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Outer-sphere $2e^-/2H^+$ transfer reactions of $Ru^{II}(\text{amine})/Ru^{IV}(\text{amido})$ complexes

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Abstract

A diverse set of $2e^-/2H^+$ reactions are described that interconvert $[Ru^{II}(\text{bpy})(\text{en}^*)_2]^{2+}$ and $[Ru^{IV}(\text{bpy})(\text{en}-H^*)_2]^{2+}$ ($\text{bpy} = 2,2'$ -bipyridine, $\text{en}^* = \text{H}_2\text{NCMe}_2\text{CMe}_2\text{NH}_2$, $\text{en}^*-H = \text{H}_2\text{NCMe}_2\text{CMe}_2\text{NH}^-$), forming or cleaving different O-H, N-H, S-H and C-H bonds. The reactions involve quinones, hydrazines, thiols and 1,3-cyclohexadiene. These proton-coupled electron transfer (PCET) reactions occur without substrate binding to the ruthenium center, but with precursor complex formation by hydrogen bonding. The free energies of the reactions vary over more than 90 kcal mol^{-1} , but the rates vary more with the kind of X-H bond involved than with this ΔG^\ddagger . There is a kinetic preference for substrates that have the transferring H's in close proximity, such as *ortho*-tetrachlorobenzoquinone over its *para* isomer and 1,3-cyclohexadiene over its 1,4-isomer, perhaps hinting at the potential for concerted $2e^-/2H^+$ transfers.

TOC image

$2e^-/2H^+$ Transfer Reactions: Multi-electron redox chemistry is central to many catalytic and energy storage processes. A variety of $2e^-/2H^+$ reactions are reported, with substrates that have or form two O-H, N-H, S-H or C-H bonds. The reactions interconvert ruthenium(II)-bis(amine) and ruthenium(IV)-bis(amido) complexes.



Keywords

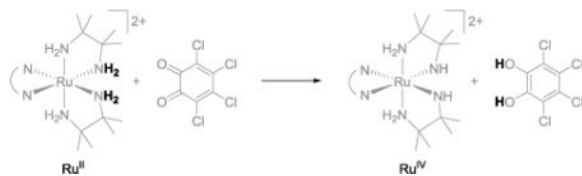
multielectron; multiproton; proton-coupled electron transfer (PCET); ruthenium; amido

Many important redox reactions involve transfer of multiple electrons and multiple protons. Examples of such proton-coupled electron transfer (PCET) reactions in chemical energy, organic chemistry and biochemistry include the interconversions of O_2 and water, N_2 and ammonia, alkenes and alkanes, and quinones and hydroquinones. The study of PCET reactions is a diverse and rapidly growing field,^{1–7} yet almost all of the well-characterized examples studied in detail involve the transfer of a single electron and a single proton (sequentially or in a single step). The transfer of two electrons and two protons together would often be very advantageous, bypassing high energy intermediates. Reported here is an exploration of net $2e^-/2H^+$ redox reactions that interconvert a Ru^{II} amine complex $[Ru^{II}(bpy)(en^*)_2]^{2+}$ (Ru^{II}) and a Ru^{IV} bis(amido) complex $[Ru^{IV}(bpy)(en^*-H)_2]^{2+}$ (Ru^{IV}), where $bpy = 2,2'$ -bipyridine, $en^* = 2,3$ -dimethyl-2,3-butanediamine, and $en^*-H = 2,3$ -dimethyl-2-amido-3-aminobutane(1-).

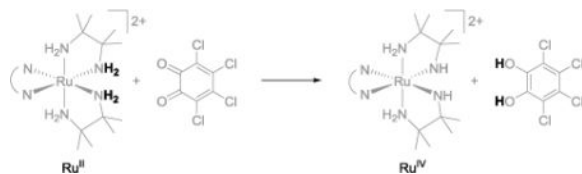
The Ru^{II} and Ru^{IV} complexes were first reported by Che *et al.*,⁸ including spectroscopic characterization, the X-ray crystal structure of Ru^{IV} , and the aqueous electrochemistry. The rich optical and 1H NMR spectra of these compounds, their electrochemical $2e^-/2H^+$ interconversion in aqueous pH 2–7, and their stability make this a valuable system for the study of multielectron PCET. Since the ruthenium centers are substitution inert and the substrates are therefore very unlikely to coordinate to the metal, the PCET chemistry occurs in an outer-sphere sense, directly to the amine ligand. The Ru^{IV}/Ru^{II} couple is particularly attractive because the two reactive N atoms have a *cis* orientation, and Ru^{IV}/Ru^{II} interconversion does not involve a change in the inner coordination sphere of the complexes. The Ru^{IV}/Ru^{II} system thus in some ways resembles the $2e^-/2H^+$ donor N_2H_2 ($HN=NH$, diazene), which is known to do symmetrical concerted transfers of two hydrogen atoms ($2e^-$

$-/2\text{H}^+$) to C–C π bonds.⁹ The most common concerted multi-electron PCET processes are hydride transfers ($2e^-/1\text{H}^+$).¹⁰ There is debate over whether Noyori-type ketone/alcohol interconversions that occur by concerted H $^-$ /H $^+$ transfers.¹¹ Noyori systems are among the ruthenium-amido complexes that have been explored for multi-redox chemistry and catalysis.¹²

Our initial studies focused on quinones and hydroquinones as prototypical $2e^-/2\text{H}^+$ couples. **Ru^{II}** reacted with one equivalent of *ortho*-tetrachloroquinone in acetone, acetonitrile or thf to quantitatively form **Ru^{IV}** and the corresponding hydroquinone within minutes at room temperature (eq 1). The *para*-tetrachloroquinone isomer reacted to form an equilibrium mixture with **Ru^{IV}** and the hydroquinone (eq 2). Remarkably, the reaction of the *p*-isomer is *ca.* 2000–3000 times slower, requiring a few hours. These and the other reactions reported here were monitored by ¹H NMR and UV-vis spectroscopies, and by mass spectrometry (see ESI). Reactions with other quinones or hydroquinones proceeded similarly, by oxidation of **Ru^{II}**, reduction of **Ru^{IV}**, or formation of an equilibrium mixture, as summarized in Table 1 (and Table S1 in the ESI). With *p*-benzoquinone in acetone, for instance, equilibrium was obtained after 2 weeks with $K_{\text{eq}} = 4.6$ ($G^\circ = -0.90$ kcal/mol; $E^\circ = 0.019$ V, Figure 1).



(1)



(2)

Other reactions that involve formation or cleavage of O–H bonds are the oxidations of **Ru^{II}** to **Ru^{IV}** by hydrogen peroxide or *meta*-chloroperbenzoic acid (mCPBA), yielding water and (in the latter case) *m*-chlorobenzoic acid. With O₂, however, the rate of oxidation is almost undetectable at ambient temperatures. The hydroxylamine TEMPO-H (2,2,5,5-tetramethyl-*N*-hydroxy-piperi-dine) reduced **Ru^{IV}** to **Ru^{II}** over hours in acetone with some decomposition.

The free energies of these reactions (G°_{react}) in acetone or thf can be in large part understood by comparison with the known thermochemistry in aqueous media.

Extrapolating Che's aqueous electrochemical results to pH 0 and converting to SHE gives the $2e^-/2\text{H}^+$ **Ru^{IV}/Ru^{II}** reduction potential $E^\circ = 0.74$ V.⁸ This is quite close to the well-known $2e^-/2\text{H}^+$ aqueous potential for *p*-benzoquinone/*p*-hydroquinone, $E^\circ = 0.70$ V.¹³ The

$E^{\circ}_{\text{aq}} = -0.040$ V is only 60 mV different from the value in acetone, equivalent to a difference of 2.7 kcal/mol in G° ($= nFE^{\circ}$, $n = 2$). Alternatively, some of the G°_{react} values are more easily analyzed using X–H bond dissociation free energies (BDFE). TEMPO–H, for instance, is a good reductant because it has a low O–H BDFE of 71.0 kcal/mol in aqueous solution.⁵ The G° for $\text{XH} \rightarrow \text{X} + \text{H}\cdot$ is thermodynamically equivalent to $\text{XH} \rightarrow \text{X} + e^{-} + \text{H}^{+}$ when the electrochemical reference is SHE).⁵ The aqueous $\text{Ru}^{\text{IV}}/\text{Ru}^{\text{II}}$ $2e^{-}/2\text{H}^{+}$ reduction potential of +0.74 V⁸ corresponds to average aqueous N–H BDFEs in Ru^{II} of 74.6 kcal/mol. Therefore, the transfer of two H atoms from TEMPO–H to Ru^{IV} is downhill by $G^{\circ} = -7.2$ kcal mol⁻¹ (typical uncertainties in BDFEs ~1 kcal/mol).

Table 1 shows that the overall reactivity of the $\text{Ru}^{\text{IV}}/\text{Ru}^{\text{II}}$ couple, for the O–H reactions above and other processes presented below, is typically well predicted by the G°_{react} values. This is true even when using aqueous electrochemical potentials for reactions in acetone solvent, illustrating the general pattern that thermodynamic solvent effects are typically small when equal numbers of e^{-} and H^{+} are transferred. BDFEs, for instance, are known to vary only small amounts with solvent.⁵ This is because $ne^{-}/n\text{H}^{+}$ ($n\text{H}\cdot$) reactions do not involve change the charge of the reagents, so the difference between the solvation energies of the reactants and products are not large.⁵ Therefore, comparisons between PCET systems in different conditions are better done with BDFE or G°_{react} values rather than individual E° or $\text{p}K_{\text{a}}$ values. For instance, this principle should facilitate comparisons of aqueous enzymatic PCET processes with model systems in organic solvents.

This thermochemical framework is often predictive for reactions of other X–H bonds. S–H bonds are weak and therefore thiols rapidly reduce Ru^{IV} to Ru^{II} . Benzenethiol and 1,2-benzenedithiol are converted to the dimers PhSSPh or $\text{C}_6\text{H}_4(\text{SS})_2\text{C}_6\text{H}_4$, respectively, along with some polymeric products. Bubbling H_2S through a solution of Ru^{IV} in acetone immediately leads to precipitation of elemental sulfur.

Hydrazine, methylhydrazine, 1,1-dimethylhydrazine, phenylhydrazine and 1,2-diphenylhydrazine all have weak N–H bonds and all reduced Ru^{IV} to Ru^{II} in THF- d_8 . Most of these proceeded at ambient temperatures over hours or days, though the PhNHNHPh reaction requires heating to form azobenzene and a small amount of PhNH₂. PhNHNH₂ and CH₃NHNH₂ make sub-stoichiometric amounts of benzene and methane, respectively, the products expected from unstable RN=NH intermediates.

Only substrate with weak C–H bonds was observed to undergo C–H bond oxidation. Ru^{IV} oxidized 1,3-cyclohexadiene over 4 days at 100 °C in acetone- d_6 a closed J. Young NMR tube, giving 30–50% Ru^{II} and somewhat lower yields of benzene. The formation of Ru^{II} was confirmed by both NMR and mass spectrometry. In contrast, heating similar solutions of 1,4-cyclohexadiene, dihydroanthracene and dihydrophenanthrene showed no conversion to Ru^{II} or oxidized organic products, only slow decomposition at high temperatures. Similarly, all attempts to reduce Ru^{IV} with H_2 , under a variety of different conditions, did not form any Ru^{II} . This is despite the reaction being quite exoergic, $G^{\circ}_{\text{react}} = -34$ kcal/mol.

Overall, these $2e^-/2H^+$ reactions typically occur at ambient temperatures in the direction indicated by the aqueous thermochemistry (Table 1). The speed of the reactions, however, does not parallel the thermochemistry. The reactions of H_2 and the C–H bond substrates are very exoergic (in one direction or the other), yet only the 1,3-cyclohexadiene reaction (days at 100 C) is observed to occur faster than decomposition. While a full mechanistic study of any of the reactions is beyond the scope of this report, a few initial kinetic studies are presented in the Supporting Information. The reduction of Ru^{IV} by excess hydrazine appeared to follow simple second-order kinetics, but the oxidation of Ru^{II} by excess H_2O_2 in buffered water displayed kinetics apparently zero-order in $[Ru^{II}]$, even when done in the presence of EDTA or picolinic acid to chelate trace iron (Figures S25-S28). Despite this complexity, some conclusions can be drawn. The faster oxidation of Ru^{II} by H_2O_2 vs. O_2 is quite unusual for Ru^{II} amine complexes, which typically undergo outersphere electron transfer to O_2 .^{14,15} This pathway is less favorable for Ru^{II} due to its unusually positive $Ru^{III/II}$ $1e^-$ reduction potential.¹⁶

Many of these reactions are marked by rapid formation of an intermediate, in which the 1H NMR signals for the NH groups of the ruthenium compounds are shifted and/or split. In Figure 1, for instance, the blue arrows indicate the shifts of the N-H signals of Ru^{II} and the breaking of their accidental degeneracy in the presence of hydroquinone (see also Figure S23). Similar NMR shifts are observed for N-H bonds in both Ru^{II} or Ru^{IV} in the hydrazine reactions (Figure S14). Shifts have also been observed in UV-vis spectra, such as the LMCT band of Ru^{IV} in CH_3CN at 20 °C in the presence of hydrazine (Figure S19). These spectral changes are most likely due to the formation of hydrogen-bonded adducts between the Ru complexes and the reagents, which presumably serve as precursor complexes on the pathway for their respective reaction.

The lower reactivity of H_2 and the C–H bond substrates is likely due in part to their inability to form hydrogen bonds with the Ru complexes, destabilizing the precursor complexes. The reactions are also quite sensitive to steric effects, for instance in the much lower reaction rate of $PhNHNHPh$ vs. $PhNHNH_2$. This is likely also due to destabilization of the precursor complex as well as the transition state. The sensitivity to steric crowding is not surprising since each of the reactive nitrogen atoms is bound to both a poly-coordinated Ru center and to a tertiary alkyl group.

The hydrazine reduction of Ru^{IV} could be slow because it may have to proceed via diazene, N_2H_2 , a high energy intermediate. Based on the aqueous potentials G°_{react} to form diazaene is only -9.2 kcal/mol while the reaction to form N_2 is very exoergic, -48.4 kcal/mol (Table 1).

Whether any of these reactions occur by one-step (concerted) $2e^-/2H^+$ mechanisms will require addition study. Studies of Nyori- and Shvo-type catalysis have shown that this is a challenging question to address convincingly.^{11,18} Still, it is clear that the reactions above proceed more readily when the two transferring hydrogen atoms are nearby. *Ortho*-tetrachloroquinone reacts substantially faster than its *para*-substituted isomer, even more than would be expected from its somewhat higher driving force. The vicinal hydrogens in

1,3-cyclohexadiene are more reactive than the more separated H's in the 1,4-isomer, where driving force is essentially the same.

In sum, a wide range of $2e^-/2H^+$ transfer reactions have been discovered using a Ru(II)-bis(amine)/Ru(IV)-bis(amido) couple, including oxidations and reductions and spanning over 90 kcal/mol in G°_{react} . The G°_{react} is well estimated by aqueous reduction potentials or BDFEs, as the solvent effects on the $2e^-/2H^+$ transfer thermodynamics are small. The speed of reactions varies with the nature of the X-H bonds involved, roughly S-H > O-H > N-H \gg C-H, but does not parallel the G° of reaction. NMR and optical spectra suggest the formation of hydrogen bonded adducts for many of the O-, S- and N-containing substrates, which is suggested to be part of the reason for their faster reactions. A strong kinetic preference is seen when the transferring H's are in close proximity, for *ortho*-tetrachlorobenzoquinone over its *para* isomer and 1,3-cyclohexadiene over its 1,4-isomer. Future mechanistic studies will explore whether this proximity effect is an indication that concerted $2e^-/2H^+$ processes are possible in this or related systems.

Experimental Section

Preparations and purifications of materials, and representative spectra of reactions are given in the ESI. Reactions were typically conducted anaerobically with a 10-fold excess of substrate, in THF-*d*₈ or acetone-*d*₆, in J. Young NMR tubes, and were protected from light.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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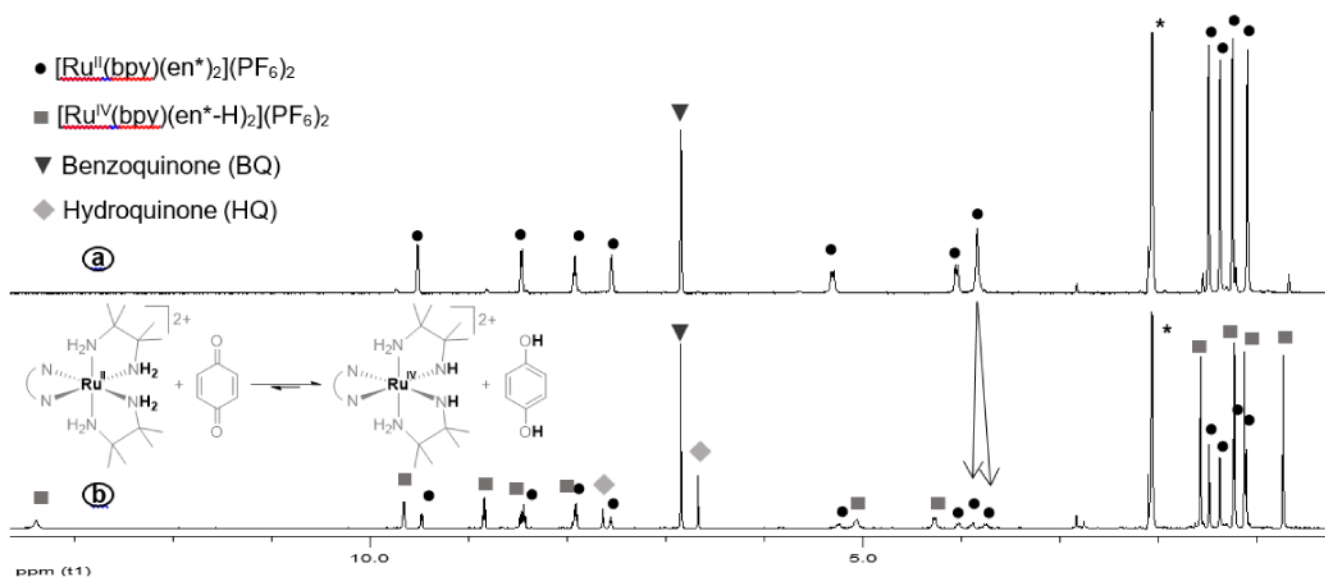


Figure 1. ^1H NMR spectra of the reaction of Ru^{II} and p-benzoquinone in acetone- d_6 at room temperature: a) initial; b) after 6 d.

Table 1

Reaction Summary and Aqueous Thermochemistry.^[a]

$2e^-/2H^+$ Redox Couple	(E°) ^[b]	$Ru^{II} \rightleftharpoons Ru^{IV}$	G^\bullet_{react} ^[c]
<u>Oxidations of Ru^{II}</u>			
$H_2O_2 + 2e^-/2H^+ \rightleftharpoons 2H_2O$	(1.78)	✓	-47.8
$o\text{-Cl}_4\text{BQ} + 2e^-/2H^+ \rightleftharpoons o\text{-Cl}_4\text{H}_2\text{Q}$	(0.79)	✓	-2.3
$p\text{-Cl}_4\text{BQ} + 2e^-/2H^+ \rightleftharpoons p\text{-Cl}_4\text{H}_2\text{Q}$	(0.76)	$K_{\text{eq}} = 16$	-0.9
$p\text{-BQ} + 2e^-/2H^+ \rightleftharpoons H_2\text{Q}$	(0.70)	$K_{\text{eq}} = 4.6$	+2.0
<u>Reductions of Ru^{IV}</u>			
$2,3\text{-naphthoquinone} + 2e^-/2H^+ \rightleftharpoons \text{naphthalene-2,3-diol}$	(0.81)	NR ^[e]	-3.2
$o\text{-BQ} + 2e^-/2H^+ \rightleftharpoons \text{catechol}$	(0.783)	NR ^[e]	-2.0
$O_2 + 2e^-/2H^+ \rightleftharpoons H_2O_2$	(0.69)	NR	2.3
$p\text{-3,5-}^t\text{Bu}_2\text{BQ} + 2e^-/2H^+ \rightleftharpoons p\text{-3,5-}^t\text{Bu}_2\text{HQ}$	(0.58)	$K_{\text{eq}} = 0.08$	7.4
$1,2\text{-naphthoquinone} + 2e^-/2H^+ \rightleftharpoons 1,2\text{-naphthohydroquinone}$	(0.579)	$K_{\text{eq}} \approx 0.001$	7.4
$\text{TEMPO}^\bullet + 1e^-/1H^+ \rightleftharpoons \text{TEMPOH}$		✓	7.2
$N_2H_2 + 2H^+/2e^- \rightleftharpoons N_2H_4$	(0.54)	✓	9.2
$N_2 + 4H^+/4e^- \rightleftharpoons N_2H_4$	(-0.33)		49.3
$S + 2e^-/2H^+ \rightleftharpoons H_2S$	(0.14)	✓	27.6
$2H^+ + 2e^- \rightleftharpoons H_2$	(0)	NR	34.1
$C_6H_6 + 2e^-/2H^+ \rightleftharpoons 1,3\text{-}C_6H_8$		✓ ^[f]	48.6
$C_6H_6 + 2e^-/2H^+ \rightleftharpoons 1,4\text{-}C_6H_8$		NR	48.6

^[a] Oxidations and reductions in various solvents at ca. 20 C; see ESI. Reacting couples written as reductions but reactions in the bottom half of the table proceed from right to left. BQ = benzoquinone; H₂Q = hydroquinone.

^[b] Aqueous E° in V vs. SHE; references in the ESI.

^[c] G^\bullet for the aqueous reaction of $X + Ru^{II} \rightarrow Ru^{IV} + XH_2$, in kcal/mol, from $-nFE^\circ$ or from BDFEs.

^[d] Ref. 8.

^[e] There is no reaction of the diol with Ru^{IV} , as predicted by the aqueous G^\bullet ; the *o*-quinone forms of these couples are unstable and their reactions could not be studied.

^[f] 4 d at 100 C.