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J. Am. Chem. Soc., Just Accepted Manuscript • DOI: 10.1021/jacs.9b08189 • Publication Date (Web): 06 Oct 2019

Downloaded from pubs.acs.org on October 7, 2019

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Elucidating Proton-Coupled Electron Transfer Mechanisms of Metal

Hydrides with Free-energy and Pressure Dependent Kinetics

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Abstract

Proton-coupled electron transfer (PCET) was studied in a series of tungsten hydride complexes with pendant pyridyl arms ([($PyCH_2Cp$)WH(CO)_3], $PyCH_2Cp$ = pyridylmethylcyclopentadienyl), triggered by laser flash-generated Ru^{III}-trisbipyridine oxidants, in acetonitrile solution. The free energy dependence of the rate constant and the kinetic isotope effects (KIEs) showed that the PCET mechanism could be switched between concerted and the two stepwise PCET mechanisms (electron-first or proton-first) in a predictable fashion. Straightforward and general guidelines for how the relative rates of the different mechanisms depend on oxidant and base are presented. The rate of the concerted reaction should depend symmetrically on changes in oxidant and base strength, *i.e.* on the overall ΔG^{0}_{PCET} , and we argue that an "asynchronous" behavior would not be consistent with a model where the electron and proton tunnel from a common transition state. The observed rate constants and KIEs were examined as a function of hydrostatic pressure (1-2000 bar) and were found to exhibit qualitatively different dependence on pressure for different PCET mechanisms. This is discussed in terms of different volume profiles of the PCET mechanisms as well as enhanced proton tunneling for the concerted mechanism. The results allowed for assignment of the main mechanism operating in the different cases, which is one of the critical questions in PCET research. They also show how the rate of a PCET reaction will be affected very differently by changes of oxidant and base strength, depending on which mechanism dominates. This is of fundamental interest as well as of practical importance for rational design of e.g. catalysts for fuel cells and solar fuels formation, which operate in steps of PCET reactions. The mechanistic richness shown by this system illustrates that the specific mechanism is not intrinsic to a specific synthetic catalyst or enzyme active site, but depends on the reaction conditions.

Introduction

Proton-coupled electron transfer (PCET) is a ubiquitous elementary process in chemistry and biology.¹⁻³ It is at the heart of biological energy conversion processes such as photosynthesis⁴⁻⁷, respiration⁸⁻¹² and nitrogen fixation¹³⁻¹⁵ in nature and in the corresponding artificial catalytic transformations.¹⁶⁻²⁴ In the last decades, high resolution structures of many of the enzymes involved in these processes have been reported, such as hydrogenases^{25, 26}, carbon dioxide reductase^{27, 28} and dioxygen reductases^{29, 30}. Their structures indicated that proton relays in the second coordination sphere of the cofactors of many enzymes might have an effect on PCET reactions at the active site. Inspired by this, the use of acid/base groups as putative proton relays in the second coordination sphere of catalysts has become an increasingly popular motif, intended to accelerate protonation and deprotonation of metal-bound hydrido (M-H)^{22,} ³¹⁻³³, carboxylates (M-CO₂)³⁴⁻³⁷, dioxygen (M-O₂)³⁸ or agua species (M-OH/M-OH₂)³⁹⁻ ⁴¹. However, the exact mechanism by which these acid/base groups accelerate catalytic reactions is often not clarified, and is often not even related to proton transfer^{42, 43}. Understanding these fundamental processes is important towards the rational design of faster and more efficient catalysts for the production of solar fuels or for fuel cells.

Moreover, an important but often challenging task when studying PCET is to elucidate whether the reaction occurs sequentially, through electron transfer followed by proton transfer (ETPT), proton transfer followed by electron transfer (PTET); or in a single, concerted electron-proton transfer step (CEPT). CEPT avoids the high energy barriers often associated with the initial steps in stepwise reactions. However, this requires tunneling of both electron and proton in the transition state, which may lower the probability compared to tunneling of a single electron or proton. The rate of PCET of a catalyst will respond very differently to modifications of the catalyst or reaction conditions, depending on the mechanism of its PCET steps. Determining and steering the operative PCET mechanism in catalysis is a promising strategy for catalyst improvement, as avoiding the high energy barriers associated with stepwise mechanisms can lower the overpotential of the reaction of interest. Therefore, methods for elucidating the PCET mechanism for the reaction in question are highly desirable.

Only in a few cases of interest is it possible to directly monitor the intermediates of the stepwise reactions⁴⁴, because of an unusually slow second step, which then provides conclusive mechanistic evidence for or against a reaction intermediate. Instead, thermodynamic arguments are frequently employed to exclude the stepwise reactions⁴⁵. The argument is that the first step is sufficiently uphill, as estimated from relative pK_a or E^0 values, that the predicted rate is at least one order of magnitude slower than the observed overall rate constant. However, relative pK_a values in hydrogen-bonded systems are often different from those of the isolated components. A significant kinetic isotope effect (KIE) upon proton/deuteron substitution is commonly used to argue that

rate-determining step^{1, 46-48}. Free energy relationships, where the rate is studied as a function of driving force, show characteristic dependencies on the ΔE^0 and $\Delta p K_a$ for the different mechanisms.^{45, 49} In cases where both these parameters can be varied independently over a sufficient range, a clear mechanistic assignment can often be made, but often the E^0 and $p K_a$ values of a PCET reactant show strong co-variation upon synthetic substitutions.

Our group has reported several systems with tyrosine or tryptophan residues covalently linked to a Ru^{II}-polypyridine photosensitizer, with water as primary proton acceptor, for which the PCET mechanism could be switched between CEPT and ETPT by varying the strength of the photogenerated Ru^{III} oxidant.^{44, 50, 51} In one study, the mechanism shifted between all three mechanisms (ETPT, CEPT and PTET) depending on the pH of the solution.⁵² In a later paper, the proton-coupled oxidation of a tungsten hydride complex [(Cp)WH(CO)₃] by a series of Fe^{III}- and Ru^{III}-trisbipyridine oxidants and pyridine bases was studied in acetonitrile49. This allowed for well-defined variations of the PCET driving force by varying both the oxidant and the base. By using weak oxidants and weak bases, the reaction was steered to follow a CEPT mechanism. This was the first demonstration that a metal hydride could undergo a CEPT reaction, with the electron and proton transferred to different acceptors. In a recent study, inspired by proton relays in natural catalysts, the pyridine bases were linked to the Cp ring ($[(PyCH_2Cp)WH(CO)_3]$)⁵³. This resulted in a strong increase of the PCET rate. In contrast to the previous study, a PTET dominated at low oxidant strengths, whereas a CEPT reaction only arose when the oxidant strength was increased. The difference in mechanistic preferences between the systems with intra- and intermolecular pyridine bases is interesting, and suggests that the hydrogen bond geometry between the W-H and pyridine units is somewhat different in the respective transition states, resulting in differences in proton vibrational wavefunction overlap. It seems that the intramolecular base then favors proton tunneling, making both CEPT and PTET more competitive than in the system with external bases. Despite its importance, the concerted pathway remains elusive in many systems. The very similar [(Cp)WH(CO)₂(PMe₃)] system studied by Dempsey and co-workers⁵⁴ differs from our motif only in the substitution of one CO ligand by PMe₃. Interestingly, CEPT was shown to give only a minor contribution to the rate, in a very similar range of ΔE^0 and $\Delta p K_a$ values between the tungsten complex, oxidants and bases, as that in ref. 49, which was attributed to a larger reorganization energy associated with deprotonation of [(Cp)WH(CO)₂(PMe₃)].⁵⁴

The present study uses stronger oxidants than previously employed to measure the PCET rate constants of $[(PyCH_2Cp)WH(CO)_3]$ derivatives with covalently attached bases of different strength. The variation in electron transfer driving force tunes the system to display additional mechanistic regions, from PTET, via CEPT to ETPT even

in a single compound. The mechanistic assignments are based on free energy relationships and KIEs within the framework of electron-proton tunneling theories for PCET. We point out that within a tunneling theory for CEPT, the rate constant must respond symmetrically to changes in driving force from changes in the oxidant and base strength (ΔG^{0}_{FT} and ΔG^{0}_{PT} , respectively), as opposed to a so-called asynchronous CEPT. Moreover, hydrostatic pressure is used for the first time as a tool to distinguish the stepwise and concerted PCET reactions. The pressure dependence of the rate constants reveals information about the volume profile of the PCET reaction, *i.e.* volume changes between reactants, transition states and products. PTET and ETPT shows distinctly different experimental activation volumes, such that the rate of the former increases with pressure while that of the latter decreases. For some combinations of oxidant and base the PCET mechanism is mixed, but increasing pressure resulted in an increasing contribution from CEPT, which could not be identified by only varying oxidant and base strength or determining the KIE. The acceleration of CEPT with increasing pressure may be attributed to a shorter proton tunneling distance due to compression of the W-H complex. Our study shows an unprecedented mechanistic richness for a single PCET system. Compared to our previous studies^{49, 53} all three mechanisms are displayed by a single WH-pyridine compound by just varying the oxidant, and also the pre-equilibrium kinetic limit of ETPT is shown. Moreover, with the combined use of free-energy and pressure dependence, our study shows methods to distinguish experimentally which mechanism is dominating under the given conditions. This also suggests the possibility to analyze and steer the PCET mechanism of catalysts with metal-hydride intermediates.

Results and discussion

E^{*θ*} and *p*Ka values. The tungsten hydride complexes **1a-e** with internal pyridine bases (Scheme 2, labeled **1a-e** in order of increasing base strength) and the reference complex [(MeCp)WH(CO)₃] that does not contain an internal base were prepared as reported earlier⁵³. The thermodynamic data for the latter compound in acetonitrile from our previous report is given in Scheme 1, together with data for [(Cp)WH(CO)₃] from the groups of Tilset and Norton.⁵⁵⁻⁵⁹ The methylene substituent on the Cp ring shifts the potentials cathodically by 30-50 mV, and increases the *pK_a* value by about 0.4 units. The first oxidation of [(Cp)WH(CO)₃] is irreversible with a peak potential at +0.76 V, and this was used to estimate the *E*⁰ value.⁵⁷ An exact value of *E*⁰ is not critical to the present study as it is based on free-energy correlations, *i.e.* relative values of Δ*E*⁰ in the reactions with different oxidants. Oxidation of the deprotonated complex [(Cp)W(CO)₃]⁻ occurs at ca. 1.10 V more negative values, showing that the thermodynamic coupling of the transferred electron and proton is strong. The *pK_a* value of [(Cp)WH(CO)₃] (*pKa* = 16.1) shows a corresponding downshift by ca. 19 units upon oxidation, rendering the oxidized hydride [(Cp)W•H(CO)₃]⁺ very acidic (*pKa* ≈ -3).

The potentials and pK_a values of the tungsten hydride in **1a-e** are assumed to be very similar to those of [(MeCp)WH(CO)₃]. The pyridine group shows a pK_a for the free conjugate acid of 9.55-14.23. A new oxidation peak appeared in the cyclic voltammograms of **1a-e**, at ca. 0.8-1.0 V lower values (-0.08 to -0.33 V vs. Fc^{+/0}) than the first oxidation for [(MeCp)WH(CO)₃] (+0.71 V).⁵³ This peak was attributed to metal oxidation coupled to transfer of the hydride proton to the pyridine base. Indeed, the observed electrochemical peak shift from [(MeCp)WH(CO)₃] to **1a-e** agreed within experimental error with that predicted from the relative pK_a values of the W•H⁺ (ca. - 2.5) and free pyridinium, assuming 59 mV shift per unit of pK_a difference. Moreover, the peak potential in the series **1a-e** showed a near-Nernstian shift of ca. -52 mV per pK_a unit of the free pyridinium. This shows that the relative driving forces for PCET in **1a-e** agree well with what is expected from the E^0 and pK_a values determined for the components.

In our previous study, we used Fe^{III}- and Ru^{III}-tris(bipyridine) complexes with M^{III/II} potentials of 0.36-0.73 V vs. Fc^{+/0} to study the proton-coupled oxidation of **1a-e**. These potentials are thus low enough that an initial electron transfer step to generate W[•]H⁺ would be uphill or near isoenergetic. At the same time, the pyridinium pK_a values are all at least two units lower than the pK_a of W-H, making an initial intramolecular proton transfer step uphill. In contrast, the concerted PCET is downhill for all combinations of oxidant and base. The overall stepwise ETPT and PTET processes are obviously also downhill by the same amount as CEPT, thanks to the second step on both those pathways being strongly exergonic: PT-b from W[•]H⁺ and ET-a from W⁻ (cf. Scheme 2), respectively. With these oxidants, most of the reactions with **1a-e** occurred via pre-equilibrium PTET, and some via CEPT. In the present study, we use four Ru^{III}-

tris(bipyridine) complexes that are stronger oxidants ($E^{0}_{Ru(III/II)} = 0.82-1.03$ V vs. Fc^{+/0}; Table 1) in an attempt to shift the reaction in favor of CEPT and possibly also of ETPT.



Scheme 1. (A) PCET square scheme showing the mechanistic pathways for **1a-1e**: stepwise PTET (pathway a, black), stepwise ETPT (pathway b, red), and concerted electron-proton transfer (CEPT; pathway in blue). The thermodynamic data given are for the previously studied [CpWH(CO)₃] in CH₃CN (E^0 vs. Fc^{+/0} and p K_a),⁵⁵⁻⁵⁹ with data for [(MeCp)WH(CO)₃] in brackets.⁵³ p K_a values for the free pyridinium groups of **1a-e** are given in Scheme 2. (B) The free energy for the ET, PT and PCET steps of panel (A) can be estimated from the E^0 and p K_a values of the W-species relevant for each step, E^0 of the oxidants and p K_a of the pyridinium groups.



Scheme 2. Reaction scheme for the photoinduced PCET reactions.

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Kinetic PCET measurements. The PCET kinetics of compounds 1a-e with the different Ru^{III}-bipyridine-based oxidants were investigated with the commonly used laser flashquench photolysis method (Scheme 2).60-62 In our experiment, the RuIII oxidant was prepared in-situ by laser flash excitation, followed by oxidative quenching. A typical sample contained 0.5-12 mM of the tungsten hydride [WH···B], 50 µM of the Ru^{II} photosensitizer (Table 1), here denoted [Ru]²⁺, and 100 mM of the diquat electron acceptor (1,1'-butylene-2,2'-bipyridine, BDQ²⁺ or 1,1'-propylene-2,2'-bipyridine, PDQ^{2+}) as quencher Q^{2+} in deoxygenated acetonitrile. The samples were prepared in a 10×10 mm quartz cuvette and sealed in an argon glove box. For the measurements at elevated pressure (1-2000 bar), the samples were put in 9 mm diameter round quartz cells, filled to the brim and sealed with a plastic septum in the glove box. The septum transmits pressure from the pressure cell, while containing the reaction solvent. In the experiments, the sample was flashed with a 10 ns laser pulse at 460 nm (see SI), exciting the Ru-based photosensitizer. The excited state of the sensitizer, [Ru]^{2+*} was oxidatively quenched by Q^{2+} , on a time scale of 100 ns. The resulting products were the oxidized form of the Ru-complex, $[Ru]^{3+}$, and the quencher monocation radical, $Q^{\bullet+}$. The $[Ru]^{3+}$ generated (<10 μ M in one laser shot) reacted in a pseudo-first order PCET reaction with $[WH \cdots B]$, which is in great excess, on a time scale of a few μ s.

Figure 1 gives examples of transient absorption and photoluminescence traces used to follow these reactions. The emission of [Ru]^{2+*} can be followed at 600 nm. It decays in a mono exponential fashion:

$$I(t) = I_0 \exp\left(-\left(k_q [Q^{2+}] + k_0\right) \cdot t\right)$$
(1)

where k_q is the second-order rate constant for excited state quenching by Q²⁺ and k_0 is the rate constant for exited state decay in the absence of Q²⁺. The recovery of [Ru]²⁺ was followed at 450 nm. Note that, while both [Ru]^{2+*} and [Ru]³⁺ have small extinction coefficients at 450 nm compared to the [Ru]²⁺ ground state, the yield of free [Ru]³⁺ in the quenching process is only around one third (the rest returns to [Ru]²⁺), which leads to significant bleach recovery at 450 nm also during the quenching process.⁶² Thus, the traces were fit to a double exponential decay model, where the first component represents quenching of [Ru]^{2+*} to form [Ru]³⁺, and the second component represents the PCET reaction of [Ru]³⁺ with [WH···B], regenerating [Ru]²⁺:

$$\Delta A_{450}(t) = A_1 \exp\left(-\left(k_q[Q] + k_0\right) \cdot t\right) + A_2 \cdot \exp\left(-k_{\text{PCET}}[\text{WH} \cdots \text{B}] \cdot t\right) (2)$$

The pseudo-first order time constant for the second component was typically ten times larger than for the first, which made the fits robust. Kinetic traces and residual plots from the fits are shown in the Supporting Information. From these fits, the observed PCET rate constant could be extracted. At 550 nm, the absorption of the reduced quencher $Q^{\bullet+}$ was followed. Under the experimental conditions used, $Q^{\bullet+}$ does not

decay significantly during the recovery kinetics of the [Ru]²⁺ bleach (Figure 1, blue symbols; vide infra) and does not affect the 450 nm recovery.



Figure 1. Typical kinetic traces of the reaction between compound **1d** and laser flashquench generated $[Ru(Me_2bpy)_2(bpy)]^{3+}$ in acetonitrile, showing the decay of $[Ru(Me_2bpy)_2(bpy)]^{2+*}$ emission at 600 nm (black squares; the black line is a single exponential fit) and formation of BDQ^{•+}, monitored at 550 nm (blue triangles; the blue line is a single exponential fit to the rise), due to oxidative quenching by BDQ²⁺. The recovery of $[Ru(Me_2bpy)_2(bpy)]^{2+}$ monitored at 450 nm (red dots) is fitted with a biexponental function (red line), where the excited state quenching reaction during the first ca. 0.1 µs is followed by the much slower PCET reaction with **1d**.

In the absence of [WH···B], the oxidized sensitizer recombines with Q^{•+} in a diffusioncontrolled bimolecular reaction, with a half-life of around 20 μ s (SI, figure S2). With [WH···B] present, [Ru]³⁺ reacts with [WH···B] by PCET before it can recombine with Q^{•+}. Charge recombination between the diquat radical Q^{•+} and the [W[•]···H⁺B] that is formed by the PCET reaction is also possible. However, [W[•]···H⁺B] rapidly dimerizes upon formation; we could follow the formation of the W-W dimer by transient mid-IR spectroscopy, giving a formation half-life of ca. 1 us for the dimeric product (see SI, pages S24-S27). The large excess of [WH···B] over [Ru]³⁺, and rapid dimerization of [W[•]···H⁺B], results in a clean PCET reaction to give [Ru]²⁺ and W-W dimer, without significant secondary oxidation of the radical. The Q^{•+} generated in these studies are not reducing enough to react with the tungsten dimer, resulting in accumulation of Q^{•+} when the PCET reaction is triggered (SI figure S3). Significant accumulation of Q^{•+} will result in accelerated recovery of the [Ru]²⁺ bleach due to direct reaction between Q^{•+} and [Ru]³⁺. For this reason, the samples were kept in the dark during preparation and measurement. It was found that the observed PCET kinetics did not change

significantly within the first four laser shots (SI, figure S5), and thus maximally four measurements per sample were conducted to avoid interference from accumulated $Q^{\bullet+}$ and tungsten dimer complex. We noted that methyl viologen (MV²⁺) was reduced to the radical form MV^{$\bullet+$} already in the dark, probably by the small fraction of deprotonated **1a-e.** In contrast, PDQ²⁺ and BDQ²⁺ have a 100 and 200 mV more negative potential for their first reduction, respectively, and did not react in the dark.

The following will first describe the qualitative trends of the kinetic data. In the next section, theoretical predictions for the difference in free-energy dependencies of the k_{PCET} between the PCET mechanisms are presented, and how their rates may depend on pressure. Thereafter, the experimental data are compared with the predictions and mechanistic assignments are made.

The second-order rate constants of the photoinduced PCET reactions in compounds 1ae with all oxidants are given in Table 1. The data obtained with $[Ru(Me_2bpy)_2(bpy)]^{3+}$ and $[Ru(bpy)_3]^{3+}$ are compared to those obtained with weaker oxidants from a previous study (Figure 2).53, 63 A clear increase in the PCET rate constants is observed when stronger oxidants are used, which is, however, much greater for the compounds with weaker bases (1a-b). As a consequence, the rate dependence on pyridine base strength becomes weaker with stronger the oxidants. This is highlighted in Figure 2 by the linear fits to data with the same oxidants. The kinetic isotope effects (KIE = k_H/k_D , measured with a series of W-D analogues of **1a-1e**) in the reactions with [Ru(dmb)₂(bpy)]³⁺ decreased from ca. 0.90 to 0.51, going from 1a to 1d. With $[Ru(bpy)_3]^{3+}$, the KIEs of compound **1a** and **1b** were 1.13 and 1.05, increased slightly to 1.27 for **1c**, and then dropped to 0.89 and 0.74 for 1d and 1e, respectively. In Figure 3, the rate constants are instead plotted as a function of oxidant strength (E^0) . Here it is obvious that the rates for **1a-b** are much more sensitive to changes in E^0 than are those of **1c-d**. However, it is also clear that the strength of this dependence for each compound 1a-d varies in different regions of oxidant E^0 . These results indicate that the main reaction mechanism varies with the strength of both oxidant and base.



Figure 2: Dependence of the observed second-order PCET rate constant on the pK_a value of the pyridinium derivative residue (Scheme 2). The standard deviation of k_{PCET} is smaller than the size of the data points. The lines are linear fits to the data with the same oxidant (fits for $[Fe(dmb)_3]^{3+}$ and $[Fe(bpy)_3]^{3+}$ are omitted for clarity. Kinetic isotope effect (KIE) values are given where measured. All rate constants are given in Table 1.



Figure 3. Dependence of the observed second-order PCET rate constant on the oxidant strength (E^0). The standard deviation of k_{PCET} is smaller than the size of the data points. The lines are linear fits to the data: for **1c-d** the data with $E^0 = 0.35-0.73$ V were used, while for **1a-b** linear fits are made in two different regions: $E^0 = 0.50-0.73$ and 0.73-0.90 V, respectively. All rate constants are given in Table 1.

Complex	
$(pK_a)^{d}$	1a
Oxidant	(9.55)
$(E^o)^{c)}$	
	1.1×10 ⁴
$[Fe((OMe)_2bpy)_3]^{3+}$	(0.38)
(0.36V)	-0.36 eV
	3.0×10 ⁴
$[Fe(Me_2bpy)_3]^{3+}$	
(0.51V)	-0.51 eV
	5.6×10 ⁵
$[Fe(bpy)_{3}]^{3+}$	(0.88)
(0.66V)	-0.66 eV
	1.6×10 ⁶
$[Ru(Me_2bpy)_3]^{3+}$	(2.4)
(0.73V)	- 0.73 eV
	1.2×10 ⁸
$[Ru(Me_2bpy)_2(bpy)]^{3+}$	(0.90)
(0.82 V)	-0.82 eV
	ND ^{e)}
$[Ru(Me_2bpy)(bpy)_2]^{3+}$	
(0.85 V)	

s⁻¹)^{a)}, kinetic isotope effects (KIEs, shown in ons of complexes **1a-e** with different oxidants oxidants are from ref. 53.

$(\mathbf{p}K_a)^{\mathbf{d}}$	1a	1b	1c	1d	1e
Oxidant	(9.55)	(9.93)	(12.53)	(13.32)	(14.23)
$(E^o)^{c)}$					
	1.1×10 ⁴	4.8×10 ⁴	2.3×10 ⁷	1.1×10 ⁸	5.4×10 ⁸
$[Fe((OMe)_2bpy)_3]^{3+}$	(0.38)	(0.31)	(0.14)	(0.19)	
(0.36V)	-0.36 eV	-0.38 eV	-0.54 eV	-0.58 eV	-0.64 eV
	3.0×10 ⁴	6.9×10 ⁴	6.9×10 ⁷	3.4×10 ⁸	ND ^{e)}
$[Fe(Me_2bpy)_3]^{3+}$					
(0.51V)	-0.51 eV	-0.53 eV	-0.69 eV	-0.73 eV	
	5.6×10 ⁵	6.7×10 ⁵	5.4×10 ⁷	3.4×10 ⁸	ND ^{e)}
$[Fe(bpy)_{3}]^{3+}$	(0.88)	(0.99)	(0.19)		
(0.66V)	-0.66 eV	-0.68 eV	-0.84 eV	-0.88 eV	
	1.6×10 ⁶	2.7×10 ⁶	7.2×10 ⁷	3.7×10 ⁸	ND ^{e)}
$[Ru(Me_2bpy)_3]^{3+}$	(2.4)	(1.2)	(0.28)		
(0.73V)	- 0.73 eV	-0.75 eV	-0.91 eV	-0.95 eV	
	1.2×10 ⁸	1.6×10 ⁸	3.3×10 ⁸	6.0×10 ⁸	ND ^{e)}
$[Ru(Me_2bpy)_2(bpy)]^{3+}$	(0.90)	(0.88)	(0.91)	(0.51)	
(0.82 V)	-0.82 eV	-0.84 eV	-1.00 eV	-1.04 eV	
	ND ^{e)}	6.0×10 ⁸	5.9×10 ⁸	9.8×10 ⁸	ND ^{e)}
$[Ru(Me_2bpy)(bpy)_2]^{3+}$					
(0.85 V)		-0.87 eV	-1.03 eV	-1.07 eV	
	5.8×10 ⁸	6.4×10 ⁸	1.3×10 ⁹	1.3×10 ⁹	1.6×10 ⁹
$[Ru(bpy)_3]^{3+}$	(1.1)	(1.1)	(1.3)	(0.89)	(0.74)
(0.89 V)	-0.89 eV	-0.91 eV	-1.07 eV	-1.11 eV	-1.17 eV
	7.2×10 ⁸	1.2×10 ⁹	4.9×10 ⁹	2.0×10 ⁹	ND ^{e)}
$[Ru(bpy)_2((EtO_2C)_2bpy)]^{3+}$					
(1.03 V)	-1.03 eV	-1.05 eV	-1.21	-1.25	

a) Standard deviations of rate constants were $\pm 5-10\%$, from an average of fits to single traces for three independent samples, and are given in Table S1.

b) For combinations when KIE was not determined the field is left blank.

c) $M^{3+/2+}$ reduction potentials in CH₃CN versus Fc⁺/Fc^{49, 64, 65}. bpy = 2,2'-bipyridine, (OMe)₂bpy = 4,4'-dimetoxy-2,2'-bipyridine, Me₂bpy = 4,4'-dimethyl-2,2'-bipyridine; (EtO₂C)₂bpy = 4,4'diethylester-2,2'-bipyridine.

d) pK_a of the conjugate acid of the corresponding pyridine derivative residue in CH₃CN⁵³. e) Not determined.

In our previous study,⁵³ we assigned the PCET mechanism for **1a-e** and the weakest oxidants to pre-equilibrium PTET (Figure 2: grey line for $[Fe((OMe)_2bpy)_3]^{3+}$). With intermediate oxidants, the mechanism was assigned to CEPT for **1a-b**, and a mix of CEPT and PTET for **1c-e** (blue line for $[Ru(Me_2bpy)_3]^{3+}$). With the stronger oxidants used here, we assign the mechanism for **1a-b** to ETPT, while there is evidence for both CEPT and ETPT for **1c-e**, depending on the strength of oxidant and base. These assignments, and their theoretical background, are described in the following sections.

Further indication that the mechanism changes was obtained from the pressure dependence of k_{PCET} (Table 2). We found a linear variation of ln k_{PCET} with pressure, and the slope of that line equals $-\Delta V^{\ddagger}/RT$, where ΔV^{\ddagger} is the activation volume (i.e. the difference in volume between the transition state and the reactants). While the compounds with weaker bases showed rates that decreased with increasing pressure, the rates for compounds with stronger bases the rate increased instead (Figure 4). This can be related to the different signs of the activation volume that are predicted for the different mechanisms, based on the changes in charge density and solvation of the different intermediates and transition states, as explained below. Interestingly, for some combinations of compounds, (**1c** with [Ru(Me₂bpy)₃]³⁺, and **1d** with [Ru(bpy)₃]³⁺) the protonated and deuterated compounds showed different dependences on pressure, giving rise to strongly pressure dependent KIEs. This may be related to changes in proton tunneling probability as the W-H complex is compressed.^{1, 48}

Table 2. Apparent activation volumes for the W-H and W-D complexes **1a-e** from analysis of pressure dependent rate constants (eq. 12), and kinetic isotope effects (KIE) at 1 bar.

	[Ru(]	$u(Me_2bpy)_2(bpy)]^{3+}$		[Ru(bpy) ₃] ³⁺		
Compound	$\Delta V^{\ddagger}(cm)$	³ /mol) ^{a)}	KIE	$\Delta V^{\ddagger}(cm)$	^a /mol) ^{a)}	KIE
	W-H	W-D	(1 bar)	W-H	W-D	(1 bar)
1 a	2.2	2.6	0.9	3.6	4.0	1.1
1b	3.8	5.1	0.89	5.2	4.1	1.1
1c	-1.2	-4.2	0.91	3.0	2.1	1.3
1d	-7.7	-7.7	0.51	-4.8	0.65	0.87
1e	-	-	-	-0.54	-0.44	0.76

a) For comparison, the volume of acetonitrile is 52,9 cm³ mol⁻¹ at 25 °C and 1 bar.⁶⁶



Figure 4: The observed pseudo-first order rate constants for the W-H (black symbols) and W-D (red symbols) compounds at different applied pressure from the samples containing (left) 67 μ M [Ru(bpy)₃]²⁺, 50 mM [BDQ]²⁺ and 1 mM Compound **1a**; (right) 40 μ M [Ru(dmb)₂(bpy)]²⁺, 50 mM [BDQ]²⁺ and 6 mM compound **1d**. The lines are linear fits to the data (cf. eq. 12). Data for the other pressure dependent experiments are shown in the SI.

Predicted free energy dependence of concerted and stepwise PCET mechanisms

In this section, we describe theoretical predictions for the free-energy dependence of PCET reactions. PCET can occur in a single elementary step or in two sequential steps (see Scheme 1). The observed rate constant is the sum of the contributions from these three mechanisms:

$$k_{\rm PCET} = k_{\rm ETPT} + k_{\rm PTET} + k_{\rm CEPT} \qquad (3)$$

The stepwise PCET reaction may be rate-limited by the initial ET or PT step:

$$k_{\text{ETPT}} = k_{\text{ET}-b}$$
 (rate limiting first step) (4)
 $k_{\text{PTET}} = k_{\text{PT}-a}$ (rate limiting first step) (5)

They can also occur in the kinetic pre-equilibrium limit, where their rate constants are given by the equilibrium constant for the initial reaction multiplied by the rate constant for the following step:

$$k_{\text{ETPT}} = K_{\text{ET}} \cdot k_{\text{PT}-b}$$
 (pre-equilibrium) (6)
 $k_{\text{PTET}} = K_{\text{PT}} \cdot k_{\text{ET}-a}$ (pre-equilibrium) (7)

The CEPT pathway is always thermodynamically favored because it uses all the available PCET free energy in a single reaction step; therefore, it may have a lower reaction barrier. In contrast, the initial steps of the ETPT and PTET have lower driving force and are often even uphill reactions. On the other hand, the tunneling probability of CEPT can be smaller because it involves both electron and proton. A balance between these two factors can often explain the competition between the mechanisms. A strong oxidant favors ETPT while a strong base favors PTET, if both oxidant and base are weak, however, CEPT can be favorable. The energetic part of this argument, and how this can be used to switch the preferred mechanism, are clarified in this section.

Eq. 8 gives the general rate expression for non-adiabatic ET, PT or CEPT:

$$k_{i} = A_{i} \cdot \exp\left(-\frac{\Delta G_{i}^{*}}{RT}\right)$$

$$\Delta G_{i}^{\ddagger} = \frac{\left(\Delta G_{i}^{0} + \lambda_{i}\right)^{2}}{4\lambda_{i}}$$
(8a)
(8b)

where the index *i* indicates ET, PT or CEPT.^{1, 67, 68} This expression is also valid for the cases of rate-limiting ET or PT in the stepwise PCET mechanisms (eq. 4-5). For simplicity and clarity, eq. 8 does not explicitly include variations in contributions from

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different vibronic states. The relative contribution from different vibronic states to the CEPT reaction may also vary with driving force; see Concluding Remarks. The freeenergy dependence can also be expressed by the derivative form of eq. 8:

$$\frac{\partial \ln k_i}{\partial (-\Delta G_i^0)} = \frac{1}{2RT} \left(1 + \frac{\Delta G_i^0}{\lambda_i} \right) \tag{9}$$

At moderate driving force, and sufficiently small range of ΔG^0 values, eq. 9 shows an approximately linear behavior (Scheme 3). At $\Delta G^0 = 0$ the slope equals (2 RT)⁻¹, which at room temperature is (50 meV)⁻¹, or 20 eV⁻¹. For a plot of log(k_{CEPT}) vs. p K_a , where ΔG^0 changes by 59 meV per p K_a unit, this will give a slope of 0.51 p K_a^{-1} , very close to what is observed for the CEPT reactions of **1**, and (Cp)WH(CO)₃ with external pyridines and the weaker oxidants.⁴⁹

The cases of ETPT and PTET with a rate-limiting first step (eq. 4-5) will also follow eqs. 8-9, but as the driving force is smaller than for CEPT, the slope according to eq. 7 will be larger (assuming that the reorganization energies are similar). Therefore, ratelimiting ETPT or PTET will be more sensitive to changes in oxidant and base strengths, respectively, than a CEPT reaction. Indeed, we showed in our previous work⁴⁹ that k_{ET} depends on ΔG^0 more strongly than does k_{CEPT} : $\partial(\ln k)/(-\Delta G^0) = 23 \text{ eV}^{-1} vs.$ 15 eV⁻¹, respectively. Therefore, if both the oxidant and base are weak, this tends to favor CEPT.

In the pre-equilibrium limit instead (eq. 6), k_{ETPT} will decrease by a factor of ten for each 59 mV decrease in oxidant strength (E_{ox}^{0}) . This gives $\partial(\ln k)/(-\Delta G^{0}) = 39$ eV^{-1} (i.e. (25.6 meV)⁻¹), which is a much stronger driving force dependence than for the single step reactions; see Scheme 3. Analogously, in the case of pre-equilibrium for PTET (eq. 7), k_{PTET} will decrease by a factor of ten for each pK_a unit decrease of the pyridinium group. The latter behavior is seen when comparing the rates as a function of base strength for **1a-e** with a weak oxidant (Figure 2). This makes pre-equilibrium PTET even more sensitive to changes in base pK_a than a CEPT mechanism (Scheme 3). However, if the oxidant strength is increased, the PTET is less strongly affected because oxidation of the basic form of **1a-e** (W⁻) already has a large driving force. Thus, the value of $-\Delta G^0$ is close to λ and the reaction lies close to the top of a Marcus parabola (cf. blue curve of Scheme 3).⁶⁷ This behavior is seen when comparing the rates as a function of oxidant strength for 1c or 1d with the four weaker oxidants used (Figure 3). Thus, by changing oxidant and base, we may have the possibility to make the same species react via either ETPT, PTET or CEPT. This was shown for the first time in our previous studies,^{49,53} by combining data from inter- and intramolecular pyridine bases.



Scheme 3. Illustration of the differences in free energy dependence for the different PCET mechanisms (eq. 3-9). The x-axis shows differences in either ΔG^{0}_{PT} (orange background) or ΔG^{0}_{ET} (yellow background).

Predicted pressure dependence of k_{PCET} The pressure dependence of rate constants of chemical reactions has previously been shown to be a powerful mechanistic indicator.^{69, 70} Traditionally, pressure dependence has been used to construct volume profiles for chemical reactions with great advances by the groups of le Noble, van Eldik, Swaddle and many others.⁶⁹⁻⁷¹ Theoretical approaches to analyzing the pressure dependencies are well described in multiple reviews and will thus not be discussed in detail here.⁶⁹⁻⁷⁶

Briefly, the pressure dependence of a reaction equilibrium constant can be related to the molar volume change of the reaction (reaction volume) through the Maxwell relation:

$$\frac{\delta \ln K}{\delta P} = -\frac{\Delta V}{RT} \tag{10}$$

where for the reaction:

$$A + B \leftrightarrows C$$

 ΔV is given by:

$$\Delta V = V_C - (V_A + V_B) \tag{11}$$

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In a transition state theory picture, where the reactants are in thermal quasi-equilibrium with the transition state, the pressure dependence of the rate constant reports on the molar volume difference between the transition state and the reactants (activation volume):

$$\frac{\delta \ln k}{\delta P} = -\frac{\Delta V^{\dagger}}{RT} \qquad (12)$$

where for the reaction:

$$A + B \rightleftharpoons [AB]^{\ddagger} \longrightarrow C$$

 ΔV^{\ddagger} is given by:

$$\Delta V^{\ddagger} = V_{[AB]^{\ddagger}} - (V_A + V_B) \tag{13}$$

For a pre-equilibrium mechanism, the experimentally observed activation volume will equal the sum of ΔV for the first reaction step and ΔV^{\ddagger} for the second.

Many activation and reaction volumes for electron transfer reactions have been reported.⁶⁹⁻⁷¹ It has been found that not only intrinsic volume changes of the reactants, but also solvent electrostriction effects due to a change in charge, affect the volume profiles of electron transfer reactions. Thus, highly charged species will be more solvated, with degree of solvation proportional to $(ze)^2/r$ (ze = ionic charge, r = ionic radius), which decreases the volume of the solvent.^{74, 76, 77} For an ETPT reaction in the present case, the encounter complex has Ru³⁺ and WH, going to Ru²⁺ and W•H⁺. Although the ruthenium complex has a larger radius, the main effect will be due to a decrease in charge, and a loss of solvation as Ru³⁺ goes to Ru²⁺. Thus, this ETPT reaction can be expected to have a positive reaction volume (ΔV), as the follow-up PT reaction is just shifting the proton in the oxidized **1a-e**. For the PTET reaction, the neutral [WH...py] complex becomes zwitterionic ([W⁻...H⁺py]) in the first step, which is expected to become more strongly solvated and show a negative reaction volume. The follow-up ET reaction of PTET has a large enough driving force to be nearly activationless, and thus the effects on the overall PTET rate from that step will be small. Thus, one may expect to observe an overall negative activation volume.

There are fewer pressure dependence studies of PCET reactions in small molecular systems^{76, 78} or proteins⁷⁹⁻⁸² but it can be expected that CEPT would have a different volume profile. In the present case, the different solvation of Ru³⁺ and Ru²⁺ should dominate ΔV , similar to ETPT, but CEPT is a single step reaction, and volume changes for the transition state (ΔV^{\ddagger}) should be smaller than ΔV . In addition to volume changes related to solvation, an increased pressure may accelerate a CEPT reaction by increasing the proton tunneling probability. Pressure-dependent KIEs of PT and PCET

reactions have previously been assigned to be the result of the involvement of proton tunneling.^{70, 79, 80, 83, 84} As an increased pressure favors more compressed configurations of molecules, where the proton donor-acceptor distance may be shorter, the pressure dependence in such systems may provide information about the distance dependence of the CEPT rate constants without the need to synthetically vary the molecular structure.

In conclusion, the observed PCET rate constants can be expected to have fundamentally different pressure dependencies, depending on which reaction mechanism is followed. In the present case, the PTET reaction rate should increase with pressure, while that of ETPT should decrease. For the CEPT reaction, the effects of solvation and proton tunneling distance will work in opposite direction, and the net effect cannot be predicted at the present point.

Mechanistic assignment of the PCET reactions The mechanistic assignment will begin from the rate vs. driving force correlations. First, trends with the protonic part of the driving force $(-\Delta G^0_{PT})$ will be discussed, i.e. the variation in rate with pK_a of the pyridiniums, together with KIEs. Then the electronic part of the driving force $(-\Delta G^0_{ET})$ will be discussed, i.e. the variation in rate with E^0 of the oxidant. Finally, the pressure dependence will be discussed, and how this may help in assignment of the PCET mechanism. It is important to note that, when a mechanism is assigned, this refers to the main mechanism. The observed PCET rate constant is always a sum of the different contributions (eq. 1). In most cases, one mechanism clearly dominates the reaction, i.e. it is at least ten times faster than the others are. In other cases, there are clearly simultaneous contributions from more than one mechanism.

As noted above, the variation in rate with the base strength of the pyridine group is very different for the different oxidants (Figure 2). With the two weakest oxidants, the mechanism can clearly be assigned to pre-equilibrium PTET (eq 7), as discussed before.⁵³ This is because the rate increases by a factor of ca. 10 per pK_a unit of the pyridinium group $(\Delta(\log k)/\Delta pK_a = 1.03 \text{ with } [Fe((OMe)_2 bpy)_3]^{3+})^{53}$, which is a far too strong dependence to agree with any of the other mechanisms. Noting that one pK_a unit corresponds to 59.2 meV of driving force (and that $\ln k \approx 2.30 \cdot \log k$), the slope corresponds to $\Delta(\ln k)/\Delta(-\Delta G^0) = 40 \text{ eV}^{-1}$ (see linear fit in Figure 2), in excellent agreement with the predicted value from eq. 6 of 39 eV⁻¹. Additional support for the mechanistic assignment comes from the inverted KIE values (0.14-0.38), which can be explained by an equilibrium isotope effect on the initial PT step. Based on differences in vibrational zero point energy from spectroscopic data for W-H and H⁺-pyridine vibrations, these were predicted to be ca. 0.25.⁵³ For CEPT reactions, different rate contributions from higher vibronic states for protonated and deuterated compounds, and

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compression of the proton donor-acceptor distance, can result in inverse KIE values,⁸⁵⁻⁸⁸ but it is unlikely that they would be as small as observed here. We note that Norton and coworkers have reported normal KIEs (~3-4) for proton and hydrogen atom transfer from various metal hydrides to carbon radicals as well as in in self-exchange reactions.^{59, 89} Chen and Bullock reported normal KIEs (~1.7) for hydride transfer from tungsten and molybdenum complexes to Ph_3C^+ , but in one case a clear invested value of KIE = 0.47 was found.⁹⁰ They discussed this result in terms of either a single-step reaction with a high zero-point energy of the transition state, or a step-wise reaction with a hydrogen atom transfer equilibrium followed by electron transfer, as observed for several hydrogenation reaction involving metal hydrides (see ref. 90 and references therein). In the latter case, the intermediate C-H bond has a higher frequency than the reactant W-H bond in analogy to the present study, giving rise to an equilibrium isotope effect <1.

When changing to the medium strength oxidants, the rate increased substantially for **1a-b**, but more moderately for **1c-e**. A linear fit to the data with $[Ru(Me_2bpy)_3]^{3+}$ showed only about half the slope compared to that with $[Fe((OMe)_2bpy)_3]^{3+}$. Moreover, the KIEs where larger with $[Ru(Me_2bpy)_3]^{3+}$ and even larger than unity for **1a-b** (KIE = 2.4 and 1.2, respectively). This is not consistent with pre-equilibrium PTET. Rate limiting PT can also be excluded for these reactions, because of the large observed rate constants for what would then have to be strongly uphill reactions: $\Delta p K_a > 6$ for **1a-b** and >3.5 for 1c. Thus, the second order rate constant for reverse PT from the pyridinium group to W⁻ in **1a-b** would have to be at least six orders of magnitude faster than the observed rate constants (Table 1), i.e. $\geq 1.10^{12}$ M⁻¹s⁻¹ ($\geq 1.10^{11}$ M⁻¹s⁻¹ for 1c with $[Ru(Me_2bpy)_3]^{3+}$). This would be significantly faster than the diffusion limit of ca. 1.10¹⁰ M⁻¹s⁻¹, and rate-limiting PT can therefore be ruled out. Instead, the dependence of k_{PCET} on pK_a , as well as on E^0 for **1a-b** (see below), is in good agreement with a CEPT mechanism, as discussed before.⁵³ The KIE >1 for **1a-b** also agrees with a CEPT reaction, caused by different tunneling probabilities for proton and deuteron.⁹¹ For 1ce, however, we noted that the reaction proceeds probably through a mixed mechanism, where also PTET contributes significantly. This is seen from the relatively small difference in k_{PCET} for **1c-e** with [Fe((OMe)₂bpy)₃]³⁺ vs. [Ru(Me₂bpy)₃]³⁺, and the small KIEs also with the latter oxidant. Thus, the slope of the fitted blue line in Figure 2 (Δ (ln $k/\Delta(-\Delta G^0) = 22 \text{ eV}^{-1}$) is somewhat larger than expected for just the CEPT contribution, which is predicted to be 20 eV⁻¹ or smaller.

With the four strongest oxidants, as measured in the present study, k_{PCET} for **1a-b** increases even more, by a few orders of magnitude. Across the series **1a-e**, k_{PCET} shows just a modest increase with increasing pK_a when the same oxidant is used (red lines in Figure 2). The reaction is still not diffusion-limited, except possibly for **1c** with the strongest oxidant [Ru((EtO₂C)₂bpy)₃]³⁺ ($k_{PCET} = 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$), as $k_{PCET} \le 2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$

in all other cases and still varies with e.g. oxidant strength and isotopic substitution. The very weak dependence on base strength for the same oxidant is therefore not consistent with either PTET or CEPT. Instead, we can safely assign the main mechanism to ETPT. The KIE = 1.0 ± 0.1 for **1a-b** agrees with that assignment. The weak increase in rate for **1c-e** might be explained by a small acceleration of the second PT step of a pre-equilibrium ETPT mechanism (k_{PT-b} in Scheme 1). However, based on the KIE values, and the dependence of the rate on oxidant strength and pressure discussed below, we propose that contributions from CEPT and PTET are the reason why k_{PCET} is larger in **1c-e** than in **1a-b** also with the strongest oxidants. Interestingly, with [Ru(bpy)₃]³⁺, KIE=1.1 for **1a**, then slightly larger for **1c** (KIE=1.3) and finally less than 1 for **1d-e** (KIE=0.9 and =0.7, respectively). This behavior agrees with participation of more than one mechanism, as is further supported below.

In this paragraph, we discuss the dependence of the rate on oxidant strength. In Figure 3 we see that for **1c-d**, the rate is only little affected by E^0 : $\Delta(\ln k)/\Delta(-\Delta G^0_{\rm ET}) \approx 3 \text{ eV}^{-1}$ (where $-\Delta G^{0}_{\text{ET}} = e\Delta E^{0}$) for the weaker oxidants ($E^{0} \le 0.73 \text{ V}$), which is consistent with pre-equilibrium PTET. The initial PT equilibrium is independent on E^0 , and the subsequent ET from W⁻ (k_{ET-a} in Scheme 1) is sufficiently exergonic to already be close to barrierless (close to the top of the Marcus parabola, where $-\Delta G^0 = \lambda$; eq. 8). With stronger oxidants ($E^0 > 0.73$), the dependence on E^0 is stronger: the slope of a linear fit to the data for 1c with the four oxidants in the range $E^0 = 0.73 \cdot 0.89$ V is 19 eV⁻¹, close to slope expected for a CEPT a reaction, and the KIE changes from 0.28 to 1.27 for 1c (to 0.89 for 1d). This is clear evidence that another mechanism different from PTET gradually becomes dominating, and both the dependence on E^0 and the KIE suggest that this is CEPT. Further support for this assignment is given by the pressure dependence, as discussed below. Turning to 1a-b, these show a very weak dependence on E^0 in the region $E^0 = 0.35-0.50$ V, consistent with a pre-equilibrium, PTET with the two weakest oxidants, as was discussed above. For $E^0 = 0.50-0.73$ V, the dependence is much stronger, and a linear fit to the data in Figure 3 gives a slope of 16 eV⁻¹. This slope is consistent with a CEPT reaction with a small driving force, and is consistent with our assignment above based on the KIE values and dependence on pK_a . Interestingly, when E^0 is further increased, the dependence on E^0 becomes even stronger. The fitted line in the region $E^0 = 0.73-0.90$ V has a slope of 40 eV⁻¹, which is in within experimental error of the slope predicted for a pre-equilibrium ETPT (39 eV-¹). No other PCET mechanism is consistent with such a strong dependence on E^0 . This kinetic limit requires that the reverse ET from W[•]H⁺ to Ru^{II} (k_{-ET-b}) in the encounter/successor complex is faster than PT from W[•]H⁺ to the pyridine base (k_{PT-b}). For an Eigen acid, *i.e.* a common oxygen or nitrogen acid with small intrinsic barriers, that would seem unlikely, as they become diffusion controlled already at moderate

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driving force $(\Delta p K_a > 2)$.⁹² However, proton transfer in these WH complexes is intrinsically much slower than that, in both the neutral and oxidized forms; see Concluding Remarks. In Figure 3, the rate levels off at abut $E^0 = 0.90$ V, which would be consistent with an equilibrium constant $K_{\rm ET}=1$ at around that value. This seems to be in some disagreement with the value of E^0 for [(Cp)W(CO)₃H] that was estimated to +0.76 V (+0.71 V for [(MeCp)W(CO)₃H]; Scheme 1). However, the potential for [(Cp)W(CO)₃H] was estimated from an irreversible peak potential in ref. 55, and we assumed that the 50 mV cathodic shift in E_{peak} for [(MeCp)W(CO)₃H] equals the shift in E^0 . Moreover, the columbic work term in the encounter/successor complex disfavors ET, as the ET products are both cationic, while the **1a-e** reactant is charge neutral. This means that ΔG^{0}_{ET} is slightly less favorable than estimated from just the difference in E^{0} values. Thus, pre-equilibrium ETPT seems reasonable for 1a-b with oxidants with E^0 > 0.73 V, and it explains both the larger slope in Figure 3 and the fact that k_{PCET} levels off with the strongest oxidant (which is still slower than diffusion control). We note that this pre-eq ETPT mechanism must be operative with at least similar rates in 1c-e, but the observed rates for these compounds is higher, and the KIEs different, consistent with our assignment above that other mechanisms come into play for 1c-e. As noted above, a constant shift of $E^0(W^{\bullet}-H^+/W-H)$ is no concern as our analysis is based on *relative* ΔG^0 values for the different combinations of oxidants and pyridines.

Finally, in this paragraph we use the pressure dependence of the rate constants and KIEs to discuss the PCET mechanism (Table 2). Complexes 1a-d show a clear trend in activation volumes: a positive experimental activation volume ΔV^{\ddagger} with the weakest bases turning gradually into a negative ΔV^{\ddagger} for the strongest bases. This is fully consistent with ETPT for the weaker bases and PTET for the stronger bases, due to the different charge density and solvation changes of their intermediates, as explained in the background on pressure dependence above. We note that the data for 1e shows a less negative ΔV^{\ddagger} than 1d. We speculate that this might be because ΔpK_a is already small at 1 bar, and that $K_{\rm PT}$ increases with pressure to become close to 1. Interestingly, for 1d and $[Ru(bpy)_3]^{3+}$, ΔV^{\ddagger} is distinctly different for WH and WD leading to a change from KIE=0.89 at ambient pressure to KIE=1.30 at 2 kbar (Figure 5). We already assigned the mechanism at 1 bar to PTET, with significant contribution from pre-equilibrium ETPT. Because PTET has a negative ΔV^{\ddagger} (rate increases with pressure) and ETPT has a positive ΔV^{\ddagger} (rate decreases with pressure), a higher P should favor PTET and lead to even lower KIEs, which is opposite to our observations. This suggest that a different mechanism starts contributing more at higher pressure, and because KIE increases above KIE = 1.0, we suggest that this mechanism is CEPT. CEPT should also have a slightly positive ΔV^{\ddagger} based on solvation changes (see above), but compression of the complex may lead to a shorter proton tunneling distance

and increased CEPT rates, and the KIE > 1.0 would reflect a better vibrational overlap for WH than for WD. The data thus suggests that we have an interesting situation for **1d** and $[Ru(bpy)_3]^{3+}$ where all three mechanisms give rather similar contributions to the rate, and their relative rates are sensitive to small changes in conditions. For **1c** with the same oxidant, CEPT could compete with PTET already at ambient pressure, because the base is slightly weaker in **1c**. Also, for **1c** with $[Ru(dmb)_2(bpy)]^{3+}$ as oxidant, Table 2 shows a clear difference in activation volumes between the protonated and deuterated compounds. Increasing the pressure from 1 bar to 2 kbar decreases the KIE from 0.9 to 0.7. ETPT is slowed down with pressure, whereas the PTET contribution is accelerated, and therefore the KIE decreases with pressure. It appears that the rates of both mechanisms are matched well enough with this combination of base and oxidant to significantly alter their respective contributions with an increase in pressure.



Figure 5: (left) Cartoon representing the effect of pressure on the compression of the W-H – pyridine distance; (right) Pressure dependence of the KIEs for PCET oxidation of **1d** by $[Ru(dmb)_2(bpy)]^{3+}$ (black dots), **1b** by $[Ru(bpy)_3^{3+}]$ (red squares) and **1d** by $[Ru(bpy)_3]^{3+}$ (blue triangles).

Concluding remarks

Understanding and elucidating the mechanisms, and to steer and control them, is of key importance in PCET research. The present system showed an unprecedented richness in mechanistic variation, where all three PCET mechanisms were displayed by varying the strength of oxidant and base. Straightforward and general guidelines for how the relative rates of the different mechanisms depend on oxidant and base, expected

theoretically and from our earlier studies, have been presented and they seem to hold in practice. This has not been experimentally shown before as clearly as is done in the present study. The results should be of great and general relevance for a range of PCET reactions, including synthetic catalysts or enzymes operating with PCET reaction steps. The results illustrate that the mechanism for a reactant undergoing PCET is not intrinsic to that species. Instead, it depends strongly on the reaction conditions, such as the strength of the reductant/oxidant and the acid/base used. Moreover, the different responses to changes in oxidant and base strengths for the different mechanisms underscore the importance of knowing the mechanism of the rate determining steps when e.g. designing a catalyst that should be optimized with respect to E^0 and pK_a values, or when data for enzyme mutants should be interpreted.

It is intriguing that all three mechanisms showed closely similar rate constants for some combinations of oxidants and pyridines. It is often a great challenge, both for theoretical and experimental methods, to distinguish and determine the dominating mechanism. Free energy correlations, using both variations in the strengths of oxidant and base, were important in this study to assign the mechanisms, and were supported by KIEs. Pressure dependence was used for the first time to distinguish PCET mechanisms of small molecules. It was rewarding that mechanistic predictions based on changes in charge density and solvation were useful to distinguish the mechanisms. The effect of pressure on proton tunneling for the CEPT reaction is very complicated to analyze in quantitative detail, both because of contributions from multiple vibronic transitions, and because of a likely pressure dependence of other parameters such as driving force, reorganization energy and the diffusional reaction steps. A theory describing the dependence of the CEPT rate constant on pressure, that consider these parameters, is lacking. Instead, in one approach, the pressure dependence of KIEs has been analyzed to assess proton tunneling, assuming that most pressure effects are independent on H/D isotope and thus cancel out.^{79, 80, 93} In this study, we would similarly argue that the pressure dependence of many parameters in the homologous series **1a-e** should be the same, so that differences in the relative rates and how they depend on pressure can be attributed to changes in mechanism. Indeed, clear systematic changes were found in how the activation volume varied with base strength, and thus with PCET mechanism. Data on the variation in KIE with pressure could be obtained, which indicated an enhanced proton tunneling for a CEPT reaction as the pressure increased. This can tentatively be attributed to compression of the W-H complex along the H...B coordinate to give a shorter proton tunneling distance.^{86, 87, 93} The compression presumably involves a combination of several normal modes of predominantly low frequency.⁹⁴ Identification of these modes would require a computational effort that is beyond the scope of the present study. Development of a theory to describe the pressure

dependence of CEPT reactions, combined with a wider range of experimental data where CEPT is the main reaction, would be a complement to the temperature dependence that is included in current theories,¹ and be valuable to make progress in our understanding and interpretation of PCET reactions.

Regarding the pressure dependence, it is not only an analytical tool for reactions that normally occur at one bar. Instead, we note that energy transformations in deep-sea creatures occur under substantial hydrostatic pressure and it is of fundamental interest to understand the pressure effects on these PCET reactions.⁹⁵⁻⁹⁷ Methane production in certain methanogens has been reported to be enhanced at high pressure, up to 20 MPa (200 bar)⁹⁸ or 76 MPa (760 bar).⁹⁹ We are not aware of any *in vitro* mechanistic studies of the pressure dependence of the proteins involved in these reactions. Human exploration of the deep sea in the future may rely on fuel cell powered submarine vehicles, which depend on catalytic PCET reactions at high pressure.¹⁰⁰⁻¹⁰²

It is interesting to compare our data for $[(Cp)WH(CO)_3]^{49}$ with similar data from Dempsey and coworkers on [(Cp)WH(CO)₂(PMe₃)].⁵⁴ The electron donating PMe₃ ligand decreased E^0 and increased pK_a of the complex. Nevertheless, by using weaker oxidants and stronger bases than in ref 49, they obtained very similar ΔG^{0}_{PCET} values, but found that CEPT was exclusively a minor pathway. Dempsey and coworkers suggested that the difference between the two W-H complexes is related to the rate of proton transfer. In contrast, the present study shows cases where CEPT is the major pathway. Proton transfer to and from metal hydrides is in general slow, compared to that of Eigen acids, which has been attributed to large electronic and nuclear rearrangements.^{59, 103-106} Bourrez et al. showed that proton transfer from [(Cp)W(CO)₃H] to aniline ($\Delta pK_a = 2$) was much slower than diffusion controlled: k_{PT} . $_{a} = 1 \times 10^{5} \text{ M}^{-1} \text{s}^{-1}$.⁴⁹ Dempsey and coworkers estimated that proton transfer from both the neutral [(Cp)WH(CO)₂(PMe₃)] and the oxidized complex to nitrogen bases had large reorganization energies.⁵⁴ They also found that the self-exchange proton transfer three orders of magnitude slower for the [(Cp)WH(CO)₂(PMe₃)]/ was $[(Cp)W(CO)_2(PMe_3)]$ couple than for the $[(Cp)WH(CO)_3]/[(Cp)W(CO)_3]$ couple. This led them to suggest that a larger reorganization energy for proton transfer in the PMe₃ complex is related to a more sluggish CEPT. We propose instead that the more sterically demanding PMe₃ ligand makes the distance between the hydride and the pyridine nitrogen in the encounter complex longer, which would decrease the proton wavefunction overlap between the reactant and product states, and thus slow down CEPT. With a smaller proton tunneling probability, it is less likely that CEPT can compete with the stepwise pathways. For designing PCET systems, such as catalysts with acid/base groups in their second coordination sphere, it is interesting to understand

exactly how large the proton wavefunction overlap needs to be in order to make CEPT competitive, and if hydrogen bonds are required to achieve sufficient overlap.

The predicted free-energy relationships in this study assume that a CEPT reaction responds equally to changes in ΔG^{0}_{ET} and ΔG^{0}_{PT} . This was also shown to be the case in our previous study of [(Cp)WH(CO)₃],⁴⁹ as well as in several other studies of PCET reactions with small organic compounds.107-111 Dempsey and coworkers instead found that k_{CEPT} for [(Cp)WH(CO)₂(PMe₃)] showed very different dependence on $\Delta G^{0}_{\text{CEPT}}$ for two different oxidants, one giving a Brønsted slope (in a plot of log k_{PCET} vs log K_{PCET}) of $\alpha = 0.49$ and the other $\alpha = 0.29$.⁵⁴ For a CEPT reaction at modest driving force, one expects $\alpha \approx 0.4$ -0.5, which corresponds to 16-20 eV⁻¹ in eq. 9. Therefore, they suggested that CEPT in the case of one of the oxidants is asynchronous, i.e. that the rate constant would respond differently to equal changes in ΔG^{0}_{ET} and ΔG^{0}_{PT} . Mayer and coworkers showed a first example of C-H activation by CEPT, where the electron and proton were transferred to different acceptors.¹¹² They also found a small Brønsted slope of $\alpha = 0.23$, and suggested an asynchronous reaction. A similarly small α -value was reported by Knowles and co-workers for the PCET reduction of ketones.¹¹³ However, "asynchronous" has no meaning in the electron-proton tunneling theory for PCET.^{1,114} The concept is reminiscent from (semi-)classical theories of proton transfer where proton-base bond elongation is an important part of the reaction coordinate. In the tunneling theory for CEPT, however, the reaction coordinate that defines the transition state is exclusively composed of the reorganization of solvent and the other nuclei (except the tunneling proton). Both electron and proton tunnel from the same transition state, and any "asynchronicity" in the tunneling process has no meaning. Even if the electron and proton transfer parts of the CEPT reaction would contribute different amounts to the reorganization energy, a variation in ΔG^{0}_{ET} and ΔG^{0}_{PT} will give the same change in ΔG^{0}_{PCET} , and consequently move the transition state up or down by the same amount. If a Brønsted coefficient much smaller than 0.5 is found experimentally, a different explanation should be considered. For example, the reaction could proceed in a step-wise fashion (ETPT or PTET). Alternatively, it has been shown that variations in the participation of excited vibronic states can reproduce a Brønsted coefficient <0.5.¹¹⁵ Both $\Delta G^{0}_{\rm ET}$ and $\Delta G^{0}_{\rm PT}$ should be varied separately over a sufficiently large range, to verify any asymmetry in the dependence of the rate on those two parameters. Reports of an asymmetric dependence of the rate on changes in $\Delta G^{0}_{\rm ET}$ and ΔG^{0}_{PT} has recently reported by several groups, ¹¹⁶⁻¹¹⁹ which appears to be at odds with the tunneling model. However, other effects such as hydrogen bond lengths can also vary when the relative pKa values are changed, which could be investigated by computational methods. It is an interesting topic for further theoretical and experimental investigation, whether CEPT reactions more generally can show an

asymmetric dependence of ΔG^{0}_{ET} and ΔG^{0}_{PT} , and whether that can be described by the tunneling model, or if a different description is more appropriate.

To conclude, the present study shows an unprecedented richness and variation of PCET mechanisms. The systematic variation of oxidant and base strengths, as well as hydrostatic pressure, offered correlations of rate vs. free energy and pressure that, together with KIEs, allowed for clear distinction between mechanisms in most cases. The study provides rational guidelines for elucidating and controlling the mechanism that are important for understanding and designing enzymes and synthetic catalysts that operate with PCET reaction steps.

Supporting Information

Synthesis of photosensitizers and electron acceptors, experimental details, additional characterization, spectroscopic and kinetic data.

Acknowledgements

The authors thank Dr. Starla Glover for drawing the TOC figure. This work was supported by the Swedish Research Council (grant 2016-04271) and the Foundation Olle Engkvist Byggmästare (granted 2016/3). S.W. gratefully acknowledges a grant from the Chinese Scholarship Council.

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TOC Graphics

