Lability and Basicity of Bipyridine-Carboxylate-Phosphonate Ligand Accelerate Single-Site Water Oxidation by Ruthenium-Based Molecular Catalysts

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Supporting Information

ABSTRACT: A critical step in creating an artificial photosynthesis system for energy storage is designing catalysts that can thrive in an assembled device. Single-site catalysts have an advantage over bimolecular catalysts because they remain effective when immobilized. Hybrid water oxidation catalysts described here, combining the features of single-site bis-phosphonate catalysts and fast bimolecular bis-carboxylate catalysts, have reached turnover frequencies over 100 s⁻¹, faster than both related catalysts under identical conditions. The new [(bpHc)Ru(L)2] (bpH₂cH = 2,2′-bipyridine-6-phosphonic acid-6′-carboxylic acid, L = 4-picoline or isoquinoline) catalysts proceed through a single-site water nucleophilic attack pathway. The pendant phosphonate base mediates O–O bond formation via intramolecular atom-proton transfer with a calculated barrier of only 9.1 kcal/mol. Additionally, the labile carboxylate group allows water to bind early in the catalytic cycle, allowing intramolecular proton-coupled electron transfer to lower the potentials for oxidation steps and catalysis. That a single-site catalyst can be this fast lends credence to the possibility that the oxygen evolving complex adopts a similar mechanism.

INTRODUCTION

As humanity continues to improve in renewable technologies for harvesting energy, so too must we improve in methods to store that energy for later use. A promising yet largely unrealized strategy for effective energy storage is through its conversion to chemical potential energy. The conversion of water to hydrogen or carbon dioxide to reduced carbon products such as methanol or ethanol can form the basis for a carbon-neutral fuel cycle. The development of catalysts for these fuel-forming reactions is an active area of research. In addition, an effective water- or CO₂-reducing system also requires an excellent oxidant-forming catalyst. The natural choice of oxidant is O₂, produced by the oxidation of water. Water oxidation is a 4-electron, 4-proton process that requires an excellent oxidant-forming catalyst. The natural water oxidation is catalyzed by the oxygen-evolving complex (OEC) in photosystem II (PSII). Two general mechanisms have been proposed for the key O–O bond formation step in the OEC: (1) water nucleophilic attack (WNA) of a free or Ca-bound water molecule on a Mn⁵-oxo or Mn⁷-oxyl and (2) O–O radical coupling between either Ca and Mn-oxyl radicals, or between a Mn-oxyl radical and a bridging Mn-oxo (I2M). Artificial molecular catalysts form O–O bonds through analogous mechanisms. Llobet and co-workers reported a dinuclear Ru catalyst for which O–O bond formation takes place via intramolecular interaction of two Ru⁵-oxo moieties with significant Ru⁴⁺-oxyl character (intramolecular I2M). Sun and co-workers reported a family of mononuclear catalysts ([[(bda)Ru(L)₂]]; bda²⁻ = 2,2′-bipyridine-6,6′-dicarboxylate, L = a monodentate ligand) with water oxidation rates comparable to that of the OEC using high concentrations of Ce⁴⁺ as the sacrificial oxidant. O–O bond formation for these catalysts also takes place via radical coupling of two Ru⁴⁺-oxo moieties with significant Ru⁴⁺-oxyl character, but in this case this key step is bimolecular (intramolecular I2M). While in solution these catalysts exhibit high turnover frequency (TOF) and turnover number (TON) values, when tethered to a surface their bimolecular mechanism is severely inhibited and TOF decreases by more than 3 orders of magnitude.

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It was demonstrated relatively recently that only a single metal active site is needed to catalyze water oxidation. This revelation opened the door for the development of a large number of mononuclear single-site catalysts. Reported by Meyer and co-workers, the accepted mechanism for these single-site catalysts involves the generation of an electrophilic Ru oxo, which then undergoes nucleophilic attack by a water molecule (WNA). The key aspect of the WNA mechanism is a concerted oxygen-atom proton transfer (APT) step in which the Ru oxo transfers an oxygen atom to the incoming water molecule while an external base accepts a proton from the water molecule in a concerted fashion. This nomenclature originates from the analogy of this reaction to previously studied oxygen-atom transfer reactions from Ru oxo to phosphines, dimethyl sulfoxide, and dimethyl sulfide, in which the nucleophilic substrate attacks the electrophilic oxo. The highly organized nature of the APT step imposes a significant entropic barrier, consistent with the fact that single-site catalysts are typically quite slow, especially at low pH. Rates greater than 1 s⁻¹ have only been measured electrochemically and at high pH, where proton transfer is facile due to better proton-accepting buffers, or completely avoided due to significant concentrations of hydroxide. Several important questions arise: First, considering that the OEC oxidizes water on the millisecond time scale, is it reasonable to consider WNA as a potential mechanism for the OEC? Second, is it reasonable to pursue single-site catalysts that might never reach the required TOFs for potential applications in artificial photosynthesis? Batista and co-workers showed that some single-site catalysts are slowly but irreversibly converted to more robust oxo-bridged dinuclear catalysts and posed the question: Is one site really enough?

Local proton management is of key importance in the APT step for single-site catalysts. Recognizing this led to enhancements of up to ~10⁴ in the rate constant for base-mediated APT by changing the pH of the base of the buffer acting as the proton acceptor in this step (with catalytic rates increasing from 3.5 × 10⁻³ to 4.8 s⁻¹ with H₂O and HPO₄²⁻, respectively). Nevertheless, a significant entropic penalty is paid due to a highly organized transition state (TS) where the Ru oxo, the incoming water molecule, and the base are required to arrange in a specific orientation. We were able to circumvent this problem by strategically positioning the base as part of the ligand in catalysts of the type [(bpaH₂)Ru(L)₂] as well as faster oxidations in the catalyst activation steps via intramolecular proton-coupled electron transfer (i-PCET). The combination of these features results in the fastest single-site catalysts reported in acidic solution to date with the hybrid systems outperforming both the [(bpaH₂)Ru(L)₂] and the [(bda)Ru(L)₂] "parent" compounds under identical conditions.

**RESULTS AND DISCUSSION**

**Synthesis and Characterization.** The hybrid ligand precursor 6-carboxy-6′-phosphono-[2,2′-bipyridine]-6-carboxylic acid (bpaH₄) and its derivatives were synthesized in three steps with 62% overall yield from the known compound 6′-bromo-[2,2′-bipyridine]-6-carboxylic acid, as shown in Figure S1. Following esterification of the acid in methanol, palladium-catalyzed coupling with diethylphosphonate converted the bromo to a phosphonate acid ester. Treatment with hydrochloric acid hydrolyzed both the phosphonate and carboxylate esters, providing the free protonated phosphonic-carboxylic acid bpaH₄HCl.

Ruthenium(II) complexes [(bpHc)Ru(L)₂] were synthesized in 51% (L = 4-picoline) and 86% (L = isoquinoline) yield from bpaH₄HCl-[4-picoline]²⁺-[isoquinoline]²⁺. NMR spectroscopy and elemental analysis characterized the complexes. These new catalysts retain the base-assisted, low-activation-energy i-APT pathway for O₂-O bond formation while also allowing water coordination at the Ru³⁺ state, leading to a significant reduction in overpotentials with respect to [(bpa)RuIII(L)₂] as well as faster oxidations in the catalyst activation steps via i-PCET.

**Figure 1.** Ligands 2,2′-Bipyridine-6,6′-dicarboxylic Acid (bdaH₂), 6′-Phosphono-[2,2′-bipyridine]-6-carboxylic Acid (bpaH₄), and Their Corresponding Ruthenium(V)-Oxo Complexes

L is a monodentate ligand, typically 4-picoline or isoquinoline.
[(HNET$_3$)][(bpc)Ru(L)$_2$] were then redissolved in aqueous NaOH and precipitated with acid. Aerobic oxidation of [(bpHc)Ru$_{III}$(L)$_2$] produced ruthenium-(III) complexes, which were isolated and characterized crystallographically. Solutions of [(bpHc)Ru$_{III}$(L)$_2$] are slowly oxidized in air, producing the ruthenium(III) complexes [(bpc)Ru(L)$_2$] (or [(bpHc)Ru$_{III}$(L)$_2$]$^+$ at low pH), and then uncharacterized further oxidized products. Cooling to 4 °C effected crystallization of the Ru$_{III}$ complexes. Figure 1 (left) shows the [(bpHc)Ru$_{III}$(pic)$_2$]$^+$ cation with an adjacent water molecule, which is hydrogen-bonded to the phosphonic acid group. [(bpc)Ru$_{III}$(isq)$_2$] was crystallized as the neutral deprotonated complex at neutral pH, shown in Figure 1 (right).

The major structural difference between the bpc-ruthenium-(III) complexes and their diphosphonate and dicarboxylate counterparts is the decrease of the O$^-$Ru$^-$O angle from [(bda)Ru$_{III}$(pic)$_2$]$^+$ (126.39(7)°) and [(bda)Ru$_{III}$(isq)$_2$]$^+$ (126.0(3)°) to [(bpc)Ru$_{III}$(isq)$_2$] (117.63(10)°) to [(bpa)-Ru$_{III}$(isq)$_2$]$^-$ (112.09(6)°). This is the result of the longer C$^-$P and P$^-$O bond distances in the phosphonate group compared to the C$^-$C and C$^-$O bond distances in the carboxylate group as well as the smaller C$^-$P$^-$O angle (sp$^3$ hybridization at P) compared to the C$^-$C$^-$O angle (sp$^2$ hybridization at C) in the carboxylate group. A comparison of the bond distances and O$^-$Ru$^-$O angle between [(bpc)Ru(isq)$_2$] and [(bda)Ru(isq)$_2$]$^+$ is shown in Figure 2. Protonation of the uncoordinated P$^-$O group causes a small contraction of the bound P$^-$O from 1.563(3) Å in [(bpc)Ru$_{III}$(isq)$_2$] to 1.537(5) Å in [(bpHc)Ru$_{III}$(pic)$_2$]$^+$ and an elongation in the Ru$^-$O bond from 2.012(2) Å in [(bpc)Ru$_{III}$(isq)$_2$] to 2.049(3) Å in [(bpHc)Ru$_{III}$(pic)$_2$]$^+$. The Ru$^-$N$_{np}$ bond is also 0.04 Å longer in the protonated complex. As a result, the O$^-$Ru$^-$O angle is widened in [(bpHc)-Ru$_{III}$(pic)$_2$]$^+$ to 120.05(17)°.

Electrochemical Characterization and Catalytic Water Oxidation. Electrochemical measurements showed that while the Ru$_{III/II}$ oxidation potential for the bpc complexes are similar to those of the bpa complexes, the Ru$_{IV/III}$ couple and the onset for water oxidation catalysis for the bpc complexes are both about 200 mV lower in potential. Figure 3 shows cyclic voltammograms (CVs) and square wave voltammograms (SWVs) for [(bpHc)Ru(pic)$_2$][ClO$_4$] and [(bpHc)Ru(isq)$_2$]$^+$ at pH 1 (0.10 M HClO$_4$). The Ru$_{IV/III}$ couples for the bpc complexes are reversible and similar in potential to the bpa complexes, appearing at 0.65 V for [(bpHc)Ru(pic)$_2$] and 0.68 V for [(bpHc)Ru(isq)$_2$] (all potentials are reported vs NHE). The Ru$_{IV/III}$ couple appears at 1.40 V for [(bpHc)Ru(pic)$_2$] and at 1.41 V for [(bpHc)Ru(isq)$_2$] and is not chemically reversible on the CV time scale. Immediately following the Ru$_{IV/III}$ wave is a sharp increase in current corresponding to catalytic water oxidation. The onset of catalysis at approximately 1.50 V corresponds to an overpotential of 330 mV at pH 1. SWV finds the Ru$_{IV/III}$ potential at
stopped-catalysts, 50 supporting the notion that the water binding and showed a slope close to 1 (see Figure S11), consistent with 

\[ \text{rate law for the cerium(IV)-driven catalytic water oxidation by} \]

M HNO₃ due to their poor solubility in HClO₄ (see Figures S8 and S9). A plot of background-corrected catalytic current \( (i_{\text{ca}}) \) at 1.60 V vs \([(bpHc)Ru(pic)_2][ClO_4] \) catalyst concentration showed a linear dependence and a plot of \(-\log\left(i_{\text{ca}}\right)\) vs \(-\log\left([\text{catalyst}]\right)\) showed a slope close to 1 (see Figure S11), consistent with stopped-flow measurements and the first-order single-site mechanism proposed below.

Kinetics of \([(bpHc)Ru(L)_2]\)-Mediated Water Oxidation.

Stopped-flow kinetic measurements were used to determine the rate law for the cerium(IV)-driven catalytic water oxidation by the bpc-Ru catalysts. Aqueous solutions of catalyst with concentrations 6 μM to 150 μM were mixed with 1.5 mM ceric ammonium nitrate (CAN, \( E = 1.6 \text{ V} \)) in 0.20 M HNO₃ and the consumption of cerium(IV) was monitored using its absorption at 360 nm. Under these conditions, the cerium(IV) was consumed with a first-order dependence, and the rate was found to be first order in catalyst as well, as shown in eq 1 (see Figures S13 and S14).

\[ \frac{-d[\text{Ce}^{IV}]}{dt} = k_{1,1}[\text{catalyst}][\text{Ce}^{IV}] \tag{1} \]

The rate law suggests that the rate-determining step (RDS) is an oxidation of the catalyst by cerium(IV). The experimental rate constants \( k_{1,1} \) for this step are \( 1.2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1} \) for \([(bpHc)Ru(pic)_2][ClO_4] \) and \([(bpHc)Ru(isq)_2] \), respectively. This constitutes a 10-fold improvement over the bpc catalysts and a ~10-fold improvement over the bda catalysts, 50 supporting the notion that the water binding and more accessible r-PCET oxidations of the bpc complexes result in faster oxidations.

According to the experimental rate law, the TOF \( (= \text{[O}_2]/\text{dt}/[\text{catalyst}] \) for the bpc catalysis should be proportional to \([\text{Ce}^{IV}] \) and up to 107 s⁻¹ was reached for 100 μM \([(bpHc)Ru(isq)_2] \) with 1.5 mM cerium. For comparison, TOF = 65 s⁻¹ for 100 μM \([(bda)Ru(isq)_2] \) and TOF = 0.77 s⁻¹ for 100 μM \([(bpaH2)Ru(isq)_2] \) with 2.0 mM cerium. Table 1 shows a comparison of TOFs under various conditions for the three families of catalysts.

| catalyst | \( k_{1,1} \) (M⁻¹ s⁻¹) | [catalyst] (μM) | \( k_{obs} \) (s⁻¹) | TOF (s⁻¹) | TON | conditions^
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<td>50</td>
<td>1.11</td>
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<td>10</td>
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\(^{a}\)\( k_{obs} = -\left(d[\text{Ce}^{IV}]'/dt\right)\)\([\text{catalyst}] = k_{1,1}[\text{catalyst}] \)

\(^{b}\)\( \text{TOF} = \left(d[\text{O}_2]/\text{dt}\right)/([\text{catalyst}] = \left(k_{obs}[\text{Ce}^{IV}]\right)/(4[\text{catalyst}] \)

Conditions: A = 1.5 mM CAN, 0.10 M HNO₃; B = 2.0 mM CAN, 0.10 M HNO₃; and C = 2.0 mM CAN, 0.10 M HClO₄ with 10% CH₃CN. 50

Oxygen production was verified in separate experiments using gas chromatographic analysis of the headspace after reactions in closed vessels and the yields were 93% with \([(bpHc)Ru(pic)_2][ClO_4] \) and 88% with \([(bpHc)Ru(isq)_2] \) with respect to CeIV used. High yields were also recorded by pressure measurements with CAN concentrations up to 0.365 M; however, these conditions actually led to lower TOFs for \([(bpHc)Ru(L)_2] \), revealing an inverse relationship between the rate and \([\text{Ce}^{IV}] \) under these conditions. This is indicative of an inhibitory reaction pathway involving the cerium. Indeed, experimental TONs with cerium(IV) were limited to 67 for \([(bpHc)Ru(isq)_2] \) and 28 for \([(bpHc)Ru(pic)_2][ClO_4] \). We suppose this may be due to interaction between the cerium and the deprotonated phosphonate ligand, 59–64 blocking its pendant base function (vide infra). Results of catalytic cerium(IV)-driven experiments showed the catalysts to be fast and efficient but raised questions about their durability.

To determine whether the low TON values are general for bpc catalysts or are the result of specific interactions with cerium, we explored \([\text{CoIII/II(OH}_2)_6]^{3+/2+} \) or the catalyst. 57 On the other hand, the TOF reaching only 0.44 s⁻¹ for \([(bpaH2)Ru(isq)_2] \) with 2.0 mM cerium (vide infra) shows a comparison of TOFs under various conditions for the three families of catalysts.

The rate law suggests that the rate-determining step (RDS) is an oxidation of the catalyst by cerium(IV). The experimental rate constants \( k_{1,1} \) for this step are \( 1.2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1} \) for \([(bpHc)Ru(pic)_2][ClO_4] \) and \([(bpHc)Ru(isq)_2] \), respectively. This constitutes a 10-fold improvement over the bpa catalysts and a ~10-fold improvement over the bda catalysts, 50 supporting the notion that the water binding and more accessible r-PCET oxidations of the bpc complexes result in faster oxidations.

According to the experimental rate law, the TOF \( (= \text{[O}_2]/\text{dt}/[\text{catalyst}] \) for the bpc catalysis should be proportional to \([\text{Ce}^{IV}] \) and up to 107 s⁻¹ was reached for 100 μM \([(bpHc)Ru(isq)_2] \) with 1.5 mM cerium. For comparison, TOF = 65 s⁻¹ for 100 μM \([(bda)Ru(isq)_2] \) and TOF = 0.77 s⁻¹ for 100 μM \([(bpaH2)Ru(isq)_2] \) with 2.0 mM cerium. Table 1 shows a comparison of TOFs under various conditions for the three families of catalysts.
**Figure 4. Proposed mechanism for water oxidation by \([\text{bpHcRu(L)}_2]\) catalysts at pH 1, showing only the immediate coordination environment in the plane of the active site, with transient intermediates in brackets (bpH_2CH = 6′-phosphono-\[2,2′\]-bipyridine]-6-carboxylic acid, L = 4-picoline or isoquinoline). Values for \(E^\circ\), \(\Delta G\), and \(pK_a\) are from DFT calculations.**

Similarly in cobalt-driven reactions, with the former reaching a higher TON (see Figure S16). These results show that the bpc catalysts can achieve relatively high TON. Together, the electrochemical, cerium-driven, and cobalt-driven experiments indicate that the bpc single-site catalysts are both fast and durable.

**Water Oxidation Mechanism.** The mechanism of water oxidation by \([\text{bpHcRu(L)}_2]\), established by complementing the aforementioned kinetic studies with DFT calculations. Experimental studies of higher oxidation state intermediates were stymied by the proximity and overlapping signals of the Ru IV/III couple, the Ru V/IV couple, and the catalytic water oxidation wave. Consequently, the most favorable pathway for O_2 production was probed computationally and is shown in Figure 4. The mechanism can be separated into a few phases that are common to all water oxidation catalysts: (1) oxidative activation of the catalyst, (2) O–O bond formation, (3) oxidation of hydroperoxide/peroxide intermediates, and (4) O_2 evolution.

**Oxidative Activation of the Catalyst.** Beginning from \([\text{bpHcRu}^0(L)_2]\), the first step toward catalysis is oxidation to ruthenium(III). The calculated redox potential for the couple \([\text{bpHcRu}^{III}(py)_2]/[\text{bpHcRu}^{II}(py)_2]\) at pH 0 is 0.53 V, close to the experimental value of 0.66 V for \([\text{bpHcRu}^{III}(pic)_2]/[\text{bpHcRu}^{II}(pic)_2]\). The pK_a of the phosphonic acid in \([\text{bpHcRu}^{III}(pic)_2]\) is about 1.0 (calc 1.03), as shown in the Pourbaix diagram (Figure S11). Above pH 1, the Ru IV/III potential decreases with increasing pH until the pK_a of \([\text{bpHcRu}^{III}(pic)_2]\) is reached (expt \(\approx 4\), calc = 3.8).

The steps preceding O–O bond formation require binding of a water molecule and oxidative activation to reach a reactive metal-oxo. The bound water molecule also serves to moderate the rate of a water molecule and oxidative activation to reach a reactive metal-oxo. The bound water molecule also serves to moderate the rate of the overall charge.

Our previous generation single-site catalyst, \([\text{bpaH}_2\text{Ru(L)}_2]\), binds a water molecule at the ruthenium(IV) state, and oxidation of \([\text{bpaRu}^{II}(L)_2]^–\) to \([\text{bpaRu}^{III}(L)_2]\) is pH-independent, taking place at \(1.6\) V.\(^{54}\) For the well-known bimolecular catalysts \([\text{bdaRu(L)}_2]\), this water binding occurs at \([\text{bdaRu}^{II}(L)_2]^+\) to generate \([\text{bdaRu}^{III}(L)_2(OH)_2]^+\). A 20-electron \([\text{bdaRu}^{II}(L)_2(OH)_2]\) complex has been proposed;\(^{59,60}\) however, our calculations find this to be \(\sim 10\) kcal/mol higher in energy relative to \([\text{bdaRu}^{III}(L)_2]\). In \([\text{bdaRu}^{III}(py)_2(OH)_2]^+\), the free carboxylate is hydrogen-bonded to the coordinated water molecule, and proton transfer from the water molecule to the carboxylate to form \([\text{bdaRu}^{III}(py)_2(OH)]^+\) at pH 0 is 0.53 V, \(pK_a = -1.4\). As a result, oxidation of \([\text{bdaRu}^{III}(py)_2(OH)]^+\) to seven-coordinate \([\text{bdaRu}^{IV}(py)_2(OH)]^+\) is facile and pH-dependent.

Similiar water-binding behavior is observed here for \([\text{bpcRu}^{III}(py)_2]\) (step A in Figure 4), but the equilibrium favors \([\text{bpcRu}^{III}(py)_2(OH)]^+\) over \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) with \(pK_a = 0.15\). This is consistent with the more sluggish Ru IV/III couple for \([\text{bpHcRu(L)}_2]\) observed by voltammetry compared to that of \([\text{bdaRu(L)}_2]\). The calculated potential for oxidation of \([\text{bpcRu}^{III}(py)_2(OH)]^+\) to seven-coordinate \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) is 1.15 V, while that of \([\text{bpcRu}^{III}(py)_2(OH)]^+\) to seven-coordinate \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) is 1.37 V (step B), closer to the experimental value of 1.4 V. The calculated pK_a values for \([\text{bpcRu}^{III}(py)_2(OH)]^+\) and \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) are \(-0.08\) and \(-1.41\), respectively, and deprotonation ultimately provides seven-coordinate \([\text{bpcRu}^{IV}(py)_2(OH)]^+\), regardless of the oxidation pathway (step C).

The final step in the oxidative activation process is a PCET oxidation from \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) to \([\text{bpcRu}^{IV}(py)_2(O)]^+\). The phosphate arm of the bpc^− ligand acts as the initial proton acceptor in an intramolecular PCET process (i-PCET), with the potential for oxidation of \([\text{bpcRu}^{IV}(py)_2(OH)]^+\) to \([\text{bpcRu}^{IV}(py)_2(O)]^+\) calculated as 1.28 V (step D). The low potential is consistent with the overlapping waves observed electrochemically. The calculated pK_a for \([\text{bpcRu}^{IV}(py)_2(O)]^+\) is 0.45, and proton transfer to the bulk follows to generate \([\text{bpcRu}^{IV}(py)_2(O)]^+\), the active form of the catalyst (step E).

**O–O Bond Formation.** While the kinetic data do not definitively establish the nature of the O–O bond-forming step, when combined with TS calculations, strong support for single-site WNA catalysis emerges. Selected free energies of activation from DFT calculations are listed in Table 2, and the WNA and 12M TS structures for \([\text{bpcRu}^{IV}(isq)_2(O)]\) are shown in Figure 5. The cerium(IV)-driven experiments down to 6 μM catalyst exhibit a first-order dependence on both catalyst and cerium(IV). Electrochemical experiments also find a first-order
WNA mechanism predict this to be the favored pathway for the case. Furthermore, calculated barriers for the catalysts were a bimolecular step involved, which is not the second-order behavior for the bpc catalysts. The barriers for nucleophilic attack of a water molecule on [(bpc)Ru\(\text{V}(\text{py})(\text{O})\)] and [(bpc)Ru\(\text{V}(\text{isq})(\text{O})\)] with concomitant proton transfer to the phosphate, which temporarily decoordinates, to generate [(k\textsuperscript{3-bp}Hc-Ru\textsuperscript{III}(L)\textsubscript{2}(OOH))] (step F) are 11.7 and 9.1 kcal/mol, respectively, similar to the 10.2 kcal/mol barrier calculated for [(bpa)Ru\(\text{V}(\text{py})(\text{O})\)]\textsuperscript{+}.\textsuperscript{41} The oxo-oxo coupling barriers are significantly higher (21.0 and 16.5 kcal/mol for [(bpc)-Ru\(\text{V}(\text{py})(\text{O})\)] and [(bpc)Ru\(\text{V}(\text{isq})(\text{O})\)], respectively), although they are significantly lower than that for [(bpa)-Ru\(\text{V}(\text{py})(\text{O})\)]\textsuperscript{+}. In contrast, for [(bda)Ru\(\text{V}(\text{isq})(\text{O})\)]\textsuperscript{+}, the single-site APT pathway with proton transfer to an external water molecule is much less favorable (\(\Delta G\textsuperscript{\ddagger}\) = 29.8 kcal/mol) than the bimolecular I2M (\(\Delta G\textsuperscript{\ddagger}\) = 13.2 kcal/mol). A difference of 3.2 kcal/mol in free energies of activation for the O–O coupling step between [(bda)Ru\(\text{V}(\text{isq})(\text{O})\)]\textsuperscript{+} (\(\Delta G\textsuperscript{\ddagger}\) = 13.2 kcal/mol) and [(bpc)Ru\(\text{V}(\text{isq})(\text{O})\)] (\(\Delta G\textsuperscript{\ddagger}\) = 16.5 kcal/mol) is actually significant. Similar differences in calculated free energies of activation between members of the series [(bda)Ru\(\text{V}(4-X-\text{py})(\text{O})\)]\textsuperscript{+} (X = H, Cl, Br, I) and [(bda)-Ru\(\text{V}(6-X-\text{isq})(\text{O})\)]\textsuperscript{+} (X = H, F, Cl, Br, OMe) result in differences of an order of magnitude or more for the experimentally determined O–O coupling rate constants.\textsuperscript{46} Once again, if the bimolecular mechanism was operational for [(bpc)Ru\(\text{V}(\text{L})(\text{O})\)], we should expect to see evidence for it at much higher concentrations than for the corresponding [(bda)Ru\(\text{V}(\text{L})(\text{O})\)]\textsuperscript{+} catalysts.

The single-site mechanism is expected to be operational for all pH \(\geq 1\) because the APT step is only accelerated in the presence of additional base, while the I2M step should not be pH-dependent. However, the rate-determining step may change with increasing pH as the PCET oxidations become faster and the non-proton-coupled steps remain unaffected.

A hydrogen-bonding interaction between the protonated phosphonate of the intermediate hydroperoxide, [(k\textsuperscript{3-bp}Hc-Ru\textsuperscript{III}(py)(OOH))]\textsuperscript{+}, results in a pK\(\text{a}\) much higher than the preceding [(bpc)Ru\textsuperscript{III}(py)(OOH)]\textsuperscript{+} intermediate (3.73 vs 1.03). Thus, this is the most stable species under catalytic conditions. From this point, additional oxidation steps are required for the reaction to progress toward O\(_2\) release.

O\(_2\) Evolution. Additional oxidation and proton loss steps are required until oxygen release becomes favorable. These steps are not expected to be rate-limiting because the calculated potentials required are all lower than those to reach Ru\textsuperscript{III}=O. The calculated potential for one-electron oxidation of six-coordinate [(k\textsuperscript{3-bp}Hc-Ru\textsuperscript{III}(py)(OOH))] to seven-coordinate [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+} is 1.20 V, below the preceding Ru\textsuperscript{IV/III} and Ru\textsuperscript{V/IV} oxidative activation potentials. [(bpc)-Ru\textsuperscript{V}(py)(OOH)]\textsuperscript{+} has a calculated pK\(\text{a}\) of –0.68 for the phosphonic acid. Consequently, oxidation of [(k\textsuperscript{3-bp}Hc)-Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+} is most likely a PCET process, forming [(bpc)Ru\textsuperscript{IV}(py)(OOH)] (step G), and the calculated [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+}/[(k\textsuperscript{3-bp}Hc-Ru\textsuperscript{IV}(py)(OOH)] potential of 1.20 V is an upper limit. In addition, the triplet [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+} is more stable than the singlet [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+} by 6.6 kcal/mol.

Oxygen evolution from [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+} to generate O\(_2\) and [(bpc)Ru\textsuperscript{IV}(py)(OOH)] is a spin-allowed and energetically favorable process with \(\Delta G = –20.1\) kcal/mol, but it is kinetically inhibited at low pH where [(bpc)-Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+}, which has a pK\(\text{a}\) of 3.24, is the dominant species. Yet this is not an impediment because only 1.06 V is required for the i-PCET oxidation of [(bpc)Ru\textsuperscript{IV}(py)(OOH)]\textsuperscript{+}.
to $\Delta^1$(bpHc)Ru(V)(py)(OO)$^-$ (step H). The calculated $k_F$ for the latter is $-0.82$ and proton transfer to the bulk yields $\Delta^1$(bpRuV)(py)(OO)$^-$ (step I).

Oxygen release (step J) is facile and spontaneous from both the doublet and quartet spin states of $\{($bpRuV)(py)$_2$(OO)$\}$. Attempts to optimize $\{($bpRuV)(py)$_2$(OO)$\}^+$ led to spontaneous $^3$O$_2$ release and regeneration of $\{($bpRuV)(py)$_2$(OO)$\}^-$ and $^3$O$_2$ release from $\{($bpRuV)(py)$_2$(OO)$\}^+$ is very favorable with $\Delta G = -34.6$ kcal/mol. The resulting $\{($bpRuV)(py)$_2$(OO)$\}^-$ re-enters the catalytic cycle.

The kinetic data discussed above suggest that the RDS is one of the oxidation steps. Based on the potentials, the Ru(V) = Ru(IV) oxidation should be the most difficult, but ruthenium-IV/III oxidations are known to be particularly slow.62

### CONCLUSION

Single-site water oxidation catalysts featuring the new hybrid bpy−phosphinate−carboxylate ligand (bpHc) improve upon bpy-bisphosphonate (bpHc) catalysts with 200 mV lower overpotential (330 mV at pH 1) and 50x faster catalysis. Though turnover numbers for our new catalysts were limited to TONs up to 1600 were reached with cobalt(III) as the oxidant. When properly designed, one site is still enough for bimolecular catalysis, which tend to struggle when confined on semiconductor surfaces. Surface studies with these catalysts are ongoing.

### EXPERIMENTAL SECTION

#### Synthetic Methods and Materials.

The complexes described below are mild air-sensitive. Reactions were carried out under argon using standard Schlenk techniques at ambient temperature (21±2°C), unless otherwise noted. Workup and purification were performed in air. A vacuum desiccator was used for long-term storage.

#### Physical Methods.

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 400 spectrometer. $^1$H NMR spectra were referenced to TMS using the residual protio impurities of TMS as the reference. $^13$C NMR spectra were referenced to TMS using the $^13$C natural abundance of the solvent. $^{31}$P and $^{31}$P NMR spectra, and $^13$C NMR spectra in D$_2$O, were referenced to CFC$_3$H$_2$PO$_4$ and TMS, respectively, using the $\delta$ scale with the corresponding $^1$H spectra. All chemical shifts are reported in the standard $\delta$ notation in parts per million; positive chemical shifts are a higher frequency than the reference. Electronic absorption spectra were recorded using an Agilent 8453 UV−vis spectrophotometer. Electrospray ionization mass spectrometry (ESI-MS) was performed on a Thermo Finnigan LC Advantage LC/MS/MS using methanol as the eluent, or at the Institute of Chemical Biology and Drug Discovery Analytical Instrumentation Laboratory in the Chemistry department at SUNY-Stony Brook on an Agilent LC-MSD using a methanol/aqueous eluent. Elemental analyses were performed by Robertson Microlit Laboratories (Ledgewood, NY, USA). Crystal structure data files have been deposited at the Cambridge Crystallographic Data Centre as CCDC 1541006 and CCDC 1541007 and can be obtained via www.ccdc.cam.ac.uk/structures/.

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. The reference electrode was calibrated to the ruthenium(III)/II couple of an internal [Ru(bpy)$_3$]$_2^+$ standard at 1.26 V vs NHE.63 Unless otherwise noted, solutions contained 1.0 mM analyte in aqueous solution containing nitric acid, phosphate buffer, or acetate buffer solutions.

Stopped-flow kinetic measurements were performed at 25 ± 0.1°C with an Olis rapid scanning monochromator (Oils RSM-1000) equipped with an Olis USA stopped-flow. Pressure measurements were obtained with a Honeywell SDX047A-A or SDX052-A pressure sensor connected via an instruNet 1555 data acquisition system. TOFs were calculated from the observed rate constants ($k_{obs}$) extracted from the data fitted with SPECFIT/32. Rate laws and overall rate constants ($k_{obs}$) were determined from plots of log[initial rate] vs log[catalyst] and $k_{obs}$ vs [Ru], respectively. Gaseous products were analyzed by gas chromatography (GC) on an Agilent 6890N GC system.

#### Synthesis of (bpHc)Ru(isq)(isq)$_2$:[RuCl$_2$(C$_6$H$_6$)]$_2$ ($149.7$ mg, $0.38$ equiv) was suspended in 16 mL anhydrous methanol. The mixture was degassed by bubbling with argon for 10 min, then heated to reflux for 3 h. The dark purple reaction mixture was removed from heat and treated with triethylamine ($518 \mu$L, $3.72$ mmol, $6.8$ equiv) and isquinoline ($149 \mu$L, $1.27$ mmol, $2.32$ equiv). After an additional 11.5 h reflux, the dark orange reaction mixture was cooled to room temperature and filtered. The filtrate was evaporated to dryness. The resulting residue was redisolved in 3 mL 0.05 M NaOH(aq) and filtered with a syringe filter. An additional 2 x 1 ml of 0.05 M NaOH(aq) was used to rinse the remaining residue from the flask and filter. To the resulting solution was added 1.5 mL 0.5 M HClO$_4$ which effected precipitation of the product. After filtration, the brown solid was washed with 3 x 2 mL of 0.1 M HClO$_4$ and 2 x 5 mL of Et$_2$O and then dried in vacuo. Elemental analysis showed that the solid retained approximately 1 equiv H$_2$O ($339.1$ mg, $93\%$).

$^1$H NMR (400 MHz, 0.10 M NaOD) δ (ppm): $8.33$ (d, $J_{HH} = 8.0$ Hz, 1H, aryl−H), $8.24$ (d, $J_{HH} = 7.8$ Hz, 1H, aryl−H), $8.01$ (s, 2H, isoquinoline−H), $7.81$ (d, $J_{HH} = 5.9$ Hz, 1H, aryl−H), $7.66$−$7.59$ (m, 2H, aryl−H), $7.55$ (d, $J_{HH} = 6.5$ Hz, 2H, isoquinoline−H), $7.44$ (t, $J_{HH} = 7.9$ Hz, 1H, aryl−H), $7.22$−$7.04$ (m, 5H, isoquinoline−H), $7.01$ (t, $J_{HH} = 7.4$ Hz, 2H, isoquinoline−H), $1.5H_2O$: $298$ (35 900), $164.3$ (d, $J_{HC} = 217$ Hz, aryl−C), $161.0$ (aryl−C), $158.9$ (d, $J_{HC} = 9$ Hz, aryl−C), $155.3$ (aryl−C), $155.1$ (aryl−C), $143.0$ (aryl−C), $140.0$ (aryl−C), $132.9$ (d, $J_{HC} = 8$ Hz, aryl−C), $131.5$ (aryl−C), $130.4$ (aryl−C), $127.9$ (aryl−C), $127.8$ (aryl−C), $127.3$ (d, $J_{HC} = 17$ Hz, aryl−C), $126.6$ (aryl−C), $125.8$ (aryl−C), $125.8$ (aryl−C), $124.8$ (aryl−C), $124.1$ (aryl−C), 31P{1H} NMR (162 MHz, 0.10 M NaOD) δ (ppm): $25.4$ UV−vis (0.1 M HNO$_3$) $\lambda_{max}$ (nm) (ε/M cm$^{-1}$): $298$ (35 900), $406$ (14 500), $331$ (7560). ESI-MS (H$_2$O) m/z (calcd, found): $\{$(bpHc)Ru(isq)$_2$$\}^+$, $+1^+$ (639.0, 638.9), $\{$(bpHc)Ru(isq)$_2$$\}^+$, $+2^+$ (660.0, 660.9). Analysis (calcd, found): for C$_{15}$H$_{26}$O$_7$ (M+H)$_2^+$ $C$ (52.41, 52.53), $H$ (3.64, 3.52), $N$ (8.43, 8.40).

### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b06096.

Additional methods, including syntheses and characterization, electrochemical data, kinetic data, crystallographic details, computational details, and structures, including Figures S1−S19 and Tables S1–S6 (PDF).
X-ray crystallographic data for [(bpHc)Ru(pic)2][ClO4]-H2O (CIF)

X-ray crystallographic data for [(bpc)Ru(isq)2]·5H2O (CIF)

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The authors declare no competing financial interest.

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■ REFERENCES

(58) Pyridine is used in place of picoline due to the facile rotation of the methyl group. Results are generally in agreement with experiment where available.


