system at 2.59 (1H, d, 13) and 2.44 (1H, d, 13), 2.34 (3H, s), 1.08 (3H, s), 0.88 (3H, s), 0.86 (3H, d, 6); EIMS *m/z* 400 (3, M^+), 358 (7), 211 (15), 191 (35), 168 (98), 95 (100).

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