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Articles

Electrochemically Controlled Hydrogen Bonding. *o*-Quinones as Simple Redox-Dependent Receptors for Arylureas

Yu Ge, Laura Miller, Teresa Ouimet, and Diane K. Smith*

Department of Chemistry San Diego State University San Diego, California 92118-1030

dsmith@sciences.sdsu.edu

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9,10-Phenanthrenequinone and acenaphthenequinone are shown to act as simple redox-dependent receptors toward aromatic ureas in CH_2Cl_2 and DMF. Reduction of the *o*-quinones to their radical anions greatly increases the strength of hydrogen bonding between the quinone carbonyl oxygens and the urea *N*-hydrogens. This is detected by large positive shifts in the redox potential of the quinones with no change in electrochemical reversibility upon addition of urea guests. Cyclic voltammetric studies with a variety of possible guests show that the effect is quite selective. Only guests with two strong hydrogen donors, such as O−H bonds or amide N−H bonds, that are capable of simultaneously interacting with both carbonyl oxygens give large shifts in the redox potential of the quinones. The electronic character and conformational preference of the guest are also shown to significantly affect the magnitude of the observed potential shift. In the presence of strong proton donors the electrochemistry of the quinone becomes irreversible indicating that proton transfer has taken place. Experiments with compounds of different acidity show that the pK_a of the protonated quinone radical is about 15 on the DMSO scale, >4 pK_a units smaller than that of 1,3-diphenylurea. This is further proof that hydrogen bonding and not proton transfer is responsible for the large potential shifts observed with this and similar guests.

Hydrogen bonds are one of the most important types of intermolecular interactions. Due to their strength and directionality, they are ubiquitous in biological systems, providing essential recognition, structural and control elements needed to coordinate and run the complex molecular machinery required for life. In recent years there has been tremendous interest in utilizing hydrogen bonds for similar purposes in synthetic systems. They have been used extensively as recognition elements in the design of synthetic receptors[1,2] and as structural elements in the creation of large molecular assemblies in solution[3,4] and "engineered" solid-state materials.[5,6] In contrast, hydrogen bonds have not been used extensively as control elements in synthetic systems, even though they are often used as such in biological ones. For example, in flavin-containing redox proteins, hydrogen bonds are used to modulate the redox potential of the

(1) For reviews see: (a) Webb, T. H.; Wilcox, C. S. *Chem. Soc. Rev.* **1993**, 383−395. (b) Rebek, J. *Angew. Chem., Intl. Ed. Engl.* **1990**, *29*, 245−255. (c) Hamilton, A. D. *J. Chem. Educ.* **1990**, *67*, 821−828. (d) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609−1646.

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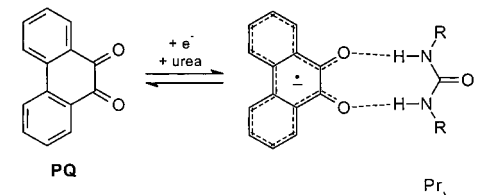
flavins by stabilizing one oxidation state relative to another. This has been demonstrated by Rotello and coworkers in several model systems.[7]

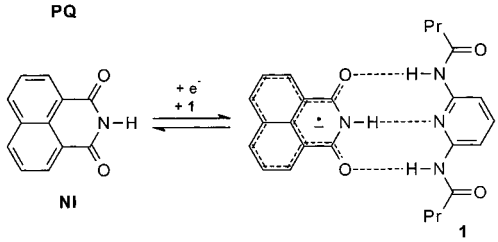
Previously, we have showed how hydrogen bonds coupled with electrochemistry can create a powerful control element in synthetic receptor-substrate systems.[8] The concept, which is also being actively explored by Rotello[9] and others,[10] is straightforward. Hydrogen bonds are known to have substantial electrostatic character. Therefore, a reduction or oxidation process that leads to a change in partial charge on one of the components in a hydrogen bond will have a significant effect on the strength of that hydrogen bond. In particular, if the negative charge on the hydrogen acceptor or the positive charge on the hydrogen donor is increased, the strength of the hydrogen bond will be increased. Alternatively, if the negative charge on the hydrogen acceptor or the positive charge on the hydrogen donor is decreased, the strength of the hydrogen bond will be decreased.

In our earlier work,[8] we showed that substantial effects can be produced even in very simple systems. Specifically we looked at the behavior of 9,10-phenanthrenequinone, PQ, and 1,8-naphthalimide, NI. Both PQ and NI undergo reversible one-electron reductions in aprotic media to form radical anions, eqs 1 and 2. Although the radical is



(1)

PQ



(2)

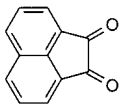
NI 1

delocalized, most of the negative charge resides on the oxygens due to their greater electronegativity. For this reason, substrates with appropriately positioned NH groups hydrogen bond with the carbonyl oxygens much stronger in the reduced states. Examples of good substrates are urea derivatives with PQ[11] and the diamidopyridine derivative 1 with NI. The increase in binding strength is detected by large positive shifts in the redox potential of PQ and NI in the presence of the substrates. In effect, the substrates stabilize the radical anions through hydrogen bonding, making it easier to reduce the quinone or diimide in their presence.

Positive shifts in the redox potential of quinones in the presence of hydrogen bond donors have been studied previously.[12] The difference here is the large magnitude of the observed shifts at very low concentrations of hydrogen bond donor. The maximum potential shift is related to the ratio of binding constants in the oxidized (K_{ox}) and reduced states (K_{red}) as given in eq 3.[13] On the basis of this, the binding strength of PQ with the oxidized

$$\Delta E^{\circ}_{max} = \frac{59mV}{n} \log\left(\frac{K_{red}}{K_{ox}}\right) \qquad (3)$$

diphenylurea increases by >2000 times upon reduction of PQ to its radical anion in CH_2Cl_2, and the binding strength of NI to 1 increases by >100 times upon reduction.



ANQ

In this paper, we report the results of our full study on the redox-dependent binding properties of the orthoquinone/radical anion redox couple. In addition to PQ, we studied acenaphthenequinone, ANQ, which also undergoes a reversible, one-electron reduction in aprotic media. A large variety of substrates were studied with both quinones in order to better understand the nature of the binding interaction. We also explored in detail the question of hydrogen bonding vs proton transfer in these systems.

Experimental Section

Synthetic Procedures. Elementary analyses were performed by Desert Analytics, Tucson, AZ. Et_2O was dried and freshly distilled from CaH_2. 1-Phenyl-3-(4-methoxyphenyl)-urea,[14] 1,3-di-(4-methoxyphenyl)urea,[15] 1-phenyl-3-(4-trifluoromethylphenyl)urea,[16] 1,3-di-(4-trifluoromethylphenyl)urea,[17] 1-phenyl-3-(2,5-di-*tert*-butylphenyl)urea, 1-phenyl-3-propyl-

(4) For some recent examples, see: (a) Gong, B.; Yan, Y.; Zeng, E.; Skrzypczak-Jankunn, E.; Kim, Y. W.; Zhu, J.; Ickes, H. *J. Am. Chem. Soc.* **1999**, *121*, 5607−5608. (b) Corbin, P. S.; Zimmerman, S. C. *J. Am. Chem. Soc.* **1998**, *120*, 9710−9711. (c) Martin, T.; Obst, U.; Rebek, J. *Science* **1998**, *281*, 1842−1845. (d) Clark, T. D.; Buriak, J. M.; Kobayashi, K.; Isler, M. P.; McRee, D. E.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1998**, *120*, 8949−8962. (e) Sakai, N.; Majumbar, N.; Matile, S. *J. Am. Chem. Soc.* **1999**, *121*, 4294−4295.

(5) For reviews see: (a) Aakeroy, C. B.; Seddon, K. B. *Chem. Soc. Rev.* **1993**, 397−407. (b) MacDonald, J. C.; Whitesides, G. M. *Chem. Rev.* **1994**, *94*, 2383−2420. (c) Zaworotko, M. J. *Chem Soc. Rev.* **1994**, 283−288. (d) Bishop, R. *Chem Soc. Rev.* **1996**, 311−319.

(6) For some recent examples, see: (a) Holy, P.; Zavazka, J.; Cisarova, I.; Podlaha, J. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 381−383. (b) Brunet, P.; Simara, M.; Wuest, J. D. *J. Am. Chem. Soc.* **1997**, *119*, 2737−2738. (c) Evans, C. C.; Sukarto, L.; Ward, M.. D. *J. Am. Chem. Soc.* **1999**, *121*, 320−325. (d) Aoyama, Y.; Endu, K.; Anzai, T.; Yamaguchi, Y.; Sawaki, T.; Kobayashi, K.; Kanehisa, N.; Hashimoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 5562−5571.

(7) (a) Breinlinger, E.; Niemz, A.; Rotello, V. M. *J. Am. Chem. Soc.* **1995**, *117*, 5379−5380. (b) Breinlinger, E.; Rotello, V. M. *J. Am. Chem. Soc.* **1997**, *119*, 1165−1166.

(8) (a) Ge, Y.; Lilienthal, R. R.; Smith D. K. *J. Am. Chem. Soc.* **1996**, *118*, 3976−3977. (b) Ge, Y.; Smith D. K. *Anal. Chem.* **2000**, *72*, 1860−1865..

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(10) Carr, J. D.; Lambert, L.; Hursthouse, M. B.; Malik, K. M. A.; Tucker, J. H. R. *Chem. Commun.* **1997**, 1649−1650.

(11) Ureas are known to strongly hydrogen bond with oxygens that carry partial negative charges, so they are often used as key components in receptors for oxyanions. See, for example: (a) Hughes, M. P.; Shang, M.; Smith, B. D. *J. Org. Chem.* **1996**, *61*, 4510−4511. (b) Nishizawa, S.; Buhlmann, P.; Iwao, M.; Umezawa, Y. *Tetrahedron Lett.* **1995**, *36*, 6483−6486.

(12) See Gupta, N.; Linschitz, H. *J. Am. Chem. Soc.* **1997**, *11*, 6384−6391, and references therein.

(13) Miller, S. R.; Gustowski, D. A.; Chen, Z.-H.; Gokel, G. W.; Echegoyen, L.; Kaifer, A. E. *Anal. Chem.* **1988**, *60*, 2021−2024.

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(17) Lin, H. C.; Cotter, B. R.; Bieron, J. F.; Krishnamurti, R. *J. Fluorine Chem.* **1991**, *52*, 107−116.

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urea,[18] and 1-phenyl-3-dibutylurea[19] were prepared from the appropriate isocyanates and amines using the general procedure described below. Other solvents and chemicals were of reagent grade and used as supplied from the manufacturers.

General Procedure for the Preparation of Ureas. A stirred solution of the amine (10 mmol) in ethyl ether (10 mL) was cooled to 0 °C. The isocyanate (10 mmol) in ethyl ether (10 mL) was added dropwise over 15 min. The solution was then allowed to warm to room temperature and stirred for 1−24 h. The solvent was removed in vacuo and the residue recrystallized from ethanol to yield a crystalline solid. All compounds, except 1-phenyl-3-(2,5-di-*tert*-butylphenyl)urea, are known, and analytical data are in accordance with literature values.[14−19]

1-Phenyl-3-(2,5-di-*tert*-butylphenyl)urea. 2,5-Di-*tert*-butylaniline and phenyl isocyanate were used as starting materials. The reaction was finished in 2 h with 90% yield: mp 232.0−232.5 °C; ^{1}H NMR 1.321 (s, 9 H), 1.326 (s, 9 H), 7.007 (tt, J = 9.6, 1.6 Hz, 1 H), 7.21−7.46 (m, 8 H); ^{13}C NMR 31.74, 32.28, 35.85, 36.55, 121.30, 124.69, 125.61, 128.37, 128.57, 130.08, 135.75, 139.20, 144.75, 151.82, 155.65; IR ($CHCl_3$) 3320, 2965, 1644, 1600, 1557, 1505,1235; MS m/z 325 (M^+) Anal. Calcd for $C_{21}H_{28}N_2O$: C, 77.73; H, 8.70; N, 8.63. Found: C, 77.80; H, 9.00; N, 8.60.

Instrumental Procedures. Instrumentation and Reagents. Cyclic voltammetry (CV) experiments were performed with a PAR Model 263 digital potentiostat using the Model 270 electrochemistry software package. The acquisition mode was set to "ramp" in order to simulate an analogue experiment. CH_2Cl_2 was freshly distilled from P_2O_5 and filtered through a column of activated alumina immediately before use. Anhydrous grade *N*,*N*-dimethylformamide (DMF) was purchased from Aldrich and also filtered through an activated alumina column immediately before use. NBu_4PF_6 (0.1 M) was used as the electrolyte. All measurements were conducted at 22 °C under N_2 in a jacketed, one-compartment cell with a Au disk working electrode (2 mm diameter) and a Pt wire counter electrode. A Ag wire was used as a pseudo-reference in most experiments. Ferrocene, *N*,*N*,*N*′,*N*′-tetramethylphenylenediamine and cobalticinium hexafluorophosphate were used as internal references. For the CVs used for computer simulation, a Ag wire in a fritted tube containing 10 mM $AgNO_3$ in 0.1 M Bu_4NPF_6/DMF was placed in a separate compartment and used as a reference. The cell for these experiments was covered with a black cloth to prevent photodegradation of the quinones.

General Procedure for Measurement of $\Delta E_{1/2}$ Values. Electrolyte and solvent were added to a cell with working, reference and counter electrodes protected under N_2. The solvent was degassed by purging with N_2 for a few minutes. After taking a background scan, the quinone and internal reference were added and a CV taken. Then the guest was added to the cell and another CV taken. The difference in half-wave potentials of the quinone relative to the internal reference before and after adding the guest, $\Delta E_{1/2}$, was then calculated.

CV Simulation. DigiSim v2.1 software (BioAnalytical Systems) was used to simulate the CVs and calculate the binding constants of PQ and ANQ with 1,3-diphenylurea. Background subtracted CVs of the quinones in the presence of 0, 0.5, 1.0, 2.0, 5.0, 10, 20 and 50 mM diphenylurea were fit to the following "square-scheme", eq 4. The formal redox potential of the quinone, E_Q, the diffusion coefficient of the quinone, D, and the uncompensated resistance in the cell, R_u,[20] were determined by fitting the CVs with no added urea at scan rates between 200 and 1000 mV/s, assuming Butler−Volmer kinetics with an electron-transfer rate constant, k_s, = 10 cm/s and alpha = 0.5. The E_Q, D, and R_u values were then used to fit the CVs in the presence of urea by adjusting K_{ox} and K_{red} to give the best fit to the experimental CVs at different values of k_f. All species were assumed to have equal D, $\sim 5 \times 10^{-6}$ cm^2/s. Values of $k_f \leq 10^5$ M/s resulted in much poorer fits to the experimental voltammograms. In the final simulations k_f values of 10^6 were used for both the oxidized and reduced quinones.

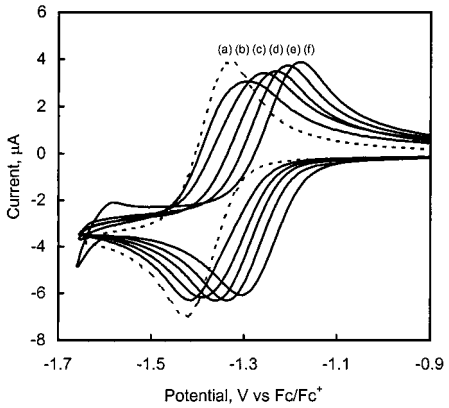
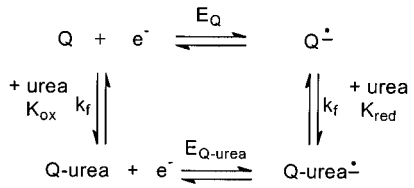


Figure 1. Cyclic voltammograms of 1 mM ANQ in CH_2Cl_2 in the presence of increasing amounts of 1,3-diphenylurea. Scan rate = 100 mV/s. [1,3-Diphenylurea] (mM) = (a) 0, (b) 0.5, (c) 1, (d) 2, (e) 5, (f) 10.



(4)

Results and Discussion

Voltammetry of Quinones in the Presence of 1,3-Diphenylurea. Figure 1 shows cyclic voltammograms (CVs) of acenaphthenequinone (ANQ) in the presence of different amounts of 1,3-diphenylurea in CH_2Cl_2. The CVs of ANQ are similar to the previously reported CVs of phenanthrenequinone (PQ) in the presence of 1,3-diphenylurea.[8a] CV (a) in Figure 1 (dashed line) is ANQ by itself. Addition of 0.5 equiv of 1,3-diphenylurea, CV (b), causes noticeable broadening of the anodic peak, and, in the presence of 1 equiv of 1,3-diphenylurea, CV (c), the half-wave potential ($E_{1/2}$) is shifted significantly positive of the original. The wave continues to shift positive as more 1,3-diphenylurea is added until at 10 mM, which is close to the solubility limit, the wave is 170 mV positive of the original, CV (f).

The behavior observed in Figure 1 is consistent with strong binding of the urea to the ANQ radical anion. However, attempts to simulate the CVs of PQ and ANQ in the presence of different amounts of 1,3-diphenylurea in CH_2Cl_2 resulted in unsatisfactory fits to the experimental data. We believe this is due to self-aggregation of the urea in CH_2Cl_2. This hypothesis is supported by a concentration dependence study of 1,3-diphenylurea in CD_2Cl_2 using ^{1}HNMR. The peak for the urea N-hydrogens moved upfield by 0.19 ppm when the urea solution was diluted from 1 mM to 20 μM. It then moved downfield by 0.03 ppm upon dilution from 20 μM to 10

(19) Van Landeghem, H.; de Aguirre, I. *Bull. Soc. Chim. Fr.* **1967**, 172−178.

(20) Since quinones are known to have very fast electron-transfer rate constant in aprotic solvents (see, for example, Howell, J. O.; Wightman, R. M. *Anal.Chem.* **1984**, *56*, 524−529), ΔE_p's > 60 mV at these relatively slow scan rates were assumed to be entirely due to the R_u in the cell. R_u values of 800−900 Ω were typically determined in this fashion.

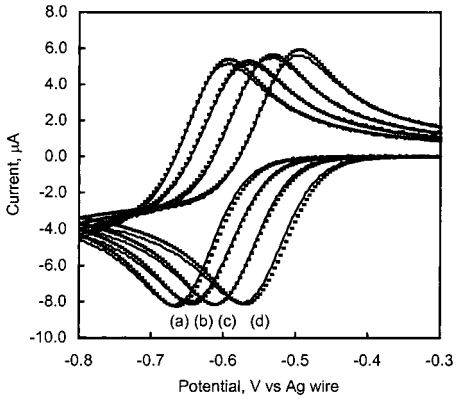


Figure 2. Experimental (solid lines) and simulated (dashed lines) cyclic voltammograms of 1 mM PQ in DMF in the presence of increasing amounts of 1,3-diphenylurea. Scan rate = 200 mV/s. [1,3-Diphenylurea] (mM) = (a) 0, (b) 2, (c) 10, (d) 50. The simulated CVs correspond to $K_{ox} = 1$ and $K_{red} = 905$ M^{-1}.

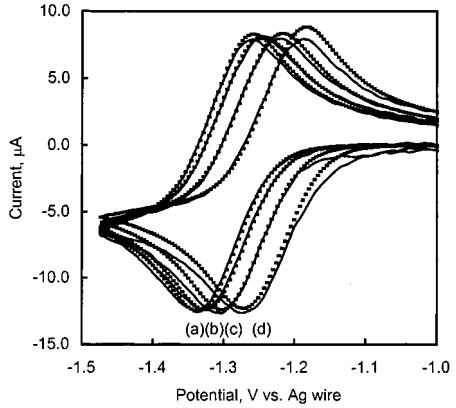


Figure 3. Experimental (solid lines) and simulated (dashed lines) cyclic voltammograms of 1 mM ANQ in DMF in the presence of increasing amounts of 1,3-diphenylurea. Scan rate = 200 mV/s. [1,3-Diphenylurea] (mM) = (a) 0, (b) 1, (c) 5, (d) 20. The simulated CVs correspond to $K_{ox} = 1$ and $K_{red} = 715$ M^{-1}.

μM. Further dilution resulted in the chemical shift moving upfield again. This behavior indicates that the urea does aggregate in CD_2Cl_2 and the aggregation mode is complicated.

Since self-aggregation competes with binding to the quinone radical anion, successful fitting of the experimental CVs in CH_2Cl_2 would require incorporating aggregation into the mechanism. In contrast, ^{1}H NMR data of 1,3-diphenylurea in DMF-d_7 shows no concentration dependence over the same concentration range, which indicates urea self-aggregation does not occur in DMF. This simplifies the binding, and, as a result, we are able to fit the experimental CVs reasonably well in DMF.

Figure 2 shows CVs of PQ in DMF in the presence of different amounts of 1,3-diphenylurea (solid lines) overlapped with the corresponding simulated CVs (dotted lines). Similar CVs for ANQ are shown in Figure 3. For both quinones, the $E_{1/2}$ shift in DMF is significantly smaller than in CH_2Cl_2, indicating weaker binding. This is expected since DMF should solvate the hydrogen bonding sites much more effectively than CH_2Cl_2. With PQ the simulated CVs fit the observed ones very well. The fits are not as good with ANQ due to problems with background subtraction.[21] However the peak potentials in the simulated CVs fit the experimental CVs nicely.

The simulated CV's shown in Figures 2 and 3 correspond to $K_{ox} = 1$ M^{-1} and $K_{red} = 905$ M^{-1} for PQ and $K_{ox} = 1$ M^{-1} and $K_{red} = 715$ M^{-1} for ANQ.[22] It should be noted that it is not possible to accurately determine K_{ox} from the simulations since values ranging from 0.01 to 1 M^{-1} produce very little change in the voltammograms. Despite this, the values for K_{red} appear reliable since varying K_{ox} over this range only causes K_{red} to vary between 893 M^{-1} and 905 M^{-1} for PQ and 700 M^{-1} and 715 M^{-1} for ANQ. Values of $K_{ox} > 1$ lead to larger values for K_{red}, but the quality of the fit deteriorates.

The lack of any significant interaction between the neutral quinones and diphenylurea in DMF is confirmed by ^{1}H NMR. Adding up to 30 mM PQ to a 1mM solution of diphenylurea in DMF-d_7 produced a less than 0.01 ppm change in the chemical shift of the urea protons.

The above studies indicate that reduction acts essentially as an on/off switch for *o*-quinone/urea binding in DMF. Binding is "off" in the oxidized state and "on" in the reduced state.

The simulations also suggest that the PQ radical anion binds the urea slightly better than the ANQ radical anion.[23] This appears general since consistently larger $E_{1/2}$ shifts are observed with PQ for a variety of ureas. (See Tables 2 − 4.) The reason for this difference may be structural, electrostatic, or both. Semiempirical molecular orbital calculations (AM1) indicate that the O−O distance in the PQ radical anion (2.754 D) is smaller than in the ANQ radical anion (2.951 D). This makes the O−O distance in PQ more comparable to the urea H−H distance in diphenylurea (2.633 D), allowing at least the possibility of forming two more linear hydrogen bonds with PQ than ANQ. In addition, a slightly larger percentage of the excess negative charge appears localized

(21) This was a greater problem with ANQ because of its more negative redox potential. Increases in the background current due to increasing moisture and other changes during long experiments result in an actual background that is greater than the original background taken at the beginning of the experiment, particularly at the negative limit. As a result the background subtraction is incomplete and causes the experimental currents to be larger than the simulated ones on the forward scan and smaller on the reverse.

(22) In our earlier paper (ref 8a), we reported a value of $K_{red} = 660$ M^{-1} for PQ under the same conditions. There are several reasons for the different value reported here. The first and most significant involves a mistake that was made with the diffusion coefficients in the original simulations. Specifically, while the diffusion coefficients of PQ, PQ− and the urea were set at 5.45×10^{-6} cm^2/s, the value determined for PQ in this solvent system, the diffusion coefficients of the PQ-urea complexes, PQ-urea and PQ-urea$^-$, were mistakenly left as 1×10^{-5} cm^2/s (the program's default value). Since it is usually the solvent system that has the greatest effect on diffusion coefficients, the standard assumption is that the diffusion coefficients of all the species are the same and this more reasonable assumption was made in the simulations reported here. In addition to the above, a number of other changes were made which we believe make the simulation more realistic, although they have less effect on the value of Kred. First, in our original simulations we only used three equilibria, Q + e- $\rightleftarrows$ Q$^-$, Q + urea $\rightleftarrows$ Q-urea, and Q$^-$ + urea $\rightleftarrows$ Q-urea$^-$, to fit the data rather than the complete square scheme (eq 4) used here. Second, we assumed everything was at equilibrium and set all the rate constants very large. The electron-transfer rate constant, k_s, was set at 1×10^4 cm/s and the forward rate constants for complex formation, k_f, were set at 1×10^9 M/s. In these simulations we set k_s to the more reasonable value of 10 cm/s and we explored the effect of changing k_f. This lead us to choosing a value of 1×10^6 M/s for both k_f's.

(23) The value of K_{red} for ANQ reported here (715 M^{-1}) is actually larger than the original value (ref 8a) reported for K_{red} for PQ (660 M^{-1}). This is because of differences in the simulation model as described in footnote 22. It should be noted that if the ANQ and PQ data are fitted to the *same* model, whether it is the old or new one, the ANQ data always gives a smaller value for K_{red}.

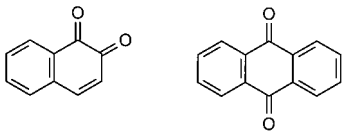
Table 1. Shift in Half-Wave Potential, $\Delta E_{1/2}$, for Different Dicarbonyl Compounds in the Presence of 5 mM Diphenylurea[a]

dicarbonyl (1.0 mM)	$\Delta E_{1/2}{}^{0/1-}$ (mV) CH_2Cl_2	DMF
phenanthrenequinone, PQ	131 ± 13	61 ± 2
1,2-naphthoquinone, **2**	141 ± 9	58 ± 3
acenaphthenequinone, ANQ	117 ± 4	40 ± 6
anthraquinone, **3**	49 ± 5	8 ± 7
benzil, **4**	irreversible	5 ± 17

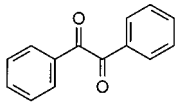
[a] The reported $\Delta E_{1/2}$ values are the average of at least three independent measurements. The ranges correspond to the 95% confidence limits.

on the O's in the PQ radical anion than in the ANQ radical anion (32.8% in PQ^- vs 30.4% in ANQ^-).

For comparison, the voltammetry of another o-quinone, 1,2-naphthoquinone, **2**, and two other related dicarbonyl compounds, anthraquinone, **3**, and benzil, **4**, were studied. Like the *o*-quinones, anthraquinone and benzil can



2 **3**



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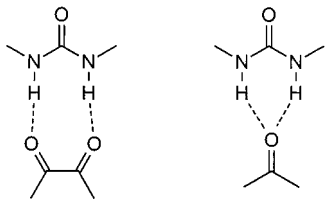
be reversibly reduced to radical anions in aprotic media resulting in increased negative charge on the oxygens. With the o-quinones one urea can simultaneously hydrogen bond with two oxygens as shown in structure A below. However, with anthraquinone one urea can only hydrogen bond to one oxygen at a time as shown in structure B. This is likely to be the case with benzil as well, since rotation about the central C−C bond will be hindered in the radical anion due to partial double bond formation and the lower energy structure will have the oxygens trans due both to electrostatic repulsion and steric effects.



A **B**

The results with benzil, anthraquinone, and *o*-naphthoquinone are summarized along with PQ and ANQ in Table 1, which lists the change in $E_{1/2}$ of the neutral/radical anion redox couples upon addition of 5 mM diphenylurea. The data show that 1,2-naphthoquinone behaves almost identically to PQ. This is not surprising given the structural similarities between the two and it offers further evidence that the angles of the carbonyls in this type of o-quinone provide a somewhat better fit to urea than the angles in ANQ. However, despite these slight differences, all the *o*-quinones give $E_{1/2}$ shifts that are considerably larger than those with anthraquinone and benzil. Anthraquinone does gives a significant, albeit much smaller, positive shift in CH_2Cl_2, presumably due to the hydrogen bonding motif depicted in structure B. However, no significant shift is observed in DMF. It is not possible to evaluate the redox-dependent binding behavior of benzil in CH_2Cl_2 since the CV becomes irreversible upon the addition of 1,3-diphenylurea. However, it also gives no significant $E_{1/2}$ shift in DMF.

Table 2. Shift in Half-Wave Potentials, $\Delta E_{1/2}$, for Phenanthrenequinone, PQ, and Acenaphthenequinone, ANQ, in the Presence of Various NH- and OH-Containing Substrates[a]

substrate (50 mM)	$\Delta E_{1/2}$ **PQ**$^{0/1-}$ (mV) CH_2Cl_2	DMF	$\Delta E_{1/2}$ **ANQ**$^{0/1-}$ (mV) CH_2Cl_2	DMF
benzophenone	6	1	11	3
1,4-dicyanobenzene	11	−2	12	1
water	15 ± 13	2 ± 5	10 ± 9	5 ± 4
ethanol	14 ± 7	2 ± 2	11 ± 5	2 ± 9
ethylene glycol	111 ± 4	11 ± 2	109 ± 6	14 ± 6
propylamine	0 ± 1	1 ± 3	2 ± 1	2 ± 1
1,2-diaminobenzene	18 ± 14	7 ± 2	6 ± 5	3 ± 4
1,3-diaminobenzene	2 ± 18	9 ± 8	3 ± 3	1 ± 8
propionamide	20 ± 9	5 ± 7	20 ± 11	5
benzamide	31 ± 11	7	25 ± 2	4
formanilide	60 ± 5	22	61 ± 5	16
butylurea	80 ± 12	20 ± 9	63 ± 10	14 ± 9
1,3-dipropylurea	51 ± 4	28 ± 10	39 ± 11	10 ± 7
1-phenyl-3-propylurea	156 ± 11	66 ± 17	144 ± 4	54 ± 12
1,3-diphenylurea (5 mM in CH_2Cl_2)	131 ± 13	107 ± 28	117 ± 4	90 ± 5
1-phenyl-3-(2,5-di-*tert*-butylphenyl)urea (5 mM in CH_2Cl_2)	52 ± 6	21 ± 5	41 ± 3	11 ± 7
1,1-dibutyl-3-phenylurea	4 ± 5	5 ± 2	5 ± 9	5 ± 5

[a] $\Delta E_{1/2}$ values reported with ranges are the average of at least three independent measurements. The ranges correspond to the 95% confidence limits.

The much larger $E_{1/2}$ shifts observed for the o-quinones compared to anthraquinone and benzil support the hypothesis that both carbonyl oxygens in the o-quinones are hydrogen-bonded to the urea. Anthraquinone and benzil give smaller shifts because the urea is only able to interact with one carbonyl at a time.

Voltammetry of *o*-Quinones in the Presence of Other Substrates. Table 2 lists the shifts in $E_{1/2}$ observed for PQ and ANQ upon addition of 50 mM of various compounds in CH_2Cl_2 and DMF. These data shows that despite their simple structure PQ and ANQ are rather selective redox-dependent receptors. Most compounds, even those that contain hydrogen bonding sites, do not produce significant shifts in the $E_{1/2}$ of the quinone/radical anion redox couple.

As shown in Table 2, addition of electron-poor aromatic substrates that do not have N−H or O−H bonds (1,4-dicyanobenzene and benzophenone) result in small, positive shifts in the $E_{1/2}$'s of the quinones in CH_2Cl_2, but not in DMF. However, these shifts are much, much smaller than those observed with the ureas. This supports our assumption that the interaction with diphenylurea is primarily due to hydrogen bonding and not due to a donor−acceptor or other type of π-π interaction between the aromatic systems of the relatively electron-rich radical anion and the somewhat electron-poor urea.

The data in Table 2 also show that the presence of a N−H or O−H bond in the substrate is not sufficient to produce a significant $\Delta E_{1/2}$. (For the purpose of this discussion we define "significant" as a shift of at least

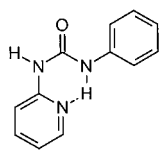
10 mV after the error limits are taken into consideration.) Of those substrates that contain an O−H bond, water, ethanol, and ethylene glycol, only the latter produces a significant shift. Unlike the others, ethylene glycol has two O-hydrogens that could simultaneously hydrogen bond to both quinone carbonyl oxygens.

A greater variety of compounds containing N−H bonds were examined. With these it is obvious that the type of bond also plays a role. None of the amino compounds produced a significant shift, including 1,2-diaminobenzene which should be able to hydrogen bond with both carbonyls. (Ethylenediamine was also tried as a substrate but it could not be studied due to rapid reaction with the quinones.)

Amides are better hydrogen donors than amines due to the electron-withdrawing nature of the carbonyl. As a result, the simple amides propionamide and benzamide do produce small but significant shifts in CH_2Cl_2. Amides formed from arylamines should be even better hydrogen donors, and indeed, formanilide, which has only one N−H bond, gives much larger shifts than the other amides. In fact the magnitude of the shift is equivalent to that observed with the alkylureas, butylurea and dipropylurea. The N-hydrogen in these compounds should be less positively charged than the N-hydrogen in formanilide, but there are two of them making it possible to form two hydrogen bonds with the o-quinones. Not surprisingly, even larger shifts are observed when one of the urea nitrogens has an aryl substituent as in phenylpropylurea and the largest shift is observed when both nitrogens have aryl substituents as in diphenylurea. This compound has two highly polarized N−H bonds capable of forming two strong hydrogen bonds with the *o*-quinones.

The importance of forming two strong hydrogen bonds is supported by the behavior of 1,1-dibutyl-3-phenylurea. This arylurea only has one N-hydrogen and gives insignificant potential shifts. However, part of the reason for the small shifts with this urea is that there is likely to be a considerable amount of steric hindrance at the binding site.

A better argument supporting the importance of both urea N-hydrogens being able to hydrogen bond to the o-quinones can be made by considering the behavior of the two pyridylureas **5** and **6**. The electronic character of both compounds should be very similar. However, with **5**, a strong intramolecular hydrogen bond will be formed between the 2-pyridyl nitrogen and one of the urea N-hydrogens.[24] This means that only one hydrogen will be available for intermolecular hydrogen bonding. In contrast, with **6**, both N-hydrogens will be available for intermolecular hydrogen bonding.



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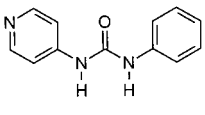

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Table 3 lists the observed $\Delta E_{1/2}$ values for these two pyridyl ureas along with 1,3-diphenylurea. Compound **5** gives significantly smaller shifts than both 6 and 1,3-diphenylurea. These results provide further evidence that the structure of the o-quinone-urea complex is as depicted in eq 1 with the urea in the trans-trans conformation and both N-hydrogens simultaneously bonded to the carbonyl O's.

Table 3. Shift in Half-Wave Potentials, $\Delta E_{1/2}$, of Phenanthrenequinone, PQ, and Acenaphthenequinone, ANQ, in the Presence of Ureas with Different Conformations[a]

	$\Delta E_{1/2}$ **PQ**$^{0/1-}$ (mV)		$\Delta E_{1/2}$ **ANQ**$^{0/1-}$ (mV)	
substrate (5.0 mM)	CH_2Cl_2	DMF	CH_2Cl_2	DMF
1-phenyl-3-(2-pyridyl)urea, **5**	42 ± 6	16 ± 8	18 ± 10	6 ± 1
1,3-diphenylurea	131 ± 13	61 ± 2	117 ± 4	40 ± 6
1-phenyl-3-(4-pyridyl)urea, **6**	141 ± 6	85 ± 4	130 ± 5	60 ± 5

[a] The reported $\Delta E_{1/2}$ values are the average of at least three independent measurements. The ranges correspond to the 95% confidence limits.

The data in Table 3 also show that the phenylpyridylurea 6 binds more strongly than diphenylurea itself. This can be attributed to an electronic effect. The greater electronegativity of nitrogen compared to carbon makes a pyridyl group more electron-withdrawing than a phenyl group. This causes the urea N-hydrogen to be more positive in 6 than diphenylurea. (A similar effect is seen in the pK_a's of related compounds—the N-hydrogen of 2-aminopyridine and 4-aminopyridine have pK_a's in DMSO of 27.6 and 26.5, respectively, considerably smaller than the pK_a of aniline (30.5).[25])

This electronic effect was explored further by testing diphenylurea derivatives containing electron-donating methoxy groups and electron-withdrawing trifluoromethyl groups. Table 4 lists the shifts in $E_{1/2}$ observed for PQ and ANQ upon addition of 5 mM of these substrates in CH_2Cl_2 and DMF. As expected, the magnitude of the shift steadily increases going from the urea with the most electron-donating substituents,1,3-di(4-methoxyl)phenylurea, to the urea with the most electron-withdrawing substituents,1,3-di(4-trifluoromethyl)phenylurea. The former would be expected to have the least positively charged N-hydrogens and the latter the most positively charged.

Proton Transfer vs Hydrogen Bonding. In an attempt to find even stronger bonding substrates for the o-quinones, diphenylthiourea was also tried as a guest with PQ. As with the oxyureas, a large positive shift in the cathodic peak potential of PQ was observed, but, unlike the oxyureas, this was accompanied by substantial changes in wave shape.[26] Most notably the cathodic peak current doubled in size, the original anodic peak disappeared and another anodic peak appeared at more positive potentials. Such behavior is strongly indicative of proton transfer. Indeed, very similar behavior is observed when 1,3-diphenyl-1,3-propanedione is added to PQ, Figure 4. This compound should not hydrogen bond to the urea, but the methylene protons have an acidity comparable to diphenylthiourea.

The behavior seen in Figure 4, has also been observed upon addition of acids to other quinones in aprotic solvents.[27] It can be explained by an ECE mechanism,

(24) (a) Singha, N. C.; Sathyanarayana, D. N., *J. Chem. Soc., Perkin Trans. 2* **1997**, 157−162. (b) Sudha, L. V.; Sathyanarayana, D. N. *J. Mol. Struct.* **1985**, *131*, 253−259. (c) Sudha, L. V.; Sathyanarayana, D. N. *J. Mol. Struct.* **1984**, *125*, 89−96. (d) Camilleri, P.; Odell, B.; Rzepa, H. S.; Sheppard, R. N. *Chem. Commun.* **1988**, 1132−1133.

(25) Bordwell, F. G. *Acc. Chem. Res.* **1988**, 21, 456−463.

(26) Similar electrochemical behavior was recently reported for the addition of thioureas to ubiquinone in CH_2Cl_2. Greaves, M. D.; Niemz, A.; Rotello, V. M. *J. Am. Chem. Soc.* **1999**, *121*, 266−267.

Table 4. Shift in Half-Wave Potentials, $\Delta E_{1/2}$, of Phenanthrenequinone, PQ, and Acenaphthenequinone, ANQ, in the Presence of Different Substituted Ureas[a]

	$\Delta E_{1/2}$ $\mathbf{PQ}^{0/1-}$ (mV)		$\Delta E_{1/2}$ $\mathbf{ANQ}^{0/1-}$ (mV)	
substrate (5.0 mM)	CH_2Cl_2	DMF	CH_2Cl_2	DMF
1,3-di-(4-methoxy)phenylurea	90 ± 7	50 ± 2	68 ± 4	30 ± 7
1-phenyl-3-(4-methoxy)phenylurea	121 ± 17	57 ± 6	105 ± 2	35 ± 4
1,3-diphenylurea	131 ± 13	61 ± 2	116 ± 4	40 ± 6
1-phenyl-3-(*p*-trifluoromethyl)phenylurea	171 ± 9	84 ± 8	136 ± 13	56 ± 4
1,3-di-(4-trifluoromethyl)phenylurea	193 ± 4	100 ± 12	169 ± 4	68 ± 9

[a] The reported $\Delta E_{1/2}$ values are the average of at least three independent measurements. The ranges correspond to the 95% confidence limits.

Table 5. Reversibility of the CV of PQ and ANQ in DMF and CH_2Cl_2 in the Presence of Compounds with Different p*K*a Values[a]

		DMF		CH_2Cl_2	
substrate	p*K* (DMSO)	$PQ^{0/1-}$ reversible?	$ANQ^{0/1-}$ reversible?	$PQ^{0/1-}$ reversible?	$ANQ^{0/1-}$ reversible?
1,3-diphenylurea	19.55	yes	yes	yes	yes
diethyl malonate	16.4	yes	yes	yes	yes
dimethyl methylmalonate	15.05	yes	yes	yes	yes
ethyl acetoacetate	14.4	no	no	no	no
1,3- diphenyl-1,3-propanedione	13.35	no	no	no	no
benzoic acid	11.0	no	no	no	no

[a] CV conditions: 1 mM quinone + 10 mM acid in 0.1 M NBu_4PF_6 in either DMF or CH_2Cl_2; 100 mV/s scan rate. [b] pK_a values in DMSO, from ref 25.

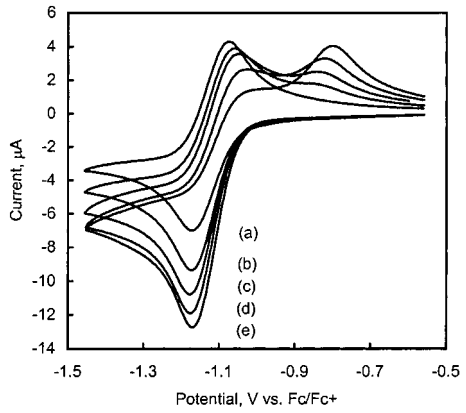


Figure 4. Cyclic voltammograms of 1 mM PQ in CH_2Cl_2 in the presence of increasing amounts of 1,3-diphenyl-1,3-propanedione. Scan rate = 100 mV/s. [1,3-Diphenyl-1,3-propanedione] (mM) = (a) 0, (b) 0.4, (c) 1, (d) 2, (e) 5.

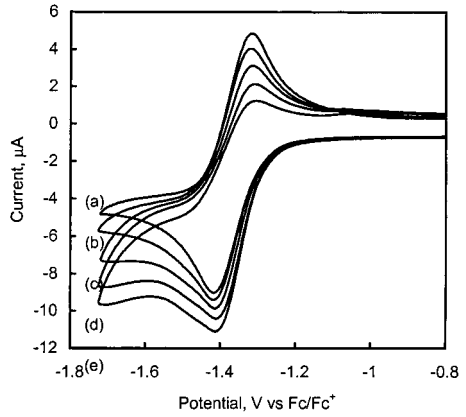
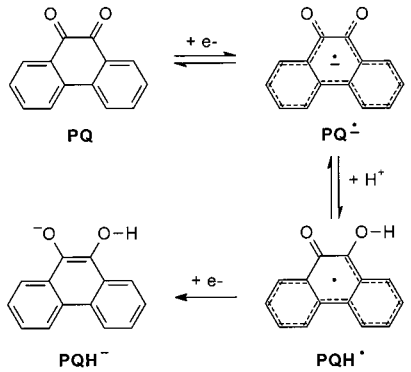


Figure 5. Cyclic voltammograms of 1 mM ANQ in CH_2Cl_2 in the presence of increasing amounts of 1,3-diphenyl-1,3-propanedione. Scan rate = 100 mV/s. [1,3-Diphenyl-1,3-propanedione] (mM) = (a) 0, (b) 0.4, (c) 1, (d) 2, (e) 5.

eq 5. In the absence of proton donors, PQ is reversibly reduced to the radical anion, PQ^-. In the presence of a strong enough acid, PQ^- is protonated to form the neutral radical PQH. PQH is easier to reduce than the original quinone, so at the potential of PQ reduction, PQH is immediately reduced to PQH^-. Thus the cathodic peak current doubles and the original anodic peak disappears since PQ^- is no longer present. The irreversible oxidation peak at more positive potentials has been ascribed to the oxidation of the final anion, PQH^- in this case.[27]



Addition of 1,3-diphenyl-1,3-dione to ANQ in CH_2Cl_2 also causes the quinone reduction to become irreversible, but the voltammetry differs substantially from that observed for PQ. As shown in Figure 5, instead of the original cathodic peak doubling in size, a new, broad, irreversible reduction peak is observed at more negative potentials. This is accompanied by a decrease in the original anodic peak, but no new anodic peak appears.

The behavior of ANQ also suggests proton transfer is occurring, but it is accompanied by a different mechanism than in the case of PQ. This is not that surprising given the structural differences. In the case of PQ, addition of the second electron creates the 14 e^- aromatic phenanthrene ring system, but adding a second electron to ANQ only gives a 12 e^- system, so the new double bond is not aromatic. The resulting bond length changes may cause significant reorganizational energy

(27) Eggins, B. R.; Chamber, J. Q., *J. Electrochem. Soc.* **1970**, *117*, 186−191.

leading to slow electron transfer kinetics. It is also possible that the protonated radical anion dimerizes and the second electron addition is due to reduction of the dimer product. Further investigation would be necessary to clarify the mechanism. The main point at present is that protonation clearly occurs and leads to an irreversible CV.

By taking CVs of the quinones in the presence of proton sources with different pK_a's, it is possible to estimate the pK_a of the protonated radical anion. Table 5 gives the results of this study. The pK_a values for these compounds in DMSO[25] are used since not all the values in DMF and CH_2Cl_2 are available. It is assumed that the relative acidity scale will be the same in DMF and CH_2Cl_2 even though the actual pK_a's will be different. Based on these results the protonated radical for both quinones appears to have a pK_a of about 15 on the DMSO scale. It is noteworthy that this is >4 pK_a units smaller than that of the ureas. Therefore, the positive redox potential shifts we observe are indeed the result of hydrogen bonding and not due to proton transfer.

Conclusions

We have shown that two simple *o*-quinones, phenanthrenequinone and acenaphthenequinone, act as quite selective redox-dependent receptors toward aromatic ureas in aprotic solvents. Whereas essentially no interaction is observed between diphenylurea and the neutral quinones in DMF, strong binding to the quinone radical anions is observed even in this highly competitive solvent. Even stronger binding is observed in CH_2Cl_2, a solvent more comparable to the solvents normally used for the study of hydrogen bonding receptors.

The present work leaves little doubt that the strong bonding between the ureas and quinone radical anions is due to the formation of two strong, partially ionic hydrogen bonds between the urea NH's and the quinone carbonyl O's. To see such strong binding it is necessary to have the two carbonyls aligned in the same direction as well as two strong hydrogen donors on the guest that can also align in the same direction.

Beyond the specific example of the o-quinone-urea complex, this study, along with the work of Rotello and others, illustrates the powerful role electrochemistry can play in creating and characterizing strongly hydrogen bonded complexes. Reversibly reducible carbonyl compounds such as quinones and imides are not the only examples of redox-dependent hydrogen bonding receptors and in future papers we will report examples of other simple compounds that also can be converted electrochemically into strong hydrogen bonding receptors.

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