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XESTOSAPROL C, A NEW PENTACYCLIC HYDROQUINONE SULFATE FROM A MARINE SPONGE *XESTOSPONGIA SAPRA*

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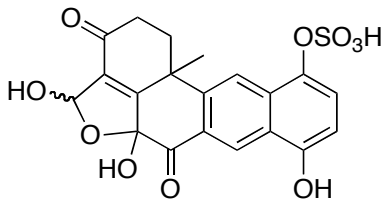
Abstract - A new pentacyclic hydroquinone sulfate with a 2,5-dihydro-2,5-furandiol ring, xestosaprol C (**1**), has been isolated from an Okinawan marine sponge *Xestospongia sapra*. The structure of **1** was elucidated by the spectroscopic data.

INTRODUCTION

Marine sponges are a rich source of bioactive secondary metabolites with unprecedented skeletons.[1] A variety of pentacyclic quinone and hydroquinone compounds with antimicrobial, cardiotonic, and cytotoxic activities, have been isolated from marine sponges of the genera *Xestospongia*[2-5] and *Adocia*.[6] In our continuing search for bioactive metabolites from marine sponges,[7] we have isolated a new pentacyclic hydroquinone sulfate with a 2,5-dihydrofuran-2,5-diol ring, xestosaprol C (**1**), from the sponge *Xestospongia sapra* (SS-241). Here we describe the isolation and structure elucidation of **1**.



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RESULTS AND DISCUSSION

The sponge (SS-241) collected off Kerama Islands, Okinawa, was extracted with MeOH. The MeOH extract was partitioned between EtOAc and H_2O, and the aqueous layer was subsequently extracted with *n*-BuOH. Repeated purification of *n*-BuOH-soluble materials with SiO_2 gel column chromatographies

furnished xestosaprol C (**1**, 0.0001%, wet weight) together with a known related compound, halenaquinol sulfate.[4]

Xestosaprol C (**1**) {$[\alpha]_D^{24}$ -9.9 (*c* 1.0, MeOH)} was obtained as a yellowish amorphous solid. The molecular formula, $C_{20}H_{16}O_{10}S$, of **1** was established by HRESIMS [*m/z* 447.03647 $(M-H)^-$, Δ -2.12 mmu]. UV absorptions (λ_{max} 219, 277, and 398 nm) of **1** were similar to those of halenaquinol sulfate.[4] IR absorptions indicated the existence of OH (3261 cm^{-1}) and carbonyl (1684 and 1627 cm^{-1}) functionalities. The molecular formula and the chromatographic behavior of **1** suggested the presence of a sulfate group, which was supported by IR absorptions (1347 and 1108 cm^{-1}).[5] In the ^1H and ^{13}C NMR spectra of **1** (Table 1) a pair of signals were observed due to the presence of an epimeric hydroxyl group at C-1. The ^1H NMR (Table 1) spectrum of **1** showed signals due to a methyl group (CH_3-20), aromatic protons (H-11, H-14, H-15, and H-18), and methylene protones (H_2-4 and H_2-5). The ^{13}C NMR spectrum of **1** revealed signals due to two carbonyl carbons, eight sp^2 quaternary carbons, four sp^2 methines, two sp^3 quaternary

Table 1. ^1H and ^{13}C NMR Data for Xestosaprol C (**1**).

Position	δ_C [a]		δ_H [a]	δ_H [b]
1	101.7, 101.7 [c]	t	6.10 (s), 6.37 (s) [c]	5.89 (d, 7.7), 6.16 (d, 9.1) [c]
1-OH				7.05 (d, 7.7), 6.70 (d, 9.1) [c]
2	136.8, 137.4 [c]	s		
3	196.9, 197.0 [c]	s		
4a	37.7, 38.0 [c]	t	2.58 (m)	2.07 (m)
4b			3.01 (m)	2.07 (m)
5a	40.7, 41.3 [c]	t	2.23 (m)	2.89 (m)
5b			2.81 (m)	2.89 (m)
6	39.8, 40.0 [c]	s		
7	164.4, 164.9 [c]	s		
8	104.0, 105.3 [c]	s		
8-OH				7.69 (s), 7.87 (s) [c]
9	193.8	s		
10	146.0	s		
11	127.1, 127.2 [c]	d	8.96 (s), 9.01 (s) [c]	8.72 (s), 8.76 (s) [c]
12	134.1	s		
13	154.7	s		
13-OH				10.44 (brs)
14	109.5	d	6.82 (d, 8.6)	6.82 (d, 8.4)
15	126.0	d	7.52 (d, 8.6)	7.33 (d, 8.4)
16	142.5	s		
17	128.7	s		
18	122.8	d	8.42 (s), 8.43 (s) [c]	8.19 (s), 8.21 (s) [c]
19	146.1	s		
20	27.1, 27.5 [c]	q	1.96 (s), 2.01 (s) [c]	1.96 (s), 2.01 (s) [c]

[a] in CD_3OD. [b] in DMSO-d_6. [c] signals due to a minor isomer.

carbons, an sp^3 methine, two sp^3 methylenes, and a methyl group. Among them, two sp^2 quaternary carbons (δ_C 154.7, δ_C 142.5) were ascribed to those bearing an oxygen atom, while two pare of sp^3 quaternary carbons (δ_C 101.0 and 101.7, and 104.0 and 105.3) were assigned as hemiacetal carbons.

The ^{1}H-^{1}H COSY spectrum of **1** revealed connectivities of C-1 to 1-OH, C-4 to C-5, and C-14 to C-15 as shown in Figure 1. HMBC correlations of H-11 to C-13 and C-19, H-14 to C-12 and C-13, H-15 to C-16 and C-17, and H-18 to C-10 and C-16 indicated the existence of a naphthalene ring (C-10 to C-19). The HMBC correlation of H_2-5 to C-3 suggested the connection of C-3 to C-4, while connectivities of C-5, C-7, C-19, and C-20 to C-6 were implied by HMBC cross-peaks of H_3-20 to C-5, C-6, C-7, and C-19, and H-18 to C-6. HMBC cross-peaks of H-1 to C-7 and C-8 revealed connectivities of C-1 to C-8 via O-1 and C-1 to C-7 via C-2, respectively. Connections of C-7 and C-9 to C-8 were deduced from HMBC correlations of 8-OH to C-7, C-8, and C-9, while connectivities of C-8 and C-10 to C-9 were implied by HMBC cross-peaks of 8-OH and H-11 to C-9. The presence of a sulfate group at C-16 was deduced from comparison of ^{13}C NMR data of C-13 (δ_C 154.7) and C-16 (δ_C 142.5) for **1** with those of C-13 (δ_C 150.8) and C-16 (δ_C 141.1) for halenaquinol sulfate,[4] which was supported by a NOESY correlation observed between a methoxy group at C-13 and H-14 of 13-*O*-methyl derivative of **1** (Scheme 1). Thus, the gross structure of xestosaprol C was elucidated to be **1**.

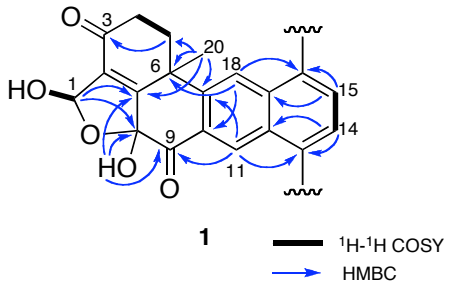
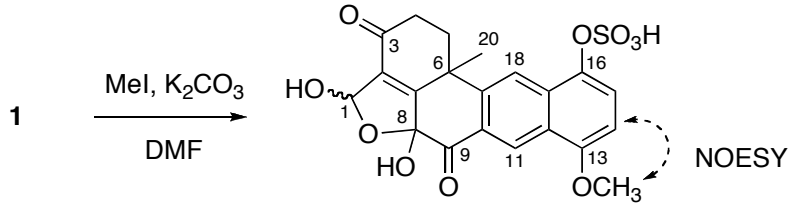


Figure 1. Selected 2D NMR correlations for xestosaprol C (**1**).



Scheme 1. Methylation at 13-OH of xestosaprol C (**1**)

Molecular mechanics calculations for four possible diastereomers of **1** were carried out by using Sybyl 6.5 (MMFF94 force-field),[8] indicating that two diastereomers with a *syn*-relationship between CH_3-20 and 8-OH were relatively more stable than the other two possible diastereomers with an *anti*-relationship between CH_3-20 and 8-OH.

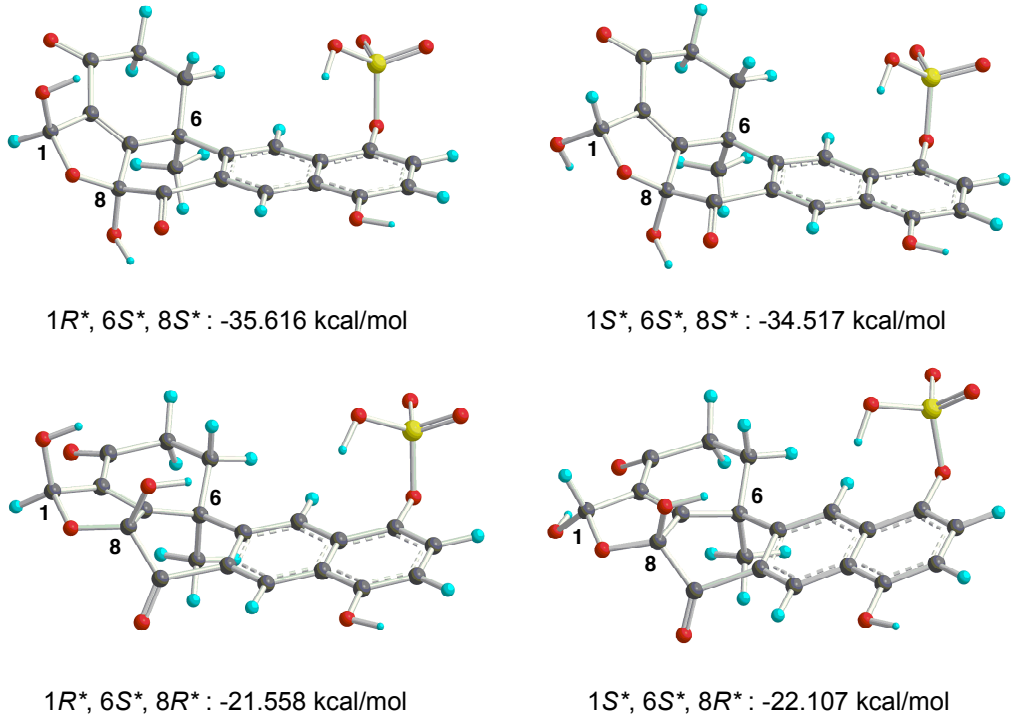


Figure 2. Minimum energy for four possible stereoisomers for xestosaprol C (**1**).

Xestosaprol C (**1**) is a new pentacyclic hydroquinone sulfate with a 2,5-dihydrofuran-2,5-diol ring, although some related compounds have been isolated from marine sponges.[2-6] Biological activity of **1** is currently investigated.

EXPERIMENTAL

General Experimental Procedures

Optical rotation was recorded on a JASCO P-1030 polarimeter. IR and UV spectra were recorded on a JASCO FT/IR-5300 spectrophotometers and Shimadzu UV-1600PC, respectively. ^{1}H, ^{13}C and 2D NMR spectra were measured on a JEOL JMN-EX400, a JEOL ECA500, and a Bruker AMX-600 spectrometers. The 3.35 and 49.8 ppm resonances of residual CD_3OD and 2.49 and 39.5 ppm resonances of residual DMSO-d_6 were used as internal references for ^{1}H and ^{13}C NMR spectra, respectively. ESI mass spectra were obtained on a JEOL JMS-700TZ spectrometer.

Collection, Extraction, and Isolation

The sponge *Xestospongia sapra* (SS-241) was collected off Kerama Islands, Okinawa, and kept frozen until used. The sponge (1.6 kg, wet weight) was extracted three times with MeOH (3 L) and then evaporated to give a residue (103 g). The extract was partitioned between EtOAc (500 mL x 3) and H_2O (1 L), and then H_2O-soluble portion was extracted with *n*-BuOH (500 mL x 3). A part (2.0 g) of the *n*-BuOH-soluble fraction (7.56 g) was purified repeatedly by silica gel column chromatographies (Wako gel C-300, Wako Pure Chemical, 2 x 30 cm) with $CHCl_3$/MeOH/H_2O/AcOH to afford xestosaprol C (**1**, 0.0001%, wet weight) and halenaquinol sulfate.

Xestosaprol C (1): yellowish amorphous solid; $[\alpha]_D^{24}$ -9.9 (*c* 1.0, MeOH); IR (film) ν_{max} 3261, 1684, 1627, 1347, and 1108 cm^{-1}; UV (MeOH) λ_{max} 219 nm (ε 23000), 277 (20400), and 398 (2900); ^1H and ^{13}C NMR (see Table 1); ESIMS *m/z* 447 $(M-H)^-$, HRESIMS *m/z* 447.03647 [calcd. for $C_{20}H_{15}O_{10}S$, $(M-H)^-$, 447.03859].

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