Chemistry of Natural Compounds, Vol. 47, No. 1, March, 2011 [Russian original No. 1, January–February, 2011]

SESQUITERPENE QUINONES FROM A VIET NAM SEA SPONGE *Spongia* SP.

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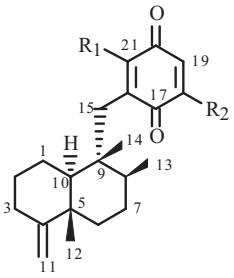
UDC 547.567+547.913.5+593.4

The $CHCl_3$ extract from a Viet Nam sea sponge *Spongia* species (Order Dictyoceratida) that was collected during the fifth cruise of the RS Akademik Oparin was investigated in a search for antioxidants in marine organisms.

The sea sponge (100 g) was extracted with $CHCl_3$. The extract was separated over a column of Sephadex LH-20 using $CHCl_3$:MeOH (3:1) to afford **1** (35 mg), which was active for trapping DPPH radicals (2,2-diphenyl-1-picrylhydrazyl). Inactive compounds **2** (300 mg) and **3** (35 mg) were also isolated. These were readily identified as ilimaquinone [1, 2] and smenospongiarin [3].



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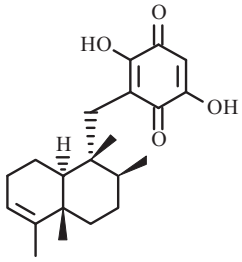

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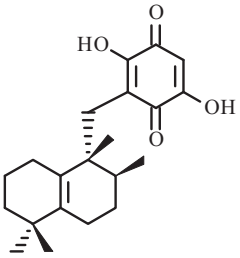

6

1: $R_1 = R_2 = OH$
2: $R_1 = OH$, $R_2 = OCH_3$
3: $R_1 = OH$, $R_2 = NHCH_2CH_2CH(CH_3)_2$
4: $R_1 = R_2 = OCH_3$

Compound **1**, orange crystals, mp >350°C ($CHCl_3$:EtOH), $[\alpha]_D^{20}$ –9.8° (*c* 0.46, $CHCl_3$), showed a peak for the molecular ion with *m*/*z* 344.1991 (HR-EI-MS) that corresponded to the empirical formula $C_{21}H_{28}O_4$. The PMR spectrum of **1** (Table 1) was very reminiscent of that of **2**. The difference was the lack of a methoxyl resonance in the spectrum of **1**. However, the ^{13}C NMR spectrum showed resonances for only 17 C atoms. 2D NMR spectroscopy experiments (HSQC, HMBC) enabled all resonances of the sesquiterpenoid part to be assigned. These agreed fully with the corresponding resonances of **2** [1, 4].

Methylation of **1** by diazomethane in Et_2O gave the corresponding dimethyl ether **4**, $[\alpha]_D^{20}$ –27° (*c* 0.59, $CHCl_3$), the spectral properties of which agreed with the literature for the synthetic methyl ether of **2** [5] and the dimethyl ether of smenoquinone (**1**), which was isolated from a sea sponge *Smenospongia* species [3]. Thus, it was confirmed that **1** was smenoquinone. Table 1 presents the full assignment of proton and carbon resonances in smenoquinone and its dimethyl ether [3, 5] because these have not been reported.

A comparison of the PMR and ^{13}C NMR spectra of **1** taken in CD_3OD with the published spectra for smenoquinone [3] showed that the resonances in the quinoid parts of the molecules were different. Thus, the ^{13}C NMR spectrum of **1** showed only the resonance for C-16 (δ 117.7) for the quinoid ring C atoms, in contrast with the published spectrum for the same C atoms in smenoquinine [δ 114.45 (C-16), 182.82 (C-17), 179.65 (C-18), 101.79 (C-19), 174.72 (C-20), 166.80 (C-21)] in CD_3OD [3]. The PMR spectrum of **1** lacked a resonance for quinoid proton H-19, in contrast with the published value for this proton at δ 5.71 [3].

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0009-3130/11/4701-0135

Table 1. ^{13}C NMR (125 MHz), PMR (500 MHz), and HMBC Spectra of **1** and **4** ($CDCl_3$)

C atom	**1**			**4**		
	δ_C	δ_H (J/Hz)	HMBC	δ_C	δ_H (J/Hz)	HMBC
1	23.3 (CH_2)	2.08 m, 1.47 m	3, 5, 9	23.2 (CH_2)	2.08 m, 1.47 m	3, 5, 9
2	28.7 (CH_2)	1.87 m, 1.16 m	4, 10	28.5 (CH_2)	1.86 m, 1.16 m	4, 10
3	32.9 (CH_2)	2.33 m, 2.08 m	1, 5, 11	32.9 (CH_2)	2.32 m, 2.08 m	1, 5, 11
4	160.2 (C)			160.3 (C)		
5	40.5 (C)			40.6 (C)		
6	36.7 (CH_2)	1.53 m, 1.37 m	4, 8, 10, 12	36.6 (CH_2)	1.53 m, 1.39 m	4, 8, 10, 12
7	27.9 (CH_2)	1.41 m	5, 9, 13	28.1 (CH_2)	1.42 m	5, 9, 13
8	38.2 (CH)	1.16 m	6, 10, 14, 15	38.3 (CH)	1.17 m	6, 10, 14, 15
9	43.3 (C)			43.6 (C)		
10	50.2 (CH)	0.75 (d, J = 11.7)	2, 5, 9, 12, 14, 15	50.7 (CH)	0.74 (d, J = 11.7)	2, 5, 9, 12, 14, 15
11	102.8 (CH_2)	4.45 m	3, 4, 5	102.7 (CH_2)	4.44 m	3, 4, 5
12	20.6 (CH_3)	1.05 s	4, 5, 6, 10	20.6 (CH_3)	1.04 s	4, 5, 6, 10
13	17.9 (CH_3)	0.97 (d, J = 6)	7, 8, 9	18.0 (CH_3)	0.93 (d, J = 6.5)	7, 8, 9
14	17.3 (CH_3)	0.85 s	8, 9, 10, 15	17.3 (CH_3)	0.83 s	8, 9, 10, 15
15	32.6 (CH_2)	2.54 (d, J = 14), 2.45 (d, J = 14)	8, 9, 10, 14, 16	32.8 (CH_2)	2.53 (d, J =13.3), 2.46 (d, J = 13.3)	8, 9, 10, 14, 16, 17, 21
16	114.9 (C)			128.9 (C)		
17	170 (C)[a]			182.7 (C)		
18	170 (C)[a]			159.3 (C)		
19	102.1 (CH)	6.02 s		105.2 (CH)	5.72 s	17, 18, 21
20	170 (C)[a]			183.4 (C)		
21	170 (C)[a]			157.5 (C)		
22				56.5 (CH_3)	3.80 s	18
23				60.9 (CH_3)	4.01 s	21
OH		7.87 br.s				

[a]Observed as a very broad resonance in the processed spectrum (LB = 30 Hz).

The ^{13}C NMR spectrum of **1** taken in $CDCl_3$ lacked resonances for four C atoms of the quinoid ring (C-17, C-18, C-20, and C-21) that were bonded to O atoms. The lack of these resonances in ^{13}C NMR spectra ($CDCl_3$) was noted earlier for acid-rearrangement products of ilimaquinone, i.e., **5** [δ 115.1 (C-16), 102.1 (C-19)] [6] and **6** [δ 115.8 (C-16), 102.3 (C-19)] [6]. The ^{13}C NMR spectrum ($CDCl_3$) of natural dihydroxyavarone **5** [δ 121.8 (C-16), 185.4 (C-17), 152.7 (C-18), 130.6 (C-19), 181.8 (C-20), 144.5 (C-21)] that was isolated from the sea sponge *Dysidea cinerea* [7] had chemical shifts for the quinoid C atoms that did not agree with those for smenoquinone isolated from the sea sponge *Smenospongia* sp. [3], **5** [6], **6** [6], and **1**.

A literature search for other examples of 3-substituted 2,5-dihydroxy-1,4-benzoquinones revealed a series of 2,5-dihydroxy-3-alkyl-1,4-benzoquinones isolated from plants of the genus *Embelia* [8, 9]. The ^{13}C NMR spectra of these compounds gave resonances for *O*-containing quinoid C atoms as a very broad peak at δ 170 and chemical shifts for the other C atoms (δ 117.0, 102.2) that agreed with those of C-16 and C-19 in **1**. Expansion of the resonance lines by processing the ^{13}C NMR spectrum of **1** (use of exponential window function LB = 30 Hz) showed in the spectrum also a broad resonance at δ 170. The lack of a resonance for H-19 in the PMR spectrum (CD_3OD) of **1** was due to replacement of quinoid H-19 with deuterium. In fact, adding CD_3OD to the $CDCl_3$ solution of **1** caused the resonance of not only the hydroxyl protons at δ 7.87 but also that of quinoid H-19 at δ 6.02 to disappear. Replacement of H-19 with deuterium also explained the lack of a resonance for C-19 in the ^{13}C NMR spectrum taken in CD_3OD.

The antioxidant activity of **1** was tested using bleaching of solutions of DPPH radical [10] and $ABTS^{\bullet+}$ [2,22-azinobis (3-ethylbenzothiazolin-6-sulfonic acid)] [11]. Compound **1** exhibited moderate activity for trapping DPPH radicals (IC_{50} 3.7×10^{-4} M) that was comparable with that of ionol (IC_{50} 3.6×10^{-4} M). The antioxidant activity of **1** for reduction of $ABTS^{\bullet+}$ radical cations corresponded to 0.15 mmol/L of trolox equivalents (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid).

ACKNOWLEDGMENT

The work was supported by Grant 09-III-A-05-145 (FEB RAS) and the RAS Presidium Program "Molecular and Cellular Biology."

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