Ferrocenyl-amidinium compound as building block for aqueous proton-coupled electron transfer studies

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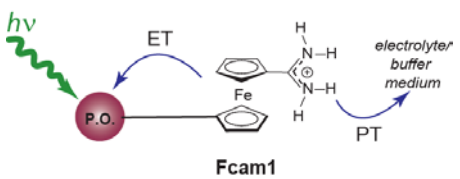
Abstract: A water-soluble amidinium-appended ferrocene moiety is characterized in which the amidinium functionality is fused directly to the ferrocene ring (Fcam1). This species is designed to form a building block for aqueous proton-coupled electron transfer in which proton transfer occurs to the bulk and electron transfer occurs to a chemical oxidant. pH-dependent absorption spectroscopy and electrochemistry show that the electrochemical potential is directly linked to the protonation state of the amidinium. A thermodynamic square scheme is constructed for Fcam1. The square scheme serves as motivation and provides direction for incorporating this species into a covalently-bound system for the study of proton-coupled electron transfer.

Keywords: Ferrocene, Ferrocene-derivative, proton-coupled electron transfer (PCET), pH-dependent oxidation potential, square scheme, pH-dependence

[1]Ferrocene derivatives have been incorporated into a large number of electron transfer model systems due to their rich redox properties, reversible oxidation and general photostability and thermal stability [1- 9]. Previous efforts have revealed that appended acid groups impart pH-dependent oxidation behavior to the ferrocene redox unit [10]. Accordingly, the use of ferrocenyl moieties appended with hydrogen-bonding functionalities is appealing for mechanistic study of proton-coupled electron transfer (PCET). The synthesis of a ferrocenyl amidinium derivative in which the protonic group is fused directly to the redox center enables PCET studies using ferrocene to be carried out in aqueous conditions.

Early mechanistic studies of proton coupled electron transfer (PCET) have focused primarily on assemblies of donor–acceptor (D–A) pairs juxtaposed by hydrogen-bonded interfaces [11-13] formed by carboxylic acid dimers [14,15], and amidinium–carboxylate salt bridges [16- 21]. The inspiration for these PCET studies lies in a host of biological systems that employ guanine–cytosine base-pairs [22] and arginine–aspartate salt bridges [23- 31]. Mechanistic investigation of PCET through hydrogen bonded interfaces addresses the impact of proton motion on through-bond electron transfer (ET) in a co-linear PCET arrangement, in which ET and proton transfer (PT) occur in the same direction. Assembly of these hydrogen-bonded systems, however, requires the use of aprotic solvents of low dielectric constant in order to facilitate efficient binding. Mechanistic interrogation of aqueous PCET systems requires an alternative architectural strategy to co-linear PCET in hydrogen-bonded systems, as water disrupts formation of amindinum–carboxylate hydrogen bonds and prevents formation of D–A dyads. A strategy that can be employed to study PCET that does not necessitate formation of hydrogen-bonded D–A dyads is the use of a bi-directional PCET motif. Specifically, a bi-directional system of relevance to aqueous studies consists of a covalently bound D–A pair to establish an ET coordinate and a PT coordinate that is established through loss of an amidinium proton to the bulk. The ferrocenyl-amidinium species presented in these studies, **Fcam1**, (Scheme 1) is a building block for such bi-directional aqueous PCET. This system is akin to the bi-directional PCET systems involving deprotonation of tyrosine to the bulk concomitant with oxidation by a Re polypyridyl photo-oxidant [32,33].



Scheme 1 Cartoon depiction of photo-induced bi-directional PCET, in which deprotonation of the appended amidinium functionality facilitates ET to an electron acceptor photo-oxidant (P.O.).

Prior to incorporation of the ferrocenyl-amidinium component into a PCET assembly, it is necessary to characterize the individual **Fcam1** moiety, specifically its electronic absorption and electrochemical oxidation potential and their dependence on pH. Significant electronic communication between the ferrocene sub-unit and the pendant amidinium is revealed by UV–visible absorption spectroscopy through observation of spectral shifts that occur upon protonation or deprotonation of the amidinium functionality. pH-Dependent absorption spectroscopy yields the pK_a of the amidinium functionality in water, while pH-dependent electrochemistry clearly reveals that the oxidation potential of the compound is linked to the protonation state of the amidinium functionality. Formation of the oxidized species, **Fcam1$^+$,** is monitored by electronic absorption spectroscopy during bulk electrolysis experiments. A thermodynamic square scheme that provides a complete thermodynamic characterization of **Fcam1** is presented and serves as an important guide to incorporation of **Fcam1** into covalently-bound photo-induced PCET systems.

[1]Abbreviations: PCET, proton-coupled electron transfer; ET, electron transfer; PT, proton transfer; D–A, donor–acceptor, NHE, normal hydrogen electrode.

pH-Dependent electronic absorption spectroscopy [34]: Absorption spectra of ferrocene-amidinium (**Fcam1**) in aqueous 100 mm phosphate solutions buffered at pH 8 exhibit absorption peaks at 221 nm (ε_{221nm},12,100 $M^{-1}cm^{-1}$), 265 nm (ε_{265nm}, 4230 $M^{-1}cm^{-1}$), 320 nm (ε_{320nm}, 1180 $M^{-1}cm^{-1}$), and 443 nm (ε_{264nm}, 365 $M^{-1}cm^{-1}$). Under basic conditions (pH 11.41) absorption peaks at 264 nm (ε_{264nm}, 4380 $M^{-1}cm^{-1}$), 311 nm (ε_{311nm}, 1860 $M^{-1}cm^{-1}$), and 428 nm (ε_{228nm}, 414 $M^{-1}cm^{-1}$) are produced (Figure 1). **Fcam1** is stable for extended periods in water in this pH range (Figure S1 in the Supporting Information).

pH-Dependent electrochemistry [34]: The electrochemical oxidation potential of **Fcam1** obtained via differential pulse voltammetry (DPV) reveals oxidation potentials that range from 752 mV vs NHE at pH 7.18 to 672 mV vs. NHE at pH 11 (Figure 2). All redox potentials are reported versus NHE.

Spectroelectrochemistry [34]: The UV–visible absorption spectrum of the **Fcam1** species is monitored during bulk electrolysis at 850 mV (vs. NHE) to reveal a new spectral feature at 570 nm that arises upon the disappearance of the ground state absorption of **Fcam1** at 450 nm (Figure 3).

UV–visible absorption spectroscopy (Figure 1) and electrochemical experiments (Figure S2 in the Supporting Information) performed on the ferrocenyl-amidinium compound **Fcam1** reveal marked variation with pH. The spectral and electrochemical behaviors are closely correlated. Oxidation potentials plotted versus pH (Figure 2) track the spectral shifts observed in UV–visible spectra (Figure 2) thereby confirming that oxidation of the **Fcam1** is gated by deprotonation of the amidinium functionality. A pK_a value of 8.8 for **Fcam1** is determined from the plots in Figure 2.

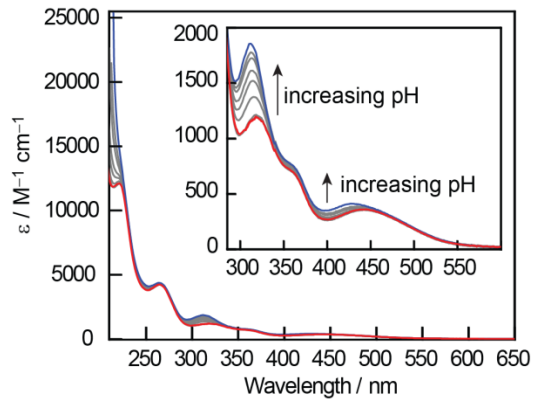


Fig. 1 pH-dependent UV–visible absorption spectra of **Fcam1** as a function of increasing pH (red spectrum, pH 7; blue spectrum, pH 11). Shifts in the spectral features are clearly seen as increasing pH causes deprotonation of the pendant amidinium functionality.

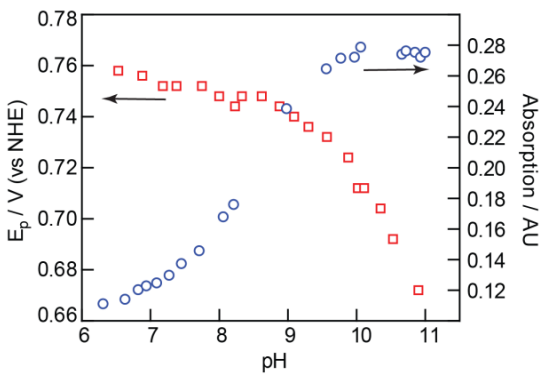


Fig. 2 The spectral shift in the UV–vis spectrum at 450 nm is plotted versus pH (circle). The spectral shifts are tracked by the redox potential (square) of **Fcam1** as a function of pH. Redox potentials obtained by DPV (E_p) are plotted versus pH. The pH-dependent studies reveal a pK_a value of 8.8 for **Fcam1**.

Spectroelectrochemistry reveals the spectral band associated with the ferrocenium-amidinium species, **Fcam1**$^+$. A red-shifted peak at 570 nm (**Fcam1**$^+$) appears concomitant with the loss of the 450 nm peak associated with **Fcam1** and confirms formation of the oxidized moiety (Figure 3). Observation of this peak thus establishes a spectral feature that may subsequently be used to monitor oxidation of **Fcam1**. The **Fcam1**$^+$ species is observed more clearly in acetonitrile, which stabilizes the ferrocenium ion (Figure S4 in the Supporting Information) and confirms spectral assignment for the peak associated with **Fcam1**$^+$.

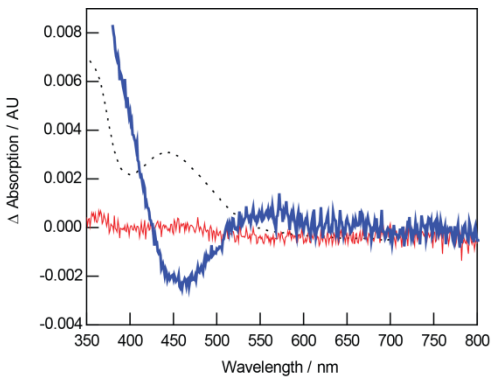
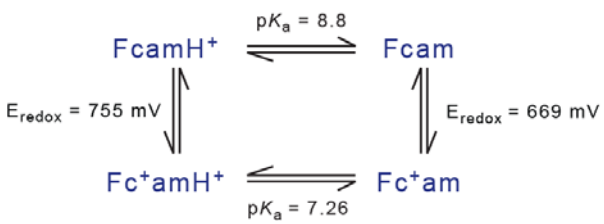


Fig. 3 Spectroelectrochemistry performed in aqueous solutions of **Fcam1** buffered at pH 7. The baseline (red, thin line) indicates the sample blanked on **Fcam1**, and the difference spectrum (blue, heavy line) is obtained upon oxidation of **Fcam1** at 850 V (vs NHE). The peak present at 570 nm is indicative of the **Fcam1**$^+$ moiety. The ground-state electronic absorption spectrum of **Fcam1** is shown (dotted line) for reference. Figure S3 in the Supporting Information shows spectroelectrochemistry performed at pH 11.

The thermodynamic properties of **Fcam1** are summarized on the square schemes shown in Scheme 2, for which complete labeling of acidity constants and oxidation potentials is presented. The pK_a value for the protonated form of **Fcam1** is experimentally determined (vide supra), as are the oxidation potentials of both protonated (755 mV vs NHE) and deprotonated



Scheme 2 Thermodynamic square scheme for **Fcam1** that fully characterizes the protonation states and redox potentials of the PCET moiety in aqueous conditions.

(669 mV vs NHE) **Fcam1** (vide supra). With three of the four values experimentally determined, the square can be completed by calculating the pK_a value for the ferrocenium-amidinium species, **Fcam1**$^+$. The value obtained from these calculations is pK_a(**Fcam1**$^+$) = 7.26. This square scheme forms the basis for designing a covalently bound D–A system for bi-directional PCET studies involving **Fcam1**.

A suitable oxidant, and its reduced radical anion, must be stable in basic aqueous conditions both above and below the pK_a of **Fcam1**, specifically in the range of pH 7-10. This stringent stability requirement precludes demonstration of ground-state diffusion controlled PCET with **Fcam1**, as appropriate chemical oxidants for this process suffer from instability at high pH conditions. Therefore, to demonstrate pH-dependent PCET, it is necessary to incorporate **Fcam1** into a covalently bound D–A system, in which ET will be initiated from the excited state of a photo-oxidant. Photo-induced ET in a bound system can then be monitored as a function of pH of the aqueous buffered solution. Current investigation is underway into an appropriate photo-oxidant that possesses the necessary driving force for ET and will undergo electron transfer with **Fcam1** and is the subject of ongoing work in this direction.

In summary, a water soluble amidinium-appended ferrocenyl moiety is presented that shows spectral and electrochemical properties that vary with pH. The pH-dependent electronic absorption spectra reveal efficient coupling between the ferrocene moiety and appended amidinium functionality. From pH-dependent spectral shifts of the absorption spectrum, the amidinium acidity constant of pK_a(**Fcam1**) = 8.8 is ascertained. The oxidation potential for **Fcam1** moves to lower potential with increasing pH, indicating that oxidation of the ferrocene moiety is facilitated by deprotonation of the acid functionality. Further analysis of the thermodynamic square scheme constructed for **Fcam1** yields an acidity constant for the ferrocenium-amidinium of pK_a(**Fcam1**$^+$) = 7.26.

The foregoing analysis provides the underpinning for construction of a PCET system through detailed characterization of the ET and PT properties of **Fcam1**. The results provide an imperative for incorporation of **Fcam1** into D–A networks of bi-directional character that will undergo photo-induced PCET. A photo-induced event will be necessary in order to reach the higher pH range where **Fcam1** demonstrates pH-dependent behavior. With the appropriate choice of photo-oxidant, a D–A system can be constructed in which the donor and acceptor are covalently linked and for which the driving force for ET is modulated by the pH of the surrounding environment. These water-based bi-directional PCET studies are of particular interest for understanding PCET in various solvent environments for applications of energy storage and modeling of biological systems.

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Notes and references

† Electronic Supplementary Information (ESI) is available online at: www.

[1] M. Kubo, Y. Mori, M. Otani, M. Murakami, Y. Ishibashi, M. Yasuda, K. Hosomizu, H. Miyasaka, H. Imahori, S. Nakashima, *Chem. Phys. Lett*, 2006, **429**, 9.
[2] W. Cao, J. P. Ferrance, J. Demas, J. P. Landers, *J. Am. Chem. Soc.* 2006, **128**, 7572.
[3] T. Fushimi, A. Oda, H. Ohkita, S. Ito, *Langmuir*, 2005, **21**, 1584.
[4] Y. Araki, Y. Yasumura, O. Ito, *J. Phys. Chem. B* 2005, **109**, 8943.
[5] E. J. Lee, M. A. Wrighton, *J. Am. Chem. Soc.* 1991, **113**, 8562.
[6] S. Fery-Forgues, B. Delavaux-Nicot, *J. Photochem Photobio A: Chemisry* 2000, **132**, 137.
[7] U. Siemling, J. Vor der Bueggen, U. Vorfeld, B. Neumann, A. Stammler, H.-G. Stammler, A. Brockhinke, R. Plessow, P. Zanello, F. Laschi, F. F. de Biani, M. Fontani, S. Steenken, M. Stapper, G. Gurzadyan, *Chemistry – A European Journal* 2003, **9**, 2819.
[8] A. Delgadillo, A. M. Leiva, B. Loeb, *Polyhedron* 2005, **24**, 1749.
[9] K. Heinze, K. Hempel, M. Beckmann, *European J. Inorg. Chem.* 2006 **10**, 2040.
[10] G. De Santis, L. Fabbrizzi, M. Liccheilli, P. Pallavicini, *Inorg. Chim. Acta* 1994, **225**, 239.
[11] C.J. Chang,. J.D.K. Brown, M.C.Y. Chang, E.A. Baker, D.G. Nocera, In *Electron Transfer in Chemistry*; Balzani, V., Ed.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 3.2.4, pp 409-461.
[12] R. I. Cukier, D. G. Nocera, *Annu. Rev. Phys. Chem.* 1998, **49**, 337.
[13] C. J. Chang, M. C. Y. Chang, N. H. Damrauer, D. G. Nocera, *Biochim. Biophys. Acta* 2004, **1655**, 13.
[14] C. Turró, C. K. Chang, G. E. Leroi, R. I. Cukier, D. G. Nocera, *J. Am. Chem. Soc.* 1992, **114**, 4013.
[15] P. J. F. de Rege, S. A. Williams, M. J. Therien, *Science* 1995, **269**, 1409.
[16] N. H. Damrauer, J. M. Hodgkiss, J. Rosenthal, D. G. Nocera, *J. Phys. Chem. B* 2004, **108**, 6315.
[17] J. A. Roberts, J. P. Kirby, D. G. Nocera, *J. Am. Chem. Soc*. 1995, **117**, 8051.
[18] J. A. Roberts, J. P. Kirby, D. G. Nocera, *J. Am. Chem. Soc*. 1997, **119**, 9230.
[19] J. A. Roberts, J. P. Kirby, S. T. Wall, D. G. Nocera, *Inorg. Chim. Acta* 1997, **263**, 395.
[20] J. P. Kirby, J. A. Roberts, D. G. Nocera, *J. Am. Chem. Soc*. 1997, **119**, 9230.
[21] J. M. Hodgkiss, N. H. Damrauer, S. Pressé, J. Rosenthal, D. G. Nocera, *J. Phys. Chem. B.* 2006, **110**, 18853.
[22] J.L. Sessler, B. Wang, S.L. Springs, C.T. Brown, In *Comprehensive Supramolecular Chemistry*; Murakami, Y., Ed.; Pergamon Press: Oxford, 1996; Vol. 4, pp. 311-336 and references therein.
[23] S. Kumar, R. Nussinov, *ChemBioChem* 2002, **3**, 604.
[24] H. R. Bosshard, D. N. Marti, I. J. Jelesarov, *Mol. Recog*. 2004, **17**, 1.
[25] J. D. Puglisi, L. Chen, A. D. Frankel J. R. Williamson, *Proc. Natl. Acad. Sci. U.S.A.* 1993, **90**, 3680.
[26] N. P. Pavletich, C. O. Pabo, *Science* 1991, **252**, 809.
[27] J. M. Berg, *Acc. Chem. Res.* 1995, **28**, 14.
[28] E. H. Howell, J. E. Villafranca, M. S. Warren, S. J. Oatley, J. Kraut, *Science* 1986, **231**, 1123.
[29] B. E. Ramirez, B. G. Malmström, J. R. Winkler, H. B. Gray, *Proc. Natl. Acad. Sci. U.S.A.* 1995, **92**, 11949.
[30] B. R. Crane, L. M. Siegel, E. D. Getzoff, *Science*, 1995, **270**, 59.
[31] P. Brzezinski, *Biochemistry* 1996, **35**, 5611.
[32] T. Irebo, S. Y. Reece, M. Sjödin, D. G. Nocera, L. Hammarström, *J. Am. Chem. Soc*., 2007, **129**, 15462.
[33] H. Ishikita, A. V. Soudackov, S. Hammes-Schiffer, *J. Am. Chem. Soc*., 2007, **129**, 11146.
[34] Experimental details can be found in the *Electronic Supporting Information*.