Synthesis of 5-Anilino-2-phenylthio-1,4-benzoquinones

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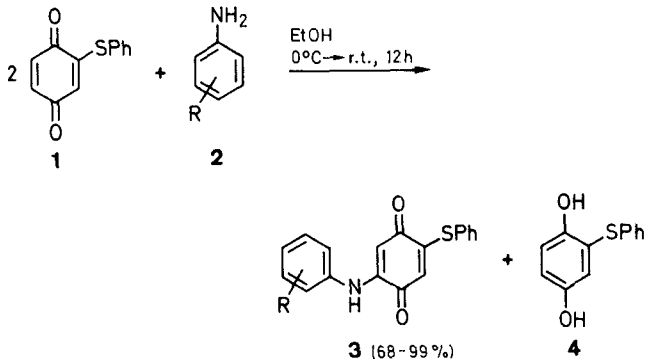
Reductive addition of substituted anilines to 2-phenylthio-1,4-benzoquinone followed by oxidation of a second molecule of the quinone, affords a series of 5-amino-2-thio-substituted 1,4-benzoquinones in good yields.

The addition of amines or sulfur nucleophiles to quinones has been studied extensively.[1] Usually, nucleophilic 1,4-attack of the Michael-type takes place, and the initial hydroquinone product is oxidized by the quinone starting material. Numerous *N*-substituted quinones were synthesized,[2] some of them with profound physiological properties. Many alkylthio and arylthio quinones were also prepared and are amply documented in the literature.[1]

Surprisingly very little is known about 1,4-quinones substituted with both thio and amino groups, and to our knowledge no compound in which the quinone is substituted both with arylthio and anilino groups (e.g., **3**) is known.

In this communication we describe the preparation and properties of a series of such compounds.

The reaction of two equivalents of 2-phenylthio-1,4-benzoquinone (**1**) with one equivalent of an aromatic primary amine **2** results in 1,4-reductive addition. The initial hydroquinone product formed is subsequently oxidized by the second equivalent of the quinone starting material. Thus, the two products obtained are the 2,5-disubstituted quinone **3**, and the hydroquinone **4**. Compounds **3** usually precipitate from the ethanolic reaction medium in high yields (based on the substituted amines **2**) and with high purity. Performing the reaction with only one equivalent of **1** and under the influence of air, results in lower yields of less pure 2,5-addition products. In the mother solutions, small quantities (2–6%) of the 6-addition products, namely the 6-anilino-2-phenylthio-



2, 3	R	2, 3	R
a	H	**f**	2-Me
b	4-Me	**g**	2-MeO
c	4-MeO	**h**	3-Cl
d	4-Cl	**i**	3-Me
e	4-Br	**j**	3,4-benzo

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Table. 5-Amino-2-phenylthio-1,4-benzoquinones **2a–j** Prepared

Product	Yield[a] (%)	mp (°C) (EtOH)	Molecular Formula[b]	IR (KBr)[d] ν (cm^{-1})	UV (CH_2Cl_2)[e] λ_{max} (nm) (log ε)	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	MS (65 eV)[f] m/z (%)
2a	89	198–199	$C_{18}H_{13}NO_2S$ (307.3)	3303, 1643, 1609	263 (4.29), 372 (4.22), 531 (3.21)	5.79 (s, 1H), 6.19 (s, 1H), 7.21–7.43 (m, 5H), 7.50 (s, 5H)	308 (MH^+, 100), 309 ($M^+ + 2$, 4)
2b	86	170–171	$C_{19}H_{15}NO_2S$ (321.4)	3310, 1651, 1610	264 (4.18), 376 (4.16), 543 (3.24)	2.36 (s, 3H), 5.80 (s, 1H), 7.15 (ABq, 4H, J = 8.3), 7.51 (s, 5H)	322 (MH^+, 100), 323 ($M^+ + 2$, 21)
2c	85	188–190	$C_{19}H_{15}NO_3S$ (337.4)	3302, 1644, 1602	264 (4.17), 380 (4.10), 550 (3.34)	3.83 (s, 3H), 5.78 (s, 1H), 6.01 (s, 1H), 7.08 (ABq, 4H, J = 8.8), 7.49 (s, 5H)	338 (MH^+, 100), 339 ($M^+ + 2$, 21)
2d	82	230–231	$C_{18}H_{12}ClNO_2S$ (341.8)	3276, 1656, 1605	272 (4.28), 375 (4.26), 529 (3.22)	5.79 (s, 1H), 6.11 (s, 1H), 7.25 (ABq, 4H, J = 8.7), 7.49 (s, 5H)	342 (MH^+, 100), 343 ($M^+ + 2$, 35), 305 ($M^+ - HCl$, 7)
2e	68	235–236	$C_{18}H_{12}BrNO_2S$ (386.3)	3284, 1655, 1605	273 (4.30), 377 (4.25), 529 (3.23)	5.80 (s, 1H), 6.14 (s, 1H), 7.25 (ABq, 4H, J = 8.6), 7.50 (s, 5H)	386 (M^+, 65), 388 ($M^+ + 2$, 100), 306 ($M^+ - Br$, 7)
2f	74	152–153	$C_{19}H_{15}NO_2S$ (321.4)	3331, 1655, 1615	260 (4.24), 364 (4.29), 524 (3.12)	2.24 (s, 3H), 5.79 (s, 1H), 5.81 (s, 1H), 7.23 (s, 4H), 7.51 (s, 5H)	322 (MH^+, 100), 323 ($M^+ + 2$, 23)
2g	83	183–184	$C_{19}H_{15}NO_3S$ (337.4)	3295, 1655, 1610	264 (4.18)[g], 386 (4.09), 546 (3.39)	3.88 (s, 3H), 5.81 (s, 1H), 6.26 (s, 1H), 6.92–7.37 (m, 4H), 7.50 (s, 5H)	338 (MH^+, 100), 339 ($M^+ + 2$, 11)
2h	88	210–211	$C_{18}H_{13}ClNO_2S$ (341.8)	3289, 1650, 1604	268 (4.28), 372 (4.21), 518 (3.13)	5.82 (s, 1H), 6.21 (s, 1H), 7.26–7.44 (m, 4H), 5.52 (s, 5H)	342 (MH^+, 100), 343 ($M^+ + 2$, 60), 306 ($M^+ - Cl$, 10)
2i	84	165–166	$C_{19}H_{15}NO_3S$ (337.4)	3323, 1649, 1599	264 (4.26), 370 (4.18), 533 (3.25)	3.81 (s, 3H), 5.80 (s, 1H), 6.22 (s, 1H), 6.72–6.81 (m, 3H), 7.25–7.33 (m, 1H), 7.51 (s, 5H)	338 (MH^+, 100), 339 ($M^+ + 2$, 31)
2j	99	204–205	$C_{22}H_{15}NO_2S$ (357.4)	3294, 1650, 1603	262 (4.47), 370 (4.13), 545 (3.41)	5.84 (s, 1H), 6.38 (s, 1H), 7.18–7.89 (m, 12H)	358 (MH^+, 100), 359 ($M^+ + 2$, 16)

[a] Yields of isolated products, not optimized.
[b] Satisfactory microanalyses obtained: C, H, N, S ± 0.21.
[c] Recorded on a Perkin-Elmer Lambda 5 UV/VIS spectrophotometer.
[d] Recorded on a Nicolet 5ZDX FT-IR spectrometer.
[e] Recorded on a Bruker WP200SY spectrometer.
[f] CI in methane; recorded on a Finnigan 4020 quadropole spectrometer.
[g] This compound shows an extra absorption at 281 nm (log ε = 4.15).

1,4-benzoquinones could be detected. The hydroquinone **4** is easily reoxidized (after isolation) to **1** by refluxing with ethanolic tetrachloro-1,4-benzoquinone(chloranil), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or even 1,4-benzoquinone. Pure analytical grade products **3** are obtained as violet or brown crystals after recrystallization from ethanol.

In contrast to the facile formation of 2,5-disubstituted quinones **3** via the procedure discussed above and the purity of the isolated products, the reverse addition *reaction, namely the addition of arenethiols to 2-anilino-*1,4-benzoquinones is much less favorable. Under the same experimental conditions, complex mixtures are formed, which consists of both the 2,5- and 2,6-addition products as well as several other unidentified products.

The electronic spectra of **3** show three typical absorptions.[3] A band of strongest intensity at λ_{max} = 260–273 nm, a somewhat weaker absorption at λ_{max} = 365–385 nm, and a band with medium intensity in the visible region with λ_{max} = 520–550 nm. Bathochromic displacements and blue shifts exerted by the substituents can be observed (see Table).

All products **3** show two IR absorptions in the carbonyl region at 1643–1656 and 1600–1615 cm^{-1}. The appearance of two absorptions is typical of disubstituted quinones and due to Fermi resonance, asymmetry of the molecule, and vibration coupling.[4]

Resonance participation by the sulfur and the nitrogen substituents shifts upfield the ^{1}H-NMR signals of the quinone protons.[5] Thus, in most compounds they are located at δ = 5.8 (for the hydrogen vicinal to S) and δ = 6.1–6.2 (for the hydrogen vicinal to NH).

As characteristic of many quinones,[6] the analytically useful M + 2 peak is observed in all mass spectra of compounds **3**.

Melting points were determined using a Thomas-Hoover capillary *apparatus and are uncorrected. 2-Phenylthio-1,4-benzoquinone* was prepared according to the literature procedure.[7]

5-Anilino-2-phenylthio-1,4-benzoquinones 2a–j; General Procedure: *To a cooled (0 °C) solution of 2-phenylthio-1,4-benzoquinone* (**1**; 1.08 g, 5 mmol) in EtOH (50 mL), a solution of the aromatic amine (**2a–j**; 2.5 mmol) in EtOH (5 mL) is added dropwise with stirring. The orange solution turns violet within a few minutes and stirring

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is continued at r.t. for 12 h. Usually, the product precipitates as dark violet or brown crystals. The mixture is cooled in ice, the product is collected by filtration and recrystallized from EtOH.

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