Proton-Coupled Electron Transfer Reactions with Photometric Bases **Reveal Free Energy Relationships for Proton Transfer**

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ABSTRACT: The proton-coupled electron transfer (PCET) oxidation of p-aminophenol in acetonitrile was initiated via stopped-flow rapid-mixing and spectroscopically monitored. For oxidation by ferrocenium in the presence of 7-(dimethylamino)quinoline proton acceptors, both the electron transfer and proton transfer components could be optically monitored in the visible region; the decay of the ferrocenium absorbance is readily monitored (λ_{max} = 620 nm), and the absorbance of the 2,4-substituted 7-(dimethylamino)quinoline derivatives ($\lambda_{max} = 370-392$ nm) red-shifts substantially (ca. 70 nm) upon protonation. Spectral analysis revealed the reaction proceeds via a stepwise electron transfer-proton transfer process, and modeling of the kinetics traces monitoring the ferrocenium and quinolinium signals provided rate constants for elementary proton and electron transfer steps. As the pK_a values of the conjugate acids of the 2,4-R-7-(dimethylamino)quinoline derivatives employed were readily tuned by varying the substituents at the 2- and 4-positions of the quinoline backbone, the driving force for proton transfer was systematically varied. Proton transfer rate constants ($k_{PT,2} = (1.5-7.5) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, $k_{PT,4} = (0.55-3.0) \times 10$ $10^7 \text{ M}^{-1} \text{ s}^{-1}$) were found to correlate with the pK_a of the conjugate acid of the proton acceptor, in agreement with anticipated free energy relationships for proton transfer processes in PCET reactions.

■ INTRODUCTION

Proton-coupled electron transfer (PCET) reactions involve the transfer of both a proton and electron and can proceed through either stepwise or concerted mechanisms. In stepwise reactions, initial electron transfer (ET) is followed by proton transfer (PT) (ET-PT) or vice versa (PT-ET). By contrast, in a concerted proton-electron transfer (CPET) reaction both the electron and proton move in a single kinetic step, circumventing charged, high-energy intermediates. These types of reactions are found throughout chemistry and biology and play an important role in the activation of small, energy-poor molecules, like H_2O and CO_2 , into energy-rich fuels.^{1,2} As such, PCET processes underpin emerging energy technologies based on photon-to-fuel conversion strategies, and thus understanding and controlling PCET reactions is a high priority for the scientific community. However, elucidating the operating mechanism of a given PCET process can be quite difficult.^{3,4} Extracting relevant kinetic information about proton and electron transfers and interpreting the reaction parameters controlling a PCET reaction is an even greater challenge. Therefore, in order to advance our understanding of PCET

reactions, more effective and versatile methods for monitoring PCET processes must be developed.

Spectroscopic monitoring of ET processes is enabled by the fact that transition metals often have unique optical signatures for each of their oxidation states. As such, time-resolved spectroscopic techniques like optical spectroscopy coupled to stopped-flow rapid mixing⁵⁻⁹ and transient absorption¹⁰⁻¹⁷ spectroscopy have been widely employed to monitor the ET component of PCET reactions. Electrochemistry has also been used to probe ET processes in PCET events.¹⁸⁻²¹ However, it is significantly more difficult to monitor the PT component of a PCET reaction through conventional methods. There are few methods available by which proton movement can be monitored on appropriate time scales; time-resolved infrared spectroscopy has been successfully employed to monitor PT,^{22–28} but when there is an accompanying ET reaction, electron transfer kinetics must generally be determined in a separate experiment. Our lab has recently reported the

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Scheme 1. General Schematic of the PCET Reaction between NH₂PhOH, Fc⁺, and R-7DMAQ^a



^{*a*}NH₂PhOH is oxidized by Fc⁺, generating NH₂PhOH radical cation (NH₂PhOH^{\bullet +}), which is then deprotonated by R-7DMAQ. Products of this initial PCET reaction are ferrocenium, *p*-aminophenol radical, and R-7DMAQH⁺.

comprehensive optical monitoring of an excited-state PCET reaction and the subsequent thermal PCET recombination, but this is a rare example of concurrent spectroscopic monitoring of electron and proton transfer processes.¹⁷ As a result, PCET reaction mechanisms are generally inferred from reaction products, KIE studies of the ET component, and thermodynamic analyses.^{3,6,11,18,29,30} This approach has inherent shortcomings; as a result, little information is typically gleaned about the role PT plays in a PCET reaction, and this has further ramifications in the broader context of PT reactions.

Recognizing the integral role PT plays in PCET reactions, control over PT may offer a clear pathway to orchestrate and manipulate PCET reaction pathways and provide avenues for the development of catalysts that can, for instance, activate inert, energy poor molecules for fuel synthesis. However, in order to control PT, the parameters that govern a PT event need to be well understood. For instance, can we develop clear correlations between the driving force $(-\Delta G_{\rm PT})$ and rate constant (k_{PT}) for PT within in a PCET process? While there have been some experimental investigations into the relationships between thermochemical parameters and reaction kinetics of PCET reaction, a unified understanding, especially one that includes concerted reaction mechanisms and nonaqueous solvents, is not yet available.^{3,4,7,9,31-39} This further underscores that to advance our understanding of PCET reactions, a technique to effectively monitor PT must be developed.

Borrowing concepts from pH indicators and acid/base chemistry, we have identified, synthesized, and characterized a series of "photometric bases" and have demonstrated that these molecules can be used to optically monitor PT processes in PCET reactions. In this work, we present a series of 7-(dimethylamino)quinoline (R-7DMAQ) derivatives that have optical signatures in the visible region that shift upon protonation. This red-shift in absorbance provides an excellent handle directly probe a PT event. While similar approaches have been utilized to study pure PT reactions (thermal and excited state, in both water and nonaqueous solvents), these studies have relied on indicator dyes, many of which are carbon-based acids/bases and have limited tunability for PT driving force and thus were not readily extendable to the PCET studies of interest here.^{40–44}

In the series of 7-(dimethylamino)quinoline derivatives studied here, variation of the R-group at the 2,4-positions of the quinoline allows the optical properties and pK_a (in CH₃CN) to be systematically tuned. This allows (1) direct access to a range of optical windows across the visible region in which PT reactions can be monitored and (2) an opportunity to vary PT driving force. The latter presents a unique opportunity to systematically examine the relationship between $-\Delta G_{\rm PT}$ and $k_{\rm PT}$ within in a PCET process. With these tools in hand, we have explored the PCET reaction between the *p*-aminophenol (NH₂PhOH), these photometric bases, and mild oxidant ferrocenium (Fc⁺) using optical spectroscopy and stopped-flow rapid-mixing (Scheme 1). Both PT and ET processes were monitored independently of one another, and free energy relationships between the proton transfer rate constants and the $pK_{\rm a}$ of the photometric base are revealed.

EXPERIMENTAL SECTION

General Considerations. All solutions for electrochemical and stopped-flow analyses were prepared in a nitrogen-filled glovebox. The acetonitrile used (Fisher Scientific, HPLC, >99.9%) was degassed with argon and dried with a Pure Process Technology Solvent System. Reagents were purchased from Sigma-Aldrich with the exception of 3,4-dimethoxyphenylboronic acid (VWR), 3,5-bis(trifluoromethyl)phenylboronic acid (Matrix), and phenylboronic acid (Chem-Impex). 2-Picoline, tetrafluoroboric acid diethyl ether, and aniline were degassed via the freeze-pump-thaw method (3+ cycles) and stored under an inert atmosphere. UV-vis spectra were collected on an Agilent Cary 60 spectrometer. Spectrophotometric titrations were carried out in a nitrogenfilled glovebox using fiber optics that feed through a glovebox port and couple to the Cary 60 spectrometer. Molar extinction coefficients were determined spectroscopically using the Carv 60 spectrometer and the Beer-Lambert relationship. Mass spectrometry was carried out with a LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer. Measurements were made on complexes dissolved in methanol. Samples were introduced via a microelectrospray source at a flow rate of 3 µL/min. Xcalibur (ThermoFisher, Bremen, Germany) was used to analyze the data.

Synthesis of 7-(Dimethylamino)quinoline Derivatives. 7-(Dimethylamino)quinoline (H-7DMAQ). H-7DMAQ was obtained via Skraup reaction as described by Picken⁴⁵ with a modification from Ozerov.⁴⁶ 1.0 g (4.8 mmol) of 3-(dimethylamino)aniline dihydrochloride was dissolved in 10 mL of H₂O, and to it 20 mL of 1.0 M sodium hydroxide was added. Dichloromethane (4×25 mL) was used to extract the basic aniline, and the combined organic layers were concentrated in vacuo to a violet oil in a round-bottom flask. Glycerol (0.5 mL, 6.8 mmol) and sodium iodide (1.08 g, 7.2 mmol) were added. The reaction flask was put on ice, and concentrated sulfuric acid (2.7 mL) was added dropwise. The mixture was heated to reflux (140–150 °C) for 3 h. After cooling, equal volumes (40 mL) of H₂O and CH₂Cl₂ were used Scheme 2. (a) General Scheme for the Synthesis of the R-7DMAQs Containing Aryl Substituents (Ph, MeO, and TMP-7DMAQ);^{*a,b*} (b) H-7DMAQ Synthesized in One Step via a Skraup Reaction;^{*b*} (c) Substituents of the R-7DMAQs and the Nomenclature Used Throughout This Article



^{*a*}The substituents at the 2,4-positions of the quinoline backbone are determined by the identity of the boronic acid employed in the third step. ^{*b*}Details of these reactions are included in the Experimental Section.

to transfer the mixture to a 250 mL Erlenmeyer flask. The Erlenmeyer flask was placed in an ice bath, and the mixture was basified with aqueous sodium hydroxide (1.0 M) until the solution was alkaline. Sodium sulfite was added to quench any remaining I₂, and the reaction mixture was filtered. CH₂Cl₂ (4 × 25 mL) was used to extract the organic product. The organic layer was dried (MgSO₄), filtered, concentrated to an oil, and purified on silica gel (eluent, chloroform/methanol 99.5/0.5 to 95/5) yielding H-7DMAQ as a yellow oil (0.39 g, 47% yield). ¹H NMR (400 MHz, CDCl₃) δ (ppm): 8.74 (d, 1H), 7.96 (d, 1H), 7.64 (d, 1H), 7.19 (dd, 1H₄), 7.16 (d, 1H), 7.10 (dd, 1H), 3.10 (s, 6H, s).

General Procedures for Aryl-Substituted 2,4-R-7-(Dimethylamino)quinoline Derivatives. The four arylsubstituted 2,4-R-7-(dimethylamino)quinoline derivatives (R-7DMAQ) were synthesized in three steps.

2,4-Dihydroxy-7-(dimethylamino)quinoline. The synthesis of 2,4-dihydroxy-7-(dimethylamino)quinoline was adapted from Knierzinger and Wolfbeis.⁴⁷ 3-(N,N-Dimethylamino)aniline dihydrochloride (2.0 g, 9.6 mmol) was dissolved in 10 mL of H₂O, and to it 40 mL of 1.0 M sodium hydroxide was added. The solution was poured into a separation funnel, and CH_2Cl_2 (4 × 50 mL) was used to extract the basic aniline. The combined organic layers were concentrated in vacuo. Diethyl malonate (1.5 mL, 9.6 mmol) was added to the round-bottom flask containing the aniline, a Dean-Stark apparatus was fitted to the flask (to distill off ethanol produced in situ), and the mixture was refluxed between 180 and 200 °C for 3 h. Upon cooling, gravish solids were left behind in the reaction flask. The solids were transferred to a Buchner funnel and washed thoroughly with H₂O. Solids retained by the funnel were placed in a beaker and stirred with acetone. This mixture was then filtered, and the resulting solids collected are 2,4-dihydroxy-7-(dimethylamino)quinoline (2,4-OH-7DMAQ) (1.4 g, 75% yield). ¹H NMR (400 MHz, CD_2Cl_2) δ (ppm): 10.83 (s, 1H, -OH), 10.70 (s, 1H, -OH), 7.54 (d, 1H, Ar-H), 6.60 (dd, 1H, Ar-H), 6.40 (d, 1H, Ar-H), 5.42 (s, 1H, Ar-H), 2.95 (s, 6H, CH₃).

2,4-Dibromo-7-(dimethylamino)quinoline. The synthesis of 2,4-dibromo-7-(dimethylamino)quinoline (2,4-Br-7DMAQ) was adapted from Janin et al.⁴⁸ To a round-bottom flask containing a Teflon-coated stir bar, 2,4-OH-7DMAQ (1.0 g, 4.9 mmol), POBr₃ (7.0 g, 24.5 mmol), and K₂CO₃ (2.0 g, 14.7 mmol) were added. This mixture was dissolved in dry

acetonitrile (60 mL) and refluxed for 3 h at 80 °C. After the mixture was cooled, water was slowly added to the reaction vessel until the solution stopped bubbling. Aqueous sodium hydroxide (2 M) was then added until the solution reached neutral pH and a precipitate formed. CH₂Cl₂ (4 × 50 mL) was then used to extract the organic product. A simple silica column with CH₂Cl₂ mobile phase separated the product mixture (typically the second yellow band to elute). 2,4-Br-7DMAQ was obtained as a green-yellow crystalline powder (0.53 g, 33%). ¹H NMR (400 MHz, CD₂Cl₂) δ (ppm): 7.89 (d, 1H, Ar–H), 7.44 (s, 1H, Ar–H), 7.14 (dd, 1H, Ar–H), 6.99 (d, 1H, Ar–H), 3.09 (s, 6H, CH₃).

2,4-R-7-(Dimethylamino)quinoline. The procedure for the Suzuki coupling of 2,4-Br-7DMAQ with arylboronic acid to vield aryl-substituted 2,4-R-7-(dimethylamino)quinoline (R-7DMAQ) was adapted from Watanabe⁴⁹ and Suzuki.⁵⁰ In a nitrogen-filled glovebox, 2,4-Br-7DMAQ (1 equiv), an arylboronic acid (2.2 equiv), Pd(PPh₃)₄ (0.04 equiv), and a Teflon-coated stir bar were added to a Schlenk flask. The flask was removed from the glovebox in a sealed vessel and placed under nitrogen flow on a Schlenk line. $Ba(OH)_2$ (3 equiv) was degassed and cannula transferred to the Schlenk flask along with a mixture of degassed dimethoxyethane/H2O (4:1, also added via cannula transfer). The mixture was refluxed at 85 °C under a N₂ atmosphere for 48 h. After cooling of the reaction mixture, water was added to the flask to aid in transfer to a separatory funnel. The mixture was then extracted with CH₂Cl₂ and purified further using column chromatography. These details, along with further characterization for each R-7DMAQ, are included in the Supporting Information.

Stopped-Flow Experiments. Stopped-Flow experiments were performed on a HI-TECH SF-61DX2 double-mixing stopped-flow spectrophotometer in single mixing mode with Kinetic Studio data acquisition software (v2.33). For single wavelength kinetics measurements, a tungsten light source and dual-beam photomultiplier tube (Hamamatsu R928) were used. For spectral analysis, a xenon light source and a photodiode array were used. Stopped-flow measurements were all performed under a nitrogen atmosphere. Samples were prepared inside of an inert-atmosphere glovebox in septum-sealed bottles. PEEK tubing was used to transfer solutions directly from sealed bottles to the stopped-flow syringes. To ensure purity of samples analyzed, each syringe was purged three times prior to each measurement. In a typical experiment,

Гable	1. Absorbance	Features,	Redox 1	Properties,	and pK_a	Values for	Each of	the R	-7DMAQs	Compounds
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base	pK_a (CH ₃ CN)	$\lambda_{\max} \to (nm)$	ε , B (M ⁻¹ cm ⁻¹)	$\lambda_{\rm max} \; {\rm BH^{+}} \; ({\rm nm})$	ε , BH ⁺ (M ⁻¹ cm ⁻¹)	$E_{\rm p,a}~({\rm V~vs~Fc^{+/0}})$
Ph-7DMAQ	14.2	392	4300	464	9880	0.45
H-7DMAQ	15.0	370	3300	432	6230	0.39
MeO-7DMAQ	15.0	389	10000	375, 465	20200, 20800	0.44
TMP-7DMAQ	15.2	374	6600	446	13300	0.51

one syringe was loaded with ferrocenium hexafluorophosphate (60 μ M) while the other was loaded with R-7DMAQ (30 μ M) and varying concentrations of NH₂PhOH (100–500 μ M). Upon injection, absorbance vs time was monitored at various wavelengths for kinetics traces. Fitting of the data was carried out in MATLAB (The MathWorks, Inc.) and is described elsewhere in the text.

Electrochemistry. All electrochemical measurements were performed in a nitrogen-filled glovebox, using electrode leads that were fed through a custom port and connected to a Pine Instruments WaveDriver potentiostat. A three-electrode cell was used for all experiments, utilizing platinum working electrodes, a glassy carbon counter electrode (CH Instruments, 3 mm diameter), and a silver wire pseudoreference immersed in a glass tube fitted with a porous Vycor tip and filled with a 0.25 M [Bu₄N][PF₆] acetonitrile solution. The glassy carbon electrodes were polished using a Milli-Q water slurry of 0.05 μ m polishing powder (CH Instruments, containing no agglomerating agents), rinsed and sonicated in Milli-Q water, and rinsed with acetone. Working electrodes were electrochemically pretreated with two cyclic scans between 1.5 and -2.5 V at 200 mV/s in 0.25 mM [Bu₄N][PF₆] solution. Background voltammograms of electrolyte-only solutions were collected for every electrode at the appropriate scan rate. All voltammograms were recorded in 0.25 M $[Bu_4N][PF_6]$ acetonitrile solutions and internally referenced to ferrocene.

RESULTS

Synthesis and Characterization of 2,4-R-7-(Dimethylamino)quinoline Derivatives. The aryl-substituted 2,4-R-7-(dimethylamino)quinoline derivatives (R-7DMAQ, R = aryl) were synthesized via the procedure outlined in Scheme 2a. *N,N*-Dimethyl-3-phenylenediamine was refluxed with diethyl malonate to form 2,4-hydroxy-7-(dimethylamino)quinoline. Bromination of the hydroxyl groups was carried out by refluxing the isolated reaction product in dry acetonitrile with phosphorus oxybromide and potassium carbonate. The final R-7DMAQ was obtained via a Suzuki coupling; a wide variety of commercially available boronic acids permits access to a range of aryl-substituted 7DMAQs. 7-(Dimethylamino)quinoline (H-7DMAQ) was synthesized in one step via a Skraup reaction (Scheme 2b).

Absorbance spectra of all the 7DMAQ derivatives exhibit a broad absorption feature centered 370–390 nm that tails into the visible region (Table 1, Figure 1, and Figures S9–S12). Protonation of the 7DMAQ species to form 7DMAQH⁺ results in a bathochromic shift of this absorbance feature of ca. 71 nm and an increase in the extinction coefficient ($\lambda_{max} = 432-465$ nm, Table 1, Figure 1, and Figures S9–S12). Of note, MeO-7DMAQH⁺ has two pronounced absorbance features ($\lambda_{max} = 375$ and 465 nm). Spectrophotometric titrations were carried out to determine the p K_a values for these compounds; values ranged from 14.2 to 15.2, with more electron-donating aryl substituents giving rise to higher p K_a values (Table 1 and Figures S17–S20).^{7,17,51}



Figure 1. UV–vis absorbance spectrum of TMP-7DMAQ (blue) in acetonitrile (78 μ M) and its conjugate acid TMP-7DMAQH⁺ (red, formed *in situ* upon the addition of 1 equiv of HBF₄).

Electrochemical analysis by cyclic voltammetry revealed irreversible waves in the anodic scans ($E_{p,a} = 0.39-0.51$ V vs Fc^{+/0}) (Table 1 and Figures S13–S16). Cathodic scans indicate the compounds are quite difficult to reduce (<–2.0 V vs Fc^{+/0}).

Time-Resolved Optical Monitoring of PCET Reactions. The termolecular PCET reaction between NH₂PhOH, R-7DMAQ, and Fc⁺ was initiated by stopped-flow rapid mixing of a solution of NH₂PhOH (100–500 μ M) and R-7DMAQ (30 μ M) with a solution of ferrocenium hexafluorophosphate (60 μ M) and monitored via optical spectroscopy. Upon mixing, Fc⁺ oxidizes NH₂PhOH, generating the aminophenol radical cation NH₂PhOH^{•+}. This radical cation is much more acidic and is readily deprotonated by basic species in solution,^{3,52,53} including R-7DMAQ, to generate R-7DMAQH⁺ and NH₂PhO[•].

This PCET reaction was first explored with Ph-7DMAQ. Absorbance spectra recorded at various time delays have prominent features corresponding to Fc⁺ ($\lambda_{max} = 620$ nm), Ph-7DMAQ ($\lambda_{max} = 392$ nm), and Ph-7DMAQH⁺ ($\lambda_{max} = 464$ nm) (Figure 2). The peaks corresponding to Fc⁺ and Ph-7DMAQ decay over the 0–100 ms time scale, while a new feature consistent with Ph-7DMAQH⁺ grows in on a similar



Figure 2. Absorbance spectra recorded at various time delays (0–100 ms, 6 ms intervals) upon rapid mixing of NH₂PhOH (100 μ M) and Ph-7DMAQ (30 μ M) with Fc⁺ (150 μ M) in CH₃CN.

time scale as the reaction proceeds. Clean conversion of Ph-7DMAQ to its conjugate acid is indicated by the well-defined isosbestic point at 415 nm.

Single wavelength kinetics traces monitoring the appearance of the 7DMAQH⁺ peak ($\lambda_{obs} = 440-460 \text{ nm}$) and the decay of the Fc⁺ peak ($\lambda_{obs} = 620 \text{ nm}$) were recorded as a function of NH₂PhOH concentration for each of the four R-7DMAQ photometric bases (representative spectra in Figures 3 and 4;



Figure 3. Stopped-flow kinetics traces monitoring the appearance of TMP-7DMAQH⁺ at 450 nm. Present in each reaction are 60 μ M Fc⁺, 30 μ M TMP-7DMAQ, and 100–500 μ M NH₂PhOH.



Figure 4. Stopped-flow kinetics traces monitoring the disappearance of Fc⁺ at 620 nm. Present in each reaction are 60 μ M Fc⁺, 30 μ M TMP-7DMAQ, and 100–500 μ M NH₂PhOH.

full data set in Figures S21–S23). At both wavelengths, the rates of reaction accelerated as the concentration of NH₂PhOH was increased. In a separate experiment, the kinetics of Fc⁺ reduction were monitored ($\lambda_{obs} = 620$ nm) as a function of R-7DMAQ concentration (with constant concentrations of NH₂PhOH and Fc⁺). Notably, changes in the concentration of the photometric base did not affect the decay kinetics of the Fc⁺ signal (Figure S24).

KINETICS ANALYSIS AND DISCUSSION

Proton-Coupled Electron Transfer Reactivity. The stopped-flow experiments described above provide kinetics data about both PT and ET processes in the oxidation of NH₂PhOH by the oxidant/base combination of Fc⁺ and R-7DMAQ (the formal bond dissociation free energies^{3,36} range from 74.4 to 75.7 kcal mol⁻¹ for these oxidant/base combinations). The observation that higher concentrations of NH₂PhOH correlate with increases in both the observed rates of PT and ET suggests that the PT and ET components are coupled. Qualitatively, however, these two processes do not appear to occur with the same reaction kinetics. Further, for samples in which the concentration of R-7DMAQ was varied as

the concentrations of NH₂PhOH and Fc⁺ were held constant, kinetics traces reveal that the decay of the Fc⁺ signal is not sensitive to base concentration. These observations indicate that this reaction is not operating under a CPET mechanism. The viabilities of stepwise PT-ET and ET-PT pathways were both considered. PT-ET would require an initial deprotonation event, yet the differences between pK_a values of NH₂PhOH (~ 30) and the R-7DMAQH⁺ species (14.2–15.2) suggest that protonation of R-7DMAQ by NH₂PhOH is highly endergonic. By contrast, an ET-PT process (eqs 1 and 2) involves a slightly endergonic ET process ($\Delta G_{\rm ET} \approx 60$ mV) followed by PT from the NH₂PhOH radical cation (NH₂PhOH^{•+}) to R-7DMAQ (rough estimation of the pK_a of $NH_2PhOH^{\bullet+}$ in CH_3CN from the pK, reported in DMSO gives a value of 15.8;^{3,54} however, observations of deprotonation by R-7DMAQ in this work suggests the value is in fact lower as PT to R-7DMAQ appears facile).

$$NH_2PhOH + Fc^+ \xrightarrow{\kappa_1} NH_2PhOH^{\bullet+} + Fc^0$$
(1)

$$NH_2PhOH^{\bullet+} + R-7DMAQ$$

$$\stackrel{k_2}{\to} \mathrm{NH}_2 \mathrm{PhO}^{\bullet} + \mathrm{R-7DMAQH}^+$$
(2)

$$\mathrm{NH}_{2}\mathrm{PhO}^{\bullet} + \mathrm{Fc}^{+} \xrightarrow{\kappa_{3}} \mathrm{NH}_{2}\mathrm{PhO}^{+} + \mathrm{Fc}^{0}$$
(3)

$$\rm NH_2PhO^+ + R-7DMAQ \xrightarrow{k_4} \rm NHPhO + R-7DMAQH^+$$
(4)

$$NH_{2}PhOH + R-7DMAQH^{+}$$

$$\stackrel{k_{5}}{\rightleftharpoons} NH_{3}PhOH^{+} + R-7DMAQ$$

$$\stackrel{k_{-5}}{\longleftarrow} (5)$$

$$NH_2PhOH^{\bullet+} + NH_2PhOH \xrightarrow{k_6} NH_2PhO^{\bullet} + NH_3PhOH^+$$
(6)

$$\mathrm{NH}_{2}\mathrm{PhO}^{+} + \mathrm{NH}_{2}\mathrm{PhOH} \xrightarrow{k_{7}} \mathrm{NH}\mathrm{PhO} + \mathrm{NH}_{3}\mathrm{PhOH}^{+}$$
(7)

2NHPhO
$$\xrightarrow{k_8}$$
 further products (8)

$$Fc^{+} + R-7DMAQ \rightleftharpoons_{k_{-9}}^{k_{9}} [Fc^{+} \cdots R-7DMAQ]$$
(9)

Our data qualitatively support an initial ET-PT mechanism for the reaction of NH₂PhOH, Fc⁺, and R-7DMAQ to form NH₂PhO[•], R-7DMAQH⁺, and Fc. However, extensive studies exploring the electrochemical oxidation of aniline and its derivatives (including NH₂PhOH) show that upon oxidation the products formed are highly favored to undergo a second one-electron, one-proton oxidation,⁵⁵⁻⁵⁹ and their twoelectron, two-proton chemistry is well precedented. $^{60-66}\ \mathrm{Our}$ own electrochemical and mass spectrometric investigations of NH₂PhOH support this hypothesis and suggest that in the presence of base, the one-electron oxidized product can be readily deprotonated before undergoing a second oxidation and deprotonation (Figures S25-S27). This observation, combined with previous reports of two-electron, two-proton reactions involving NH₂PhOH, provides compelling evidence that stopped-flow kinetics data contain details of the secondary PCET reactivity of NH₂PhO[•] to form *p*-benzoquinone imine, NHPhO (eqs 3 and 4).



Figure 5. Stopped-flow kinetics traces monitoring (left) the appearance of TMP-7DMAQH⁺ at 450 nm and (right) the disappearance of Fc⁺ at 620 nm for the reaction between 100 and 500 μ M NH₂PhOH, 60 μ M Fc⁺, and 30 μ M TMP-7DMAQ. Dotted lines represent the kinetics simulation based on the kinetics model described by eqs 1–9. Rate constants used in the simulation: k_1 , 1.2×10^5 M⁻¹ s⁻¹; k_2 , 7.5×10^8 M⁻¹ s⁻¹; k_3 , 5.0×10^5 M⁻¹ s⁻¹; k_4 , 3.0×10^7 M⁻¹ s⁻¹; k_5 , 2.7×10^3 M⁻¹ s⁻¹; k_{-5} , 3.0×10^6 M⁻¹ s⁻¹; k_6 , 3.0×10^6 M⁻¹ s⁻¹; k_7 , 1.0×10^5 M⁻¹ s⁻¹; k_8 , 1.0×10^5 M⁻¹ s⁻¹; k_{-5} , 3.0×10^6 M⁻¹ s⁻¹; k_{-5} , 3.0×10^6 M⁻¹ s⁻¹; k_{-9} , 38.9 s⁻¹.

Equations 1–4 together describe two sequential stepwise PCET reactions. A complete picture of the reactivity, and a full kinetics analysis, however, must also account for additional reactivity. While NH₂PhOH is a weaker base than R-7DMAQ, the high concentration of NH₂PhOH in these experiments requires that we take into account an equilibrium between R-7DMAQH⁺ and NH₂PhOH (eq 5). Spectrophotometric titrations (Figures S28–S31) indicate a weak equilibrium between these two reagents ($K_5 = 1 \times 10^{-2}$ – 5×10^{-4}). These titrations provide an estimation of the pK_a of NH₃PhOH⁺ in accounting Information).

The amine group of unreacted NH_2PhOH can also serve as a proton acceptor for either of the radical cations generated in eqs 2 and 4 (eqs 6 and 7). On the basis of the relative basicities of the proton acceptors in solution, we posit that PT to NH_2PhOH will be slower than PT to R-7DMAQ. However, because the concentration of 7DMAQ is half that of the oxidant Fc⁺, and NH_2PhOH in excess, NH_2PhOH must serve as a proton acceptor from both a stoichiometric and kinetic perspective.

The aforementioned product NHPhO reacts further to form oligomeric structures; we simplistically represent this complex terminal reactivity with eq 8.64,65 Lastly, when Fc⁺ is titrated into a solution of R-7DMAQ, the absorbance of R-7DMAQ decreases, and a new peak appears at 460 nm, suggesting an adduct between R-7DMAQ and Fc⁺ (Figure S32). However, upon addition of a stronger base (that does not absorb in the visible region), 1,8-diazabicycloundec-7-ene (DBU, $pK_{a} =$ 24),⁶⁷ the original absorbance spectrum of basic R-7DMAQ is recovered. Quinolines are Lewis bases⁶⁸ and can thus form adducts with Lewis acids, like Fc⁺.⁶⁹ To further confirm that the absorbance shifts arise from a Lewis acid-base interaction, and ensure the reactivity was not resulting from an endergonic electron transfer reaction, the interaction of Ph-7DMAQ with decamethylferrocenium $(Me_{10}Fc^+, a 507 \text{ mV weaker oxidant})^{69}$ was tested. Upon titration with Me₁₀Fc⁺, a similar change in absorbance of Ph-7DMAQ is observed (Figure S33). This Lewis acid-base interaction between the R-7DMAQs and Fc⁺ (eq 9) was quantified using a modified Benesi-Hildebrand analysis⁷⁰ (see Figures S34-S37) and taken into account when modeling the kinetics of the described PCET system (vide infra).

Kinetics Model for PCET Reactivity. Kinetics simulations were performed with a series of differential equations (see Supporting Information) derived from the kinetics model described in eqs 1–9 to determine rate constants for

elementary reaction steps. The rate law for the coupled series of reactions was solved numerically using an ordinary differential equation solver. Initial concentrations of reactants, intermediates, and products as well as the time interval of the reaction and rate constants were provided as inputs. Solving these equations resulted in time-dependent concentration profiles for each species—known molar extinction coefficients were used to convert time-dependent concentration profiles into simulated stopped-flow kinetics traces.

In order to minimize floating parameters, kinetics traces monitoring the loss of the Fc⁺ absorbance at 620 nm upon rapid mixing with NH₂PhOH in the absence of R-7DMAQ were simulated to quantify the rates of ET between Fc⁺ and NH₂PhOH (eq 1) and NH₂PhO[•] (eq 3) (Figure S38). To describe reactivity in the absence of R-7DMAQ, rate constants k_{2} , k_{4} , k_{5} , k_{-5} , k_{9} , and k_{-9} were set to zero in the kinetics model, and the remaining rate constants were adjusted iteratively to simulate the kinetics traces. Simulations were extremely sensitive to both k_1 and k_3 and yielded values of 1.2×10^5 $M^{-1}~s^{-1}$ and 5.0 $\times~10^5~M^{-1}~s^{-1}$, respectively, for these two rate constants. These rate constants are consistent with those predicted by the Marcus cross-relation based on the selfexchange rate constants for ferrocene/ferrocenium and phenoxyl/phenoxide (the PhOH^{+/0} self-exchange rate constant is not known; see Supporting Information).⁷

Simulations also provided rate constants for proton transfer from the oxidation products to NH₂PhOH ($k_6 = 3.0 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ and $k_7 = 1.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$; see below for further discussion). The rate constant depicting terminal oligomerization reactivity of *p*-quinone imine ($k_8 = 1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$) falls in the range estimated for oligomer formation.⁶⁵ The value of this parameter had minimal influence on the kinetic fits but was necessary to model the consumption of the *p*-benzoquinone imine.^{64,65}

To model kinetics data for samples incorporating the photometric bases ($\lambda_{obs} = 440-460$ and 620 nm), the five rate constants determined above in the absence of R-7DMAQ were held constant. Values for K_5 and K_9 , which describe the equilibria of R-7DMAQ with NH₂PhOH and Fc⁺, respectively, were used to determine the ratios of k_5 : k_{-5} and k_9 : k_{-9} . The forward rate constants k_5 and k_9 were determined through iterative simulation while the reverse rate constants k_{-5} and k_{-9} were fixed by maintaining $K_{eq} = k_5/k_{-5} (k_9/k_{-9})$. As a result, the only remaining variables in the complete kinetics model described by eqs 1–9 were the rate constants for proton transfer from the initial oxidation products NH₂PhOH^{•+} and

NH₂PhO⁺ to R-7DMAQ (k_2 and k_4 , respectively). Rate constants k_2 and k_4 were iteratively adjusted, together with k_5 and k_9 , to achieve satisfactory simulation of the single wavelength kinetics traces at both $\lambda_{obs} = 440-460$ nm and $\lambda_{obs} = 620$ nm. Simulations were repeated across a set of samples that contained varying concentrations of NH₂PhOH to obtain a self-consistent set of rate constants for each R-7DMAQ. k_2 values from these simulations fall in the range $(1.5-7.5) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ while the corresponding k_4 values are smaller, in the range $(5.5-3.0) \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ (Table 2).

 Table 2. Rate Constants Determined through Kinetics

 Modeling

	R-7DMAQ photometric base						
rate constants	Ph- 7DMAQ	H-7DMAQ	MeO- 7DMAQ	TMP- 7DMAQ			
$k_1 (M^{-1} s^{-1})$	1.2×10^{5}	1.2×10^{5}	1.2×10^{5}	1.2×10^{5}			
$k_2 (M^{-1} s^{-1})$	1.5×10^{8}	6.0×10^{8}	6.0×10^{8}	7.5×10^{8}			
$k_3 (M^{-1} s^{-1})$	5.0×10^{5}	5.0×10^{5}	5.0×10^{5}	5.0×10^{5}			
$k_4 (M^{-1} s^{-1})$	5.5×10^{6}	2.0×10^{7}	2.0×10^{7}	3.0×10^{7}			
$k_5 (M^{-1} s^{-1})$	2.0×10^{4}	3.0×10^{9}	5.7×10^{9}	$2.7 \times 10^{\circ}$			
k_{-5} (M s) k_{-5} (M ⁻¹ s ⁻¹)	1.0×10^{6}	1.0×10^{6}	3.0×10^{6}	3.0×10^{6}			
k_{6} (M ⁻¹ s ⁻¹)	1.0×10^{5}	1.0×10^{5}	1.0×10^{5}	1.0×10^{5}			
$k_8 (M^{-1} s^{-1})$	1.0×10^{5} 1.0×10^{5}	1.0×10^{5}	1.0×10^{5} 1.0×10^{5}	1.0×10^{5} 1.0×10^{5}			
$k_9 (M^{-1} s^{-1})$	3.0×10^{5}	1.2×10^{6}	1.0×10^{6}	1.4×10^{6}			
$k_{-9} (s^{-1})$	6.7	5.7	16.1	38.9			

To more closely examine the influence of individual rate constants on simulations of single-wavelength kinetics traces, the concentration profiles of individual reactants and intermediates underpinning the kinetics simulations were examined. In the studies described in this work, the concentration of Fc^+ is held constant (60 μ M) while the initial concentrations of NH₂PhOH range from 100 to 500 µM. These near pseudo-first-order conditions might suggest that all of the Fc⁺ would be consumed through the oxidation of NH₂PhOH to NH₂PhOH^{•+}, and thus the subsequent oxidation of NH₂PhO[•] would not occur as the Fc⁺ concentration would rapidly decay to zero. However, concentration profiles of Fc⁺, NH₂PhOH, NH₂PhO[•], and NHPhO show that with the rate constants determined from the kinetics simulations Fc⁺ is not immediately and completely consumed by reaction with NH₂PhOH; NH₂PhO[•] forms rapidly, and Fc⁺ oxidizes both NH₂PhOH and NH₂PhO[•] on the milliseconds time scale (Figure S42). Incorporating the oxidation of NH₂PhO[•] by Fc⁺ is critical for accurately describing the reaction of interest and obtaining good kinetics simulations.

Driving Force Dependent Rate Constants for Proton Transfer. Rate constants for proton transfer from NH₂PhOH^{•+} (k_2) and NH₂PhO⁺ (k_4) to R-7DMAQ, linear correlations are observed between ln (k_{PT}) and the pK_a values for the conjugate acids of the R-7DMAQ proton acceptors (Figure 6). While the two trend lines have identical slopes (slope = 1.65) their vertical offset reflects the difference in the unknown pK_a values of NH₂PhOH^{•+} and NH₂PhO⁺. As such, the pK_a values on the *x*-axis only linearly correlate with $-\Delta G_{PT}$ within each set of data.³ The free energy relationships observed are consistent with what is predicted by the Brønsted relation for acid–base reactivity, as well as theory developed by Bell based on the transition state model.^{41,73–75} Indeed, linear correlations between rate constants and driving force have been observed



Figure 6. For proton transfer reactions from aminophenol oxidation products, free energy relationships are observed between the rate constants and the pK_a value for the conjugate acid of the proton acceptor, which is proportional to the driving force for proton transfer within each set of reactions. Included on this plot are the values for k_2 and k_4 , the rates of PT to R-7DMAQ derivatives (\bullet , $pK_a(R-7DMAQH^+) = 14.2-15.2$), as well as k_6 and k_7 , the rates of PT to NH₂PhOH (\blacktriangle , $pK_a(NH_3PhOH^+) = 12.5$). Across the R-7DMAQ derivatives, linear free energy relationships (gray dashed lines) are observed for proton transfer from NH₂PhOH^{•+} (slope = 1.66) and from NH₂PhO⁺ (slope = 1.65). Including proton transfer from these radical cations to NH₂PhOH, the data fit best to a quadratic relationship (blue and red dashed lines).

in many examples of proton transfer, and Brønsted slopes have been traditionally used to characterize reaction mechanisms and compare proton transfer processes.^{33,34,41–43,73,75–79}

When the rate constants for proton transfer from NH₂PhOH^{•+} (k_6) and NH₂PhO⁺ (k_7) to NH₂PhOH are added to the plot $(pK_{a}(NH_{3}PhOH^{+}) = 12.5)$, these data points fall off the linear trend lines defined by the four R-7DMAQ bases, lending distinct curvature to the $\ln(k_{\rm PT}) - pK_{\rm a}$ relationship (Figure 6). While NH₂PhOH is a structurally distinct base from the R-7DMAQ class of compounds, examples of free energy relationships in proton transfer reactions involving nitrogen and oxygen acids and bases have been shown to hold across a range of proton donors/acceptors.⁸⁰ The data sets (k_2 and k_{6} , k_{4} , and k_{7}) fit well to parabolas, consistent with the quadratic correlation between ΔG^{\ddagger} (the free energy of activation) and $-\Delta G_{\text{PT}}$ predicted by Marcus for proton transfer reactions.^{41,73,75,81,82} In this context, the linear relation observed for proton transfer to the R-7DMAQ bases could simply result from the small $\Delta p K_a$ range that these data points span, across which the higher order terms of the quadratic can be neglected to give an apparent linear relationship for $d\Delta G^{\ddagger}/$ $d\Delta G_{\rm PT}^{31,75,83}$ While parabolic free energy relationships have long been theorized for proton transfer, 81,82,84,85 limited experimental examples revealing these relationships are available, especially in either nonaqueous solvents or as part of a PCET process.^{75,80,82,86} Unfortunately, the system studied in this work limits the range of driving forces that can be examined, preventing a more definitive assessment of the free energy relationship for proton transfer. Nevertheless, these data enhance our understanding of free energy relationships for proton transfer processes in PCET reactions and motivate extended study in this area.

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CONCLUSION

Utilizing a series of 7-(dimethylamino)quinoline derivatives as photometric bases, both the PT and ET components of the PCET oxidation of NH₂PhOH were optically monitored upon rapid mixing via stopped flow. Analysis of this complex multielectron, multiproton reaction was enabled by spectroscopic handles for both proton transfer and electron transfer. A comprehensive kinetics model was constructed, from which rate constants for elementary reaction steps were determined. These data reveal free energy relationships between PT rate constants and the pK_a values of the conjugate acids of the proton acceptors. Over the driving force range examined, these data suggest a Marcus relationship for proton transfer. Notably, free energy relationships for PT components of PCET reactions have recently been reported by our group for elementary proton transfer steps involved in hydrogen evolution catalyzed by transition metal complexes.^{33,34} Taken together, these experimentally determined relationships enhance our understanding of PT processes in PCET reactions and provide a framework to further study these reactions in a comprehensive fashion.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcb.6b04011.

Experimental details, compound purification and characterization (NMR, UV–vis, mass spectrometry, cyclic voltammetry), spectrophotometric titrations, additional stopped-flow kinetics, a modified Benesi–Hildebrand analysis, and additional details of kinetics modeling (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Weinberg, D. R.; Gagliardi, C. J.; Hull, J. F.; Murphy, C. F.; Kent, C. A.; Westlake, B. C.; Paul, A.; Ess, D. H.; McCafferty, D. G.; Meyer, T. J. Proton-Coupled Electron Transfer. *Chem. Rev.* **2012**, *112*, 4016–4093.

(2) Costentin, C.; Robert, M.; Savéant, J.-M. Update 1 of: Electrochemical Approach to the Mechanistic Study of Proton-Coupled Electron Transfer. *Chem. Rev.* **2010**, *110*, PR1–PR40.

(3) Warren, J. J.; Tronic, T. A.; Mayer, J. M. Thermochemistry of Proton-Coupled Electron Transfer Reagents and Its Implications. *Chem. Rev.* **2010**, *110*, 6961–7001.

(4) Kretchmer, J. S.; Miller, T. F. Tipping the Balance between Concerted versus Sequential Proton-Coupled Electron Transfer. *Inorg. Chem.* **2016**, *55*, 1022–1031.

(5) Manner, V. W.; DiPasquale, A. G.; Mayer, J. M. Facile Concerted Proton-Electron Transfers in a Ruthenium Terpyridine-4'-Carboxylate Complex with a Long Distance Between the Redox and Basic Sites. *J. Am. Chem. Soc.* **2008**, *130*, 7210–7211.

(6) Markle, T. F.; Rhile, I. J.; Mayer, J. M. Kinetic Effects of Increased Proton Transfer Distance on Proton-Coupled Oxidations of Phenol-Amines. J. Am. Chem. Soc. 2011, 133, 17341–17352.

(7) Saouma, C. T.; Kaminsky, W.; Mayer, J. M. Protonation and Concerted Proton–Electron Transfer Reactivity of a Bis-Benzimidazolate Ligated [2Fe–2S] Model for Rieske Clusters. *J. Am. Chem. Soc.* **2012**, *134*, 7293–7296.

(8) Warren, J. J.; Mayer, J. M. Hydrogen Atom Transfer Reactions of Iron-Porphyrin-Imidazole Complexes as Models for Histidine-Ligated Heme Reactivity. *J. Am. Chem. Soc.* **2008**, *130*, 2774–2776.

(9) Bourrez, M.; Steinmetz, R.; Ott, S.; Gloaguen, F.; Hammarström, L. Concerted Proton-Coupled Electron Transfer from a Metal-Hydride Complex. *Nat. Chem.* **2015**, *7*, 140–145.

(10) Zhang, M.-T.; Hammarström, L. Proton-Coupled Electron Transfer from Tryptophan: A Concerted Mechanism with Water as Proton Acceptor. J. Am. Chem. Soc. **2011**, 133, 8806–8809.

(11) Sjödin, M.; Irebo, T.; Utas, J. E.; Lind, J.; Merényi, G.; Åkermark, B.; Hammarström, L. Kinetic Effects of Hydrogen Bonds on Proton-Coupled Electron Transfer from Phenols. *J. Am. Chem. Soc.* **2006**, *128*, 13076–13083.

(12) Johannissen, L. O.; Irebo, T.; Sjödin, M.; Johansson, O.; Hammarström, L. The Kinetic Effect of Internal Hydrogen Bonds on Proton-Coupled Electron Transfer from Phenols: A Theoretical Analysis with Modeling of Experimental Data. *J. Phys. Chem. B* **2009**, *113*, 16214–16225.

(13) Gagliardi, C. J.; Westlake, B. C.; Kent, C. A.; Paul, J. J.; Papanikolas, J. M.; Meyer, T. J. Integrating Proton Coupled Electron Transfer (PCET) and Excited States. *Coord. Chem. Rev.* 2010, 254, 2459–2471.

(14) Bronner, C.; Wenger, O. S. Proton-Coupled Electron Transfer between 4-Cyanophenol and Photoexcited Rhenium(I) Complexes with Different Protonatable Sites. *Inorg. Chem.* **2012**, *51*, 8275–8283.

(15) Kuss-Petermann, M.; Wolf, H.; Stalke, D.; Wenger, O. S. Influence of Donor-Acceptor Distance Variation on Photoinduced Electron and Proton Transfer in Rhenium(I)-Phenol Dyads. *J. Am. Chem. Soc.* **2012**, *134*, 12844-12854.

(16) Wenger, O. S. Proton-Coupled Electron Transfer with Photoexcited Metal Complexes. Acc. Chem. Res. 2013, 46, 1517–1526.
(17) Eisenhart, T. T.; Dempsey, J. L. Photo-Induced Proton-Coupled

Electron Transfer Reactions of Acridine Orange: Comprehensive Spectral and Kinetics Analysis. J. Am. Chem. Soc. 2014, 136, 12221–12224.

(18) Costentin, C.; Drouet, S.; Passard, G.; Robert, M.; Savéant, J.-M. Proton-Coupled Electron Transfer Cleavage of Heavy-Atom Bonds in Electrocatalytic Processes. Cleavage of a CO Bond in the Catalyzed Electrochemical Reduction. J. Am. Chem. Soc. 2013, 135, 9023–9031. (19) Costentin, C.; Hajj, V.; Louault, C.; Robert, M.; Savéant, J.-M. Concerted Proton-Electron Transfers. Consistency between Electrochemical Kinetics and Their Homogeneous Counterparts. J. Am. Chem. Soc. 2011, 133, 19160–19167.

(20) Savéant, J.-M. Electrochemical Approach to Proton-Coupled Electron Transfers: Recent Advances. *Energy Environ. Sci.* 2012, *5*, 7718–7731.

(21) Costentin, C.; Robert, M.; Savéant, J.-M.; Teillout, A.-L. Concerted Proton-Coupled Electron Transfers in Aquo/hydroxo/oxo Metal Complexes: Electrochemistry of $[Os^{II}(bpy)_2py(OH_2)]^{2+}$ in Water. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 11829–11836.

(22) Kombarova, S. V.; Il'ichev, Y. V. Excited-State Proton Transfer in Complexes of Poly(methacrylic Acid) with Dodecyltrimethylammonium Chloride. *Langmuir* **2004**, *20*, 6158–6164.

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(23) Mohammed, O. F.; Pines, D.; Pines, E.; Nibbering, E. T. J. Aqueous Bimolecular Proton Transfer in Acid-Base Neutralization. *Chem. Phys.* **2007**, *341*, 240–257.

(24) Mohammed, O. F.; Pines, D.; Dreyer, J.; Pines, E.; Nibbering, E. T. J. Sequential Proton Transfer through Water Bridges in Acid-Base Reactions. *Science* **2005**, *310*, 83–86.

(25) Psciuk, B. T.; Prémont-Schwarz, M.; Koeppe, B.; Keinan, S.; Xiao, D.; Nibbering, E. T. J.; Batista, V. S. Correlating Photoacidity to Hydrogen-Bond Structure by Using the Local O-H Stretching Probe in Hydrogen-Bonded Complexes of Aromatic Alcohols. *J. Phys. Chem. A* 2015, *119*, 4800–4812.

(26) Prémont-Schwarz, M.; Barak, T.; Pines, D.; Nibbering, E. T. J.; Pines, E. Ultrafast Excited-State Proton-Transfer Reaction of 1-Naphthol-3,6- Disulfonate and Several 5-Substituted 1-Naphthol Derivatives. J. Phys. Chem. B **2013**, 117, 4594–4603.

(27) Mohammed, O. F.; Xiao, D.; Batista, V. S.; Nibbering, E. T. J. Excited-State Intramolecular Hydrogen Transfer (ESIHT) of 1, 8-Dihydroxy-9,10-anthraquinone (DHAQ) Characterized by Ultrafast Electronic and Vibrational Spectroscopy and Computational Modeling. J. Phys. Chem. A **2014**, *118*, 3090–3099.

(28) Genosar, L.; Cohen, B.; Huppert, D. Ultrafast Direct Photoacid–Base Reaction. J. Phys. Chem. A 2000, 104, 6689–6698.

(29) Chen, J.; Kuss-Petermann, M.; Wenger, O. S. Distance Dependence of Bidirectional Concerted Proton-Electron Transfer in Phenol-Ru(2,2'-Bipyridine) 3 2+ Dyads. *Chem. - Eur. J.* **2014**, *20*, 4098–4104.

(30) Bronner, C.; Wenger, O. S. Kinetic Isotope Effects in Reductive Excited-State Quenching of $Ru(2,2'-bipyrazine)_3^{2+}$ by Phenols. *J. Phys. Chem. Lett.* **2012**, *3*, 70–74.

(31) Fecenko, C. J.; Thorp, H. H.; Meyer, T. J. The Role of Free Energy Change in Coupled Electron–Proton Transfer. J. Am. Chem. Soc. 2007, 129, 15098–15099.

(32) Mayer, J. M. Understanding Hydrogen Atom Transfer: From Bond Strengths to Marcus Theory. *Acc. Chem. Res.* 2011, 44, 36-46.

(33) Rountree, E. S.; Martin, D. J.; McCarthy, B. D.; Dempsey, J. L. Linear Free Energy Relationships in the Hydrogen Evolution Reaction: Kinetic Analysis of a Cobaloxime Catalyst. *ACS Catal.* **2016**, *6*, 3326–3335.

(34) Rountree, E. S.; Dempsey, J. L. Reactivity of Proton Sources with a Nickel Hydride Complex in Acetonitrile: Implications for the Study of Fuel Forming Catalysts. *Inorg. Chem.* **2016**, *55*, 5079–5087.

(35) Mayer, J. M. A Simple Marcus-Theory Type Model for Hydrogen Atom Transfer/Proton-Coupled Electron Transfer. J. Phys. Chem. Lett. 2011, 2, 1481–1489.

(36) Waidmann, C. R.; Miller, A. J. M.; Ng, C.-A.; Scheuermann, M. L.; Porter, T. R.; Tronic, T. A.; Mayer, J. M. Using Combinations of Oxidants and Bases as PCET Reactants: Thermochemical and Practical Considerations. *Energy Environ. Sci.* **2012**, *5*, 7771–7780.

(37) Hammes-Schiffer, S.; Stuchebrukhov, A. A. Theory of Coupled Electron and Proton Transfer Reactions. *Chem. Rev.* **2010**, *110*, 6939–6960.

(38) Hammes-Schiffer, S. Proton-Coupled Electron Transfer: Classification Scheme and Guide to Theoretical Methods. *Energy Environ. Sci.* **2012**, *5*, 7696–7703.

(39) Hammes-Schiffer, S. Proton-Coupled Electron Transfer: Moving Together and Charging Forward. J. Am. Chem. Soc. 2015, 137, 8860–8871.

(40) Gutman, M.; Huppert, D. Rapid pH and $\Delta \mu H^+$ Jump by Short Laser Pulse. *J. Biochem. Biophys. Methods* **1979**, *1*, 9–19.

(41) Jarczewski, A.; Hubbard, C. D. A Review of Proton Transfer Reactions between Various Carbon-Acids and Amine Bases in Aprotic Solvents. J. Mol. Struct. **2003**, 649, 287–307.

(42) Sen Gupta, S. K.; Arvind, U. Equilibria and Kinetics of Reactions between Carboxylic Acids and the Carbinol Base of Crystal Violetin in Apolar Aprotic Solvents: Relative Strengths of *m*- and *o*-Substituted Benzoic Acids in Toluene. *J. Phys. Org. Chem.* **1997**, *10*, 466–472.

(43) Hojatti, M.; Leffek, K. T. Proton Transfer Reactions from 4-X-Phenyl-4-Nitrophenylcyanomethanes to Tetramethylguanidine in Acetonitrile Solvent. *Can. J. Chem.* **1984**, *62*, 2653–2656. (44) Crooks, J. E.; Robinson, B. H. Hydrogen-Bonded and Ion-Pair Complexes in Aprotic Solvents. *Faraday Symp. Chem. Soc.* **1975**, *10*, 29–40.

(45) van den Berg, O.; Jager, W. F.; Cangialosi, D.; van Turnhout, J.; Verheijen, P. J. T.; Wübbenhorst, M.; Picken, S. J. A Wavelength-Shifting Fluorescent Probe for Investigating Physical Aging. *Macromolecules* **2006**, *39*, 224–231.

(46) Lee, C.-I.; Zhou, J.; Ozerov, O. V. Catalytic Dehydrogenative Borylation of Terminal Alkynes by a SiNN Pincer Complex of Iridium. *J. Am. Chem. Soc.* **2013**, *135*, 3560–3566.

(47) Knierzinger, A.; Wolfbeis, O. S. Syntheses of Fluorescent Dyes. IX. New 4-Hydroxycoumarins, 4-Hydroxy-2-quinolones, 2H,5H-Pyrano[3,2-C]benzopyran-2,5-diones and 2H,5H-Pyrano[3,2-C]-quinoline-2,5-diones. *J. Heterocycl. Chem.* **1980**, *17*, 225–229.

(48) Janin, Y. L.; Roulland, E.; Beurdeley-Thomas, A.; Decaudin, D.; Monneret, C.; Poupon, M.-F. Synthetic Approaches to 1-(2-Chlorophenyl)isoquinolone-3-carboxylic Acid. *J. Chem. Soc. Perkin Trans.* 1 2002, 529–532.

(49) Watanabe, T.; Miyaura, N.; Suzuki, A. Synthesis of Sterically Hindered Biaryls via the Palladium-Catalyzed Cross-Coupling Reaction of Arylboronic Acids or Their Esters with Haloarenes. *Synlett* **1992**, 1992, 207–210.

(50) Suzuki, A. Organoborane Coupling Reactions (Suzuki Coupling). *Proc. Jpn. Acad., Ser. B* 2004, *80*, 359–371.

(51) McCarthy, B. D.; Martin, D. J.; Rountree, E. S.; Ullman, A. C.; Dempsey, J. L. Electrochemical Reduction of Brønsted Acids by Glassy Carbon in Acetonitrile-Implications for Electrocatalytic Hydrogen Evolution. *Inorg. Chem.* **2014**, *53*, 8350–8361.

(52) Bordwell, F. G.; Zhang, X. M.; Cheng, J. P. Bond Dissociation Energies of the Nitrogen-Hydrogen Bonds in Anilines and in the Corresponding Radical Anions. Equilibrium Acidities of Aniline Radical Cations. J. Org. Chem. **1993**, *58*, 6410–6416.

(53) Bordwell, F. G.; Cheng, J. Substituent Effects on the Stabilities of Phenoxyl Radicals and the Acidities of Phenoxyl Radical Cations. *J. Am. Chem. Soc.* **1991**, *113*, 1736–1743.

(54) Kütt, A.; Leito, I.; Kaljurand, I.; Sooväli, L.; Vlasov, V. M.; Yagupolskii, L. M.; Koppel, I. A. A Comprehensive Self-Consistent Spectrophotometric Acidity Scale of Neutral Brønsted Acids in Acetonitrile. *J. Org. Chem.* **2006**, *71*, 2829–2838.

(55) Yamada, K.; Teshima, K.; Kobayashi, N.; Hirohashi, R. Electropolymerization of Aniline Derivatives in Non-Aqueous Solution without a Proton Donor. *J. Electroanal. Chem.* **1995**, *394*, 71–79.

(56) Miras, M.; Barbero, C.; Haas, O. Preparation of Polyaniline by Electrochemical Polymerization of Aniline in Acetonitrile Solution. *Synth. Met.* **1991**, *43*, 3081–3084.

(57) Miras, M.; Barbero, C.; Kötz, R.; Haas, O. Electroactive Polyaniline Film from Proton Free Nonaqueous Solution. J. Electrochem. Soc. **1991**, 138, 335–336.

(58) Wei, Y.; Jang, G.-W.; Chan, C.-C.; Hsueh, K. F.; Hariharan, R.; Patel, S. A.; Whitecar, C. K. Polymerization of Aniline and Alkyl Ring-Substituted Anilines in the Presence of Aromatic Additives. *J. Phys. Chem.* **1990**, *94*, 7716–7721.

(59) MacDiarmid, A. G.; Epstein, A. J. Polyanilines: A Novel Class of Conducting Polymers. *Faraday Discuss. Chem. Soc.* 1989, 88, 317–332.
(60) Snead, W. K.; Remick, A. E. Studies on Oxidation-Reduction Mechanism. II. The Anodic Oxidation of *p*-Aminophenol. *J. Am. Chem. Soc.* 1957, 79, 6121–6127.

(61) Taj, S.; Ahmed, M. F.; Sankarapapavinasam, S. Poly(*para*-aminophenol): A New Soluble, Electroactive Conducting Polymer. *J. Electroanal. Chem.* **1992**, 338, 347–352.

(62) Kwon, S. J.; Yang, H.; Jo, K.; Kwak, J. An Electrochemical Immunosensor Using P-Aminophenol Redox Cycling by NADH on a Self-Assembled Monolayer and Ferrocene-Modified Au Electrodes. *Analyst* **2008**, *133*, 1599–1604.

(63) Heras, A. M.; Avila, J. L.; Ruiz, J. J.; García-Blanco, F. A Contribution to the Study of the Electrochemical Oxidation of *p*-Aminophenol on a Mercury Electrode. *Electrochim. Acta* **1984**, *29*, 541–545.

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(64) Sun, W.; Jiao, K.; Zhang, S.; Zhang, C.; Zhang, Z. Electrochemical Detection for Horseradish Peroxidase-Based Enzyme Immunoassay Using *p*-Aminophenol as Substrate and Its Application in Detection of Plant Virus. *Anal. Chim. Acta* **2001**, *434*, 43–50.

(65) Brown, K. C.; Corbett, J. F. Benzoquinone Imines. Part 16. Oxidation of *p*-Aminophenol in Aqueous Solution. *J. Chem. Soc., Perkin Trans.* 2 **1979**, 308–311.

(66) Corbett, J. F. Benzoquinone Imines. Part II. Hydrolysis of *p*-Benzoquinone Monoimine and *p*-Benzoquinone Di-Imine. *J. Chem. Soc. B* **1969**, 213–216.

(67) Kaljurand, I.; Kütt, A.; Sooväli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. Extension of the Self-Consistent Spectrophotometric Basicity Scale in Acetonitrile to a Full Span of 28 p K_a Units: Unification of Different Basicity Scales. J. Org. Chem. **2005**, 70, 1019– 1028.

(68) Raston, C. L.; Skelton, B. W.; Whitaker, C. R.; White, A. H. Lewis-Base Adducts of Main Group 1 Metal Compounds. V. Diaquabis(quinolone)lithium(I) Bromide Bis(quinoline). *Aust. J. Chem.* **1988**, *41*, 409–412.

(69) Noviandri, I.; Brown, K. N.; Fleming, D. S.; Gulyas, P. T.; Lay, P. A.; Masters, A. F.; Phillips, L. The Decamethylferrocenium/ Decamethylferrocene Redox Couple: A Superior Redox Standard to the Ferrocenium/Ferrocene Redox Couple for Studying Solvent Effects on the Thermodynamics of Electron Transfer. *J. Phys. Chem. B* **1999**, *103*, 6713–6722.

(70) Ward, W. M.; Farnum, B. H.; Siegler, M.; Meyer, G. J. Chloride Ion-Pairing with Ru(II) Polypyridyl Compounds in Dichloromethane. *J. Phys. Chem. A* **2013**, *117*, 8883–8894.

(71) Meyer, T. J.; Taube, H. Electron Transfer Reactions. In *Comprehensive Coordination Chemistry*; Pergamon Press: New York, 1987.

(72) Neta, P.; Grodkowski, J. Rate Constants for Reactions of Phenoxyl Radicals in Solution. *J. Phys. Chem. Ref. Data* **2005**, *34*, 109–199.

(73) Arnaut, L. G.; Formosinho, S. J. Understanding Chemical Reactivity: The Case for Atom, Proton and Methyl Transfers. *Chem. Eur. J.* **2008**, *14*, 6578–6587.

(74) Bell, R. P. The Proton in Chemistry; Springer: Boston, MA, 1973.
(75) Silverman, D. N. Marcus Rate Theory Applied to Enzymatic Proton Transfer. Biochim. Biophys. Acta, Bioenerg. 2000, 1458, 88-103.

(76) Gamiz-Hernandez, A. P.; Magomedov, A.; Hummer, G.; Kaila, V. R. I. Linear Energy Relationships in Ground State Proton Transfer and Excited State Proton-Coupled Electron Transfer. *J. Phys. Chem. B* **2015**, *119*, 2611–2619.

(77) Kaila, V. R. I.; Hummer, G. Energetics of Direct and Water-Mediated Proton-Coupled Electron Transfer. J. Am. Chem. Soc. 2011, 133, 19040–19043.

(78) Elgrishi, N.; McCarthy, B. D.; Rountree, E. S.; Dempsey, J. L. Reaction Pathways of Hydrogen-Evolving Electrocatalysts: Electrochemical and Spectroscopic Studies of Proton-Coupled Electron Transfer Processes. *ACS Catal.* **2016**, *6*, 3644–3659.

(79) Pearson, R. G.; Dillon, R. L. Rates of Ionization of Pseudo Acids IV. Relation between Rates and Equilibria. *J. Am. Chem. Soc.* **1953**, *75*, 2439–2443.

(80) Andrieux, C. P.; Gamby, J.; Hapiot, P.; Savéant, J.-M. Evidence for Inverted Region Behavior in Proton Transfer to Carbanions. *J. Am. Chem. Soc.* **2003**, *125*, 10119–10124.

(81) Marcus, R. A. Theoretical Relations among Rate Constants, Barriers, and Broensted Slopes of Chemical Reactions. *J. Phys. Chem.* **1968**, 72, 891–899.

(82) Peters, K. S. A Theory–Experiment Conundrum for Proton Transfer. Acc. Chem. Res. 2009, 42, 89–96.

(83) Reece, S. Y.; Seyedsayamdost, M. R.; Stubbe, J.; Nocera, D. G. Electron Transfer Reactions of Fluorotyrosyl Radicals. *J. Am. Chem. Soc.* **2006**, *128*, 13654–13655.

(84) Kiefer, P. M.; Hynes, J. T. Kinetic Isotope Effects for Nonadiabatic Proton Transfer Reactions in a Polar Environment. 1. Interpretation of Tunneling Kinetic Isotopic Effects. *J. Phys. Chem. A* **2004**, *108*, 11793–11808. (85) Borgis, D.; Hynes, J. T. Curve Crossing Formulation for Proton Transfer Reactions in Solution. J. Phys. Chem. **1996**, 100, 1118–1128. (86) Peters, K. S.; Cashin, A.; Timbers, P. Picosecond Dynamics of Nonadiabatic Proton Transfer: A Kinetic Study of Proton Transfer within the Contact Radical Ion Pair of Substituted Benzophenones/ N,N-Dimethylaniline. J. Am. Chem. Soc. **2000**, 122, 107–113.