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Exchange of Quinone and Hydroquinone Moieties in Mixed Solutions of Biquinone and Bihydroquinone

Naoto Hayashi,* Kiyomi Matsui, Akifumi Kanda, Takahiro Yoshikawa,
Hiroyuki Nakagawa, Junro Yoshino, and Hiroyuki Higuchi*
Graduate School of Science and Engineering, University of Toyama, Gofuku, Toyama 930-8555

(Received April 5, 2011; CL-110282; E-mail: nhayashi@sci.u-toyama.ac.jp, higuchi@sci.u-toyama.ac.jp)

A mixture of biquinone (**QQ*n***) and bihydroquinone (**HH*n***) bearing *tert*-butyl substituents at 5,5′- ($n = 1$) and 6,6′-positions ($n = 2$) yields hydroquinonylquinone (**HQ*n***) as an equilibrium product by quinone/hydroquinone exchange. The equilibrium constants for the formation of **HQ1** are higher than those of **HQ2** in all solvents. While the exchange between **QQ1** and **HH1** is slow, that between **HQ1**s occurs so rapidly in $CDCl_3$ that it is observed in phase-sensitive 2D NOESY NMR spectra.

In mixed solution of quinones (**Q**) and hydroquinones (**H**), the exchange of **Q** and **H** moieties occurs in the ground[1] and excited states,[2] and in mixed crystals.[3,4] The reaction proceeds via a proton-coupled electron-transfer (PCET) mechanism and PCET reactions have attracted considerable attention as they occur in various chemical and biochemical processes.[5] The **Q**/**H** exchange process is described for both quinone and hydroquinone in Figure 1. Initially, an electron transfers from **H** to **Q** to form a complex **1**$\cdots$**2**. Because **1** is more basic than **Q** and **2** is more acidic than **H**, a facile proton transfer follows to give **3** in both cases. As it is a radical species, **3** can be either be reduced or oxidized to give **4** and **5**, which finally yields **H** and **Q** by proton transfer, respectively. Because it is initiated by an electron transfer, the **Q**/**H** exchange should occur more rapidly in a mixture of biquinone (**QQ**) and bihydroquinone (**HH**) because of stronger electron–acceptor and donor character. We previously reported that the electron–acceptor character of 5,5′-di-*tert*-butyl-2,2′-biquinone (**QQ1**) (Chart 1), where *tert*-butyl groups are substituted for increasing the stability and solubility, was significantly enhanced.[6] This is because the first half-wave reduction potential (−0.78 V in DMF vs. Ag/Ag^+) is lower than that of 2,5-di-*tert*-butylquinone (−1.05 V). The **Q**/**H** exchange was actually observed in a mixed solution of bi(1,4-naphthoquinone) ($^{\mathrm{N}}$**Q**$^{\mathrm{N}}$**Q**) and bi(1,4-hydronaphthoquinone) ($^{\mathrm{N}}$**H**$^{\mathrm{N}}$**H**), which gave 2-(1,4-dihydroxynaphthyl)naphthoquinone ($^{\mathrm{N}}$**H**$^{\mathrm{N}}$**Q**) as an equilibrium product via the exchange of naphthoquinone ($^{\mathrm{N}}$**Q**) and naphthohydroquinone ($^{\mathrm{N}}$**H**) moieties, however, no mechanistic study was performed.[7] In this study, the **Q**/**H** exchange in mixtures of **QQ1** and its hydroquinone derivative, **HH1**, and their isomers **QQ2** and **HH2**, which bear *tert*-butyl groups at the 6,6′-positions, have been investigated in several solvents.

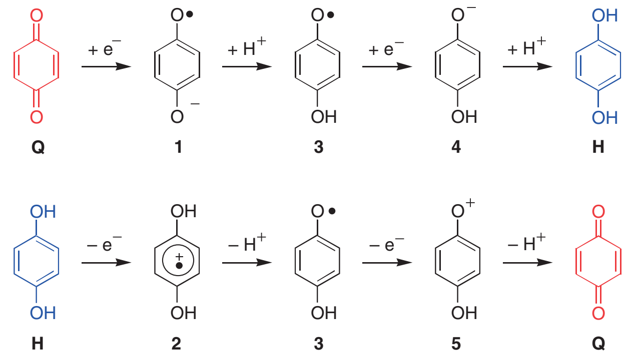

Figure 1. Mechanisms of exchange in quinone and hydroquinone.

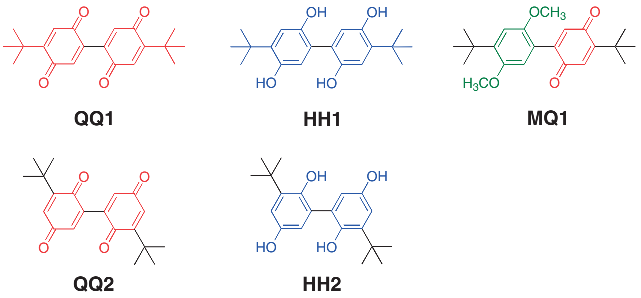

Chart 1.

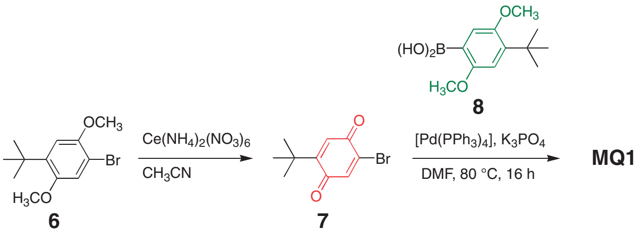

Figure 2. Synthesis of **MQ1**.

QQ1, **HH2**, and **QQ2** were prepared according to literature procedures.[6,8] Several synthetic methods of bihydroquinone are known;[9] we chose to synthesize **HH1** by demethylation of tetramethoxybiphenyl that is similar to the synthesis of **HH2**. For comparison, 5-*tert*-butyl-2-(4-*tert*-butyl-2,5-dimethoxyphenyl)-*p*-quinone (**MQ1**) was synthesized by the oxidation of bromodimethoxybenzene **6** using Ce(IV) to give bromoquinone **7** followed by the Suzuki coupling[10,11] with arylboronic acid **8** (Figure 2).

All compounds were stable in benzene, chloroform, dichloromethane, acetone, and acetonitrile for several days, therefore ^{1}H NMR spectra of the mixtures of **QQ1** and **HH1**, and **QQ2** and **HH2** were measured in these solvents. In the mixed solution of **HH1** and **QQ1**, several new peaks were observed. They were attributed to 2-(2,5-dihydroxyphenyl)-*p*-quinone (**HQ1**), indicating that **Q**/**H** exchange occurred between **QQ1** and **HH1** (eq 1, $n = 1$).

$$\mathbf{QQ}n + \mathbf{HH}n \overset{K_n}{\rightleftharpoons} 2\mathbf{HQ}n \quad (n = 1, 2) \qquad (1)$$

The presence of the molecular ion peak of **HQ1** ($m/z = 328$) in the mass spectrum confirmed the formation of **HQ1**. All attempts to isolate **HQ1** by chromatography failed and only mixtures of

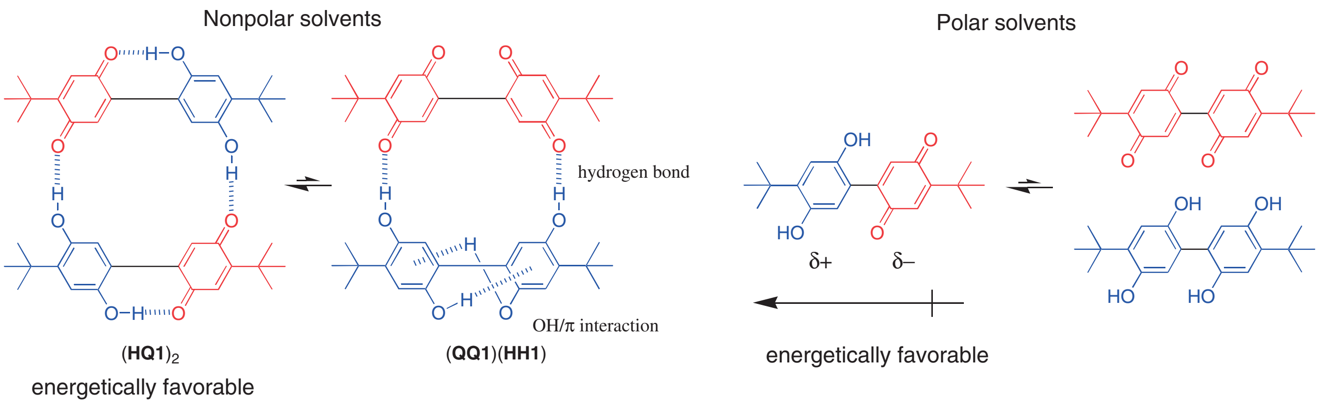

Figure 3. Hydrogen-bonded dimers existing in a **QQ1**–**HH1**–**HQ1** system in nonpolar solvents (left) and monomeric species in polar solvents (right).

HQ1, **QQ1**, and **HH1**, were detected, thus strongly indicating that **HQ1** is expected to be an equilibrium product. **HQ1** could be trapped as **MQ1** by adding dimethyl sulfate and potassium carbonate to the mixed solution of **QQ1** and **HH1**; its molecular structure was determined by comparing with that of the sample shown in Figure 2. The exchange rate was considerably slow in all solvents, and it took from a few hours to more than twenty hours to achieve equilibrium (see Supporting Information[15]). This contrasts the mixed solution of duroquinone and durohydroquinone, which reaches equilibrium imediately.[1a]

In all solvents used, **HQ1** is present as a major component and K_1 (eq 1, $n = 1$) is about 15–37 (benzene, 23; chloroform, 21, dichloromethane, 15; acetone, 37; acetonitrile, 31). This is because in nonpolar solvents with small dielectric constants (ε), there are strong hydrogen bonds between virtually all the molecules.[12] The formation of $(\mathbf{HQ1})_2$ appears to be the most favorable, because all hydroxy groups form hydrogen bonds (Figure 3). In contrast, in the hydrogen-bonded complex (**QQ1**)(**HH1**), just two hydroxy groups of **HH1** form hydrogen bonds with the carbonyl groups in **QQ1** and the other two participate in OH/π interactions as found in 2,2′-biphenyldiol,[13] thus the sum of the interaction energies is less than that of $(\mathbf{HQ1})_2$. The formation of $(\mathbf{HQ1})_2$ is also advantageous in nonpolar solvents because the molecules are aligned head-to-tail for the molecular dipole moments to cancel out. In contrast, (**QQ1**)(**HH1**) is polar. On the other hand, in polar solvents, the molecules are monomeric because of the small hydrogen-bonding energies,[12] therefore in the polar environment, **HQ1** should be favorable compared to **QQ1** and **HH1** due to its polar character (Figure 3).

Existence of $(\mathbf{HQ1})_2$ is confirmed by phase-sensitive 2D NOESY NMR spectra (303 K, mixing time = 0.5 s). As shown in Figure 4a, the cross peaks arising from the chemical exchange of the two *tert*-butyl groups of **HQ1** (Figure 4c) were observed in $CDCl_3$. In contrast, no cross peaks were observed in the $(CD_3)_2CO$ solution, as shown in Figure 4b. This result agrees with the hypothesis that **HQ1** exists as a monomer.

The **Q**/**H** exchange between **HQ1**s is so rapid as to be observable in NMR measurement, which is in marked contrast to the slow **Q**/**H** exchange between **QQ1** and **HH1**. The slow exchange in the mixed solution of **QQ1** and **HH1** is sterically hindered by the *tert*-butyl groups and the highly twisted π-planes. These prohibit the electron transfer in the initial step of the **Q**/**H** exchange. In fact, we previously reported that the torsional angle of two quinone planes was 38° in the X-ray structure of **QQ1**;[6] thus, **QQ1** did not form a charge-transfer (CT) complex with hydroquinone.[14] Nevertheless, a new absorption band was observed in UV–vis spectra of the mixed solution of **QQ1** and **HH1**, which is attributable to **HQ1** on the basis of K_1. As shown in Figure 5, the longest wavelength absorption peak ($\lambda_{\max}$) of **HQ1** is red-shifted compared to **QQ1** and **HH1**. It is seen that $\lambda_{\max}$ for **HQ1** is significantly red-shifted in the less polar solvent (chloroform) compared to that in acetone. This negative solvatochromism indicates that in **HQ1**, the ground state is more charge separated than the excited state because of electron transfer from **H** to **Q**; this is expected to allow rapid **Q**/**H** exchange in **HQ1**. Similar negative solvatochromism is observed in **MQ1**, however the shift in $\lambda_{\max}$ was smaller (19 nm whereas 25 nm in **HQ1**) because of the weak electron-donating behavior of the 2,5-dimethoxyphenyl moiety.

The **Q**/**H** exchange was also observed in the mixed solution of **QQ2** and **HH2** and yielded 2-(2,5-dihydroxyphenyl)-*p*-quinone (**HQ2**). Compared to K_1, the values of K_2 were low being about 0.36–3.1 (benzene, 0.36; chloroform, 0.75, dichloromethane, 0.85; acetone, 3.1; acetonitrile, 3.1). The positions of the *tert*-butyl groups affect the equilibrium constants, and as steric repulsions between the *tert*-butyl groups are negligible in both intra- and intermolecular processes, it is inferred that solvent interactions play a critical role. It has been reported that in the intramolecular cyclization of **QQ1** and **QQ2**,[8] the substitution of bulky *tert*-butyl groups affects the solvation of the adjacent substituents.

In conclusion, the **Q**/**H** exchange was observed in both the mixtures of **QQ1** and **HH1** and **QQ2** and **HH2** to yield **HQ1** and **HQ2**, respectively, and **HQ1** was generated more favorably than **HQ2** in all solvents. The **Q**/**H** exchange was slow between **QQ1** and **HH1** and considerably fast in the hydrogen-bonded dimer $(\mathbf{HQ1})_2$ presumably due to the intramolecular electron transfer. Our future research will focus on the substituent effect on the ratio $[\mathrm{QH}]^2$:[QQ][HH] as well as the exchange rate of intra- and intermolecular processes.

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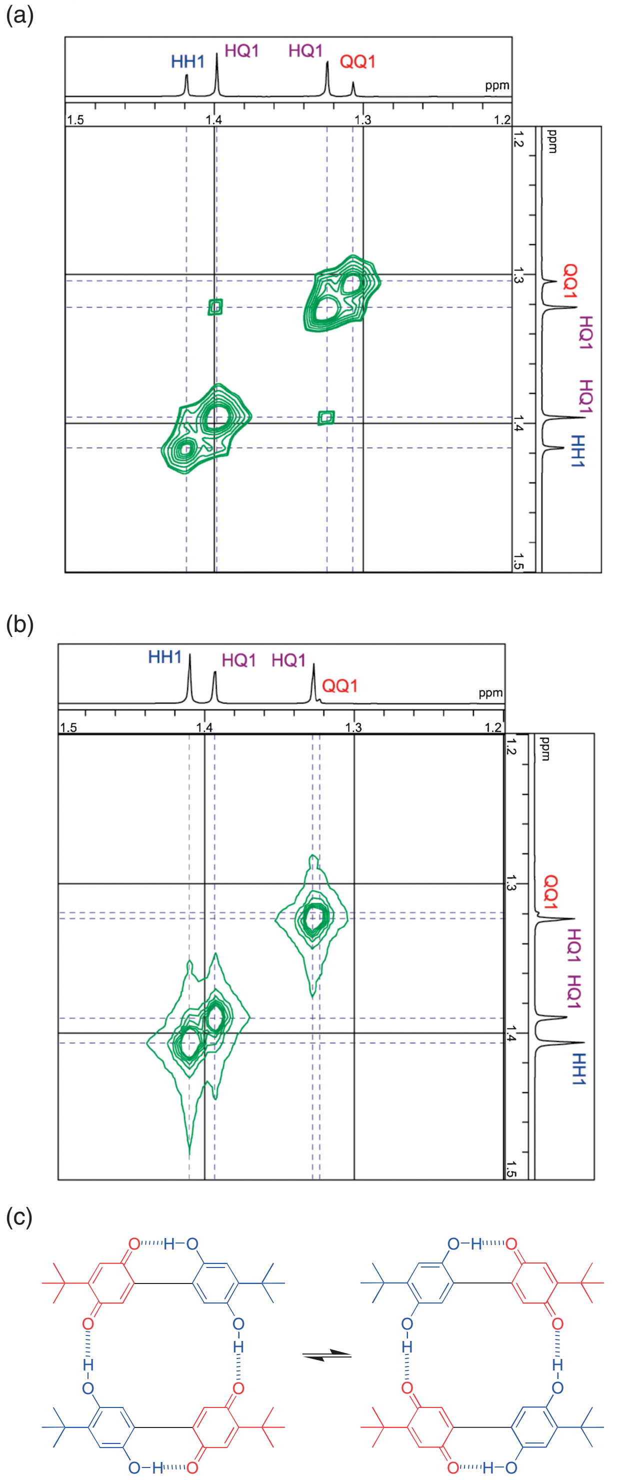

Figure 4. 2D NOESY spectra of the mixture of **QQ1** and **HH1** at 1.2–1.5 ppm in $CDCl_3$ (a) and $(CD_3)_2CO$ (b), only signals attributed to *tert*-butyl groups are shown. Schematic representation of the chemical exchange of quinone and hydroquinone moieties in $(\mathbf{HQ1})_2$ (c).

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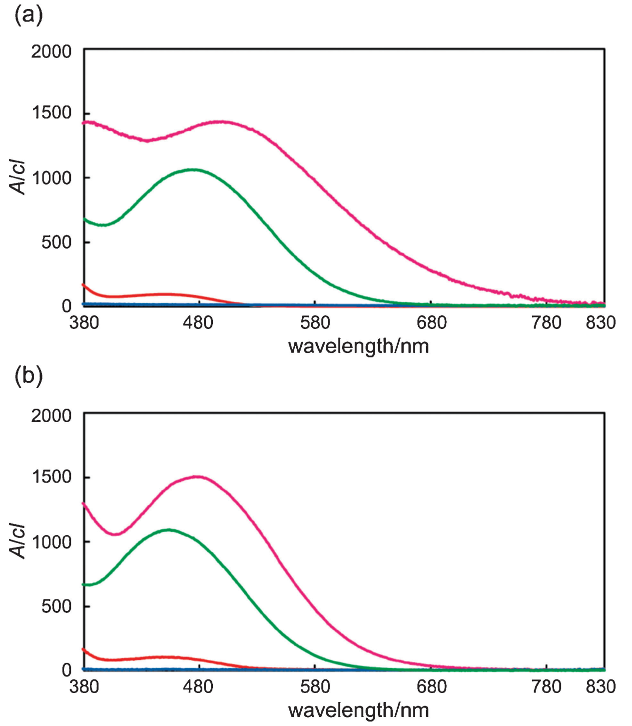

Figure 5. UV–vis spectra of the mixture of **QQ1** and **HH1** (purple, mainly **HQ1**), **QQ1** (red), **HH1** (blue), and **MQ1** (green) in $CHCl_3$ (a) and $(CH_3)_2CO$ (b). λ_{max} values are 500 (**HQ1**), 473 (**QM1**), and 452 nm (**QQ1**) in $CHCl_3$, and 475 (**HQ1**), 454 (**QM1**), and 448 nm (**QQ1**) in $(CH_3)_2CO$.

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