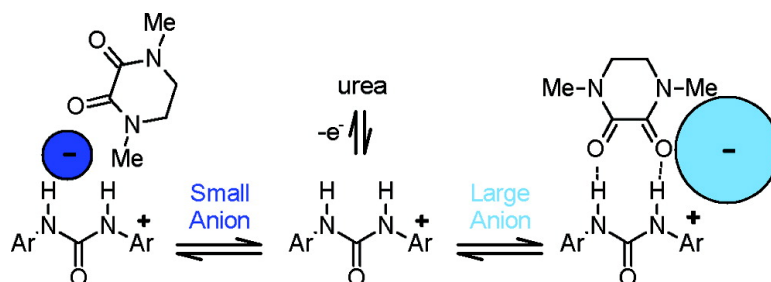


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*J. Am. Chem. Soc.*, **2008**, 130 (31), 10070-10071 • DOI: 10.1021/ja803453e • Publication Date (Web): 10 July 2008

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## Electrochemically Controlled Hydrogen Bonding. Electrolyte Effects in an Oxidation-Based Arylurea–Amide System

Jessica E. Woods, Yu Ge, and Diane K. Smith\*

Department of Chemistry and Biochemistry, San Diego State University, San Diego, California 92182-1030

Received May 9, 2008; E-mail: dsmith@sciences.sdsu.edu

Over the past decade, it has been shown that it is possible to selectively and significantly perturb the strength of H-bonding between organic molecules using electrochemistry. However, although both reduction<sup>1</sup> and oxidation<sup>2</sup> reactions have been used, reductions have generally proven more successful.<sup>3</sup> In this paper, we show that the difficulty with oxidations can be due to an electrolyte effect resulting from competition between the guest and the electrolyte anion for H-bonding to the oxidized host. Furthermore, we show that, by switching to an electrolyte with a very large anion, significant changes in binding strength are observed upon oxidation of an electroactive urea in the presence of a diamide guest.

The basic idea behind redox-dependent hydrogen bonding is to use the change in charge accompanying e-transfer to perturb the strength of H-bonds between host and guest. One possibility is to use a reduction reaction to increase negative charge on H-accepting atoms in a host. Another possibility, which is explored in this study, is to use an oxidation reaction to increase the positive charge on H-donating groups in the host. H-accepting guests will then bind more strongly to the oxidized form, making it easier to oxidize the host. This results in a negative shift in the half-wave potential,  $E_{1/2}$ , of the host in the presence of the guest.

Since the perturbation of H-bond strength relies on a change in charge, ion–ion interactions may also play a role in these systems. They can be used to advantage when the guest itself is ionic,<sup>4</sup> but with neutral guests, they may pose a problem. This is particularly an issue in electrochemical studies, where an “inert” electrolyte will be present in excess. The most common electrolytes used in these studies are  $\text{NBu}_4\text{ClO}_4$  or  $\text{NBu}_4\text{PF}_6$ .<sup>2</sup> Use of  $\text{NBu}_4^+$  is a good choice for reduction-based systems because it is a very large ion and is unlikely to significantly ion pair in the solvents commonly used for these studies.<sup>5</sup> However, the same cannot be said about  $\text{ClO}_4^-$  or  $\text{PF}_6^-$ . This has been particularly noted by Geiger in electrochemical studies of organometallic cations.<sup>6</sup>

In this work, we show that interaction with  $\text{ClO}_4^-$  or  $\text{PF}_6^-$  can also be an issue for oxidation-based, redox-dependent H-bonding. The system under investigation is based on the urea, U. This compound was chosen because diarylureas are known to be very good H-donors, and oxidation of the  $\text{NMe}_2$ -phenyl ring should lead to a significant increase in positive charge on one of the urea NH's (eq 1). For comparison purposes, we also synthesized the methylated derivative, UMe.

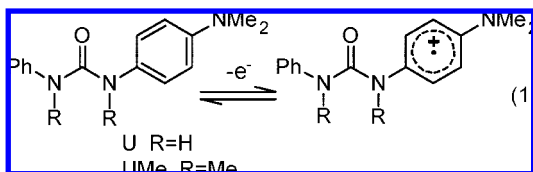
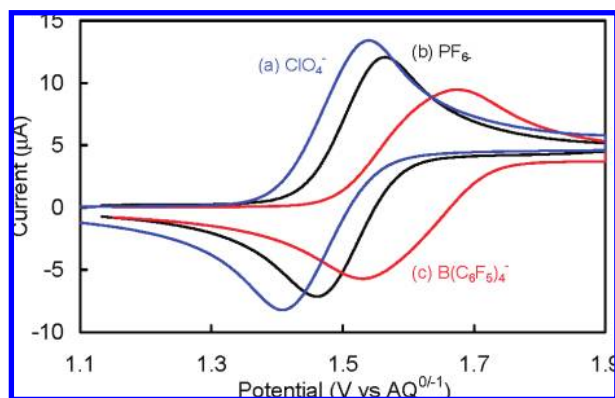
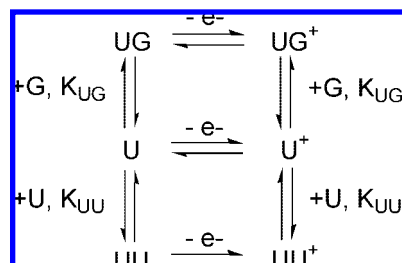


Figure 1 shows cyclic voltammograms (CVs) of U in  $\text{CH}_2\text{Cl}_2$  with (a)  $\text{NBu}_4\text{ClO}_4$ , (b)  $\text{NBu}_4\text{PF}_6$ , and (c)  $\text{NBu}_4\text{B}(\text{C}_6\text{F}_5)_4$  as the



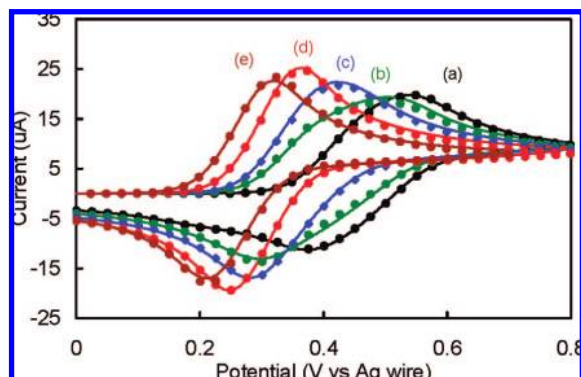
**Figure 1.** CVs (100 mV/s) of 1 mM U in  $\text{CH}_2\text{Cl}_2$  with (a) 0.1 M  $\text{NBu}_4\text{ClO}_4$ , (b) 0.1 M  $\text{NBu}_4\text{PF}_6$ , and (c) 0.1 M  $\text{NBu}_4\text{B}(\text{C}_6\text{F}_5)_4$ .

**Scheme 1.** Mechanism for U Oxidation with Guest, G, Present



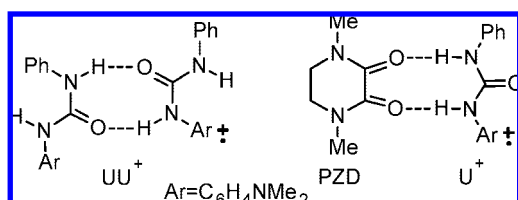
electrolyte. Clearly, the electrolyte anion has a big effect on the electrochemistry. With  $\text{ClO}_4^-$ , reversible oxidation to the radical cation,  $\text{U}^+$ , is observed at 1.47 V, with  $\text{PF}_6^-$ , the same process occurs at 1.51 V, and with  $\text{B}(\text{C}_6\text{F}_5)_4^-$ , it is at 1.60 V. In addition, the  $\text{U}^{0/+}$  wave is considerably broader with  $\text{B}(\text{C}_6\text{F}_5)_4^-$  than  $\text{ClO}_4^-$  or  $\text{PF}_6^-$ . Close inspection of the  $\text{U}^{0/+}$  wave in Figure 1c suggests that it actually represents two strongly overlapping waves of equal height. Interestingly, when the same set of CVs is run with UMe, the  $E_{1/2}$  values are much closer (within 0.03 V) and there is no significant difference in wave shape between the three electrolytes.<sup>7</sup> This strongly suggests that it is an ionic H-bonding interaction between the anions and the urea NH's that is mainly responsible for the differences between electrolytes seen in Figure 1.

A mechanism capable of explaining the differences observed in Figure 1 is given in Scheme 1. If a guest, G, is present that binds more strongly to  $\text{U}^+$  than U, the observed  $E_{1/2}$  of  $\text{U}^{0/+}$  will shift negative in the presence of G. This is what appears to happen in Figure 1a and b, with  $\text{ClO}_4^-$  or  $\text{PF}_6^-$  playing the role of G through strong interaction with the urea NH's. In contrast, if no G is present, as with  $\text{B}(\text{C}_6\text{F}_5)_4^-$ , then  $\text{U}^+$  could interact with U to form the  $\text{UU}^+$  dimer shown below. Since U would bind more strongly to  $\text{U}^+$  than another U, the  $E_{1/2}$  shifts negative as  $\text{UU}^+$  is being formed. This continues until half of the U is oxidized to  $\text{U}^+$ . Oxidation of the



**Figure 2.** Experimental (solid lines) and simulated (dots) CVs (500 mV/s) of 1 mM U in 0.1 M NBu<sub>4</sub>B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>/CH<sub>2</sub>Cl<sub>2</sub> + PZD: (a) 0 mM, (b) 0.5 mM, (c) 1 mM, (d) 5 mM, (e) 100 mM.

rest of U then occurs upon dissociation of UU<sup>+</sup>. This would occur at a slightly more positive potential, producing the broad wave observed for U<sup>0/+</sup> with B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub><sup>-</sup>.



The occurrence of U dimerization in CH<sub>2</sub>Cl<sub>2</sub> is supported by <sup>1</sup>H NMR data for U in CD<sub>2</sub>Cl<sub>2</sub> that show the NH chemical shifts are concentration-dependent. Analysis of these data gives  $K_{UU} = 22 \text{ M}^{-1}$ . Using this value, CVs of 0.5 and 1 mM U in NBu<sub>4</sub>B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>/CH<sub>2</sub>Cl<sub>2</sub> were fit to a slightly modified version<sup>7</sup> of the mechanism shown in Scheme 1, giving  $K_{UU+} = 4600 \text{ M}^{-1}$ .

The fact that U<sup>+</sup> binds so strongly to another U suggests there must be other molecular guests that will strongly bind to U<sup>+</sup> and produce large shifts in the observed  $E_{1/2}$  of U<sup>0/+</sup>. Past experience<sup>1c,d</sup> suggests that this requires a guest with two strong H-acceptor atoms preorganized to H-bond with both urea NH's. 1,4-Dimethylpiperazine-2,3-dione, abbreviated PZD, nicely satisfies these criteria as shown above.

It turns out that PZD is a good enough guest for U that large  $E_{1/2}$  shifts are observed in all electrolytes. The difference is how much PZD needs to be added. With ClO<sub>4</sub><sup>-</sup> or PF<sub>6</sub><sup>-</sup>, addition of 1 mM PZD to 1 mM U in CH<sub>2</sub>Cl<sub>2</sub> produces a -2 or -16 mV shift, respectively, in the  $E_{1/2}$  of U<sup>0/+</sup>, with little change in the shape or size of the CV wave.<sup>7</sup> As more PZD is added, the wave shifts further negative. By 400 mM PZD, the shift is significant, -60 mV with ClO<sub>4</sub><sup>-</sup> and -114 mV with PF<sub>6</sub><sup>-</sup>, but there is no evidence that the maximum shift is nearing.

Figure 2 shows experimental and simulated CVs for the same type of experiment done with NBu<sub>4</sub>B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>. Now addition of 1 mM PZD causes a -109 mV shift, almost as large as that observed with 400 mM in PF<sub>6</sub><sup>-</sup>. Along with the shift, there is a substantial sharpening of the wave, indicating that PZD binding is competing

successfully with U dimerization. By 5 mM PZD, the wave has reached full height, and by 100 mM, the system appears to be closing in on a maximum shift of about -200 mV. This corresponds to a >2000-fold increase in binding strength upon oxidation. To the best of our knowledge, this is by far the largest binding enhancement reported to date for an oxidation-based, redox-dependent H-bonding system with a neutral molecular guest. From the simulated CVs, we obtain reliable estimates of the actual binding constants in the two oxidation states:  $K_{UG} = 62 \text{ M}^{-1}$  and  $K_{UG+} = 1.6 \times 10^5 \text{ M}^{-1}$ .

In conclusion, we have demonstrated a simple redox-dependent H-bonding system in which oxidation leads to a substantial increase in binding strength to a molecular guest. Indeed, the magnitude of the effect is comparable to that observed for the better reduction-based systems. However, it is doubtful that this system is unique. The difference is the electrolyte. Binding to the commonly used electrolyte anions ClO<sub>4</sub><sup>-</sup> and PF<sub>6</sub><sup>-</sup> is strong enough to obscure the strength of binding to the guest. It is likely that other oxidation-based systems would also reveal much stronger binding if re-examined using less competitive electrolytes.

**Acknowledgment.** Acknowledgment is made to the Donors of the American Chemical Society Petroleum Research Fund for support of this research.

**Supporting Information Available:** Additional CVs, NMR titration data and analysis, general voltammetry and CV simulation procedures, synthesis and structural data for UMe. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- There are a number of examples (see ref 1) where perturbation of H bonds through reduction results in a > 10-fold change in binding strength between an electroactive host and a neutral guest. In contrast, to our knowledge, the ferrocene diamides studied by Green, Tucker, and colleagues (ref 2e) remain, until now, the only reported examples where oxidation does the same.
- Much greater success has been achieved with oxidation-based H-bonding receptors for anions. For a recent example, see Willener, Y.; Joly, K. M.; Moody, C. J.; Tucker, J. H. R. *J. Org. Chem.* **2008**, *73*, 1225–1233.
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- See Supporting Information.

JA803453E