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# Synthesis and electro-spectroelectrochemistry of ferrocenyl naphthaquinones

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ABSTRACT

A practical approach to ferrocenyl naphthaquinone derivatives involving thermal rearrangement of variously substituted 4-aryl-4-hydroxycyclobutenones was described. The reaction of 3-ferrocenyl-4-isopropoxy-3-cyclobutene-1,2-dione with different aryl lithiums gave the corresponding 4-aryl-4-hydroxycyclobutenones, which were heated in *p*-xylene at reflux open to the air to yield ferrocenyl naphthaquinones. The redox chemistry of the ferrocenyl naphthaquinones was studied by electrochemical and in situ spectroelectrochemical techniques in $CH_2Cl_2$ solution and in $CH_3CN$ solution with water, weak and strong acidic additives. Ferrocenyl naphthaquinones displayed reversible two reduction processes involving semiquinone radical anion (Fc–snq$^{\bullet-}$), dianion (Fc–nq$^{2-}$) species and a one-electron oxidation process based on the ferrocenium/ferrocene ($Fc^{+}$–nq/Fc–nq) couple in $CH_2Cl_2$. The redox reaction mechanism of the ferrocenyl naphthaquinones in the presence of the additives proceeded via hydrogen bonding or proton-coupled electron transfer. Effects of the substituents on the reduction potentials and intramolecular charge-transfer bands of ferrocenyl naphthaquinones were also discussed.



## 1. Introduction

In recent years, ferrocene and its derivatives have received considerable attention since they have found potential applications in the fields of asymmetric synthesis,[1] bioorganometallic chemistry,[2] and particularly in materials science.[3] Ferrocene has become one of the most preferred components of molecular electron transfer systems in artificial photosynthesis studies[4] and in the development of optoelectronic devices.[5] As an electron-donor unit having chemical versatility, thermal stability as well as a reversible electrochemical redox couple, ferrocene participates in electron transfer systems with various electron acceptors and redox-active species such as fullerene,[6] BODIPY,[7] porphyrins,[8] phthalocyanines,[9] and corroles.[10] Dithiafulvalene[11] and tetrathiafulvalene[12] derivatives of ferrocene have been reported as donor conducting materials for charge-transfer complexes. Moreover, ferrocene has been combined with good electron acceptor quinones covalently or by various spacers. Ferrocene–benzoquinone[13] and ferrocene–anthraquinone[14] donor–acceptor systems with or without a spacer are quite common. Both quinones and ferrocene exhibiting well-established reversible electrochemical redox couples are the most important and well-studied examples of an organic/organometallic redox system.[15] From a fundamental standpoint, these model molecules have played an important role in developing our current understanding of organic and organometallic redox chemistry.[16] Additionally, as remarkable electron donor–acceptor pairs, ferrocene, and quinones provide tunable redox potentials through judicious choice of substituents. Thus, coupling ferrocene and quinones intramolecularly would then offer interesting candidates for studying electron transfer reactions and optical properties.[17]

Electron transfer plays a pivotal role not only in chemical processes but also in biological redox processes that have tremendous relevance to our life, such as photosynthesis and respiration.[18] To understand the factors for controlling important electron-transfer processes in biological systems, electron-transfer dynamics between donor and acceptor molecules bound to proteins have been studied extensively.[19] Considering the redox chemistry of quinone-based couples, these species are closely related to biological processes as electron-proton transfer agents in the oxidative phosphorylation of ADT to ATP, or photosynthesis, which themselves are directly affected the by acid–base properties of quinone, semiquinone, and hydroquinone species.[20]

It has been determined that the electrochemical behavior of quinone is strongly influenced by environmental conditions that regulate the potentials and reaction pathways of the reduced/oxidized species appearing in a proton-coupled electron transfer.[15f,g,20a,21] A deep insight into the redox processes of quinones can be gained by performing detailed studies on the electrochemical behaviors of quinones, particularly, in non-aqueous media using aprotic solvents, which are useful in mimicking the non-polar environments in the cell where many biological electron-transfer processes occur.[20a] In dry, neutral and aprotic media, quinones

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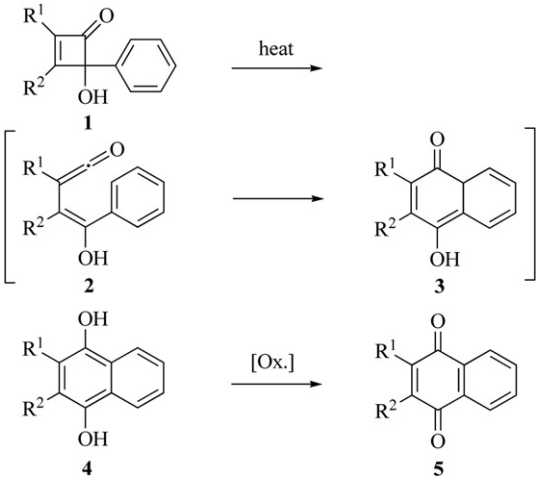
typically show two cathodic chemically reversible waves, which correspond to the formation of the semiquinone radical anion ($sq^{\bullet -}$) and dianion ($q^{2-}$), respectively.[15f] The potentials of these reductions depend on several parameters, such as the solvent, supporting electrolyte and electrode material as well as the electron-withdrawing or -donating substituents appended on the quinone unit.[15f,20a,21a] The course of electroreduction for quinones is remarkably complex in the acidic medium as described in numerous studies.[15d,f,g,20a,21,22] Several recent studies reported hydrogen bonding and protonation effects on the redox behavior of quinones through electrochemical investigations.[15d,20a,23] Hydrogen bonds are particularly important for biological systems where they provide essential recognition, structural, and control elements needed to coordinate and run the complex molecular machinery required for life.[20a,23a,24] Moreover, the hydrogen bonding can be viewed as a first step toward proton transfer.[15d,20a] The electrochemical and spectroelectrochemical investigations on the quinone redox system involving the electron transfer coupled with the hydrogen bonding give much information concerning the effect of molecular structure and environment on these basic processes.[23,25] It is well-known that the combination of electrochemical and spectroelectrochemical methods provides a powerful tool to reveal the complementary nature of the molecular structure. Moreover, these methods supply detailed electrochemical information to clarify mechanism of electron transfer reactions.[26]

In this study, we have devoted our interests to the synthesis of new ferrocenyl naphthaquinone derivatives via a well-established regiospecific method, which offers an easy access to highly substituted quinones.[27] Generally, the method entails thermal rearrangements of reactive 4-alkenyl-, 4-(aryl or heteroaryl)-4-hydroxycyclobutenones, such as **1**, to the naphthaquinone derivative **5** after the oxidation of the initially formed hydroquinone **4** (Scheme 1). We employed this method, for the first time, to achieve various ferrocenyl naphthaquinones (**10a**–**k**, **11g**, and **13**) starting from 3-ferrocenyl-4-isopropoxy-3-cyclobutene-1,2-dione (**6**) and aryl lithiums **7a**–**k**. The method has been applied before for the synthesis of ferrocenyl benzoquinones by Zora et al.[13c] However, to the best of our knowledge, only three ferrocenyl naphthaquinone derivatives have been prepared by the reaction of Fischer-type chromium carbene complexes with ethynylferrocene.[28] Here, we have also presented an electrochemical approach to the mechanistic study of hydrogen bonding and proton-coupled electron transfer of ferrocenyl naphthaquinones in non-aqueous solutions in the absence and presence of acidic additives.

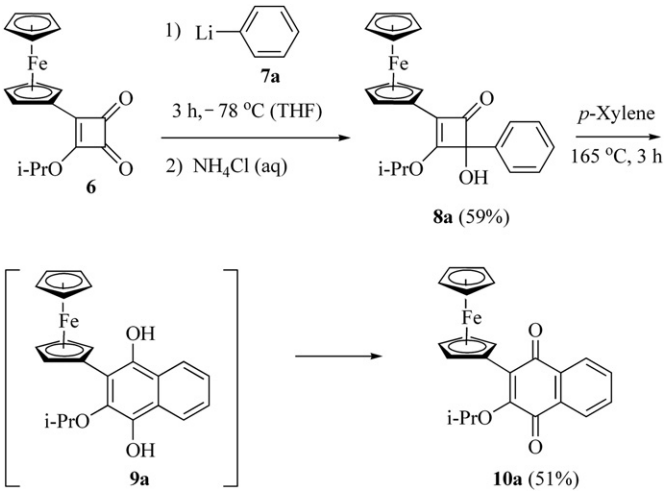



**Scheme 1.** Thermal rearrangement of 4-aryl-4-hydroxycyclobutenone **1** to the naphthaquinone derivative **5** ($R^1$, $R^2$=alkyl, aryl, heteroaryl, alkoxy, etc.).

## 2. Results and discussion

### 2.1. Synthesis of ferrocenyl naphthaquinone derivatives

We initially attempted the synthesis of ferrocenyl-substituted 4-hydroxy-4-phenylcyclobutenone **8a** by the reaction of 3-ferrocenyl-4-isopropoxy-3-cyclobutene-1,2-dione (**6**)[13c,29] with phenyllithium (**7a**) according to well-documented literature procedures.[27,30] Surprisingly, thermolysis of the isolated ferrocenyl-substituted 4-hydroxy-4-phenylcyclobutenone (**8a**), even under a nitrogen atmosphere, furnished directly the oxidized product ferrocenyl naphthaquinone **10a** in 51% yield instead of a hydroquinone derivative **9a** (Scheme 2). However, isolating the 4-hydroxycyclobutenone **8a** by column chromatography was quite tedious and we noticed that the alcohol **8a** was prone to decompose slowly when it was stored, particularly at rt.




**Scheme 2.** Synthesis of ferrocenyl naphthaquinone **10a** via a thermal rearrangement of the isolated 4-hydroxy-4-cyclobutenone intermediate **8a** in *p*-xylene.

A more practical synthetic approach to the ferrocenyl naphthaquinone derivative **10a** was achieved without isolation and purification of ferrocenyl-substituted 4-hydroxy-4-phenylcyclobutenone **8a**. The crude material obtained by treatment of a THF solution of **6** at −78 °C with phenyllithium (**7a**), followed by an ammonium chloride quench, was directly dissolved in *p*-xylene and the resulting solution was heated at reflux open to the air to promote oxidation of intermediate hydroquinone **9a** (Scheme 3). During heating, the color of the solution slowly turned deep green and the color change persisted with disappearance of the ferrocenyl-substituted 4-hydroxy-4-phenylcyclobutenone **8a** in 4 h. After evaporation of *p*-xylene and column chromatography, the ferrocenyl naphthaquinone **10a** was obtained in 45% overall yield from 3-ferrocenyl-4-isopropoxy-3-cyclobutene-1,2-dione (**6**).

To investigate the scope and limitations of this short synthetic approach to ferrocenyl naphthaquinone derivatives, we performed the reaction of cyclobutenedione **6** with differently substituted aryl lithiums **7a**–**g**, which were in situ prepared (except for **7a**) by the reaction of a slight excess of *n*-BuLi with the corresponding aryl bromides in dry THF at −78 °C. The thermolyses of crude mixtures of 4-aryl-4-hydroxycyclobutenones **8a**–**g** were completed within 4 h and gave the ferrocenyl naphthaquinone derivatives **10a**–**g** and **11g** in moderate yields (40–53%). In all attempts, a ferrocenyl hydroquinone derivative of type **9a** was not observed (Scheme 3).

Although the thermal rearrangements of 4-aryl-4-hydroxycyclobutenones (**8e**–**g**) are open to give two regioisomeric naphthaquinones via ring closure at two different positions of aryl groups, for example, α or β in **8g**, only the thermolysis of the cyclobutenone **8g** gave the angularly-fused ferrocenyl naphthaquinone derivative