Communications to the Editor

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HALENAQUINOL AND HALENAQUINOL SULFATE, PENTACYCLIC HYDROQUINONES FROM THE OKINAWAN MARINE SPONGE *XESTOSPONGIA SAPRA*

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Two new pentacyclic hydroquinones named halenaquinol (1) and halenaquinol sulfate (2) were isolated from the Okinawan marine sponge *Xestospongia sapra* and their structures were elucidated on the basis of chemical and physicochemical evidence which included a quantitative photo-oxidative conversion of 1 to halenaquinone (3).

KEYWORDS —— halenaquinol; halenaquinol sulfate; hydroquinone containing pentacyclic acetogenin; marine sponge; *Xestospongia sapra*; hydroquinone photo-oxidation

In a continuing search for new bioactive substances from marine organisms,[1] we have isolated two new yellow pigments of pentacyclic hydroquinone acetogenins named halenaquinol (1) and halenaquinol sulfate (2) from the Okinawan marine sponge *Xestospongia sapra*. This paper reports the elucidation of their structures.[2]

An acetone extract of the titled fresh sponge (collected in July at Zamami-jima, Okinawa Prefecture) was partitioned in a water-AcOEt mixture and the water phase was further partitioned with n-BuOH. Since the constituents in the organic phases were found to be photo-sensitive, the chromatographic separations were carried out in the dark. Lobar column chromatography (LiChroprep DIOL, hexane-AcOEt) of the AcOEt soluble portion furnished halenaquinol (1) (30% from the AcOEt extract), whereas TOYOPEARL HW-40 (super fine) column chromatography (MeOH) of the n-BuOH soluble portion furnished halenaquinol sulfate (2) (36% from the n-BuOH extract).

Halenaquinol (1), a yellow solid, $C_{20}H_{14}O_5$,[3] $[\alpha]_{577}$ +179° (acetone), was fairly unstable for light and heat (even at 40°C). It showed complex UV absorption maxima (MeOH) at 228 nm (ε 36000), 284 (sh) (20000), 302 (23000), and 431 (4000), suggestive of the presence of a polycyclic ring system with aromatic ring(s) in 1. The IR spectrum (KBr) of 1 showed hydroxyl [3360 (br) cm^{-1}] and conjugated carbonyl (1656, 1627 cm^{-1}) absorption bands.

The ^{1}H-NMR spectrum (d_6-DMSO)[4] of halenaquinol (1) showed three one-proton singlets assignable to aromatic protons [δ 9.04 (11-H), 8.75 (1-H), 8.31 (18-H)],

an AB quartet due to two neighboring aromatic protons on a *p*-hydroquinone skeleton (δ 6.97, 6.87, both 1H, J=8.0 Hz, 14,15-H), a three-proton singlet due to a methyl group (δ 1.65, 6-CH_3), and signals ascribable to methylene protons [δ 2.29 (1H m), 2.5-3.0 (3H m)].

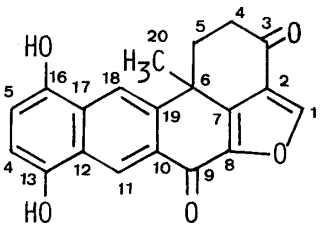
Acetylation of halenaquinol (1) afforded an amorphous diacetate (4), $C_{24}H_{18}O_7$, IR (1764, 1695, 1678 cm^{-1}), δ ($CDCl_3$): 2.58, 2.55 (both 3H s), 7.42, 7.34 (both 1H ABq, J=8.5 Hz, 14,15-H), whereas reduction of 1 with $NaBH_4$-$CeCl_3$[5] at -78°C in MeOH furnished a dihydro derivative (5), $C_{20}H_{16}O_5$ [δ 4.76 (1H m, 3-H) in CD_3OD]. Halenaquinol (1) was readily decomposed in the air. However, irradiation of its acetone solution (in a quartz tube) with a fluorescent lamp (15 W) at 20°C for 12 h provided a quinone, *m/z* 332 (M^+), δ (d_6-DMSO) 7.16 (2H s, 14,15-H). The physicochemical data (including the optical rotation) for this photo-oxidized product were found to be identical with those reported for halenaquinone (3),[6] which was isolated as an antibiotic principle from the Hawaiian marine sponge *Xestospongia exigua* and the structure was determined by X-ray analysis.[7] Consequently, the structure of halenaquinol has been determined as 1 comprising a *p*-hydroquinone moiety.

Halenaquinol sulfate (2), a yellow solid, $[\alpha]_{577}$ +106° (MeOH), gave a UV absorption spectrum: λ_{max}^{MeOH} nm (ε): 225 (41000), 275 (20000), 296 (22000), 318 (sh) (12000), 398 (6000), and ^{1}H-NMR signals (d_6-DMSO): δ 9.04 (1H s, 11-H), 8.75 (1H s, 1-H), 8.38 (1H s, 18-H), 7.49, 6.92 (both 1H d, J=8.0 Hz, 14,15-H), 1.67 (3H s, 6-CH_3), 2.2-2.8 (4H m). These spectral properties are very similar to those of 1. The SIMS (glycerol) of 2 gave ion-peaks at *m/z* 437 $(M+H)^+$, 459 $(M+Na)^+$, 529 (M+H+glycerol)$^+$, and 551 (M+Na+glycerol)$^+$. Solvolysis of 2 with DMSO at 35°C furnished halenaquinol (1) quantitatively.[8] Thus, 2 has been shown to be a Na salt of a monosulfate of halenaquinol (1).

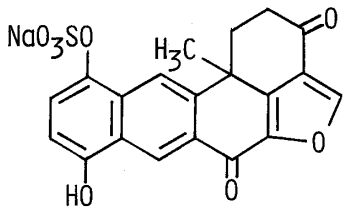
In order to determine the location of the sulfate group in 2, we have undertaken extensive ^{13}C-NMR studies including selective decoupling experiments and low power selective decoupling (LPSD) experiments monitored by ^{13}C-^{1}H long-range couplings.[9] Thus, in the ^{13}C-NMR spectrum of halenaquinol (1), upon D_2O treatment, signals due to C-12 and C-17 were observed as St while signals due to C-14 and C-15 were deformed. When respective proton signals were irradiated in the LPSD method, the following ^{13}C-^{1}H long-range couplings were eliminated: *e.g.* irr. at 1-H: C-2 & C-8 → Ss, C-7 → deformed; irr. at 4,5-H: C-3 → Ss; irr. at 11-H: C-9 → Ss, C-17 → Sd, C-13 → deformed; irr. at 14,15-H: C-12 & C-17 → Sd, C-13 & C-16 → deformed: irr. at 18-H: C-10 → Ss, C-12 & C-16 → deformed. Furthermore, comparisons in detail of the ^{13}C-NMR data for 2-5 have led us to assign carbon signals of 1-5 as shown in Table I.

In the ^{13}C-NMR spectrum of halenaquinol sulfate (2), when the signal due to 11-H (δ 9.04, s) was irradiated by the LPSD method, signals due to C-9 and C-17 were altered to Ss and Sd, respectively, and signals due to C-13 and C-19 were deformed, whereas irradiation of 18-H signal (δ 8.38, s) resulted in changes of C-10 and C-12 signals to Ss and St and deformation of C-16 signal. Furthermore, the *ipso* and *meta* carbon signals of the sulfated hydroxyl group were observed in a higher field and the *ortho* and *para* carbon signals in a lower field in the ^{13}C-NMR spectrum of 2 as compared with that of 1.

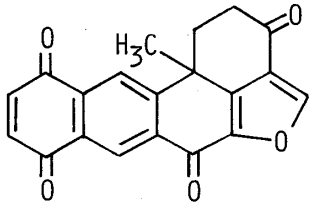
Based on the above-described evidence, the location of the sulfate group in



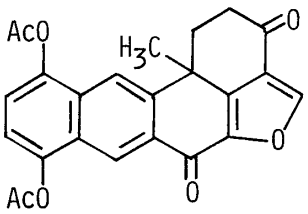
halenaquinol (1)



halenaquinol sulfate (2)



halenaquinone (3)



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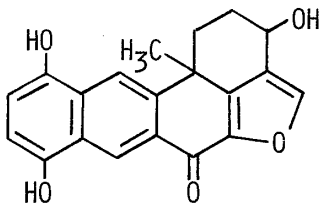

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Table I. ^{13}C-NMR Data for 1, 2, 3, 4, and 5[a)]

Carbon	1	2	3	4	5
1	150.0 Ds	150.4 Ds	150.8 Ds	150.1 D	147.2 Dd
2	122.4 Sd	122.4 Sd	122.3 Sd	122.2 S	126.3 Sd
3	192.3 Sm	192.3 Sm	191.3 Sm	191.5 S	61.5 Dm
4	36.7 Tm	36.5 Tm	36.2 Tm	36.3 T	32.9 Tm
5	33.7 Tm	33.8 Tm	32.2 Tm	32.8 T	30.5 Tm
6	35.6 Sm	35.7 Sm	36.6 Sm	35.9 S	36.2 Sm
7	143.7 Sm	144.5 Sm	148.3 Sm	143.6 S	145.4 Sm
8	144.9 Sd	144.8 Sd	143.8 Sd	144.9 S	144.1 Sd
9	172.2 Sd	172.0 Sd	169.6 Sd	170.7 S	172.3 Sd
10	129.5 Sd	129.5 Sd	136.2 Sd	131.4 S	130.4 Sd
11	124.1 Ds	123.9 Ds	125.0 Ds[c)]	122.3 D	124.0 Ds
12	123.5 Sq	123.4 Sq	130.0 St[d)]	125.3 S	123.7 Sq
13	147.3 Sm	151.4 Sm	183.9 Sm[e)]	145.9 S[c)]	147.5 Sm[c)]
14	112.0 Dd[c)]	108.4 Dd	139.0 Ds	121.1 D[d)]	111.8 Dd[d)]
15	109.0 Dd[c)]	121.6 Ds	139.0 Ds	118.6 D[d)]	108.9 Dd[d)]
16	145.3 Sm	141.1 Sm	183.5 Sm[e)]	144.2 S[c)]	145.4 Sm
17	126.5 Sq	130.0 St	133.3 St[d)]	128.1 S	126.5 Sq
18	119.0 Ds	120.3 Ds	123.6 Ds[c)]	118.8 D	118.1 Ds
19	147.7 Sm	147.8 Sm	154.3 Sm	147.8 S	147.4 Sm[c)]
20	31.9 Qm	31.7 Qm	29.8 Qm	31.0 Q	34.7 Qm

a) Measured at 22.5 MHz in d_6-DMSO.
b) Abbreviations given in the columns denote the signal patterns (capital letters refer to the pattern arising from directly bonded protons, and lower-case letters to long-range ^{13}C-^{1}H coupling): S or s = singlet, D or d = doublet, T or t = triplet, Q or q = quartet, m = multiplet.
c)~e) These assignments may be interchanged.

halenaquinol sulfate has been shown to be attached to the 16-OH of halenaquinol (1) and consequently, the structure of halenaquinol sulfate has been elucidated as 2. The absolute configurations at C-6 in halenaquinol (1) and halenaquinol sulfate (2) are now under investigation.

We have extensively examined the constituents of the titled marine sponge by TLC. However, we could not detect halenaquinone (3) in our sponge extracts. Taking into consideration the reported isolation procedure of halenaquinone (3) from the marine sponge *Xestospongia exigua*[7] and the present facile conversion of halenaquinol (1) to 3 either by irradiation or heating in the air, halenaquinone (3) seems to be a secondary product which may be formed during the isolation procedure.

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2) Presented at the 34th Annual Meeting of Kinki Branch, the Pharmaceutical Society of Japan, Nishinomiya, Nov. 3, 1984. Abstract Papers p. 51.
3) The molecular compositions of compounds with the chemical formulae were determined by high resolution mass spectrometry.
4) The ^{1}H-NMR spectra were measured at 90 MHz except halenaquinol diacetate (4) which was measured at 500 MHz.
5) J. Luche, L. Rodriguez-Hahn, and P. Crabbé: J. Chem. Soc., Chem. Commun., 1978, 601.
6) The chemical shifts in the ^{13}C-NMR spectra of both compounds were identical. However, some of our assignments (Table I) are different from those reported by Roll, *et al.*[7]
7) D. M. Roll, P. J. Scheuer, G. K. Matsumoto, and J. Clardy, J. Am. Chem. Soc., 105, 6177 (1983).
8) The sample of halenaquinol sulfate (2) was hygroscopic and the sulfate linkage was actually hydrolyzed during the procedure to yield 1.
9) E. Breitmaier and W. Voelter, "^{13}C-NMR Spectroscopy: Methods and Applications," 2nd ed., Verlag Chemie, Weinheim, New York, 1978, pp. 92-101.

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