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Manipulating the Rate-Limiting Step in Water Oxidation Catalysis by Ruthenium Bipyridine- Dicarboxylate Complexes

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In order to gain a deeper mechanistic understanding of water oxidation by [(bda)Ru(L)₂] catalysts (bdaH₂ = [2,2'-bipyridine]-6,6'-dicarboxylic acid; L = pyridine-type ligand), a series of modified catalysts with one and two trifluoromethyl groups in the 4-position of the bda²⁻ ligand were synthesized and studied using stopped-flow kinetics. The additional –CF₃ groups increased the oxidation potentials for the catalysts and enhanced the rate of electrocatalytic water oxidation at low pH. Stopped-flow measurements of cerium(IV)-driven water oxidation at pH 1 revealed two distinct kinetic regimes depending on catalyst concentration. At relatively high catalyst concentration (ca. $\geq 10^{-4}$ M), the rate determining step (RDS) was a proton-coupled oxidation of the catalyst by cerium(IV) with direct kinetic isotope effects (KIE > 1). At low catalyst

concentration (ca. $\leq 10^{-6}$ M), the RDS was a bimolecular step with $k_H/k_D \sim 0.8$. The results support a catalytic mechanism involving coupling of two catalyst molecules. The rate constants for both RDSs were determined for all six catalysts studied. The presence of $-\text{CF}_3$ groups had inverse effects on the two steps, with the oxidation step being fastest for the unsubstituted complexes and the bimolecular step being faster for the most electron-deficient complexes. Though the axial ligands studied here did not significantly affect the oxidation potentials of the catalysts, the nature of the ligand was found to be important not only in the bimolecular step, but also in facilitating electron transfer from the metal center to the sacrificial oxidant.

Introduction

The development of alternative energy sources requires the concomitant development of efficient energy storage solutions. In the last decade, research has blossomed in battery technologies and other forms of energy storage, but chemical bonds remain the ideal choice in terms of the required worldwide scale, particularly when it comes to transportation. Among the most simple and attractive systems is the splitting of water into hydrogen and oxygen, which can later be recombined in fuel cells to release the stored energy. Efficient water splitting requires highly active and robust catalysts for both hydrogen and oxygen generation. The performance of molecular catalysts for oxygen evolution ($4\text{e}^-/4\text{H}^+$ process) lags behind those for hydrogen evolution ($2\text{e}^-/2\text{H}^+$) in terms of rate, robustness, and efficiency.¹

From the mechanistic perspective, there are two major classifications of water oxidation catalysts based on how the key O-O bond formation step takes place: single-site catalysts, involving water nucleophilic attack at a single metal-oxo fragment (WNA), and two-site catalysts, where the O-O bond is formed via radical coupling interaction of two metal-oxo moieties with oxyl radical character (I2M).^{2, 3} Both of these mechanisms can be followed by a

variety of catalyst types, and it is important to make a clear distinction between the mechanistic classification (single-site WNA vs two-site I2M) and the nuclearity of the catalyst (mononuclear, dinuclear/multinuclear, etc.). The single-site pathway has been proposed for mononuclear,⁴⁻⁷ multinuclear,⁸⁻¹⁰ and nanoparticle^{11, 12} catalysts. In the single-site mechanism, a water molecule attacks an electron-deficient metal-oxo species with simultaneous proton transfer to a hydrogen-bound proton acceptor, generating an intermediate metal-hydroperoxide, Scheme 1.¹³⁻¹⁵ The proton acceptor can be another water molecule,^{16, 17} the basic form of a buffer,^{14, 18} a strategically positioned base,¹⁹ or another nearby metal-oxo moiety, as is the case for the ruthenium “blue dimer”.⁸⁻¹⁰ Single-site catalysts typically display H/D kinetic isotope effects if the O-O bond formation is rate-limiting and the overall rate of water oxidation is sensitive to both the nature (pK_a) and concentration of the buffer.

Scheme 1. O-O bond formation via single-site water nucleophilic attack (WNA) pathways for (A) mononuclear catalysts and (B) dinuclear catalysts. BL represents a bridging ligand.

In the second class, the interaction of two metal-oxyl radicals (I2M) results in O-O coupling to form a peroxo bridge between the two metal centers, Scheme 2. These two metals can be a part of the same molecule in a multinuclear complex,²⁰ a cluster,²¹ or a nanoparticle,²² or two independent molecules,⁴ as reported for [(bda)Ru(L)₂] (*vide infra*).²³ When the O-O bond

formation is rate-limiting, catalysts in this class should not display H/D kinetic isotope effects and the overall rate of water oxidation should be insensitive to both the nature and concentration of the buffer.

Scheme 2. O-O bond formation via radical coupling interaction of two metal-oxo/oxyl fragments (12M) for (A) mononuclear and (B) dinuclear catalysts. BL represents a bridging ligand.

Ruthenium polypyridyl complexes hold a special place in the landscape of molecular water oxidation catalysts (WOCs). Not only is the first molecular WOC, the blue dimer, a ruthenium polypyridyl complex, but they are among the most widely studied, with new developments continuing to be made.^{8, 24-26} A relatively recent advance was the introduction of carboxylate groups on bipyridine to provide a planar, tetradentate, dianionic, bipyridyl-dicarboxylate (bda²⁻) ligand. Ruthenium complexes with the formula [(bda)Ru(L)₂], where L is a neutral pyridine-based donor, were first reported by the Sun group in 2009, and WOCs of this type remain among the fastest to date.^{27, 28} Since its initial report, [(bda)Ru(L)₂] complexes have attracted a great deal of interest from the Sun group²³ and others,²⁹⁻³⁴ and related systems are an active area of research.^{19, 35-39}

Several mechanisms for water oxidation by [(bda)Ru(L)₂] have been proposed, which differ in the nature of the O-O bond-forming step, shown in Scheme 3. A common thread among the proposed mechanisms is that the majority of oxidation steps proceed via proton-coupled electron-transfer (PCET), a key consideration for realizing the remarkably low overpotentials of

these catalysts. Initial reports from Sun and coworkers proposed a mechanism for cerium-driven water oxidation that proceeds through radical O-O coupling between two ruthenium(V)-oxo complexes, labelled A in Scheme 3 and corresponding to A in Scheme 2.²⁸ The rate-determining step (RDS) under catalytic conditions was proposed to be a bimolecular coupling of two $\text{Ru}^{\text{V}}=\text{O}$ molecules for $[(\text{bda})\text{Ru}(\text{pic})_2]$ (pic is 4-picoline). Due to a faster bimolecular step, the isoquinoline complex $[(\text{bda})\text{Ru}(\text{isq})_2]$ was proposed to be rate-limited by the oxidation of the resulting $[\text{Ru}^{\text{IV}}-\text{O}-\text{O}-\text{Ru}^{\text{IV}}]$ dimer after O-O coupling. This was based on UV-Vis absorption spectral-fitting and stopped-flow kinetic studies with sub-micromolar catalyst concentrations.

Scheme 3. Proposed mechanisms for water oxidation catalyzed by $[(\text{bda})\text{Ru}(\text{L})_2]$ complexes.

The Meyer group has proposed involvement of a water nucleophilic attack mechanism based on solution and surface electrochemical experiments, labelled B in Scheme 3 and corresponding to A in Scheme 1.³⁰⁻³² Depending on the conditions, the RDS was proposed to be the O-O bond formation step or proton-coupled oxidation of $\text{Ru}^{\text{IV}}-\text{OH}$ to $\text{Ru}^{\text{V}}=\text{O}$. Evidence for this mechanism include an observed first-order dependence on catalyst concentration, rate enhancement with higher concentration of base, and slow electron transfer for the higher oxidation states of ruthenium.

Support for a third mechanism involving blue-dimer-like Ru-O-Ru intermediates was recently reported by our group, pathway C in Scheme 3.³³ Spectroelectrochemical experiments and electrochemical comparison of solution and surface-bound catalysts suggested the formation of a μ -oxo dimer from two Ru^{IV}-OH molecules. In this mechanism, the dimerization step involves proton-loss and precedes O-O bond formation. Because the O-O bond is formed after the RDS, it is difficult to determine the nature of this step, specifically whether it proceeds through a single-site nucleophilic attack like the blue dimer (Scheme 1, B),⁸⁻¹⁰ or whether terminal and bridging oxygen atoms come together (a variation of Scheme 2, B). It is also possible that the formation of a Ru-O-Ru dimer requires loss of one of the axial ligands, in which case the active catalytic cycle may not involve cycling through the same monomeric [(bda)Ru(L)₂] intermediates.

The determination of the rate law for catalysis under a given set of conditions may help to establish the operating mechanism. Of the three mechanistic pathways in Scheme 3, A and C involve bimolecular coupling between two catalyst molecules. Therefore, a second-order dependence on catalyst concentration would rule out pathway B. On the other hand, pathway B is the only one of the three that may exhibit first-order behavior with respect to catalyst while having zero-order dependence on oxidant. All of the proposed mechanisms involve proton-coupled oxidation steps. In this work, we report stopped-flow kinetic data for the cerium(IV)-driven homogenous water oxidation by [(R-bda)Ru(L)₂] catalysts that supports a mechanism involving proton-coupled oxidation steps and a bimolecular step. This could correspond to Pathway C or Pathway A. Furthermore, we find clear concentration-dependent switching of the rate-determining step between a proton-coupled oxidation and a bimolecular step, which is consistent with the seeming discrepancies observed in the literature between electrochemical (millimolar catalyst concentrations) and stopped-flow absorption studies (sub-micromolar

catalyst concentrations). In addition, we observe a direct kinetic isotope effect (KIE) in the high concentration regime and an inverse KIE in the low concentration regime. The latter is not straightforward in the context of a radical O-O coupling as the rate limiting bimolecular step observed at low catalyst concentrations.

Towards reaching a deeper understanding of the factors controlling the efficacy of these catalysts we examine here a series of catalysts with zero, one, and two electron-withdrawing trifluoromethyl groups on the bda^{2-} ligand. Sun^{40, 41} and others^{29, 42} have shown that changing the nature of the axial pyridine donors can significantly affect the rate of chemical and photochemical catalysis. However, if these catalysts indeed proceed through a bimolecular step facilitated by π -stacking interactions, it can be difficult to parse the electronic and π -stacking aspects of axial ligand modification. In addition, the active site for water oxidation is in the equatorial plane occupied by the $\text{Ru}(\text{bda})$ framework. Therefore, modification of the bda^{2-} backbone is expected to have a significant electronic effect on the metal center, but should be relatively innocent in terms of intermolecular interactions. In spite of this, there has been relatively limited study of variations in the plane of the bda^{2-} ligand.^{43, 44} In studies of another WOC, $[(\text{bpy})\text{Ru}(\text{tpy})\text{OH}_2]^{2+}$, Berlinguette and coworkers showed that substituents *trans* to the complex's active site had a more pronounced effect than those *cis* to the active site on oxidation potentials, catalytic rate, and robustness.⁴⁵ Furthermore, DFT calculations and X-ray crystallography show that electronic and structural changes upon oxidation of the $[(\text{bda})\text{Ru}(\text{L})_2]$ platform are primarily localized in the plane containing the ruthenium center and bda^{2-} ligand.^{27, 33, 46} Thus, the variation of substituents in the bda^{2-} ligand is expected to have a pronounced effect on the catalytic activity of the complexes. We present here experimental rate constants for

both the slow oxidation step and the bimolecular coupling step, each showing different trends with respect to the number of electron-withdrawing trifluoromethyl groups on the bda^{2-} ligand.

Results

Synthesis and Characterization of $(\text{R-bda})\text{Ru}(\text{L})_2$. The $4,4'\text{-CF}_3\text{-bdaH}_2$ ligand ($4,4'\text{-CF}_3\text{-bda}^{2-}$ is 6,6'-dicarboxy-4,4'-bistrifluoromethyl-2,2'-bipyridine) was synthesized from the commercially available 2-chloro-6-methyl-4-trifluoromethylpyridine, Scheme 4. Treatment with hydriodic acid effected replacement of the chlorine for iodine,⁴⁷ allowing for subsequent Ullmann coupling to provide 6,6'-dimethyl-4,4'-bis(trifluoromethyl)-2,2'-bipyridine.⁴⁸ Oxidation of the methyl groups with dichromate provided the free diacid $4,4'\text{-CF}_3\text{-bdaH}_2$ as a white solid in 76% yield.⁴⁹ Characterization is consistent with a previously reported procedure.⁵⁰

Scheme 4. Synthesis of $4,4'\text{-CF}_3\text{-bdaH}_2$ and $4\text{-CF}_3\text{-bdaH}_2$.

The nonsymmetric ligand $4\text{-CF}_3\text{-bdaH}_2$ ($4\text{-CF}_3\text{-bda}^{2-}$ = 6,6'-dicarboxy-4-trifluoromethyl-2,2'-bipyridine) was synthesized using Stille coupling of 2-methylpyridyl and 2-methyl-4-

trifluoromethylpyridyl units followed by dichromate oxidation of the methyl groups, Scheme 4. Coupling of 2-methyl-6-(trimethylstannyl)pyridine⁵¹ with commercially available 2-chloro-6-methyl-4-(trifluoromethyl)pyridine was mediated by palladium(0) tetrakis(triphenylphosphine) in refluxing toluene. Pure 6,6'-dimethyl-4-trifluoromethyl-2,2'-bipyridine was obtained in 67% yield after an acid extraction followed by precipitation after neutralization.⁵² Oxidation with sodium dichromate in sulfuric acid provided 4-CF₃-bdaH₂ in 84% yield.

The synthesis of the complexes [(R-bda)Ru(pic)₂] and [(R-bda)Ru(isq)₂] (pic is 4-picoline; isq is isoquinoline) was achieved by reaction of R-bdaH₂ with [(C₆H₆)RuCl₂]₂, triethylamine, and the appropriate axial ligand, Scheme 5. The benzene-chloro ruthenium(II) dimer was first refluxed in methanol with the free ligand under argon, presumably producing [(κ₂-CF₃-bdaH₂)RuCl(C₆H₆)] [Cl] *in situ*.^{53, 54} Addition of excess triethylamine and axial ligand and further reflux provided a deep burgundy solution. In the case of [(4,4'-CF₃-bda)Ru(L)₂], the reaction mixture was filtered, removing a small amount of orange RuCl₂L₄,⁵⁵ and taken to dryness. In the case of [(4-CF₃-bda)Ru(L)₂], which are less soluble in methanol than their symmetrical counterparts, the reaction mixtures were simply reduced to dryness to yield crude product. Column chromatography provided pure [(4,4'-CF₃-bda)Ru(pic)₂] (52% yield), [(4,4'-CF₃-bda)Ru(isq)₂] (45% yield), [(4-CF₃-bda)Ru(pic)₂] (62% yield), and [(4-CF₃-bda)Ru(isq)₂] (72% yield).

Scheme 5. Synthesis of $[(\text{R-bda})\text{Ru}(\text{L})]$ complexes.

The identities of the products were confirmed by mass spectrometry, X-ray crystallography, and ^1H , ^{13}C , and ^{19}F NMR. Electrospray ionization mass spectrometry (ESI-MS) confirmed the formulation of the four new complexes, displaying $[\text{M}+\text{H}]^+$ signals with the expected isotopic distributions for $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ (m/z : 667.0), $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ (m/z : 739.0), $[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ (m/z : 598.9), and $[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ (m/z : 671.0). NMR spectra for $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ and $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ are consistent with their C_{2v} symmetry, having two singlets corresponding to the protons on the $4,4'\text{-bda}^{2-}$ backbone, and a single set of resonances for the two equivalent axial ligands. The ^{19}F NMR spectra for both complexes display a single resonance at 64 ppm corresponding to the $-\text{CF}_3$ groups. The reduced symmetry in $[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ and $[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ results in NMR spectra similar to a combination of the corresponding bda^{2-} and $4,4'\text{-CF}_3\text{-bda}^{2-}$ complexes. The two axial ligands remain equivalent, but the protons of the $4\text{-CF}_3\text{-bda}^{2-}$ backbone are all unique, exhibiting two doublets and a triplet for the unsubstituted ring and two singlets for the $-\text{CF}_3$ ring. The purity of

$[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$, $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$, and $[(4\text{-CF}_3\text{bda})\text{Ru}(\text{isq})_2]$ were verified by elemental analysis.

The structure of $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ was further confirmed by single-crystal X-ray diffraction analysis of crystals obtained from slow diffusion of *n*-hexane into a CH_2Cl_2 solution of the complex. Figure 1 shows the structure of $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ and Table 1 lists selected bond distances alongside those for $[(\text{bda})\text{Ru}(\text{pic})_2]$.²⁷ There are only minor structural differences between the two complexes, the most significant being in the ruthenium-bda distances, which are slightly shortened by up to 0.03 Å in the $-\text{CF}_3$ substituted complex. The crystal structure of $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ was also determined and is similar to the picoline congener (see Figure S14 in the Supporting Information).

Figure 1. ORTEP diagram of $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$. Thermal ellipsoids shown at 50% probability. Hydrogen atoms and cocrystallized hexane molecule omitted for clarity.

Table 1. Selected bond distances (Å) and angle (deg) for [(bda)Ru(pic)₂]²⁷ and [(4,4'-CF₃-bda)Ru(pic)₂]. Atom numbers modified for clarity of comparison.

Bond/Angle	[(bda)Ru ^{II} (pic) ₂]	[(4,4'-CF ₃ -bda)Ru ^{II} (pic) ₂]
Ru-O1 _{COO}	2.216(7)	2.187(5)
Ru-O2 _{COO}	2.172(6)	2.168(5)
Ru-N1 _{bpy}	1.949(7)	1.927(6)
Ru-N2 _{bpy}	1.914(6)	1.910(4)
Ru-N1 _{pic}	2.070(6)	2.082(6)
Ru-N2 _{pic}	2.084(6)	2.090(6)
∠O-Ru-O	123.0(2)	120.97(17)

Electrochemical Characterization and Catalytic Water Oxidation. Electrochemical analysis of [(4-CF₃-bda)Ru(L)₂] and [(4,4'-CF₃-bda)Ru(L)₂] revealed considerable anodic shifts in the oxidation potentials with respect to the parent bda²⁻ complexes. Figure 2 shows cyclic voltammograms (CVs) and square wave voltammograms (SWVs) for [(bda)Ru(pic)₂], [(4-CF₃-bda)Ru(pic)₂], and [(4,4'-CF₃-bda)Ru(pic)₂] at pH 1 and Table 2 lists oxidation potentials for [(R-bda)Ru(L)₂] at pH 1. Except for some differences discussed below, the electrochemical behavior of the isoquinoline complexes is similar to the picoline complexes and the corresponding data is shown in Figures S3-S8 in the Supporting Information. Electrochemical data were collected in aqueous solution with the addition of 10% CH₃CN to promote the solubility of the complexes.⁵⁶ Like the parent complexes,^{28, 30, 57} the trifluoromethyl derivatives exhibit two oxidations before the onset of electrocatalytic water oxidation. As shown in Figure 2, the introduction of one trifluoromethyl group increases the Ru^{III/II} oxidation potential by 70-80 mV, while the Ru^{IV/III} couple is affected by just 30 mV. Distortion of the Ru^{IV/III} wave arises from kinetic inhibition, which has been examined in detail for other monomeric ruthenium

complexes.⁵⁸ The second trifluoromethyl group effects a further shift of 80-90 mV in the $\text{Ru}^{\text{III/II}}$ potential and 0-20 mV in the $\text{Ru}^{\text{IV/III}}$ potential. This equates to a 90-115 mV increase in oxidizing power (per electron) for the doubly oxidized complex.

Table 2. Oxidation potentials (V vs NHE) for $[(\text{R-bda})\text{Ru}(\text{L})_2]$ complexes at pH 1 (0.10 M HNO_3) with 10% MeCN.

Complex	$\text{Ru}^{\text{III/II}}$	$\text{Ru}^{\text{IV/III}}$
$[(\text{bda})\text{Ru}(\text{pic})_2]$	0.85	1.10
$[(\text{bda})\text{Ru}(\text{isq})_2]$	0.86	1.09
$[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$	0.92	1.13
$[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$	0.94	1.12
$[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$	1.00	1.13
$[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$	1.03	1.15

Figure 2. Cyclic voltammograms (left) and differential pulse voltammograms (right) for $[(\text{bda})\text{Ru}(\text{pic})_2]$ (*black*), $[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ (*purple*), and $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ (*blue*) at pH 1.0 (0.10 M HNO_3 with 10% MeCN).

Scanning further anodically, all three complexes exhibit a catalytic wave positive of the ruthenium(IV/III) couple, corresponding to the oxidation of water to O₂. For the parent [(bda)Ru(pic)₂] catalyst, the catalytic current slowly grows as the potential is increased, beginning around 1.3 V (all potentials reported versus NHE). The catalytic current for [(4-CF₃-bda)Ru(pic)₂] is slightly higher, while the catalytic wave for [(4,4'-CF₃-bda)Ru(pic)₂] is drastically steeper than the more electron-rich complexes. Interestingly, while the isoquinoline complexes exhibit the same trend, the differences between the three catalysts are much less significant, with all three catalytic waves beginning at 1.22 V (see Figure S3 in the Supporting Information).

As the pH is increased, the Ru^{III/II} and Ru^{IV/III} couples merge into a single wave, and the order of the rate of catalysis based on catalytic currents between the R-bda²⁻ variants is reversed. In pH 3.9 acetate buffer, a single broad, but reversible, 2-electron wave is observed before the onset of catalysis (see Figures S5, S6, and S9 in the Supporting Information). The [(R-bda)Ru(pic)₂] catalysts obey the same trend as at pH 1, while the three [(R-bda)Ru(isq)₂] catalysts have about the same catalytic activity. In pH 7.2 phosphate buffer, the 2-electron oxidations are no longer reversible, except for the more easily oxidized unsubstituted [(bda)Ru(L)₂] complexes (see Figures S7-S9 in the Supporting Information). Interestingly, the trend in catalyst activity is reversed at pH 7 with respect to the R-bda²⁻ substituent compared to that at lower pH, with the parent [(bda)Ru(L)₂] catalysts exhibiting greater catalytic current. The isoquinoline complexes outperform the picoline complexes at all pH values.

Kinetics of [(R-bda)Ru(L)₂]-Mediated Water Oxidation. To gain further understanding of the mechanism for water oxidation catalysis, the kinetics of [(R-bda)Ru(L)₂]-catalyzed chemical water oxidation by cerium(IV) was studied using stopped-flow kinetics measurements. A 4.0

mM solution of ceric ammonium nitrate in 0.20 M HClO₄ was mixed with an equal amount of catalyst solution in 4:1 water/acetonitrile, with catalyst concentrations after mixing ranging from 200 μ M to 0.39 μ M. The rate of cerium(IV) consumption was monitored using absorption at 360 nm. The reaction order with respect to cerium(IV) is reflected in the resulting plot of [Ce] vs time, revealing either a zero-order (linear consumption) or first-order dependence (logarithmic consumption). Furthermore, the reaction order with respect to catalyst is obtained using the slope from the plot of $-\log(d[\text{Ce}^{\text{IV}}]/dt)$ vs $-\log[\text{Ru}]$ (log/log plot), where $d[\text{Ce}^{\text{IV}}]/dt$ is the initial rate and [Ru] is the catalyst concentration.

The six catalysts examined display two different kinetic regimes, with rate laws depending on the catalyst concentration: first order in both cerium(IV) and catalyst at higher concentrations and zero order in cerium(IV) and second order in catalyst at lower concentrations. For all of the variants, an exponential decay in cerium(IV) was observed at catalyst concentrations on the order of 10^{-4} M, indicating first-order dependence. As the concentrations decrease, a point is reached at which $d[\text{Ce}^{\text{IV}}]/dt$ is better fit to a linear zero-order dependence. Figure 3 shows plots of $[\text{Ce}^{\text{IV}}]$ vs time for the first order and zero order regimes with respect to cerium using [(4,4'-CF₃-bda)Ru(pic)₂] at 150 μ M and 12.5 μ M, respectively. Shown in Figure 4, the slopes of the log/log plots for [(bda)Ru(pic)₂] and [(4,4'-CF₃-bda)Ru(pic)₂] clearly transition from about 1 at higher concentrations to about 2 at lower concentrations, indicating a change between first-order and second-order dependence on catalyst concentration. Taken together, this data indicates that the rate determining step at relatively higher concentrations involves a reaction between cerium(IV) and the catalyst, presumably oxidation of the catalyst. At lower concentrations, the rate determining step is independent of cerium and bimolecular in catalyst, consistent with the coupling of two catalyst molecules. Analogous behavior has been observed for similar catalysts

with varying cerium(IV) concentration.⁵⁹ The rate laws for these two regimes are represented by equations 1 and 2, respectively. The catalyst concentration at which the rate determining step changes, represented by the red “X” in Figure 4, is the value of [Ru] for which the two rate laws are equal (eq 1 = eq 2) and depends on the rate constants of the two steps (*vide infra*), as shown in equation 3.

Figure 3. Plots of $[\text{Ce}^{\text{IV}}]$ vs time for $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ at $150\ \mu\text{M}$ (*left*) and $12.5\ \mu\text{M}$ (*right*). The slope of the dotted line represents the initial rate $d[\text{Ce}^{\text{IV}}]/dt$.

Figure 4. Plots of $-\log$ of the initial reaction rate vs $-\log[\text{Ru}]$ (log/log plots) for $[(\text{bda})\text{Ru}(\text{pic})_2]$ (left) and $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$ (right), showing the concentration-dependent rate law regimes when $[\text{Ce}^{\text{IV}}]_0 = 2.0$ mM. The red “X” represents the crossover concentration at which the rates of the two steps are equal, obtained from the calculated rate constants $k_{1,1}$ and $k_{2,0}$ defined in equations 1 and 2.

$$\text{rate} = \frac{-d[\text{Ce}^{\text{IV}}]}{dt} = k_{1,1}[\text{Ru}][\text{Ce}^{\text{IV}}] \quad (\text{eq 1})$$

$$\text{rate} = \frac{-d[\text{Ce}^{\text{IV}}]}{dt} = k_{2,0}[\text{Ru}]^2 \quad (\text{eq 2})$$

$$[\text{Ru}]_X = [\text{Ce}^{\text{IV}}] \frac{k_{1,1}}{k_{2,0}} \quad (\text{eq 3})$$

Knowing the applicable rate laws for all concentrations, the two rate constants $k_{1,1}$ and $k_{2,0}$ were calculated for each of the six catalysts and are shown in Table 3. Using the log/log plots like those shown in Figure 4, the kinetic data for each catalyst was separated into oxidation-limited (slope = 1, eq 1) and coupling-limited (slope = 2, eq 2) regimes (see Figure S10 in the Supporting Information). For the oxidation-limited regime, observed rate constants ($k_{\text{obs}} =$

$k_{1,1}[\text{Ru}]$) were determined from the slope of plots of $\ln[\text{Ce}^{\text{IV}}]$ vs time. For the coupling-limited regime, observed rate constants ($k_{\text{obs}} = k_{2,0}[\text{Ru}]^2$) were determined from plots of $[\text{Ce}^{\text{IV}}]$ vs time. The observed rate constants and catalyst concentrations were then used to determine the rate constants for the oxidation step ($k_{1,1}$, eq 1, Figure S11) and the bimolecular coupling step ($k_{2,0}$, eq 2, Figure S12), which are listed in Table 3. Values for $[\text{Ru}]_{\text{X}}$ were obtained from these rate constants and are listed in Table 3.

Table 3. Calculated rate constants for the oxidation step ($k_{1,1}$, eq 1) and bimolecular step ($k_{2,0}$, eq 2) and crossover concentrations $[\text{Ru}]_{\text{X}}$ at which the rates of the two steps are equal when $[\text{Ce}] = 2.0 \text{ mM}$, 10% CH_3CN in pH 1 HClO_4 .

Complex	$k_{1,1} (\text{M}^{-1}\text{s}^{-1})$	$k_{2,0} (\text{M}^{-1}\text{s}^{-1})$	$[\text{Ru}]_{\text{X}} (\mu\text{M})$
$[(\text{bda})\text{Ru}(\text{pic})_2]$	$1.83(4) \times 10^4$	$5.26(8) \times 10^5$	69(2)
$[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$	$1.61(6) \times 10^4$	$6.88(19) \times 10^5$	47(2)
$[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{pic})_2]$	$1.12(3) \times 10^4$	$5.99(9) \times 10^5$	37(1)
$[(\text{bda})\text{Ru}(\text{isq})_2]$	$8.39(13) \times 10^4$	$1.83(6) \times 10^7$	9.2(3)
$[(4\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$	$6.93(18) \times 10^4$	$2.41(3) \times 10^7$	5.8(2)
$[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$	$4.82(7) \times 10^4$	$3.17(13) \times 10^7$	3.1(1)
$[(\text{bda})\text{Ru}(\text{pic})_2] (\text{D}_2\text{O})$	$1.68(1) \times 10^4$	$6.52(12) \times 10^5$	52(1)
$[(\text{bda})\text{Ru}(\text{isq})_2] (\text{D}_2\text{O})$	$5.29(10) \times 10^4$	$\sim 2.61(9) \times 10^7$ [†]	$\sim 4.1(2)$ [†]

[†] Approximate values due to limited data in the second order regime. See text and ref 58.

The rate constants presented in Table 3 reveal the impact of the electron density of the R-bda²⁻ ligand and the nature of the axial ligand on the rates of both the oxidation and bimolecular steps. For each axial ligand, the rate constants for the oxidation step ($k_{1,1}$) across the series of bda²⁻, 4-CF₃-bda²⁻, and 4,4'-CF₃-bda²⁻ track as expected based on their oxidation potentials. Notably, it appears that the nature of the axial ligand has an even greater effect on the rate constant, with the

isoquinoline ligand facilitating electron transfer to cerium(IV) relative to 4-picoline, despite the complexes' similar oxidation potentials. The trends in the rate constants for the bimolecular step ($k_{2,0}$) are less straightforward. Clearly, the isoquinoline ligand greatly accelerates this step, with the rate constants being almost two orders of magnitude greater than the corresponding picoline derivatives. This is consistent with literature reports that [(bda)Ru(isq)₂] is a faster catalyst than [(bda)Ru(pic)₂], presumably due to π -stacking interactions;²⁸ however, this particular effect is irrelevant at concentrations above $\sim 10^{-5}$ M, where the oxidation step is rate limiting. Among the three isoquinoline complexes, the rate constant for the bimolecular step tracks inversely with the electron density at the metal center. Consistent with this, [(4,4'-CF₃-bda)Ru(pic)₂] exhibits a higher bimolecular rate constant than [(bda)Ru(pic)₂], although [(4-CF₃-bda)Ru(pic)₂] is faster than both. A possible explanation is that the increased polarity of the nonsymmetric complex facilitates the bimolecular step in the picoline derivatives, but is overshadowed in the isoquinoline complexes presumably due to the π -stacking interactions.

To determine whether one or both of the rate-determining steps is proton-coupled, stopped-flow measurements were also carried out in D₂O for [(bda)Ru(pic)₂] and [(bda)Ru(isq)₂]. A solution of 4.0 mM ceric ammonium nitrate in 0.20 M DClO₄ was mixed with catalyst solutions of varying concentrations in 4:1 D₂O/CH₃CN and kinetic constants, shown in Table 3, were extracted as described above. The kinetic isotope effects ($\text{KIE} = k_{\text{H}}/k_{\text{D}}$) for $k_{1,1}$ for the picoline and isoquinoline complexes are 1.1 and 1.6, respectively, indicating that there is proton loss associated with the rate-determining oxidation step. Consistent with the slower oxidation reaction, the crossover concentration between the two regimes was lowered from 69(2) to 52(1) μM for [(bda)Ru(pic)₂] and from 9.2(3) to approximately 4.1(2) μM for [(bda)Ru(isq)₂]. The calculated value of $k_{2,0}$ for [(bda)Ru(pic)₂] is $6.52(12) \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, corresponding to an inverse

KIE of 0.81. In the case of [(bda)Ru(isq)₂] the crossover concentration was much lower, preventing the collection of sufficient data points to reach a slope of 2 in the log/log plot.⁶⁰ The slope of the linear fit for the three points on the log/log plot between 1.56 μ M and 0.39 μ M is 1.69. From these points, an approximate value of $2.6 \times 10^7 \text{ M}^{-1}\text{s}^{-1}$ was obtained for $k_{2,0}$, corresponding to an inverse KIE of ~ 0.7 for the bimolecular step, comparable to the picoline complex. The inverse kinetic isotope effect observed for both bimolecular rate constants suggests the involvement of either an equilibrium preceding the bimolecular step or a secondary kinetic isotope effect related to hydrogen bonding or the slight differences in dielectric constants.

Discussion

The comparison of [(R-bda)Ru(L)₂] complexes with different bda substituents and axial ligands allows independent analysis of the effect of electron-density at the metal center and potential intermolecular effects from the axial ligand. Because different rate-determining steps were observed over the wide range of concentrations, we can make conclusions about both the electron-withdrawing nature of the R-bda²⁻ ligand and the secondary effect of the axial ligand in regards to both the rate-limiting oxidation step and the bimolecular step.

Two trends are apparent in the rate constant for the oxidation step, $k_{1,1}$, measured for cerium(IV)-driven catalysis. Of course, there is an inverse relationship between $k_{1,1}$ and the oxidation potential, resulting in a faster oxidation for the parent bda²⁻ complexes, although the differences across the series are smaller than might be expected. This is related to the diminished influence of the $-\text{CF}_3$ groups on the Ru^{IV/III} couple vs the Ru^{III/II} couple, which is consistent with less contribution from the R-bda²⁻ ligand in the HOMO of the more highly oxidized complexes. As such, the differences in Ru^{V/IV} couples are likely to be smaller still (the presence of the catalytic wave precludes accurate electrochemical determination of the Ru^{V/IV} couples). The

observed H/D KIE indicates that the rate-limiting oxidation is proton-coupled, either $\text{Ru}^{\text{III}}\text{-OH}_2$ to $\text{Ru}^{\text{IV}}\text{-OH}$ or $\text{Ru}^{\text{IV}}\text{-OH}$ to $\text{Ru}^{\text{V}}\text{=O}$.

In regard to the axial ligand, the rate of oxidation for the isoquinoline complexes is faster than the corresponding picoline complexes, demonstrating that the axial ligand can play an important role not only in secondary interactions between catalyst molecules, but also in facilitating electron transfer from the metal center. It is notable that the kinetic advantage afforded by the change in axial ligand has a greater impact on the rate constant than the thermodynamic differences caused by the installation of trifluoromethyl groups. In the concentration regime where the rate is limited by an oxidation step, $[(\text{bda})\text{Ru}(\text{isq})_2]$ is the fastest of the six catalysts studied here for cerium(IV)-driven water oxidation.

The rate of the bimolecular step, $k_{2,0}$, is also affected more by the nature of the axial ligand than the substituent on the R-bda^{2-} backbone. Consistent with previous reports,²⁸ the outstanding trend in $k_{2,0}$ is the 30-50 fold increase in the isoquinoline complexes relative to the corresponding picoline complexes for each variation of R-bda^{2-} . Among the three isoquinoline complexes studied here, a decrease in electron density appears to increase the rate of the bimolecular step, with $[(4,4'\text{-CF}_3\text{-bda})\text{Ru}(\text{isq})_2]$ being the fastest. Curiously, this trend does not hold for the picoline complexes, possibly due to an increased importance of the added dimension of polarity in $4\text{-CF}_3\text{-bda}^{2-}$ in the slower bimolecular step of these complexes.

The inverse kinetic isotope effect observed for $k_{2,0}$ indicates that hydrogen bonding and/or a pre-equilibrium play a key role in the bimolecular step. Of the three mechanisms in Scheme 3, only pathways A or C include a bimolecular step; Pathway B does not include a step that is second-order in catalyst. Because it does not include any proton transfer, Pathway A would not exhibit a primary KIE for the bimolecular coupling step, however such behavior can be

rationalized in a number of ways. An equilibrium that precedes the RDS could lead to the inverse KIE if it is affected by the stronger hydrogen bonding in D₂O or involves a protonation step that is favored in D₂O. The small differences in static and dynamic dielectric constants between H₂O and D₂O are typically insignificant, but the drastic change in dipole between a highly polar Ru=O monomer and a much less polar Ru-O-O-Ru dimer, could contribute to the small observed inverse KIE. The simplest explanation is that hydrogen bonding plays an important role in the bimolecular step and the barrier is therefore reduced by the stronger hydrogen bonding in D₂O. The intricate hydrogen bonding observed in the crystal structure of the ruthenium(IV) complex (μ -H₃O₂)[(bda)Ru^{IV}(pic)₂]₂(H₂O)₂(PF₆)₃(CH₃CN) would support such an explanation.²⁷ The reaction of two Ru^{IV}-OH molecules to form a μ -oxo dimer in pathway C requires the loss of a proton, which might be expected to exhibit a KIE greater than 1. However, if the proton loss occurs in an equilibrium step preceding a slow dimerization, an inverse KIE could result. Thus, the bimolecular dependence under these conditions clearly rules out a single-site WNA pathway (Pathway B in Scheme 3), but the exact nature of the bimolecular step cannot be explicitly determined from our data (Pathway A vs Pathway C in Scheme 3). In the case of Pathway C, $k_{1,1}$ would apply to the Ru^{III}-OH₂ to Ru^{IV}-OH oxidation, and $k_{2,0}$ would apply to the coupling of two Ru^{IV}-OH molecules. This would be consistent with our previously reported spectroelectrochemical and computational data,³³ though the spectral data was recorded for surface-bound molecules, which may behave differently than those in solution. In the case of Pathway A, proposed by Sun and coworkers,⁶¹ our calculated values of $k_{1,1}$ would apply to the oxidation of Ru^{III}-OH₂ or Ru^{IV}-OH and $k_{2,0}$ would apply to the coupling of two Ru^V=O molecules.

The two kinetic regimes observed here could potentially account for discrepancies in the literature where some reports indicate second order behavior with respect to catalyst and others propose a different mechanism due to an observed first-order dependence on catalyst in electrochemical experiments.^{28, 30} However, it does remain possible that electrochemical catalysis proceeds through a different mechanism than cerium(IV)-driven catalysis. The difference between chemical and electrochemical studies is particularly important for surface-bound molecules, since any catalyst-catalyst bimolecular pathways would be severely inhibited, at least at planar electrodes.^{33, 34} A WNA mechanism was suggested for these catalysts under electrocatalytic conditions.³⁰ However, in this mechanism one would expect little influence from the axial ligand and faster catalysis for the more electrophilic trifluoromethyl-substituted catalysts across all pH values when nucleophilic attack is rate-limiting, which is not the case in our experiments.

The electrocatalytic behavior for [(R-bda)Ru(L)₂] certainly does not obey the same trends observed in the cerium(IV)-driven experiments. At 1.0 mM catalyst concentration the oxidation step is expected to be rate limiting based on the stopped-flow kinetic data, but [(4,4'-CF₃-bda)Ru(pic)₂] produces a much greater catalytic current than the more easily-oxidized [(bda)Ru(pic)₂] at acidic pH. A likely explanation is a faster heterogeneous electron transfer between the glassy carbon electrode and the complexes with more hydrophobic groups. That the isoquinoline catalysts are all relatively fast and exhibit much smaller differences between them is consistent with this explanation (see Figure S3 in the Supporting Information). Furthermore, the catalytic waves for [(4,4'-CF₃-bda)Ru(pic)₂] are similar to [(4,4'-CF₃-bda)Ru(isq)₂] for the acidic pH values at which this trend holds. Generally, with increasing pH, the onset potentials for catalysis decrease and catalytic currents increase, as expected based on thermodynamics and

base-enhanced PCET (see Figures S5 and S7 in the Supporting Information).³⁰ At neutral pH, the isoquinoline catalysts are still more effective than the picoline catalysts, but the R-bda²⁻ series now obey the trend expected based on oxidation potential, with the unsubstituted bda²⁻ catalysts being faster. Clearly, there is a complex interplay between oxidation potential and secondary effects on electron transfer rate.

The possibility remains that the true active species is generated by decoordination of one of the axial L-type ligands. This would reduce the steric barrier to form a μ -oxo dimer, which has been proposed previously based on spectroelectrochemical experiments.³³ Consistent with this route is the report that complexes with a single labile dimethylsulfoxide ligand [(bda)Ru(DMSO)(imidazole)] are faster than [(bda)Ru(imidazole)₂], though this behavior was previously ascribed to steric effects.⁵⁹ Oxo-bridged trimers resulting from oxidation of [(bda)Ru(pic)₂] have recently been described and shown to be active WOCs, though with rates slower than the monomeric catalysts.^{62, 63}

Conclusion

Variations of the known [(bda)Ru(L)₂] WOC were prepared with one and two trifluoromethyl substituents in the 4-positions of the bda²⁻ ligand. Kinetic studies of cerium-driven water oxidation using stopped-flow kinetic measurements showed that the rate of catalytic water oxidation by [(R-bda)Ru(L)₂] is limited by a proton-coupled oxidation step at catalyst concentrations on the order of 10⁻⁴ M and by a bimolecular step at catalyst concentrations around 10⁻⁶ M. The importance of the oxidation-limited regime is notable considering the effort that has been applied to design assemblies that facilitate the bimolecular coupling step.⁶⁴⁻⁶⁷ Indeed, recent electrochemical studies have demonstrated the importance of electron transfer mediation in these systems,^{31, 32} and our electrocatalytic data support this notion.

Our data is consistent with the kinetic behavior observed in the literature in both cerium-driven and electrochemical experiments and supports a mechanism involving a bimolecular coupling of two catalyst molecules, such as Pathways A and C in Scheme 3. It remains possible that the mechanism differs depending on the nature of the oxidant, especially considering that cerium can play a non-innocent role in water oxidation catalysis.^{68, 69}

Because the RDS varies with catalyst concentration, potential improvements must consider the experimental conditions relevant to potential applications. The ideal catalyst is particular to any given system.⁷⁰ This is illustrated in the varying effects of the installation of trifluoromethyl groups in [(4,4'-CF₃-bda)Ru(L)₂] under different conditions. In cerium-mediated catalysis at pH 1, [(4,4'-CF₃-bda)Ru(L)₂] is a faster catalyst in dilute solutions but a slower one at higher catalyst concentrations. In water oxidation electrocatalysis at glassy carbon electrodes, [(4,4'-CF₃-bda)Ru(L)₂] is again faster at low pH, but at neutral pH [(bda)Ru(L)₂] is the better catalyst. Of course, practical applications for this type of catalyst would require it to be driven photo- or electro-chemically. Thus, future work aims to apply conclusions from these basic studies towards integrated systems with photosensitizers and photoanodes.

Experimental

Synthetic Methods and Materials. The complexes described below are mildly air-sensitive. Reactions were carried out under argon using standard Schlenk techniques at ambient temperature (21-24 °C), unless otherwise noted. Workup and purification was performed in air. A nitrogen-filled glovebox was used for long term storage. Samples for analysis were prepared in air and used immediately. Oxidized impurities are easily separated from ruthenium(II) complexes by dissolving in CH₂Cl₂ and washing with aqueous ascorbic acid solution. High-purity water was obtained by passing house-distilled water through a Millipore Milli-Q Synthesis

A-10 system. 2-Methyl-6-(trimethylstannyl)pyridine⁵¹ and $[\text{RuCl}_2(\text{C}_6\text{H}_6)]_2$ ⁷¹ were prepared according to the literature. All other reagents and solvents were purchased from commercial sources and used as received.

Physical Methods. Elemental analyses (EA) were performed by Robertson Microlit Laboratories. Electrospray ionization mass spectrometry (ESI-MS) was performed with a Thermo Finnigan LCQ Advantage LC/MS/MS. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 400 spectrometer. ^1H NMR spectra were referenced to TMS using the residual protio impurities of the solvent, ^{13}C NMR spectra were referenced to TMS using the natural abundance ^{13}C of the solvent, and ^{19}F NMR spectra were referenced to CFCl_3 using the Ξ scale with the corresponding ^1H spectra.⁷² All chemical shifts are reported in the standard δ notation in parts per million; positive chemical shifts are a higher frequency than the reference. Electronic absorption spectra were recorded with a UV-visible Agilent 8453 diode-array spectrophotometer and were corrected for the background spectrum of the solvent. Electrochemical measurements were performed with a CH Instruments CH-760E bipotentiostat at ambient temperature (21-24 °C) in a single compartment cell with a 3.0 mm glassy carbon disc working electrode, platinum wire counter electrode, and Ag/AgCl (3 M NaCl) reference electrode. Solutions contained 1.0 mM analyte with 10% acetonitrile in aqueous solution containing perchloric acid, nitric acid, phosphate buffer, or acetate buffer solutions. The reference electrode was calibrated to the ruthenium(III/II) couple of an internal $[\text{Ru}(\text{bpy})_3](\text{PF}_6)_2$ standard at 1.26 vs NHE.⁷³ Stopped-flow kinetic measurements were performed at 25 ± 0.1 °C with an Olis rapid scanning monochromator (Olis RSM-1000) equipped with an Olis USA stopped-flow.

Synthesis of 2-iodo-6-methyl-4-trifluoromethylpyridine. This procedure was adapted from the synthesis of 2-iodo-pyrimidine.⁴⁷ 2-chloro-6-methyl-4-trifluoromethylpyridine (5.0 g, 25.6 mmol) was added to 20 mL of hydriodic acid (57%, precooled to 0 °C). The mixture was allowed to warm up to room temperature under magnetic stirring. After 1 hour, ¹H-NMR showed no chloro-iodo conversion and the mixture was refluxed for 4 hours. At this point ¹H-NMR showed ~ 70% conversion of the chloropyridine to the corresponding iodopyridine. The mixture was allowed to cool to room temperature and then chilled in an ice bath. Saturated potassium carbonate solution was added until neutral pH was reached and the mixture was decolorized with potassium disulfite. The aqueous solution was extracted with diethyl ether (5 x 30 mL) and the combined extracts were dried over anhydrous magnesium sulfate, filtered and the diethyl ether was removed by rotary evaporation. The yellow oil contained ~ 30% of the initial chloropyridine and was used in the next step without further purification. ¹H NMR (CDCl₃) δ/ppm: 7.72 (*s*, 1H, aryl-H), 7.30 (*s*, 1H, aryl-H), 2.59 (*s*, 3H, -CH₃).

Synthesis of 6,6'-dimethyl-4,4'-bis(trifluoromethyl)-2,2'-bipyridine. This procedure was adapted from the synthesis of 4,4'-bis(trifluoromethyl)-2,2'-bipyridine.⁴⁸ The 2-iodo-6-methyl-4-trifluoromethylpyridine from the previous step was added into a Schlenk flask containing 15.0 g of activated copper bronze.⁴⁷ The mixture was flushed with argon and heated at 170 °C for 8 hours. After cooling to room temperature the mixture was extracted several times with acetone and dichloromethane. The solvents were removed by rotary evaporation and the residue was dissolved in dichloromethane. Aqueous ammonia (20 mL) was added to the mixture and the organic fraction separated. This procedure was repeated two more times. The solution was dried with anhydrous magnesium sulfate, filtered and the solvent was removed by rotary evaporation. The sticky residue was dried at 70 °C under vacuum. The product (2.5 g, 61% from 2-chloro-6-

methyl-4-trifluoromethylpyridine) was pure except for the presence of 2-chloro-6-methyl-4-trifluoromethylpyridine from the previous step. The 2-iodo-6-methyl-4-trifluoromethylpyridine underwent quantitative coupling. ^1H NMR (CDCl_3) δ/ppm : 8.52 (s, 2H, aryl-H), 7.41 (s, 2H, aryl-H), 2.73 (s, 6H, $-\text{CH}_3$). This material was used without further purification in the following step.

Synthesis of 4,4'-bis(trifluoromethyl)-[2,2'-bipyridine]-6,6'-dicarboxylic acid (4,4'- CF_3 -bdaH₂). This procedure was adapted from the synthesis of 2,2'-bipyridine-6,6'-dicarboxylic acid.⁴⁹ 6,6'-dimethyl-4,4'-bis(trifluoromethyl)-2,2'-bipyridine (1.0 g, 3.12 mmol, 1 equiv) was added to a solution of sodium dichromate (2.28 g, 7.65 mmol, 2.45 equiv) in concentrated sulfuric acid (10 mL) under magnetic stirring. The mixture was heated at 80 °C for 1 hour, allowed to cool to ~50 °C and then poured into ~100 g of ice. The precipitate was collected by filtration and rinsed with water, a small amount of ethanol, and diethyl ether to yield a white solid (0.95 g, 80%). ^1H NMR ($\text{DMSO}-d_6$) δ/ppm : 9.01 (s, 2H, aryl-H), 8.40 (s, 2H, aryl-H).

Synthesis of 6,6'-dimethyl-4-trifluoromethyl-2,2'-bipyridine. 2-Methyl-6-(trimethylstannyl)pyridine (1.212 g, 4.737 mmol, 1 equiv), 2-chloro-6-methyl-4-(trifluoromethyl)pyridine (926 mg, 4.74 mmol, 1 equiv), and $\text{Pd}(\text{PPh}_3)_4$ (275 mg, 238 μmol , 0.05 equiv) were combined in 30 mL anhydrous toluene under argon and refluxed for 21 h. The solvent was removed and the residue was redissolved in 5 mL CH_2Cl_2 . The solution was then extracted with 3 x 30 mL 6 M $\text{HCl}_{(\text{aq})}$. The combined aqueous extracts were washed with 10 mL Et_2O , then cooled to 0 °C and neutralized with NH_4OH . The light orange solid was separated by filtration, washed with water, and dried in vacuo (804 mg, 67%). ^1H NMR (CDCl_3) δ/ppm : 8.48 (s, 1H, aryl-H), 8.23 (d, $^3J_{\text{HH}} = 7.8$ Hz, 1H, aryl-H), 7.71 (d, $^3J_{\text{HH}} = 7.7$ Hz, 1H, aryl-H), 7.36 (s, 1H, aryl-H), 2.71 (s, 3H, $-\text{CH}_3$), 2.65 (s, 3H, $-\text{CH}_3$). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3) δ/ppm : 159.4 (aryl-

C), 158.3 (aryl-C), 157.5 (aryl-C), 154.6 (aryl-C), 139.5 (*q*, $^2J_{\text{CF}} = 34$ Hz, aryl-C), 137.3 (aryl-C), 124.7 (aryl-C), 123.3 (*q*, $^1J_{\text{CF}} = 273$ Hz, $-\text{CF}_3$), 118.5 (*q*, $^3J_{\text{CF}} = 4$ Hz, aryl-C), 118.5 (aryl-C), 114.2 (*q*, $^3J_{\text{CF}} = 4$ Hz, aryl-C), 24.9 ($-\text{CH}_3$), 24.8 ($-\text{CH}_3$). $^{19}\text{F}\{^1\text{H}\}$ NMR (CDCl_3) δ/ppm : 64.68 ($-\text{CF}_3$).

Synthesis of 4-trifluoromethyl-[2,2'-bipyridine]-6,6'-dicarboxylic acid (4- CF_3 -bdaH₂).

Solid 6,6'-dimethyl-4-trifluoromethyl-2,2'-bipyridine (801 mg, 3.18 mmol, 1 equiv) was added to a solution of $\text{Na}_2\text{Cr}_2\text{O}_7 \cdot 2\text{H}_2\text{O}$ (2.322 g, 7.792 mmol, 2.45 equiv) in 12 mL concentrated H_2SO_4 . The dark orange solution was stirred at room temperature for 20 min, becoming green-brown and warm. Heating at 80 °C for 1 h produced a dark green solution, which was then poured into ca. 90 mL crushed ice, producing a white solid. The mixture was filtered and the solid was washed with 3 x 10 mL H_2O and 2 x 5 mL Et_2O (838 mg, 84%). ^1H NMR ($\text{DMSO}-d_6$) δ/ppm : 13.78 (*br s*, 1H, $-\text{COOH}$), 13.43 (*br s*, 1H, $-\text{COOH}$), 9.07 (*s*, 1H, aryl-H), 8.76 (*d*, $^3J_{\text{HH}} = 7.0$ Hz, 1H, aryl-H), 8.34 (*s*, 1H, aryl-H), 8.26-8.21 (*m*, 2H, aryl-H). $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{DMSO}-d_6$) δ/ppm : 165.5 ($-\text{COOH}$), 164.8 ($-\text{COOH}$), 156.2 (aryl-C), 153.0 (aryl-C), 150.1 (aryl-C), 148.1 (aryl-C), 139.5 (aryl-C), 139.2 (*q*, $^2J_{\text{CF}} = 34$ Hz, aryl-C), 126.0 (aryl-C), 124.5 (aryl-C), 122.7 (*q*, $^1J_{\text{CF}} = 273$ Hz, $-\text{CF}_3$), 120.4 (*q*, $^3J_{\text{CF}} = 4$ Hz, aryl-C), 119.4 (*q*, $^3J_{\text{CF}} = 4$ Hz, aryl-C). $^{19}\text{F}\{^1\text{H}\}$ NMR ($\text{DMSO}-d_6$) δ/ppm : 63.31 ($-\text{CF}_3$).

Synthesis of [(4,4'- CF_3 -bda)Ru(pic)₂]. 4,4'- CF_3 -bdaH₂ (228 mg, 600 μmol , 1 equiv) and $[\text{RuCl}_2(\text{C}_6\text{H}_6)]_2$ (150 mg, 300 μmol , 0.5 equiv) were combined in 30 mL CH_3OH . The suspension was degassed by bubbling with argon, then refluxed for 2 h, producing a dark purple solution. The reaction mixture was removed from heat, treated with triethylamine (1.0 mL, excess) and 4-picoline (0.5 mL, excess), and refluxed for an additional 15 h. The reaction mixture was filtered after cooling to room temperature and then evaporated, providing a

burgundy residue. The latter was dissolved in CHCl_3 and washed three times with an aqueous solution of ascorbic acid. The CHCl_3 solution was dried with anhydrous magnesium sulfate, filtered and taken to dryness by rotary evaporation. The crude product was purified by column chromatography on silica gel with 4:1 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$. The fractions containing pure product by UV-vis absorption were combined and evaporated (208 mg, 52%). Anal. Calcd. (Found) for $\text{C}_{26}\text{H}_{18}\text{F}_6\text{N}_4\text{O}_4\text{Ru}$ (%): C, 46.92 (46.66); H, 2.73 (2.68); N, 8.42 (8.64). ESI-MS (acetone/methanol) m/z : 667.0 ($[\text{M}+\text{H}]^+$), 688.9 ($[\text{M}+\text{Na}]^+$), 704.8 ($[\text{M}+\text{K}]^+$). ^1H NMR (CD_2Cl_2) δ/ppm : 8.42 (*s*, 2H, bda aryl-H), 8.33 (*s*, 2H, bda aryl-H), 7.43 (*d*, $^3J_{\text{HH}} = 6.6$ Hz, 4H, pic aryl-H), 6.91 (*d*, $^3J_{\text{HH}} = 6.0$ Hz, 4H, pic aryl-H), 2.23 (*s*, 6H, pic $-\text{CH}_3$). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2) δ/ppm : 171.8 (bda aryl- $\text{COO}-$), 160.6 (bda aryl-C), 159.8 (bda aryl-C), 150.8 (pic aryl-C), 150.0 (pic aryl-C), 131.3 (*q*, $^2J_{\text{CF}} = 35$ Hz, bda aryl-C), 126.5 (pic aryl-C), 123.5 (*q*, $^1J_{\text{CF}} = 273$ Hz, bda $-\text{CF}_3$), 122.6 (*q*, $^3J_{\text{CF}} = 4$ Hz, bda aryl-C), 120.0 (*q*, $^3J_{\text{CF}} = 4$ Hz, bda aryl-C), 21.0 (pic $-\text{CH}_3$). $^{19}\text{F}\{^1\text{H}\}$ NMR (CD_2Cl_2) δ/ppm : 64.04 ($-\text{CF}_3$). UV-vis (CH_2Cl_2) $\lambda_{\text{max}}/\text{nm}$ ($\epsilon/\text{M}^{-1}\text{cm}^{-1}$): 306 (22000), 340 (8700), 356 (8700), 424 (10000).

Synthesis of [(4,4'- CF_3 -bda) $\text{Ru}(\text{isq})_2$]. 4,4'- CF_3 -bda H_2 (228 mg, 600 μmol , 1 equiv) and $[\text{RuCl}_2(\text{C}_6\text{H}_6)]_2$ (150 mg, 300 μmol , 0.5 equiv) were combined in 30 mL CH_3OH . The suspension was degassed by bubbling with argon, then refluxed for 2 h, producing a dark purple solution. The reaction mixture was removed from heat, treated with triethylamine (1.0 mL, excess) and isoquinoline (0.6 mL, excess), and refluxed for an additional 15 h. The reaction mixture was filtered after cooling to room temperature and then evaporated, providing a burgundy residue. The latter was dissolved in CHCl_3 and washed three times with an aqueous solution of ascorbic acid. The CHCl_3 solution was dried with anhydrous magnesium sulfate, filtered and taken to dryness by rotary evaporation. The crude product was purified by column

chromatography on silica gel with 4:1 CH₂Cl₂/CH₃OH. The fractions containing pure product by UV-vis absorption were combined and evaporated (199 mg, 45%). Anal. Calcd. (Found) for C₃₂H₁₈F₆N₄O₄Ru (%): C, 52.11 (51.92); H, 2.46 (2.68); N, 7.60 (7.53). ESI-MS (acetone/methanol) m/z: 739.0 ([M+H]⁺), 761.0 ([M+Na]⁺), 776.9 ([M+K]⁺). ¹H NMR (CD₂Cl₂) δ/ppm: 8.56 (*s*, 2H, bda aryl-H), 8.52 (*s*, 2H, isq aryl-H), 8.33 (*s*, 2H, bda aryl-H), 7.84 (*d*, ³J_{HH} = 8.3 Hz, 2H, isq aryl-H), 7.76 (*d*, ³J_{HH} = 8.2 Hz, 2H, isq aryl-H), 7.72 (*td*, ³J_{HH} = 7.5 Hz, ⁴J_{HH} = 1.1 Hz, 2H, isq aryl-H), 7.62 (*ddd*, ³J_{HH} = 8.1 Hz, ³J_{HH} = 6.6 Hz, ⁴J_{HH} = 1.1 Hz, 2H, isq aryl-H), 7.46 (*d*, ³J_{HH} = 6.6 Hz, 2H, isq aryl-H), 7.33 (*d*, ³J_{HH} = 6.5 Hz, 2H, isq aryl-H). ¹³C{¹H} NMR (CD₂Cl₂) δ/ppm: 171.8 (bda aryl-COO-), 160.6 (bda aryl-C), 159.8 (bda aryl-C), 156.2 (isq aryl-C), 142.1 (isq aryl-C), 135.5 (isq aryl-C), 132.8 (isq aryl-C), 131.7 (*q*, ²J_{CF} = 35 Hz, bda aryl-C), 129.1 (isq aryl-C), 129.0 (isq aryl-C), 128.0 (isq aryl-C), 126.7 (isq aryl-C), 123.5 (*q*, ¹J_{CF} = 273 Hz, bda -CF₃), 122.7 (*q*, ³J_{CF} = 4 Hz, bda aryl-C), 122.7 (isq aryl-C), 120.3 (*q*, ³J_{CF} = 4 Hz, bda aryl-C). ¹⁹F{¹H} NMR (CD₂Cl₂) δ/ppm: 64.00 (-CF₃). UV-vis (CH₂Cl₂) λ_{max}/nm (ε/M⁻¹ cm⁻¹): 256 (25000), 305 (28000), 409 (16000).

Synthesis of [(4-CF₃-bda)Ru(pic)₂]. 4-CF₃-bdaH₂ (402 mg, 1.28 mmol, 1 equiv) and [RuCl₂(C₆H₆)]₂ (322 mg, 644 μmol, 0.5 equiv) were combined in 30 mL CH₃OH. The suspension was degassed by bubbling with argon, then refluxed for 2 h, producing a dark purple solution. The reaction mixture was removed from heat, treated with triethylamine (0.7 mL, 5 mmol, 4 equiv) and 4-picoline (0.26 mL, 2.7 mmol, 2.1 equiv), and refluxed for an additional 15 h. The reaction mixture was then evaporated, providing a burgundy residue. The product was purified by column chromatography on silica gel with 4:1 CH₂Cl₂/CH₃OH. The fractions containing pure product by UV-vis absorption were combined and evaporated. The resulting residue was treated with 3 x 30 mL 0.05 M ascorbic acid, filtered, washed with 10 mL H₂O and

10 mL Et₂O, and dried in vacuo (479 mg, 62%). Anal. Calcd. (Found) for C₂₅H₁₉F₃N₄O₄Ru (%): C, 50.25 (49.65); H, 3.21 (3.08); N, 9.38 (9.21). ESI-MS (acetone/methanol) m/z: 598.9 ([M+H]⁺), 620.8 ([M+Na]⁺), 678.7 ([M+K]⁺). ¹H NMR (CD₂Cl₂) δ/ppm: 8.30 (*s*, 1H, bda aryl-H), 8.26 (*d*, ³J_{HH} = 8.1 Hz, 1H, bda aryl-H), 8.24 (*s*, 1H, bda aryl-H), 8.11 (*d*, ³J_{HH} = 7.6 Hz, 1H, bda aryl-H), 7.76 (*t*, ³J_{HH} = 7.9 Hz, 1H, bda aryl-H), 7.51 (*d*, ³J_{HH} = 6.4 Hz, 4H, pic aryl-H), 6.90 (*d*, ³J_{HH} = 6.1 Hz, 4H, pic aryl-H), 2.22 (*s*, 6H, pic -CH₃). ¹³C{¹H} NMR (CD₂Cl₂/CD₃OD) δ/ppm: 173.4 (bda aryl-COO-), 172.7 (bda aryl-COO-), 161.6 (bda aryl-C), 159.3 (bda aryl-C), 159.3 (bda aryl-C), 157.6 (bda aryl-C), 151.1 (pic aryl-C), 149.8 (pic aryl-C), 132.0 (bda aryl-C), 130.9 (*q*, ²J_{CF} = 35 Hz, bda aryl-C), 126.7 (bda aryl-C), 126.4 (pic aryl-C), 124.7 (bda aryl-C), 123.6 (*q*, ¹J_{CF} = 273 Hz, bda -CF₃), 122.3 (*q*, ³J_{CF} = 4 Hz, bda aryl-C), 120.0 (*q*, ³J_{CF} = 4 Hz, bda aryl-C), 20.9 (pic -CH₃). ¹⁹F{¹H} NMR (CD₂Cl₂) δ/ppm: 64.02 (-CF₃). UV-vis (CH₂Cl₂) λ_{max}/nm (ε/M⁻¹ cm⁻¹): 250 (20000), 305 (24000), 370 (9600), 415 (8300), 489 (4500).

Synthesis of [(4-CF₃-bda)Ru(isq)₂]. 4-CF₃-bdaH₂ (428 mg, 1.37 mmol, 1 equiv) and [RuCl₂(C₆H₆)₂] (343 mg, 685 μmol, 0.5 equiv) were combined in 30 mL CH₃OH. The suspension was degassed by bubbling with argon, then refluxed for 2.5 h, producing a dark purple solution. The reaction mixture was removed from heat, treated with triethylamine (0.76 mL, 5.5 mmol, 4 equiv) and isoquinoline (0.35 mL, 3.0 mmol, 2.2 equiv), and refluxed for an additional 15 h. The reaction mixture was then evaporated, providing a brown-red residue. The product was purified by column chromatography on silica gel with 4:1 CH₂Cl₂/CH₃OH. The fractions containing pure product by UV-vis absorption were combined and evaporated. The resulting residue was treated with 3 x 30 mL 0.05 M ascorbic acid, filtered, washed with 10 mL H₂O and 10 mL Et₂O, and dried in vacuo (657 mg, 72%). Anal. Calcd. (Found) for C₃₁H₁₉F₃N₄O₄Ru (%): C, 55.61 (55.36); H, 2.86 (2.60); N, 8.37 (8.33). ESI-MS

(acetone/methanol) m/z : 671.0 ($[M+H]^+$), 692.8 ($[M+Na]^+$), 708.8 ($[M+K]^+$). 1H NMR (CD_2Cl_2) δ/ppm : 8.52 (*s*, 2H, *isq* aryl-H), 8.43 (*s*, 1H, *bda* aryl-H), 8.38 (*d*, $^3J_{HH} = 8.0$ Hz, 1H, *bda* aryl-H), 8.24 (*s*, 1H, *bda* aryl-H), 8.12 (*d*, $^3J_{HH} = 7.6$ Hz, 1H, *bda* aryl-H), 7.83 (*t*, $^3J_{HH} = 7.9$ Hz, 1H, *bda* aryl-H), 7.80 (*d*, $^3J_{HH} = 7.9$ Hz, 2H, *isq* aryl-H), 7.74 (*d*, $^3J_{HH} = 8.1$ Hz, 2H, *isq* aryl-H), 7.70 (*t*, $^3J_{HH} = 7.4$ Hz, 2H, *isq* aryl-H), 7.60 (*t*, $^3J_{HH} = 7.4$ Hz, 2H, *isq* aryl-H), 7.48 (*d*, $^3J_{HH} = 6.5$ Hz, 2H, *isq* aryl-H), 7.44 (*d*, $^3J_{HH} = 6.5$ Hz, 2H, *isq* aryl-H). $^{13}C\{^1H\}$ NMR (CD_2Cl_2/CD_3OD) δ/ppm : 173.5 (*bda* aryl-COO-), 172.8 (*bda* aryl-COO-), 161.6 (*bda* aryl-C), 159.3 (*bda* aryl-C), 159.2 (*bda* aryl-C), 157.5 (*bda* aryl-C), 156.3 (*isq* aryl-C), 142.6 (*isq* aryl-C), 135.4 (*isq* aryl-C), 132.7 (*isq* aryl-C), 132.4 (*bda* aryl-C), 131.4 (*q*, $^2J_{CF} = 35$ Hz, *bda* aryl-C), 129.0 (*isq* aryl-C), 129.0 (*isq* aryl-C), 127.8 (*isq* aryl-C), 126.8 (*bda* aryl-C), 126.7 (*isq* aryl-C), 125.2 (*bda* aryl-C), 123.5 (*q*, $^1J_{CF} = 273$ Hz, *bda* -CF₃), 122.5 (*isq* aryl-C), 122.5 (*br*, *bda* aryl-C), 120.5 (*br*, *bda* aryl-C). $^{19}F\{^1H\}$ NMR (CD_2Cl_2/CD_3OD) δ/ppm : 64.16 (-CF₃). UV-vis (CH_2Cl_2) λ_{max}/nm ($\epsilon/M^{-1} cm^{-1}$): 256 (23000), 304 (31000), 419 (16000).

ASSOCIATED CONTENT

Supporting Information. NMR spectra for [(4-CF₃-bda)Ru(pic)₂], electronic absorption spectra for new complexes, additional electrochemical and stopped-flow data, crystallographic details, and cif files. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interests.

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Water oxidation catalysis by series of (R-bda)Ru(L)₂ water oxidation catalysts, including new variants with one and two trifluoromethyl groups in the 4- positions of the bda²⁻ ligand, was studied by electrochemical and stopped-flow kinetics. The rate-limiting step varied with catalyst concentration, with an oxidation step being limiting at higher concentrations (rate = $k_{1,1}[\text{Ru}][\text{Ce}^{\text{IV}}]$) and a bimolecular coupling being limiting at lower concentrations (rate = $k_{2,0}[\text{Ru}]^2$). The effects of bda²⁻ substituents and axial ligands are assessed.