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Facile Synthesis of Quinone Dimer Derivatives Substituted with Sulfanyl Groups and Their Properties

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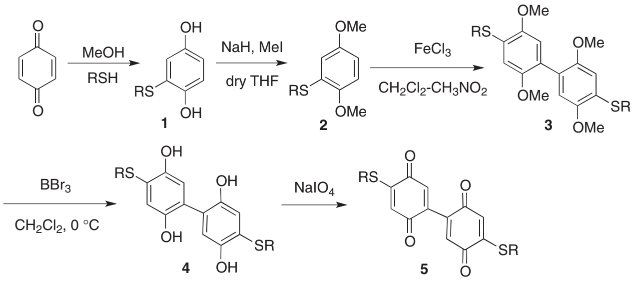
Quinone dimers are readily prepared quantitatively from 2-sulfanyl-1,4-dimethoxybenzene by oxidative treatment. The oxidative coupling progressed in a highly regioselective manner. Removal of O-protection and subsequent oxidation gave 5,5′-bis(sulfanylquinone) dimer in good yields. Physical properties of the dimer derivatives are also investigated.

Quinone derivatives are widely abundant among natural products.[1] Quinone and hydroquinone compose an interesting redox system and their properties are often observed among natural metabolic systems as well as artificial functional molecules. Quinone dimers are expected to show many unique physical properties because of a synergetic effect by combination of the two quinones.[2] However, there have been only a limited number of reports describing synthesis of quinone dimers because of their low stability.[3] Another reason is that biaryl coupling reaction for dimer formation is usually limited to transition-metal-catalyzed reactions. Recently we launched research on a new chemistry of combination of sulfur and quinones, and found a very short synthesis of quinone dimers bearing sulfur substituents. In this report we describe a new regioselective synthesis of 5,5′-disulfanyl-2,2′-bisbenzoquinone dimer derivatives and their unique physical properties.

Our synthesis started from the conjugate addition of thiol to quinone (Scheme 1).[4] The addition progressed smoothly at room temperature and 2-sulfanyl-1,4-hydroquinones **1** are obtained in almost quantitative yields. The two hydroxy groups in compound **1** were protected by treatment with excess NaH and MeI, giving hydroquinone dimethyl ether **2** in good yields. Exposure of compound **2** to $FeCl_3$ in CH_3NO_2–CH_2Cl_2 resulted in rapid consumption of compound **2** and desired dimers **3** were obtained in good yields.[5] The results are summarized in Table 1.



Scheme 1. Synthesis of quinone dimers **5**.

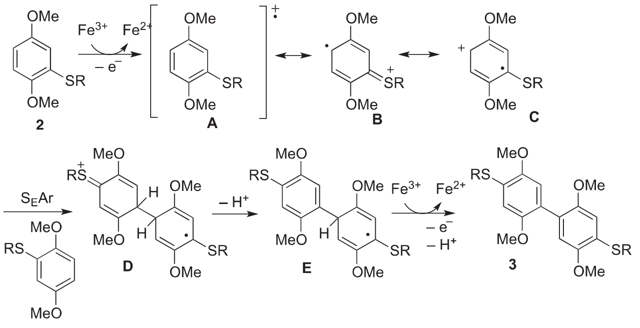
Table 1. Preparation of quinone dimers **5**

Entry	R	**1**; Yield/%[a]	**2**; Yield/%[a]	**3**; Yield/%[a]	**4**; Yield/%[a]	**5**; Yield/%[a]
1	Ph	**1a**; 100	**2a**; 92	**3a**; 99	**4a**; 100	**5a**; 100
2	*o*-BrC_6H_4	**1b**; 100	**2b**; 80	**3b**; 99	**4b**; 100	**5b**; 100
3	*p*-BrC_6H_4	**1c**; 95	**2c**; 96	**3c**; 100	**4c**; 100	**5c**; 61
4	*p*-*t*-BuC_6H_4	**1d**; 100	**2d**; 93	**3d**; 96	**4d**; 44	**5e**; 93
5	*m*-ClC_6H_4	**1e**; 81	**2e**; 95	**3e**; 100	**4e**; 79	**5e**; 62
6	*p*-ClC_6H_4	**1f**; 98	**2f**; 85	**3f**; 100	**4f**; 73	**5f**; 69
7	*n*-C_8H_{17}	**1g**; 49	**2g**; 100	**3g**; 84	**4g**; 62	**5g**; 47

[a]Isolated yield.

The dimerization reaction occurred smoothly. For example, compound **2a** underwent the oxidative dimerization to give **3a** in 99% yield (Entry 1). Compound **3a** was isolated in a single isomer, thus the regioselectivity of the coupling reaction was very high. The NMR spectrum for **3a** appeared in a very simple signal pattern and its highly symmetric structure was expected. The structure of **3a** was confirmed by X-ray crystallographic analysis, which revealed the dimer structure unambiguously.[6,10] The two hydroquinone dimethyl ether units connected at the para-position of phenylsulfanyl group and 2,2′-dimer was exclusively formed. In the X-ray structure, the torsional angle between the two hydroquinone dimethyl ether rings was estimated to be 76° so the two rings existed in an almost orthogonal conformation. Since $FeCl_3$ did not remove methyl ether groups, no further oxidation to **5** was observed. No oxidation on the sulfanyl group was observed. Other compounds **2** derived from arylsulfanyl group also gave dimer **3** in quantitative yields (Entries 2–6). The regioselectivity was equally high and only a single isomer of dimer **3** was formed. Compounds **2** derived from aliphatic thiols also underwent the dimerization to give **3** in good yield (Entry 7). Thus, the present oxidative conditions provided a useful preparation of dimer **3** in good yields. The present reaction achieved the formation of biaryl derivatives by direct C–H substitution reaction.[7] Removal of methyl groups was carried out by treatment with BBr_3 and hydroquinone dimers **4** were obtained in good yields.[6] Oxidative treatment of compounds **4** with $NaIO_4$ resulted in the formation of quinone dimers **5**.

The origin of the regioselectivity should be explained in this way (Scheme 2). Treatment of compounds **2** with $FeCl_3$ resulted in the single electron oxidation to give radical cation **A**, which has resonance structures **B** and **C**. In these structures, the sulfanyl group plays important role to stabilize the cation radical so that the para-position to the sulfanyl group became the most electrophilic. The cationic form **C** is attacked by another hydroquinone dimethyl



Scheme 2. Supposed reaction mechanism.

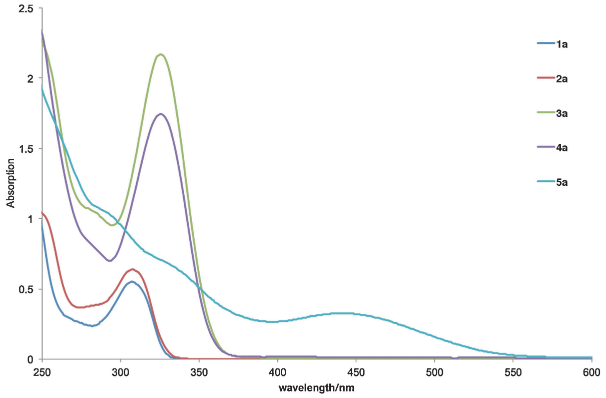


Figure 1. UV–vis spectra for compounds **1a**, **2a**, **3a**, **4a**, and **5a**. Observed in 1 × 10^{-4} M in $CHCl_3$.

ether in a Friedel–Crafts manner. The reaction occurs at the most activated position, para to the sulfanyl group, exclusively to give intermediate **D**, which release two proton and one electron to give compound **3** regioselectively.

Figure 1 shows UV–vis spectra for compounds **1a**, **2a**, **3a**, **4a**, and **5a**. Monomeric hydroquinone derivatives **1a** and **2a** showed their absorption peak at 305 and 307 nm, respectively, and their ε were almost the same values. Absorption maxima for dimeric derivatives **3a** and **4a** shifted to 326 and 325 nm. It should be noted that their ε values were more than twice those of corresponding monomeric compounds. TD-DFT calculation showed that these absorptions are based on HOMO–LUMO transition for **3a** and **4a**. UV–vis absorption of **5a** showed a very different curve from hydroquinone derivatives; a weak peak was observed at 441 nm and continuous absorption appeared between 280 to 400 nm. TD-DFT calculation indicated that the absorption at 441 nm resulted from HOMO−1 to LUMO+1 transition. Other absorption peaks are also consistent to TD-DFT calculations of the molecule.

Finally we examined fluorescent spectra for compounds **3a**, **4a**, and **5a**. Figure 2 showed fluorescent photos for compounds **3a**, **4a**, and **5a** in $CHCl_3$. A solution of **3a** and **4a** in $CHCl_3$ showed relatively strong fluorescent at 377 and 407 nm, respectively, when irradiated at 330 nm. Quantum yield $\Phi_{360\,\mathrm{nm}}$ for compound **4a** in MeOH reached 21.0%. On the other hand, **5a** showed very weak fluorescence in the irradiation at 360 nm light. The torsional angles of biaryl units for **3a** and **4a** were measured by X-ray analyses to be 76 and 67°, respectively,[8,10] while that for **5a** was estimated to be about 42° by calculation. This difference is likely to be one of the reasons of the difference of fluorescence of **3a**, **4a**, and **5a**. As compound **4a** is soluble in alkaline water and this series of derivative is potentially useful as a novel water-soluble fluorescent reagent.

Figure 2. Fluorescence of **3a** (left), **4a** (center), and **5a** (right). Observed in 1 × 10^{-4} M in $CHCl_3$. Excited at 365 nm by UV lamp.

The fluorescence of **4a** is controlled by oxidative treatment. For example, THF solution of **4a** showed strong fluorescence when irradiated with 320 nm UV light, and the fluorescence disappeared when aqueous NaClO solution, which also oxidizes **4a**, was added to the THF solution. This is probably due to the oxidative conversion of **4a** into **5a** that shows very weak fluorescence at the same UV excitation. This may open the use of the compounds as an oxidant sensor.

Redox properties were examined by CV analysis of **5a**. Compound **5a** showed clear reversible redox curve and its two $E_{1/2}^{\mathrm{red}}$ were observed at −0.14 and −0.55 V (vs. Ag/Ag^+).[9,10]

In conclusion, we have successfully synthesized quinone dimer derivatives in short-steps from quinone and thiols. Since the starting materials are commonly available reagents, which are not expensive, and the reactions progressed in high yields, this method provides a useful method for the preparation of quinone dimers. Their properties are potential for a new redox and fluorescent materials. Further study on this topic is now underway in our laboratory.

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