Xesto- and Halenaquinone Derivatives from a Sponge, *Adocia* sp., from Truk Lagoon[1]

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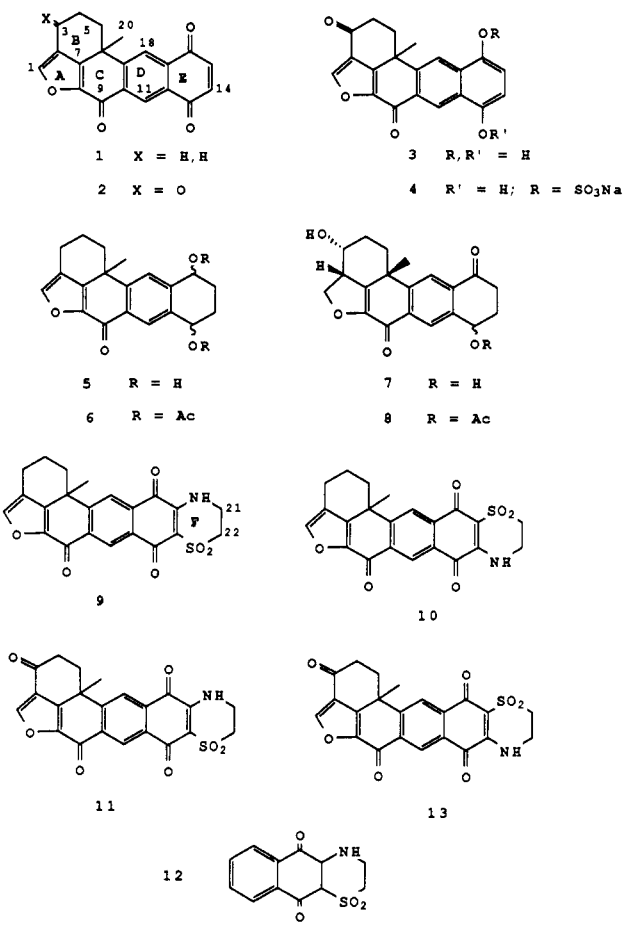
Partially reduced derivatives of the novel quinones xestoquinone (1) and halenaquinone (2) have been isolated from an *Adocia* sp. sponge from Truk Lagoon. In addition, three derivatives of 1 and 2 which each possess an added 1,1-dioxo-1,4-thiazine ring have been isolated. Structures for the latter compounds were confirmed by synthesis from 1 and 2. Cytotoxicity data are reported.

The quinone and hydroquinone compounds 1–4 have been isolated from Pacific sponges of the genus *Xestospongia*.[2-4] Kobayashi et al. have suggested that 1 and 2 may be artifacts arising from oxidation of the hydroquinones such as 3. Xestoquinone (1) exhibits cardiotonic activity, and halenaquinone (2) shows antibiotic activity. In this paper we report the isolation of five derivatives of 1 and 2 from an *Adocia* sp. collected in Truk Lagoon. Three of these possess an added 1,1-dioxo-1,4-thiazine ring; one of them is cytotoxic.

The major components obtained from two different collections of sponges were xestoquinone (1) and halenaquinone (2). Single frequency $^1H/^{13}C$ decoupling experiments established the assignments shown in Table I for the quaternary sp^2 carbon signals (except for the carbonyl carbons). The assignments for C-7 and C-8 are opposite to those made earlier,[3] as are those for C-10 and C-19. Our assignments agree with those made by Kobayashi et al.[4] for 2.

The molecular formula $C_{20}H_{20}O_4$ was established for one of the minor alcohol metabolites 5, by low-resolution MS, ^1H and ^{13}C NMR, and IR. This corresponds to a hexahydro formula of 1. ^1H and ^{13}C NMR data, Table I, indicated that 5 contained rings A–D of xestoquinone including the carbonyl group at C-9, but ring E was clearly reduced since no signals indicative of the quinone protons and carbonyl carbons of 1 were present. Instead, the proton NMR spectrum of 5 exhibited a broad two-proton multiplet at 4.91 ppm indicative of two secondary alcohols which were each coupled to two-proton multiplets, one at 2.36 ppm and the other at 1.72 ppm. The 4.91-ppm multiplet was also coupled (~0.5 Hz) to the benzenoid resonances at 8.42 and 7.64 ppm. Acetylation of 5 yielded a diacetate, 6, which exhibited resolved one-proton triplets at 6.06 and 6.12 ppm in its ^1H NMR spectrum, confirming that each acetate-bearing carbon is adjacent to a methylene group. These data are all consistent with structure 5 for this metabolite, which is thus 13,14,15,16-tetrahydroxestoquinol. The ^{13}C NMR signals of the two alcohol carbons, C-13 and C-16, appeared as four closely spaced signals in the DEPT[5] spectrum, but in the spectrum of acetate 6, C-13 and C-16 appeared as two sharp peaks. Hence, doubling of the peaks in the spectrum of the diol 5 is ascribed to slow interconversion of conformational isomers in DMSO solution, rather than the occurrence of 5 as an unresolved mixture of stereoisomers.

Chart I



A second minor alcohol metabolite, 7, was assigned the formula $C_{20}H_{20}O_5$ on the basis of LRMS (m/z 340, M^+), IR, ^{13}C, and ^1H NMR data. The ^1H NMR spectrum of this metabolite bore many resemblances to that of halenaquinone, 2. However, the absence of both furan and quinone proton signals indicated that rings A and E of 7 both were at least partially reduced. Decoupling and COSY experiments established a sequence of connectivity for carbons 1–5 and 13–15 and indicated an allylic relationship between H-11 and H-13 (Table I). A singlet at 8.33 ppm was assigned to H-18 by comparison of its chemical shift with that in 1 and 2 and from an NOE observed between this signal and the methyl protons (see below). Thus this metabolite was assigned structure 7.

Acetylation of 7 afforded the diacetate 8 (LRMS, m/z 424, M^+), whose ^1H NMR spectrum showed signals at 6.19 (dd) and 5.27 ppm (dd), for the H-13 and H-3 signals,

(1) Taken from the Ph.D. Dissertation of S. J. Bloor, University of Oklahoma, 1986.
(2) Roll, D. M.; Scheuer, P. J.; Matsumoto, G. K.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 6177.
(3) Nakamura, H.; Kobayashi, J.; Kobayashi, M.; Ohizumi, Y.; Hirata, Y. *Chem. Lett.* **1985**, 713.
(4) Kobayashi, M.; Shimizu, N.; Kyogoku, Y.; Kitagawa, I. *Chem. Pharm. Bull.* **1985**, *33*, 1305.
(5) Doddrell, D. M.; Pegg, D. T.; Bendall, M. R. *J. Magn. Reson.* **1982**, *48*, 323. Bendall, M. R.; Pegg, D. T.; Doddrell, D. M.; Williams, D. H. *J. Org. Chem.* **1982**, *47*, 3021.

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Table I. NMR Data for 5 and 7

	5		7		
	$^{13}C^a$	$^1H^b$	$^{13}C^a$	$^1H^f$	$^{13}C^g$
C-1	144.6 d	7.41 br s	70.8 t	4.78 dd (10, 10),[h] 4.74 dd (10, 6)[h]	144.9
C-2	121.2 s		46.6 d	3.66 m (ddd 10, 6, 4)[h]	121.5
C-3	17.8 t	2.85 br dd (17, 8),[h] 2.61 br dd [17, 9 (5)][h]	66.2 d[c]	4.36 br s	18.4
C-4	16.3 t	2.20 m (2 H)	28.2 t	2.09 m (2 H)	16.9
C-5	31.1 t	2.35 dt (13, 3.6),[h] 1.67 dt (13, 4.6)[h]	33.8 t	2.36 m, 1.70 ddd (13, 13, 6)[h]	31.3
C-6	35.7 s		35.7 s		37.3
C-7	146.8 s		146.8 s		147.2
C-8	143.4 s		145.5 s		143.8
C-9	171.5 s		174.2 s		170.3
C-10	138.9 s[c]		135.1 s		138.0
C-11	126.5 d	8.42 s	125.0 d	8.52 s	127.1
C-12	138.9 s[c]		142.2 s		130.4
C-13	66.4 d[d]	4.91 m	65.8 d[c]	5.29 dd (7.8, 4)[h]	183.8[a]
C-14	29.8 t[e]	2.36 m, 1.72 m (2 H each)	31.8 t	2.56 m, 2.36 m	139.4[b]
C-15	29.9 t[e]		24.3 t	3.15 ddd (19, 9, 5),[h] 2.86 ddd (19, 8, 4)[h]	138.6[b]
C-16	66.6[d]	4.91 m	197.0 s		184.7[a]
C-17	131.2 s[c]		132.6 s		133.2
C-18	124.1 d	7.64 s	123.8 d	8.33 s	123.2
C-19	149.1 s		150.1 s		156.2
C-20	32.2 q	1.48 s	24.3 s	1.63 s	32.6

[a] DMSO-d_6, 75 MHz. [b] $CDCl_3$, 300 MHz. [c] Numbers with identical letters within a column may be interchanged [d] Numbers with identical letters within a column may be interchanged [e] Numbers with identical letters within a column may be interchanged. [f] $CDCl_3$ + 10% CF_3CO_2D. [g] $CDCl_3$, 75 MHz. [h] Coupling constants in hertz.

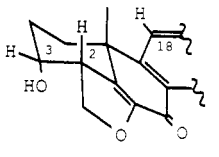
Table II. ^1H NMR Data for 9–11 and 13

	9[a]	10[b]	11[a]	13[c]
C-1	7.55 s	7.67 s	8.29 s	8.38 s
C-3	2.88 dd (17, 7.7),[d] 2.65 dd (17, 9.3)[d]	2.92 br dd (17, 7.6),[d] 2.69 br dd (17, 9)[d]		
C-4	2.2–2.4 m	2.1–2.4 m	2.90 m	2.90 m
C-5	2.57 dt (12.9, 3.7),[d] 1.74 dt (12.9, 4.5)[d]	2.59 dt (13, 4),[d] 1.76 dt (13, 4.9)[d]	3.04 ddd (14, 14, 5)[d] 2.29 ddd (14, 14, 5)[d]	3.13 m, 2.4 m
C-11	9.04 s	9.03 br s	9.06 s	9.19 s
C-18	8.38 s	8.34 s	8.41 s	8.45 s
C-20	1.53 s	1.56 s	1.69 s	1.78 s
C-21	4.16 m (2 H)	3.53 m (2 H)	4.20 m (2 H)	4.15 m (2 H)
C-22	3.39 m (2 H)	4.30 m (2 H)	3.43 m (2 H)	3.60 m (2 H)
N–H	6.94 br s		6.99 br s	

[a] $CDCl_3$. [b] $CDCl_3$ + 10% CF_3CO_2D. [c] $CDCl_3$ + 20% CD_3OD. [d] Coupling constants in hertz.

respectively, consistent with the proposed structure. The ^{13}C NMR spectrum of **8** showed only two lines for C-3 and C-13 at 72.7 and 74.4 ppm, whereas, in the spectrum of **7**, the corresponding signals were each doubled. This doubling is as ascribed to conformational isomers as in the case of **5**; see above.

The partial relative stereochemistry shown for **7** was determined from NOEs and solvent-induced ^1H NMR chemical shifts. Irradiation of the methyl signal (in Pyr-d_5; see Experimental Section) induced NOEs of 10% on H-2, a trace on H-3, and 14% on H-18. Thus the methyl and H-2 must be cis as depicted in stereostructure I with H-3



I

being equatorial (β) to be consistent with small J's of this signal. Also, the doubled triplet noted for H-5α in $CDCl_3/CD_3OD$ at 1.69 ppm was shifted downfield to ~1.90 ppm in Pyr-d_5 (largely obscured by other signals), as expected from its diaxial relationship with the 3-OH.[6] Partial reduction of the furan ring on going from **1** to **7** causes the C-20 NMR absorption to be shifted upfield significantly (Table I).

(6) Page, J. E. In *Annual Reports on NMR Spectroscopy*; Mooney, E. F., Ed.; Academic: New York, 1970; Vol. 3, p 149.

Table III. ^{13}C NMR Data for 9–11[a]

	9	10	11
C-1	146.2	146.1	150.5
C-2	121.7	121.6	122.6
C-3	17.8	17.8	191.5
C-4	16.2	16.2	32.2
C-5	30.3	30.3	36.7
C-6	37.2	37.2	36.2
C-7	147.1	147.1	146.7
C-8	142.9	143.1	143.5
C-9	169.3	169.4	169.6
C-10	135.9	137.9	135.4
C-11	125.4	124.8	125.1
C-12	128.5	131.8	128.6
C-13	177.8	173.7	177.3
C-14	111.7	147.9	111.4
C-15	147.8	111.4	147.9
C-16	173.7	178.3	173.5
C-17	134.4	130.9	134.8
C-18	122.9	123.4	123.2
C-19	157.4	154.6	155.5
C-20	31.8	31.6	29.8
C-21	48.2	40[b]	48.2
C-22	40[b]	48.3	40[b]

[a] All spectra recorded at 75 MHz in DMSO-d_6. Assignments made by comparison with xestoquinone and from single frequency decoupling experiments. [b] Signal obscured by solvent peak.

The remaining three metabolites all exhibited odd-mass molecular ions revealing the presence of nitrogen and M + 2 peaks (10–15% of M + 1) suggestive of the presence of sulfur. The first of these compounds, adociaquinone A[7] (**9**), m/z 423 (M^+), exhibited a proton NMR spectrum

that contained all the peaks observed in the spectrum of 1 except for the two quinone protons (Table II). In addition, however, the spectrum of **9** contained an isolated spin system consistent with the partial structure $NHCH_2CH_2$, i.e., exchangeable proton at 6.94 ppm (NH) coupled to a two-proton multiplet at 4.16 ppm which in turn was coupled to a two-proton multiplet at 3.39 ppm. The ^{13}C NMR spectrum of **9** (Table III), contained all the signals indicative of the entire skeleton of 1 plus two additional methylene carbons. Summing the formula elements of 1 and the $NHCH_2CH_2$ fragment gave a mass of 359, 64 amu short of the observed M^+ of 423. A facile loss of 64 amu, attributable to expulsion of SO_2 (from a sulfone), was observed in the mass spectrum of **9**, and from this a molecular formula of $C_{22}H_{17}O_6NS$ was inferred. Since this metabolite retains all the proton signals of **1** except for H-14 and H-15, the SO_2 and $NHCH_2CH_2$ units could be fused to these positions to give structure **9** (or the regioisomeric structure **10**). A definitive assignment of the regiochemistry shown for **9** was derived from NMR studies carried out on semisynthetic material (see below).

The second sulfur-containing metabolite isolated was assigned structure **10**. This metabolite is more polar (TLC) than **9**, is considerably less soluble in DMSO, and is virtually insoluble in $CHCl_3$ (**9** is easily soluble in DMSO and sparingly soluble in $CHCl_3$, ~2 mg/mL). The spectral data for this metabolite, adociaquinone B[7] (**10**) (Tables II and III), are almost identical with those of **9**, with only small differences evident in the UV and ^{13}C NMR spectra. Since **10** was not soluble in $CDCl_3$ alone, its ^1H NMR spectrum was taken in $CDCl_3/CF_3CO_2D$. In this solvent, **10** exhibited all the peaks observed for **9** and with the same multiplicities, except for the NH resonance, which exchanges under these conditions. The signals corresponding to H-11, H-21, and H-22 were also broadened; this may be due to the poor solubility of **10** and consequent clustering of solute molecules. The mass spectra of **10** and **9** exhibited the same fragment ions, although there was some variation in peak intensities. These data suggested that **10** was the regioisomer of **9** in ring F, and this was subsequently confirmed by NMR studies on semisynthetic material (see below).

The third sulfur-containing metabolite, 3-ketoadociaquinone A[7] (**11**), exhibited ^1H NMR signals corresponding to halenaquinone (**2**), except for the absence of the quinone protons and the addition of signals indicative of the hypotaurine moiety of **9** (Table II). Likewise, the ^{13}C data of **11** matched those of halenaquinone for rings A–D and corresponded to compound **9** for rings E and F; see Table III. The mass spectrum of **11** exhibited a molecular ion at m/z 437 consistent with the molecular formula $C_{22}H_{15}O_7NS$, and fragment ions at m/z 422 ($M^+ - CH_3$), 373 ($M^+ - SO_2$), and 332 [$M^+ - (SO_2 + CHCHNH)$]. On the basis of these data, structure **11**, with ring-F regiochemistry unconfirmed, was proposed for this compound.

The structures of **9–11**, but with regiochemistry unresolved, were confirmed by synthesis from **1** and **2** using the known conjugate addition reaction of amines or sulfinic acids with naphthoquinones[8] to give substituted naphthoquinones. A model reaction between naphthoquinone and hypotaurine was first carried out to test the feasibility of a bis-1,4-addition of an amino sulfinic acid to yield a 1,4-thiaza ring. Brief heating of equimolar amounts of these two reactants gave a 30% yield of a yellow solid with spectral properties consistent with structure **12**. The yield was not improved when air was bubbled into the reaction mixture to serve as an oxidant.

When xestoquinone (**1**) was heated with hypotaurine in ethanol/acetonitrile (1:1) for 1 min, two products were isolated that were identical with **9** (7%) and **10** (15%) by TLC, MS, and ^1H NMR analysis. Likewise, from reaction of halenaquinone with hypotaurine, two products were isolated, the less polar of which was identical with **11**, and the more polar of which exhibited a ^1H NMR spectrum consistent with the expected regioisomer **13**; see Table II.

The respective ring-F regiochemistries of **9** and **10** were resolved from long-range proton–carbon couplings determined for the more soluble isomer **9**. Chemical shift assignment of the benzenoid protons was made initially by comparison to xestoquinone, i.e., the H-18 signal is slightly upfield from that of H-11 as confirmed by NOE between it and the methyl signal. This assignment was confirmed for **9** when it was noted that selective irradiation of the upfield benzenoid signal (H-18) caused sharpening of only one ^{13}C carbonyl resonance (173.7 ppm in DMSO-d_6) in a fully coupled ^{13}C NMR spectrum. On the other hand, irradiation of H-11 sharpened two carbonyl signals (169.3 and 177.8 ppm). Selective irradiation of the amine proton resonance gave inconclusive results, but when the ^{13}C NMR spectrum was recorded in DMSO-d_6 with CD_3OD added to exchange the NH proton, a definite sharpening of the broad signal at 173.7 ppm to a sharp doublet was observed. Since H-18 and the NH proton are coupled to the same carbonyl carbon, structure **9** is confirmed for this isomer and hence **10** has the alternate structure as shown. The doublet character of the 173.7-ppm peak after NH exchange is due to coupling with H-18.

Since the relative order of elution of **9** and **10** on TLC would be expected to be the same for the halenaquinone adducts **11** and **13**, it follows that the less polar adduct **11** has the same ring-F regiochemistry as the less polar metabolite **9**.

Halenaquinone (**2**), the naphthoquinone derivative **12**, and adociaquinone B (**10**) are mildly cytotoxic, ED_{50} (PS)[9] = 2.9, 2.9, and 2.4 μg/mL, respectively, while xestoquinone (**1**) was inactive.

Experimental Section[10]

Sponges were collected from the Eten Island area of Truk Lagoon in January 1984 and November 1985 at 5–10-m depths and frozen within a few hours. The frozen specimens (2.9 kg) from the first collection were soaked in $CHCl_3$/MeOH (1:1) for 1 day and then again in $CHCl_3$/MeOH (2:1). The combined solutions were concentrated under reduced pressure, and the concentrate was partitioned between $CHCl_3$ and 30% aqueous MeOH. The chloroform solubles were chromatographed as outlined in Figure 1a. Specimens from the second collection were freeze-dried (932 g dry wt) and then extracted at room temperature consecutively with the following solvents: (a) *n*-hexane, 12 h; (b) *n*-hexane, 24 h; (c) $CHCl_3$, 1 day; $CHCl_3$, 2 days. The combined chloroform extracts were chromatographed as outlined in Figure 1b.

13,14,15,16-Tetrahydroxestoquinol (5): 8 mg, white solid; mp 224–229 °C; UV (ethanol) λ_{max} (nm) 304 (ε 13 600), 254 (7200), 233 (sh) (7000); IR (NaCl) 3450 (br), 2940, 1680 (br) cm^{-1}; ^1H and ^{13}C NMR data, Table I; low-resolution mass spectrum (LRMS)

(7) The names for compounds 9–11 and 13 have been changed from those assigned in ref 1 due to the fact that the sponge name has been determined and the new compound names are more appropriate.

(8) See, for example: Scribner, R. M. *J. Org. Chem.* **1966**, *31*, 3671.

(9) Gueran, R. I.; Greenberg, N. H.; Macdonald, M. M.; Schumacher, A. M.; Abbott, B. J. *Cancer Chemother. Rep., Part 3* **1972**, *3*, No. 2, 1. Effective doses (ED_{50}) in the tissue culture tests are expressed as concentrations in micrograms/milliliter of test material in the growth medium that cause 50% inhibition of cell growth. "Active" materials display an $ED_{50} < 10$ μg/mL. PS (P388) refers to in vitro lymphocytic leukemia.

(10) Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. Other instrumental and general experimental conditions are as described earlier: Ksebati, M. B.; Schmitz, F. J. *J. Org. Chem.* **1985**, *50*, 5637.

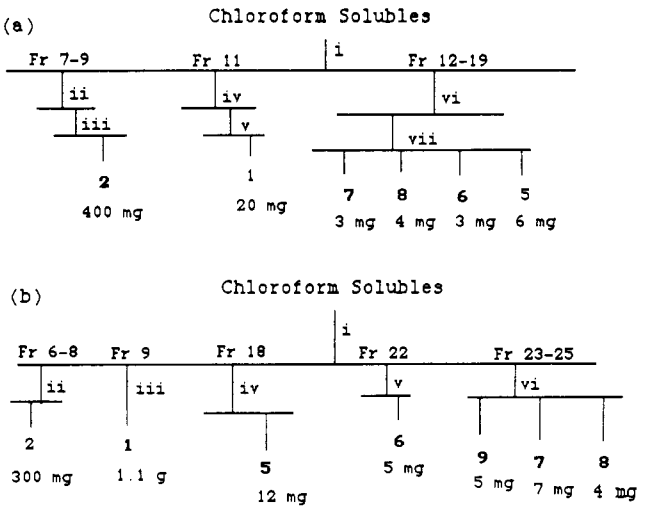


Figure 1. Fractionation of sponge extracts. (a) First collection: (i) SiO_2, acetone/hexane with step increase in acetone (0:1→1:0); (ii) SiO_2, ethyl acetate/hexane (0:1→1:0); (iii) preparative TLC, chloroform; (iv) SiO_2, methanol/chloroform (2:98); (v) preparative TLC, ethyl acetate/hexane (1:1); (vi) SiO_2, methanol/chloroform with step increase in methanol (2:98→10:90); (vii) SiO_2 HPLC, methanol/chloroform (3:97). (b) Second collection: (i) SiO_2, methanol/chloroform with step increase in methanol (0:10→1:9); (ii) SiO_2, chloroform; (iii) precipitated from chloroform/methanol solution with the addition of diethyl ether; (iv) SiO_2, methanol/chloroform (2:98); (v) SiO_2 HPLC, methanol/chloroform (3:97); (vi) SiO_2 HPLC, methanol/chloroform (4:96).

(12 eV), *m/z* (relative intensity) 324 (M^+, 15), 309 (35), 306 (100), 291 (28).

3,13-Dideoxo-1,2,14,15-tetrahydro-3,13-dihydroxyhalenaquinone (7): 5 mg, white solid; mp 235–245 °C; UV (ethanol) λ_{max} (nm) 328 (ε 9000), 252 (16 600); IR (NaCl) 3350 (br), 1650 cm^{-1}; ^1H and ^{13}C NMR data, Table I; ^1H NMR (300 MHz, Pyr-d_5) 9.04 (1 H, s, H-11), 8.45 (1 H, s, H-18), 5.21 (1 H, dd, *J* = 4, 8 Hz, H-13), 5.19 (1 H, dd, *J* = 6, 9 Hz, H-1), 4.65 (1 H, dd, *J* = 9, 11 Hz, H-1′), 4.20 (1 H, m, *J* = 2 Hz, H-3), 3.45 (1 H, m, H-2), 3.10 (1 H, m, H-15), 2.75 (1 H, m, H-15′), 2.47, 2.35 (1 H each, m, H-14, H-14′), 2.05–2.2 (2 H, m, H-4, H-5), 1.8–2.05 (2 H, m, H-4′, H-5′), 1.42 (3 H, s, H-20) ppm; LRMS (12 eV), *m/z* (relative intensity) 340 (M^+, 19), 322 (100), 307 (49), 284 (15), 279 (24).

Acetylation of 5 and 7. Approximately 2 mg of **5** or **6** was warmed in ~1:1 acetic anhydride/pyridine for about 3 h. The diacetate products were purified by silica gel chromatography using a Waters SEP-PAK cartridge (eluted with chloroform) to give diacetates **6** and **8**.

Diacetate 6: ^1H NMR 8.40 (1 H, s, H-11), 8.26 (1 H, s, H-18), 6.19 (1 H, dd, H-13), 5.27 (1 H, m, H-3), 4.67 (1 H, m, H-1), 4.37 (1 H, dd, H-1′), 3.60 (1 H, m, H-2), 2.95 (1 H, m, H-15), 2.73 (1 H, m, H-15′), 2.16, 1.99 (each 3 H, s, OAc), 1.59 (3 H, s, H-20) ppm; LRMS (12 eV), *m/z* (relative intensity) 306 (M^+ – OAc, CH_3CO, 100), 291 (55).

Diacetate 8: ^1H NMR 8.28 (1 H, s, H-11), 7.51 (1 H, s, H-18), 7.48 (1 H, s, H-1), 6.12, 6.06 (each 1 H, t, H-13, H-16), 2.80 (1 H, ddd, H-3), 2.63 (1 H, m, H-3′), 2.11, 1.99 (each 3 H, s, OAc), 1.48 (3 H, s, H-20); LRMS (12 eV), *m/z* (relative intensity) 424 (M^+, 21), 382 (60), 282 (28).

Adociaquinone A (9): 18 mg, yellow solid; slowly decomposes above 300 °C; $[\alpha]_D$ +25°; UV (ethanol) λ_{max} (nm) 294 (ε 16 800), 249 (29 200); IR (KBr) 3400 (br), 1690 (sh), 1675, 1590, 1450, 1330, 1290, 1220, 1125 cm^{-1}; ^1H and ^{13}C NMR data, Tables II and III; LRMS (12 eV), *m/z* (relative intensity) 423 (M^+, 80), 408 (M^+ – CH_3, 100), 359 (M^+ – SO_2, 61), 344 (359 – CH_3, 68), 333 (29), 318 (46), 281 (13), 207 (57).

Adociaquinone B (10): 10 mg, yellow solid; slowly decomposes above 300 °C; $[\alpha]_D$ +22°; UV (ethanol) λ_{max} (nm) 340 (ε 12 000), 288 (36 000); IR (KBr) 3360, 1690 (sh), 1675, 1585, 1335, 1310, 1290, 1130 cm^{-1}; ^1H and ^{13}C data, Tables II and III; LRMS (12 eV), *m/z* (relative intensity) 423 (M^+, 10), 408 (10), 389 (10), 383 (9), 361 (55), 359 (62), 344 (44), 333 (62), 318 (88), 207 (100); HRMS (EI) 359.114 14 ($C_{22}H_{17}NO_4$, M^+ – SO_2, requires 359.115 76) and 333.099 38 ($C_{20}H_{15}NO_4$ requires 333.100 11).

3-Ketoadociaquinone A (11): 8 mg, yellow solid; slowly decomposes above 300 °C; $[\alpha]_D$ +65.4°; UV (ethanol) λ_{max} (nm) 288 (ε 26 000), 238 (26 200); IR (KBr) 3250, 1670, 1590, 1440, 1325, 1280, 1210, 1120 cm^{-1}; ^1H and ^{13}C NMR spectral data, Tables II and III; LRMS (12 eV), *m/z* (relative intensity) 437 (M^+, 38), 422 (M^+ – CH_3, 20), 390 (13), 373 (M^+ – SO_2, 100), 358 (M^+ – SO_2, CH_3, 81), 347 (86), 322 (8.5), 319 (10), 207 (44).

Addition of Hypotaurine to Naphthoquinone. Ten milligrams (0.063 mmol) of freshly sublimed naphthoquinone was dissolved in 1 mL of 1:1 ethanol/acetonitrile to which was added 7 mg (0.065 μmol) of hypotaurine. Water (0.5 mL) was added to dissolve the hypotaurine, and the solution was heated over a steam bath for approximately 1 min. A yellow product, **12** (3.5 mg, 20% yield) precipitated from this solution after cooling for several minutes at room temperature: mp >300 °C; UV (ethanol) λ_{max} (nm) 290 (ε 3200), 255 (6200); IR (KBr) 3260, 1690, 1595, 1570, 1360, 1340, 1310, 1275, 1060, 1020 cm^{-1}; ^1H NMR ($CDCl_3$ with 10% CF_3COOD) 8.15 (dd, 7.7; 3.9), 7.91 (t, 7.7), 7.79 (t, 7.7), 4.22 (m), 3.52 (m) ppm; ^{13}C NMR (DMSO-d_6) 178.7, 174.5, 146.0, 135.6, 132.8, 132.4, 129.8, 126.3, 125.7, 111.2, 48.2, signal of methylene carbon adjacent to the sulfone is assumed to be covered by the solvent signal; LRMS (12 eV), *m/z* (relative intensity) 263 (M^+, 100), 199 (43), 171 (37), 170 (38), 154 (10).

Synthesis of 9 and 10 from Xestoquinone. To a solution of 65 mg of xestoquinone in 1.5 mL of 1:1 ethanol/acetonitrile was added a hot solution of hypotaurine (27 mg) in ethanol (0.5 mL). The mixture was heated over a steam bath for approximately 1 min. Analysis of the reaction mixture by TLC indicated that all of the xestoquinone had reacted. The solvent was evaporated and chloroform/methanol added to the residue. Filtration of this solution yielded 14 mg of a yellow solid, which was identified by TLC, NMR, and MS as **10**: FAB HRMS 424.0967 [$C_{22}H_{18}O_6NS$ ($M + H^+$) requires 424.0855], 446.0753 [$C_{22}H_{17}O_6NSNa$ ($M + Na^+$) requires 446.0674]. The filtrate was chromatographed by preparative TLC ($CHCl_3$/MeOH, 95:5) to give 6 mg of a second yellow solid, which was identified as **9** by TLC, NMR, and LRMS.

Synthesis of 11 and 13 (3-Ketoadociaquinone B) from Halenaquinone. Nine milligrams of **2** was reacted as described above for **1**. The products were separated by preparative TLC as above. The less polar product was identified as **11** by TLC and ^1H NMR. Only a small amount of a second, more polar product **13** was isolated; ^1H NMR, Table II; LRMS, *m/z* (relative intensity) 374 (29), 373 (M^+ – SO_2, 100), 347 (34), 332 (32).

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