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A New Water-soluble Fluorescent Dye Based on 2-Sulfanylhydroquinone Dimers

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In this study, a new water-soluble fluorescent dye based on 2-sulfanylhydroquinone dimers was developed, and its physical properties were investigated.

Fluorescent dyes are recognized as important tools for sensing or imaging of chemical, physical, and biological processes. So far, a wide range of dyes have been developed, and a number of these are already being applied to various fields such as bioimaging[1] and solar cells.[2] Water solubility is an important property of dyes, which is necessary for their application to biochemical and environmental research.[3] Some dyes are originally water-soluble, but others require chemical modification of the molecules. So far, many water-soluble fluorescent dyes have been reported, including BODIPY-based sulfides,[4–7] fluorescein derivatives,[8–11] rhodamines,[12,13] boronic acids,[14,15] peptides,[16] polyfluorene derivatives,[17,18] and nanoclusters.[19,20] Recently, we reported a short protocol for the synthesis of a quinone dimer bearing sulfur substituents.[21] This dimer exhibited relatively strong fluorescence in the visible light region on UV irradiation. As this molecule contained four phenolic hydroxy groups, it was expected to be a potential novel water-soluble fluorescent dye on deprotonation of the hydroxy groups. In this report, we describe the synthesis of a new type of water-soluble fluorescent dye and its physical properties. We also report an improvement in fluorescence.

Hydroquinone dimers **1a** and **1b** were prepared according to a previously reported method.[21] Oxidative coupling of 2-sulfanylhydroquinone dimethyl ether, followed by deprotection using boron tribromide, gave **1a** and **1b** in good yields. The fluorescence on excitation by 328 nm UV light was measured in methanol, and the resulting spectra are depicted in Figure 1, where it can be seen that **1a** showed almost three times stronger fluorescence than **1b**. Thus, it was deduced that the arylsulfanyl group was necessary for obtaining strong fluorescence in the UV–vis region. Next, the deprotonation of **1a** by treatment with potassium hydroxide in methanol was examined for conversion to tetrapotassium salt **2a**, which was then isolated by the removal of methanol in vacuo (Scheme 1). Compound **2a** was found to be soluble in water and showed relatively strong fluorescence; however, this decreased to zero within a second. It was speculated that this decay was due to the oxidation of **2a** by an active oxidant in water, such as oxygen, resulting in its conversion into quinone dimer **3a**, which is not excited by UV light at 365 nm.

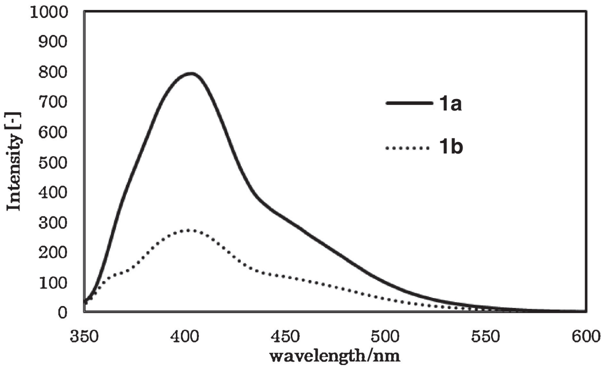
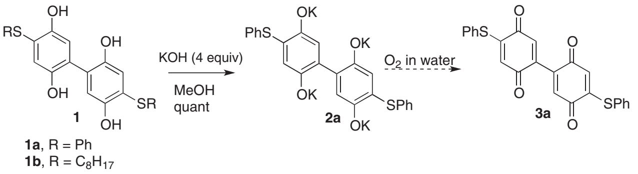
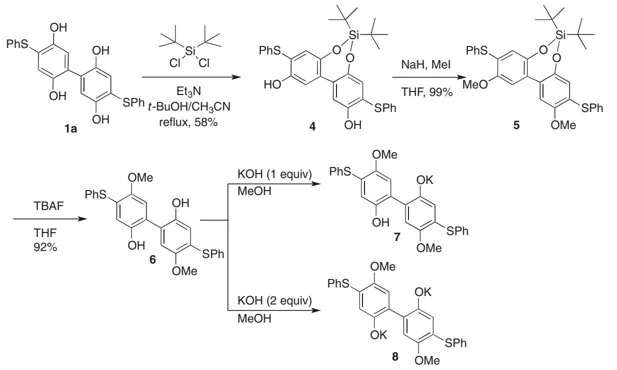


Figure 1. Fluorescence spectra for **1a** and **1b** in methanol.

This hypothesis prompted us to prepare a half-protected hydroquinone dimer, which was expected to resist oxidation to quinone derivatives. Compound **6** was therefore designed, containing a monoprotected hydroxy group on each aromatic nucleus (Scheme 2).[22] The two hydroxy groups in hydroquinone dimer **1a** were protected by treatment with di-*tert*-butyldichlorosilane in the presence of triethylamine, giving compound **4** in 58% yield. Protection of the other two hydroxy groups was carried out using the Williamson ether synthesis, and compound **5** was prepared in almost quantitative yield. Deprotection of di-*tert*-butylsilyl groups was achieved by treatment with TBAF, giving compound **6** in 92% yield. Exposure of compound **6** to one or two equivalents of potassium hydroxide gave salts **7** and **8**, which were isolated by the evaporation of methanol.



Scheme 1. Preparation of tetrapotassium salt **2a**.



Scheme 2. Synthesis of half-protected hydroquinone dimer **6** and its potassium salts.

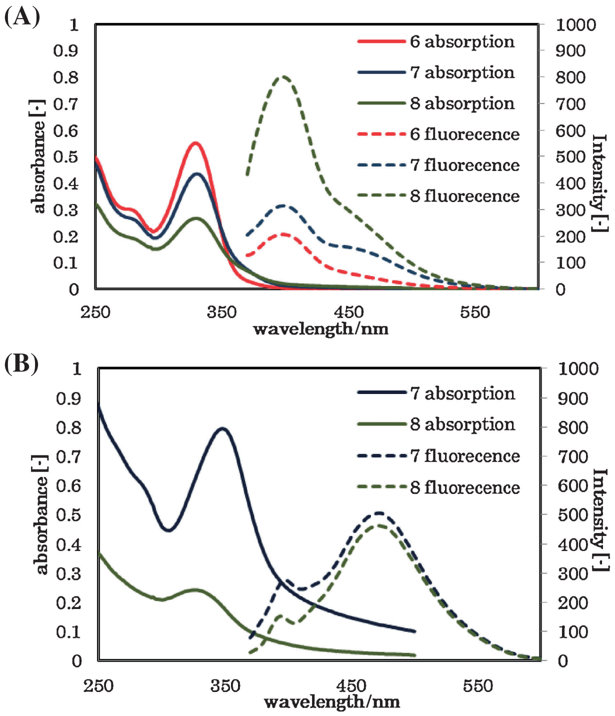


Figure 2. (A) Absorption and fluorescence spectra of compounds **6**, **7**, and **8** in methanol. Absorption spectra: concentration is 2×10^{-5} M, fluorescence spectra: concentration is 10^{-6} M. (B) Absorption and fluorescence spectra of compounds **7** and **8** in water. Absorption spectra: concentration is 5×10^{-5} M, fluorescence spectra: concentration is 10^{-6} M.

Table 1. Spectroscopic properties of compound **6**, **7**, and **8**[a]

Compound	Solvent	$\lambda_{\max}$/nm	log ε	λ_{em}/nm	Φ_{F}[b]
6	methanol	328	4.74	398	0.61
7	water	348	4.20	472	nd
	methanol	332	4.64	399	nd
8	water	328	3.69	471	0.02
	methanol	336	4.43	398	0.45

[a] UV–vis spectra: concentration is 2×10^{-5} M for methanol and 5×10^{-5} M for water, fluorescence spectra: concentration is 10^{-6} M. [b] Concentration is 10^{-5} M, excited at 360 nm.

The absorbance and fluorescence of compounds **6**, **7**, and **8** were measured in both methanol and water (Figure 2 and Table 1). Each compound can be seen to exhibit an absorption peak around 330 nm. For example, compound **6** shows a strong peak at 328 nm (solid red line), while the absorption of compound **8** is relatively low (solid green line). Fluorescence emission peaks for these compounds in methanol can be observed around 400 nm. Interestingly, the fluorescence intensities show a reverse trend toward absorbance, with dipotassium salt **8** exhibiting the strongest fluorescence out of three (dotted green line, Figure 2A). Compounds **7** and **8** were also soluble in water. Their UV absorption spectra can be seen to be similar in shape in this solvent, but their intensities are very different; monopotassium salt **7** shows strong absorption at 348 nm, while dipotassium salt **8** shows relatively weak absorption. On the other hand, these two compounds give fluorescence emission peaks with almost the same intensity at approximately 472 nm when irradiated with 360 nm UV light (Figure 2B).

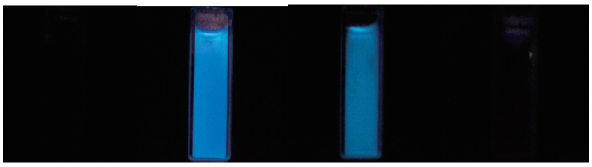


Figure 3. Fluorescence of hydroquinone dimers. From left, aqueous solution of **2a**, methanolic solution of **8**, aqueous solution of **8**, aqueous solution of **8** in the presence of an iron(III) chloride solution.

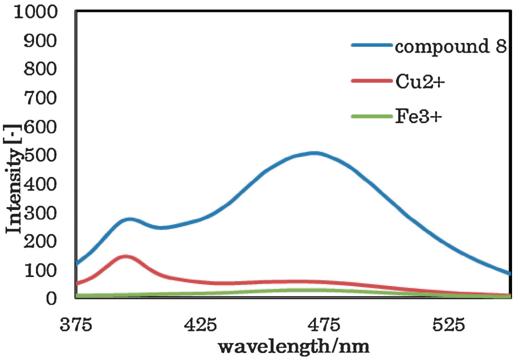


Figure 4. Fluorescence spectra of compound **8** with and without the addition of 5 equiv of Cu^{2+} and Fe^{3+}, concentration is 10^{-6} M.

The quantum yields (Φ_{F}) for these compounds were measured on excitation at 360 nm. Compound **6** in methanol showed the largest value, reaching 0.61. For compound **8**, the quantum yield in methanol was found to be 0.45; however, in water, the value reached as low as 0.02, even though similar fluorescence was observed in the two solvents. In this case, no decay in fluorescence occurred. Thus, compound **8** showed stable fluorescence in water on irradiation with 360 nm UV light. This promising result indicated that compound **8** could serve as a new, useful water-soluble fluorescent dye. Images depicting the fluorescence of the dye under black light (365 nm) illumination are shown in Figure 3.

The fluorescence of **8** in water was sensitive to the presence of certain metallic cations. For example, the fluorescence disappeared when an aqueous solution of Cu^{2+} or Fe^{3+} salt was added (Figure 4), while most alkali metal cations did not affect the fluorescence strength.

In conclusion, we have successfully developed a new water-soluble fluorescent dye based on hydroquinone dimer **1**. The preparation process was simple, and half-protection of the hydroxy groups was achieved efficiently. The present type of water-soluble fluorescent dye is expected to be applicable as a new chemical sensor in biological as well as environmental chemistry. Further studies on this topic are underway in our laboratory.

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