Colossal kinetic isotope effects in proton-coupled electron transfer

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The kinetics of reduction of benzoquinone (Q) to hydroquinone (H2Q) by Os(IV)tris(pyrazolyl)borate (trans-[OsIV(tpy)(Cl)2(N(H)N(CH2)4O)]ClO4) in 1:1 (vol/vol) CH3CN/H2O and ChClCN/D2O (1.0 M in NH4PF6/KNO3) at 25.0 ± 0.1°C. The reactions are first order in both [Q] and Os(IV) complex and occur with small driving forces kTs = 0.05, 0.08, and 0.06 eV, respectively, based on cyclic voltammetric experiments measured with the use of Princeton Applied Research (PAR) models 263A and 273 potentiostats, and bulk electrolyses were performed with a PAR model 173 potentiostat/galvanostat. All measurements were conducted in a three-compartment cell in 1:1 (vol/vol) CH3CN/H2O with 1.0 M NH4PF6 as the supporting electrolyte. A glassy carbon working electrode was used for aqueous measurements. All potentials are referenced to the saturated sodium chloride/calomel electrode (SSCE, 0.236 V vs. the normal hydrogen electrode) at room temperature and are uncorrected for junction potentials. In all cases, the auxiliary electrode was a platinum wire. The solution in the working compartment was deoxygenated by N2 or argon bubbling. All redox couple potentials are the average of four independent measurements and are ±2 mV.

Results and Discussion

The kinetics of the reactions shown in Eqs. 1–3 were studied in 1:1 (vol/vol) CH3CN/H2O mixtures at 25.0 ± 0.1°C in 1.0 M NH4PF6/HFPE mixtures. The details of the reaction in Eq. 2 with phosphorus as the proton-donor atom were reported in ref. 18, and preliminary accounts with S and N were reported in refs. 19 and 20. The structures of the Os(V) nitrogen-based electron–proton acceptor and Os(IV) sulfur-based electron–proton donor are shown in Fig. 1.

2 trans-[OsIV(tpy)(Cl)2(N(H)N(CH2)4O)]+ + Q → 2 trans-[OsIV(tpy)(Cl)2(NN(CH2)4O)]+ + H2Q

2 trans-[OsIV(Tp)(Cl)2(NP(H)Et2)] + Q → 2 trans-[OsIV(Tp)(Cl)2(NP(H)Et2)] + H2Q

2 trans-[OsIV(tpy)(Cl)2(NS(H)C6H4Me)]+ + Q → 2 trans-[OsIV(tpy)(Cl)2(NSNC6H4Me)]+ + H2Q

PCET reactions avoid high-energy redox steps (kT). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15). For PCET reactions, values of up to 30 have been observed in solution (16) and enzymatic reactions (13–15).

Abbreviations: PCET-X, proton-coupled electron transfer involving X as the donor atom; KIE, kinetic isotope effect; Q, benzoquinone; tpy, 2,2’6,2’-terpyridine; Tp, tris(pyrazol-1-yl)borate.

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with the rate law in Eq. 4 and contributions from acid-dependent and acid-independent pathways (18–20).

\[
\text{Rate} = \frac{2k_1[H^+] + 2k_2K_a}{[H^+] + K_a} [\text{Os}^{IV}] [Q]
\]

Using the reaction in Eq. 1 as the example, the acid-independent pathway \(k_1\) involves initial deprotonation with \(K_a = 6.3 \times 10^{-4}\) M, to give \(\text{trans-[Os}^{IV}(\text{tpy})(\text{Cl}_2(\text{NN}(\text{CH}_2)_4\text{O}))\text{]}\), followed by outer-sphere electron transfer. The initial electron transfer products are \(\text{trans-[Os}^{IV}(\text{tpy})(\text{Cl}_2(\text{NN}(\text{CH}_2)_4\text{O}))\text{]}^+\) and \(\text{Q}^\cdot\), Eqs. 5 and 6.

\[
\begin{align*}
\text{Os}^{IV}-\text{N} & \quad \text{N} + \text{H}^+ \\
\text{Os}^{IV}=\text{N} & \quad \text{N} + \text{Q} \\
\text{Os}^{V} & \quad \text{N} + \text{Q} + 2\text{H}^+ \\
\text{Os}^{V}=\text{N} \quad \text{N} + \text{Q} + 2\text{H}^+
\end{align*}
\]

Electron transfer is followed by a series of rapid electron/proton transfer steps to give the final products, Eq. 7.

\[
\begin{align*}
\text{Os}^{IV}=\text{N} \quad \text{N} + \text{Q} & \quad \text{N} + \text{Q} + 2\text{H}^+ \\
\text{Os}^{V}=\text{N} \quad \text{N} + \text{Q} & \quad \text{N} + \text{Q} + 2\text{H}^+ \\
\text{Os}^{V}=\text{N} \quad \text{N} + \text{Q} + 2\text{H}^+ & \quad \text{N} + \text{Q} + 2\text{H}^+
\end{align*}
\]

The pH-independent pathway is far more interesting for all three cases because it occurs with a high \(\text{H}_2\text{O}/\text{D}_2\text{O}\) kinetic isotope effect. A detectable intermediate (presumably H-bonded) intervenes in these reactions as shown by spectral measurements and the appearance of saturation kinetics in added Q, Eq. 12.

A proposed mechanism is shown in Eqs. 8–11 for the nitrogen proton-donor case. The key steps are intermediate formation followed by electron transfer. The association constant, \(K_A\), and the rate constant for the redox step, \(k_{\text{red}}\), were separated by analysis of the dependence of \(k_1\) on [Q] according to Eq. 12 (18). Similar mechanisms were identified for the acid-independent pathways for PCET-P and PCET-S.

\[
\text{Rate} = k_1[\text{Os}^{IV}][Q] = \frac{k_{\text{red}}K_A}{K_A[Q]} + 1[\text{Os}^{IV}][Q]
\]

Because \(\Delta G^o = 0\), it is possible to study the kinetics of these reactions in both the forward and reverse directions. Concentration-dependence studies reveal the rate law for the reverse reaction, shown in Eq. 13, for the nitrogen-donor case. Saturation kinetics were observed, and spectroscopic evidence for an intermediate, illustrated in Eqs. 9 and 10 as the semiquinone adduct \(\text{Os}^{IV}=:\text{N}(\text{NN}(\text{CH}_2)_4\text{O})=\text{H}^-\text{Q}^{-}\).

\[
\text{Rate} = 2k_{\text{red}} \left[ \frac{[\text{Os}^{IV}=\text{N}(\text{NN}(\text{CH}_2)_4\text{O})^+]}{[\text{Os}^{III}=\text{N}(\text{NN}(\text{CH}_2)_4\text{O})^+] + 1} \right]
\]

All of these observations are consistent with the mechanism in Eqs. 8–11. In the reverse direction, \(k_{\text{red}}\) is the rate-limiting step and \(K_1 = 3.6 \times 10^7\) from redox potential measurements. Analysis of the kinetics data in 1:1 (vol/vol) CH_3CN/\text{H}_2\text{O} in both directions gave \(k_{\text{red}} = (6.19 \pm 0.05) \times 10^{-3} \text{ s}^{-1}, K_A = (4.43 \pm 0.18) \times 10^3 \text{ M}^{-1}\) for the forward reaction and \(k_{\text{red}} = (1.03 \pm 0.02) \times 10^{-3} \text{ s}^{-1}, K_A = (2.06 \pm 0.06) \times 10^3 \text{ M}^{-1}\) for the reverse reaction, all for the N proton-donor case.

The free energy change for the proton-coupled electron transfer step in Eq. 9, \(\Delta G^o\text{(PCET)}\), is available by using electrochemical measurements to determine \(\Delta G^o\) for the reaction in Eq. 15.
under the conditions of the kinetics experiments.

\[
\text{PCET-N, 22 kcal mol}^{-1} \text{for } [\text{Os}^{IV}(\text{tpy})(\text{Cl})_2(N(H)N(CH_2)_4O)]PF_6 \text{ in 1:1 (vol/vol) CH}_3\text{CN}/\text{H}_2\text{O mixtures at 25.0 ± 0.1°C at } |Q| < 2.80 \times 10^{-3} \text{ M}.
\]

[52x379]

\[
\begin{align*}
\left[\text{Os}^{IV}(\text{tpy})(\text{Cl})_2(N(H)N(CH_2)_4O)\right]^+ + \text{H}_2\text{O} & \rightarrow \left[\text{Os}^{IV}(\text{tpy})(\text{Cl})_2(NH_2NCH_2)_4\text{O})\right]^+ \\
+ Q & \rightarrow \left[\text{Os}^{IV}(\text{tpy})(\text{Cl})_2(NH_2NCH_2)_4\text{O})\right]^+ + \text{HO}^-
\end{align*}
\]

[15]

and \( K_A \) and \( K_A' \) by the relationship

\[
\Delta G^0(\text{PCET}) = \Delta G^0 + RT \ln \left( \frac{K_A}{K_A'} \right).
\]

From the experimental data for PCET-N, the correction factor \( RT \ln(K_A/K_A') \) is negligible. Assuming this to be the case for the other two reactions, \( \Delta G^0(\text{PCET}) = 18 \text{ kcal/mol for PCET-N, 22 kcal/mol for PCET-P, and 21 kcal/mol for PCET-S under the conditions of the kinetics experiments.}^4

Kinetic studies for all three reactions in the forward direction were extended to CH\(_3\)CN/D\(_2\)O-H\(_2\)O mixtures varying from pure H\(_2\)O to “pure” D\(_2\)O with the actual mole fraction of proton in the latter determined by \(^1\text{H NMR. Rate constants } k_1 \text{ and } k_2 \text{ in Eq. 4 were separated by acid-dependent measurements and } k_{\text{red}} \text{ and } K_A \text{ by concentration-dependent measurements and Eq. 12. In Fig. 2 is shown a plot of the rate constant ratio } k_N/k_D \text{ versus mole fraction } \chi_D \text{ with } k = k_{\text{red}} \text{ for the N-proton donor with}

\[
\chi_D \text{ varied from 0 to 0.996. The linearity of these plots for all three reactions points to a solvent isotope effect dominated by transfer of a single proton. It also suggests that a single pathway dominates reactivity over the entire mole fraction range.}

Rate constants and \( K_A \) values for the three reactions involving N, S, and P proton donors in both 1:1 (vol/vol) CH\(_3\)CN/H\(_2\)O and CH\(_3\)CN/D\(_2\)O are given in Table 1. They were obtained by using the kinetic analysis described above with \( k_0 \) obtained by extrapolation of plots of \( k_N/k_D \text{ versus } \chi_D \text{.} \text{As shown by the data in Table 1, all three reactions occur with colossal H/D kinetic isotope effects in the forward direction. Within experimental error, the isotope effect appears solely in the redox step. To put the magnitudes of the isotope effects in perspective, the ratios } k_N(H_2O)/k_N(D_2O) \text{ for the outer-sphere electron transfer reactions illustrated by the reaction in Eqs. 1, 3, and 2 are 2.8, 2.0, and 3.4 for the N, S, and P-based complexes, respectively.}

Electron transfer from Os(IV) to Q in these reactions is coupled to transfer of the N–H, S–H, or P–H protons. These are proton-coupled electron transfer reactions with electron transfer occurring from a largely d\(\pi\) orbital on Q and proton transfer occurring from a \(\sigma\text{(N–H)}, \sigma\text{(S–H)}, \text{ or } \sigma\text{(P–H)} \text{ molecular orbital to a } \sigma\text{(sp\(^2\)) acceptor orbital on Q. Hydrogen atom transfer from the N–H, S–H, or P–H bonds would result in high-energy intermediates containing ligand-based radicals such as trans-[Os\(^{IV}\text{(tpy)}\text{(Cl)}_2(\text{"NN(CH}_2)_4\text{O})\text{])}^-\text{.} \text{ Although the three reactions are closely related microscopically, it is worth noting that the proton-donor atom is directly bonded to Os(IV) in the N case and is one atom removed in the other two.}

Coupled electron–proton transfer has been treated theoretically by a number of authors (21–28). The reactions studied here have been examined theoretically by use of a multistate continuum theory that treats the transferring H-atom quantum mechanically (29), developed by Hammes-Schiffer and coworkers (25–28). Important elements in this theory are the extent of electronic coupling between the electron transfer donor and acceptor, coupling with the solvent, and the extent of vibrational overlap for the transferring proton between the largely \(\pi\text{-}N_2\text{H}_3, \pi\text{-}S_2\text{H}_3, \text{ and } \pi\text{-}P_2\text{H}_3 \text{ vibrational levels in the initial state to } \pi\text{-}O_2\text{H}_3 \text{ levels in the final state; note the reaction in Eq. 9. Based on the results in ref. 29, the colossal } k_N/k_D \text{ KIEs result from a relatively small overlap between the reactant and product H or D vibrational wavefunctions arising from large hydrogen transfer distances. The pattern of isotope effects within the N–H, S–H, and P–H series is a balance of factors: (i) the proton transfer distance, which increases in the order NH < SH < PH decreasing overlap; (ii) the } \nu\text{(X–H)} \text{ frequency, which increases in the order PH < SH < NH also decreasing overlap; (iii) Boltzmann population of levels above } \nu = 0 \text{ in the reactants where overlap is greater, the importance of which increases in the order PH > SH > NH; and (iv) the driving force } \Delta G\text{. Even though the proton transfer distance is longest for PH, it has the lowest KIE because of a favorable thermal population above } \nu = 0 \text{ in } \nu\text{(P–H)}/\nu\text{(P–D)}.}

\[
\begin{array}{cccc}
\text{Table 1. Isotope effects} \\
\hline
\text{Rate constant} & \text{PCET-N} & \text{PCET-P} & \text{PCET-S} \\
\hline
k_{\text{red}}(\text{H}_2\text{O}), \text{ M}^{-1}\text{s}^{-1} & (2.74 ± 0.04) \times 10^1 & (1.48 ± 0.01) \times 10^1 & (6.77 ± 0.01) \times 10^{-1} \\
k_{\text{red}}(\text{D}_2\text{O}), \text{ M}^{-1}\text{s}^{-1} & (6.02 ± 0.03) \times 10^{-2} & (8.30 ± 0.07) \times 10^{-2} & (3.42 ± 0.05) \times 10^{-2} \\
K_N(\text{H}_2\text{O}), \text{ M}^{-1} & (4.43 ± 0.18) \times 10^3 & (2.15 ± 0.02) \times 10^3 & (1.33 ± 0.10) \times 10^3 \\
K_N(\text{D}_2\text{O}), \text{ M}^{-1} & (4.28 ± 0.04) \times 10^3 & (2.10 ± 0.02) \times 10^3 & (1.27 ± 0.08) \times 10^3 \\
k_{\text{red}}(\text{H}_2\text{O}), \text{ s}^{-1} & (6.19 ± 0.05) \times 10^{-3} & (6.94 ± 0.06) \times 10^{-3} & (5.09 ± 0.02) \times 10^{-3} \\
k_{\text{red}}(\text{D}_2\text{O}), \text{ s}^{-1} & (1.41 ± 0.04) \times 10^{-5} & (3.97 ± 0.05) \times 10^{-5} & (2.69 ± 0.02) \times 10^{-5} \\
k_{\text{red}}(\text{H}_2\text{O})/k_{\text{red}}(\text{D}_2\text{O}) & 439 ± 8 & 175 ± 5 & 189 ± 6 \\
\hline
\end{array}
\]

\*Conditions: 25.0 ± 0.1°C in 1:1 (vol/vol) CH\(_3\)CN/H\(_2\)O or 1:1 (vol/vol) CH\(_3\)CN/D\(_2\)O.

1 Obtained by extrapolation of plots of \( k_N/k_4 \text{ versus } \chi_D \text{ to } \chi_D = 1.\)
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