Oxygen Atom Transfer and Oxidative Water Incorporation in Cuboidal Mn₃MOₙ Complexes Based on Synthetic, Isotopic Labeling, and Computational Studies

Jacob S. Kanady,§‡ Jose L. Mendoza-Cortes,‡§ Emily Y. Tsui,§ Robert J. Nielsen,⊥ William A. Goddard, III,§⊥⊥ and Theodor Agapie§⊥⊥

§Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States
⊥Materials and Process Simulation Center, California Institute of Technology, Pasadena, California 91125, United States

ABSTRACT: The oxygen-evolving complex (OEC) of photosystem II contains a Mn₄CaO₄ catalytic site, in which reactivity of bridging oxidos is fundamental to OEC function. We synthesized structurally relevant cuboidal Mn₃MOₙ complexes (M = Mn, Ca, Sc; n = 3, 4) to enable mechanistic studies of reactivity and incorporation of μ-oxido moieties. We found that Mn₃IVCaO₄ and Mn₃IVScO₄ were unreactive toward trimethylphosphine (PMe₃). In contrast, our Mn³⁺Mn⁴⁺O₄ cubane reacts with this phosphine within minutes to generate a novel Mn³⁺O₄ partial cubane plus Me₂PO. We used quantum mechanics to investigate the reaction paths for oxygen atom transfer to phosphine from Mn³⁺Mn⁴⁺O₄ and Mn³⁺CaO₄. We found that the most favorable reaction path leads to partial detachment of the CH₃COO⁻ ligand, which is energetically feasible only when Mn(III) is present. Experimentally, the lability of metal-bound acetates is greatest for Mn³⁺CaO₄. These results indicate that even with a strong oxygen atom acceptor, such as PMe₃, the oxygen atom transfer chemistry from Mn³⁺Mn⁴⁺O₄ is controlled by ligand lability, with the Mn³⁺CaO₄ OEC model being unreactive. The oxidative oxide incorporation into the partial cubane, Mn³⁺O₄, was observed experimentally upon treatment with water, base, and oxidizing equivalents. ¹⁸O-labeling experiments provided mechanistic insight into the position of incorporation in the partial cubane structure, consistent with mechanisms involving migration of oxido moieties within the cluster but not consistent with selective incorporation at the site available in the starting species. These results support recent proposals for the mechanism of the OEC, involving oxido migration between distinct positions within the cluster.

1. INTRODUCTION

Artificial photosynthesis schemes generally involve water as the terminal source of electrons and protons, forming dioxygen as a byproduct.¹ In biological systems, the oxidation of water is performed by the oxygen-evolving center (OEC) of photosystem II (PSII).² The OEC consists of a Mn₄Ca cluster supported by bridging oxidos or hydroxidos and carboxylate and histidine side chains from the protein. Early crystallographic, XAS, and EPR studies³ supported a tetranuclear 3 + 1 arrangement of the four manganese centers, with more recent crystallographic studies proposing a Mn₃CaO₄ heterometallic cubane with a fourth manganese “dangler” bound by a bridging oxide.⁴ The exact structure of the cluster remains under debate, with quantum mechanics (QM) studies suggesting that the recent crystal structure corresponds to a more reduced cluster⁵ and that a more open structure is more consistent with spectroscopic data.⁶

In the catalytic cycle, or Kok cycle, four photogenerated oxidizing equivalents sequentially oxidize the OEC.⁷ Although the oxidation states are still debated,⁸ a common assignment of the intermediates, denoted as Sₙ states (n = 0–4), range in oxidation state from S₄ Mn⁴⁺Mn⁴⁺, to S₃ a putative Mn⁴⁺Mn⁵⁺ or Mn⁴⁺⁺ligand radical that promotes O=O bond formation and O₂ release.²⁹ O–O bond formation has been proposed to involve metal-bound terminal oxo/oxyl, µ₂- or µ₃-oxido moieties (Scheme 1).²⁶,⁹,¹⁰ QM investigations of the mechanism and spectroscopy have been performed in recent years. Quantum mechanics/molecular mechanics (QM/MM) studies support a cubane Mn₃CaO₄ with a Mn dangling arrangement.¹¹ A computational comparison of this¹¹ and more open structures favors an open-cuboidal arrangement.¹₀,¹¹,¹² Mechanistic and spectroscopic studies were recently interpreted most consistent with a mechanism of O–O bond formation involving such an open structure (Scheme 1b).¹²

During the catalytic cycle subsequent to O–O bond formation, new substrate water coordinates to the cluster and is deprotonated.¹³ For the latter mechanisms (Scheme 1b,c), the water must be deprotonated and incorporated into a μ₃-site, and the cluster must be oxidized. Heterogeneous catalysts for water oxidation based on Ca/Mn mixed oxides displaying structural motifs related to the biological active site have been reported,¹⁴ showing that these elementary reaction steps
relevant to practical applications. Thus, systematic studies of well-defined model clusters are an important avenue toward uncovering the reactivity of bridging oxido moieties. Additionally, the requisite oxidative incorporation of water as bridging oxido ligands into complex multimetallic structures is key to fully understanding the mechanism of the OEC and heterogeneous metal oxides.

In addition to studies of the complex biological and heterogeneous systems, synthetic metal-oxido models have provided insight into the reactivity and spectroscopy of high-oxidation state manganese clusters. Tetramanganese cubanes have been invoked in water oxidation catalysis, but more recent reports assign the heterogeneous manganese oxide deposited on the electrode as the active electrocatalyst. Herein, we introduce two new complexes: 

\[ \text{LMn}^{III}_{4} \text{O}^{3} \text{(OAc)}_{3} \] (3) and \[ \text{LMn}^{IV}_{5} \text{Scn}^{3+} \text{(OAc)}_{4} \text{(OTf)}_{5} \] (5). We targeted incomplete cubanes for studies of oxygen atom incorporation into elaborate metal oxido clusters. Addition of an equivalent of Mn(OTf)$_{2}$CH$_{2}$CN and KO$_{2}$ (2.5 equiv) to trimanganese complex 1 in THF and stirring for 20 h afforded a red-brown solution. Concentration in vacuo and extraction into benzene generated 3 as an orange-red powder (Scheme 2). Compound 3 displays paramagnetically shifted and broadened peaks between 25 and 55 ppm in the $^{1}$H NMR spectrum. ESI-MS of the reaction mixture showed peaks at 1241.0 m/z, [Mn$_{3}$O$_{5}$(OAc)$_{3}$]$^{-}$, and 1300.1 m/z, [Mn$_{3}$O$_{5}$(OAc)$_{4}$]$^{-}$, consistent with a species similar to that of Mn$_{3}$O$_{2}$ cubane 2 but with one less oxygen. Recrystallization by vapor diffusion of hexane into a THF solution afforded crystals amenable to X-ray diffraction (Figure 1).

Complex 3 displays the ligand coordination mode found in the cubane complexes. The three basal manganese centers are each square pyramidal and supported by one terminal oxido and one pyridyl group from the ligand framework; three pyridyl groups, one per arm, remain unbound. The fourth, apical manganese center is pseudo-octahedral and bound through three k$^{2}$-acetates and three $\mu$-oxides to the three basal manganese centers. This arrangement generates a partial cubane missing the “basal” oxido moiety directly above the center of the triarylbenzene motif. Analysis of the Mn ligand distances and absence of outer-sphere counterions indicate that all metal centers are Mn$^{III}$. The incomplete cubane motif Mn$_{3}$O$_{3}$ has not been isolated previously, although a [Mn$^{II}$_3Mn$^{IV}$O$_{3}$L$_{6}$]$^{+}$ (L = diphenylphosphinite) species was observed by ESI-MS. Complexes with the Mn$^{III}$Sc$^{3+}$O$_{5}$X formulation, where X is a bridging monooanion (X = Cl$^{-}$, F$^{-}$, F$_{3}$N$^{-}$, O$_{3}$CR$^{-}$, OMe$^{-}$, and OH$^{-}$) have been studied extensively. The characterization of both 2 and 3, only differing by an oxygen atom with all ancillary ligands identical, allows a unique opportunity to study systematically oxygen atom transfer from and water incorporation into a cuboidal moiety.

To extend the family of heteronuclear cubanes, we targeted a scandium variant. Treatment of a DMF solution of 4 with scandium triflate and crystallization from acetonitrile/diethyl ether yields the scandium-capped cubane cluster LScMn$^{III}_{10}$(OAc)$_{4}$(OTf) (S). The $^{1}$H NMR spectrum of a CD$_{3}$Cl$_{2}$ solution of S is similar to that of 2, with paramagneti-
cally shifted and broadened signals between −24 and 12 ppm. ESI-MS of an acetonitrile solution of 5 showed a single peak at 1306.1 m/z, [LScMn3O4(OAc)3]+, which is consistent with the assignment of 5. X-ray quality single crystals of 5 were grown by slow vapor diffusion of diethyl ether into an acetonitrile solution of 5, and an XRD study of these crystals showed that the solid-state structure of 5 maintains the Mn3MO4 cubane core moiety of 4, but the scandium center is further coordinated by an O-bound triflate anion (Figure 2). The Mn−oxido distances of 5 (1.8477(7)−1.91116(7) Å) are similar to those of 4 (1.825(2)−1.923(2) Å) and consistent with a MnIV oxidation state assignment.

2.2. O-atom Transfer to Phosphine as Comparative Probe of Mn3MO4 Reactivity. With compounds 2, 4, and 5 in hand, we investigated the reaction with phosphine as a mechanistic tool, measuring propensity of the oxide for oxygen atom transfer chemistry in these cubanes. Addition of excess (2−10 equiv) trimethylphosphine (PMe3) to complex 2 produced a color change from red-brown to orange-red. Removal of volatiles in vacuo and extraction of Me3PO with Et2O afforded 3 as a red-orange powder in near quantitative yield (Scheme 2). In the 31P NMR, ca. 1 equiv of PMe3 was converted within 15 min with respect to a tetraphenylphosphonium internal standard. The 31P NMR signal corresponding to trimethylphosphine oxide (Me3PO) was not observed in the reaction mixture of 2 and PMe3 but could be observed when the PMe3O was extracted away from the paramagnetic product into diethyl ether (Et2O). Me3PO was also observed by ESI-MS of the Et2O fraction as the Me3POH+ cation at m/z 93.1. The protonated cation mass was also observed for an authentic

Scheme 2. Reactivity and Synthesis of Cubanes 2, 4, and 5 and Partial Cubane 3

Curved lines represent 2-pyridyl groups.
manganese cluster 2 \( (E_{\text{red}} = -0.70 \text{ V vs } \text{Fc/Fc}^+) \) in DMA.\(^{19a}\) Cyclic voltammetry experiments revealed that reduction of 5 \( (E_{\text{red}} = -0.24 \text{ V vs } \text{Fc/Fc}^+) \) in DMF occurs at a much more positive potential than that of 2 and 4 (Figure 3), indicating that thermodynamically 5 is more oxidizing. Despite the significantly higher oxidizing power, 5 does not form trimethylphosphine oxide upon treatment with trimethyl phosphate, suggesting that the difference in reactivity is due to the kinetics, which is also consistent with the much slower reactivity of 2 with PEt\(_3\) versus PMe\(_3\).

2.3. QM studies of Oxygen Atom Transfer from Mn\(_4\)Mo\(_4\) to PMe\(_3\). We carried out QM studies to interrogate the differences in reactivity for oxygen atom transfer to phosphine. As described in the Supporting Information (SI), we used the B3LYP flavor of Density Functional Theory (DFT) with Poisson–Boltzmann solvation.

In order to validate this level of DFT for predicting the structures and properties of these compounds, we compare the XRD coordinates, reduction potentials, and electronic states with the minimized structures obtained from QM. The optimization of the structures was carried out for the high-spin configuration of each compound. Using this structure, we also calculated the lower spin wave functions. We found a very small splitting, <0.1 kcal, for both 2 and 4, which suggests that the coupling between high-spin manganese centers is a minor contributor to the ambient-temperature free energy surfaces computed (magnetism studies support this small splitting; see SI). For the current level of DFT the difference is too small to be significant, and hence we consider only the high-spin configuration through this discussion.

The QM optimized structure of 4 (147 atoms) is shown in Figure 4a, which differs from the XRD mainly in the THF bound to the Ca, with some small differences in the nonbonded pyridines. Considering only the core Mn\(_3\)CaO\(_4\) and the first coordination shell (21 atoms), the DFT differs from the XRD study by root-mean-square (RMS) of 0.007 Å for bonds and 0.384° for bond angles. This indicates that our level of QM reproduces the geometry of 4.
We then calculated the structure of 2 (134 atoms; Figure 4b) with the main difference involving the nonbonded pyridines with respect to the structure from XRD. Comparing only the Mn$_4$O$_4$ cluster and the first coordination shell (20 atoms), the QM agrees with XRD with RMS = 0.012 Å for bonds and 0.060° for angles. Thus again the computational model accurately describes the experimental system for the Mn$_4$ core.

Using this level of QM, we determined the transition state for the reaction with PMe$_3$ at various sites of both the Mn$_4$O$_4$ and Mn$_3$CaO$_4$ clusters. A similar QM study with smaller basis set for geometries was used for other mechanistic studies involving transition-metal complexes in enzymes (including O−O formation), leading to a typical accuracy of within 3−5 kcal/mol of experiment, with the barriers usually over-estimated. This difference is systematic not random, giving a potential energy surface similar to the exact one. Also, others have shown that DFT methods are able to reproduce accurately the crystal structures of oxo-manganese complexes.

2.3.1. Distributions of Mn$^{III}$ and Mn$^{IV}$ Sites and Redox Potentials. Comparison of the current QM methodology for single electron redox potentials in well-characterized early transition-metal metallocenes shows an absolute error deviation of 3−5 kcal/mol. The possible products are given in the upper right. The numbers in parentheses are the relative energies with respect to starting materials 4 and PMe$_3$. Boxed structures refer to products, and nonboxed structures refer to transition states.
of 0.179 V. This is equivalent to an error of 4.1 kcal/mol, which is in the range of accuracy for B3LYP (Table S1). The current B3LYP methodology systematically gives more negative potentials than experiment for the Mn$_3$O$_4$ and Mn$_3$CaO$_4$ cubanes by almost 0.2 V, an error of 4.6 kcal/mol (Table S2). This is similar to the error for single transition-metal complexes in well characterized metallocenes.$^{27}$ For each structure optimization of the redox compounds, we used the high-spin state as in the neutral case (see SI). Thus we validated our level of QM by reproducing the experimental redox potentials for these systems. We were also able to determine how the redox processes affects the geometry of the structure by reducing the MnIV atoms to MnIII (see SI).

2.3.2. QM Reaction Profiles for Reaction With PMe$_3$ to Form OPMe$_3$. 2.3.2.1. PMe$_3$ Attacking the Mn$_3$CaO$_4$ Compound. We consider first the reaction profile for PMe$_3$ attacking the Mn$_3$CaO$_4$ compound 4. We found that reacting away any of the three ‘top’ oxygens has a barrier of 28.7 kcal/mol while reacting with the ‘bottom’ oxygen leads to a barrier of 90.2 kcal/mol (pathways A* and B*, respectively; Figure 5a). The attack of ‘bottom’ oxygen is very unfavorable due to the presence of the trinucleating ligand L. Removing a ‘top’ oxygen gives the most stable product B. On the other hand, removing the ‘bottom’ oxygen leads to a product, A, that is 13.2 kcal/mol less stable because the MnIV is forced to be five coordinate. Also, the O vacancy at the top is likely stabilized by the trans-axial alkoxide and pyridine ligands.

2.3.2.2. PMe$_3$ Attacking the Mn$_3$O$_4$. We found that attacking the ‘top’ oxygens leads to three distinct barriers of 23.7, 24.5, and 28.4 kcal/mol, giving the products D, C, and E, respectively (Figure 5b). These results are very similar to the lowest barrier B* (28.7 kcal/mol) of the Mn$_3$CaO$_4$ complex. However, for the Mn$_3$O$_4$ complex we found a new lower barrier reaction path G involving partial detachment of the CH$_3$COO$^-$. This new path leads to a transition state G* (Figure 5b) with a barrier of 18.3 kcal/mol. This barrier is 5–10 kcal/mol lower than any of the barriers for direct PMe$_3$ attack on Mn$_3$O$_4$ and Mn$_3$CaO$_4$. In contrast, reacting with the ‘bottom’ oxygen gives product F (equivalent to the experimentally observed compound 3) with a high activation barrier F* (63.6 kcal/mol) due to the presence of the trinucleating ligand L, similar to results for the CaMn$_3$O$_4$ cubane. We found that F (or 3) is the lowest energy product, consistent with experiment. The products of removing ‘top’ oxygen atoms are less energetically favorable by 30.5, 23.9, and 15.8 kcal/mol for C, D, and E, respectively, with respect to F (Figure 5b). These differences arise because the MnIII centers prefer to have the elongated axis along the empty coordination site and away from the electron-rich alkoxide donors (as is the case for F).

Based on these results we propose the following reaction mechanism for oxygen atom transfer from Mn$_3$O$_4$ cubane 2 to PMe$_3$ (Figure 6). First, partial detachment of CH$_3$COO$^-$Mn$^{III}$ and CH$_3$COO$^-$.Mn$^{IV}$ involves barriers of 13.2 and 18.6 kcal/mol, respectively. This partial detachment is not observed for the CH$_3$COO-Mn$^{IV}$ of Mn$_3$CaO$_4$ complex 4 because the barrier is 27.1 kcal/mol. That indicates that the CH$_3$COO-Mn$^{III}$ and CH$_3$COO-Mn$^{IV}$ bonds in the Mn$_3$O$_4$ system are more labile than in 4. This leads to the transition-state G* with barriers of 7.5 kcal/mol, leaving behind the vacancy at the bottom which is the product observed experimentally F (or 3).

2.4. Carboxylate Exchange Studies. The difference in the dissociation energies of acetate oxygen from Mn predicted by QM was further explored experimentally by comparison of exchange properties. Solutions of complexes 2, 4, and 5 were treated with deuterated acetate ([nBu$_4$N][CD$_3$COO]) in 10:1 THF/CH$_3$CN, while the incorporation of isotopic label into the complexes was monitored by ESI-MS. In agreement with QM, we found rapid equilibration (<1 min) to a statistical mixture of isotopologues for complex 2, whereas 4 and 5 did not reach equilibrium within 50 min (Figure S24). These results are consistent with the Mn$^{II}$ sites of 2 being more labile due to electrons in the σ-antibonding orbital, leading to weaker metal–ligand bonds.

2.5. Oxidative Incorporation of H$_2$O into 3. Incorporation of water into the OEC during turnover is fundamental to the catalysis. Therefore, we studied conversion of partial cubane 3 to 2 to elucidate the mechanism for such oxido-ligand
incorporation into multinuclear manganese-oxido systems. This transformation corresponds formally to low S-state (S→1 to S→2) conversion. The metal oxidation states (MnII and MnVI), the nature of the bridging oxido moiety, and the complexity of the cluster are all relevant to the mode of action of the OEC during catalysis. Preliminary studies found that trimethylamine-N-oxide, tert-butylhydroperoxide, and cumene hydroperoxide did not react with 3 over days, whereas exposure to iodosobenzene generated 2 in 1 h (Scheme 2). Treatment of 3 with a stoichiometric amount of water resulted in no reaction (1H NMR spectroscopy). In the presence of hydroxide and water (ca. 30 equiv H2O and 2 equiv NR4OH, R = Me, Et) in THF/CH3CN, we observed decomposition of complex 3 over hours. Ferrocenium matches the potential window for the oxidation of 3 but not of the desired product, 2 (see Figure S12). Addition of ferrocenium hexafluorophosphate to 3 in the presence of water in THF/CH3CN (10:1) led to formation of 2 but in low yield and in a mixture with unidentified products. Finally, when we added an excess of ferrocenium hexafluorophosphate (4 equiv) alongside water (20–30 equiv) and hydroxide (2 equiv), we found that 2 was generated as the major product within minutes (Scheme 2). These experiments indicate that both base and oxidant are necessary for incorporation of oxygen from water in this system.

Oxidative incorporation of water has been demonstrated for a diamanganese system; if dissolved in water and exposed to air, a MnIII−(μ-O)−MnIII complex turned into a MnII−(μ-O)−MnV complex.28 Also, addition of chloride to a MnIII−O2− ‘butterly’ complex facilitated a disproportionation that gave a one-electron oxidized MnIII,MnIVO3Cl cubane.22a The present protocol mimics the biological incorporation of an oxido ligand into the OEC: water, oxidizing equivalents, and base are all necessary in this two-electron, two-proton process with a tetramanganese cluster. This reaction is important both to OEC turnover and to assembly. Although highly efficient, the OEC must be reassembled frequently under full solar flux due to photooxidative damage to the inorganic cluster and D1 peptide.29 The process by which the OEC is assembled, called photoactivation,30 uses MnIII, Ca2+, Cl−, bicarbonate, water, and oxidizing equivalents generated by light absorption.31 Significant advances have defined kinetically distinct species in photoactivation,31 and the current transformation corresponds conceptually to the putative final steps, the conversion of S→1 to S→2.

2.6. Isotopic Labeling Studies of H2O Incorporation

The above results illustrate a synthetic cycle between Mn3O4, 3 and Mn4O4, 2 by oxidative incorporation of water and μ− oxygen atom transfer. With an understanding of the oxygen atom transfer mechanism (Figure 6), an 18O-labeling study was devised to determine where the water oxygen atom is incorporated into the cluster with respect to the ligand framework (i.e., at one of the three ‘top’ positions or at the central, ‘bottom’ position close to the central arene of the ligand). The location of 18O once incorporated provides information about extent of oxido reorganization during water incorporation into these Mn4O4 systems, which is relevant to the OEC. We interrogated the regiochemistry of incorporation by subsequent oxygen atom abstraction with phosphine and evaluation of 18O/16O distribution in the products.

Labeled base and water (NMe418OH and H218O) were utilized in the water incorporation conditions (Scheme 3, in box). ESI-MS analysis of the products shows a shift by two units of m/z vs the experiment with natural abundance water and base (Figure 7a). This indicates generation of the Mn416O318O isotopologue, 2*, as the major product in a mixture of higher isotopologues (labeled 2T* and 2B*, in Scheme 3 for 18O incorporation at the “top” and “bottom” positions, respectively); see SI for quantification of isotopologue ratios and ESI-MS data.32 Higher 18O-content isotopologues of 2* could form from water exchange in the starting material 3, product 2, or from an intermediate species under the oxidizing water incorporation conditions. Control experiments showed no exchange of 18O from water into either 3 or 2 over the time frame of the water incorporation reaction (<1 h; Scheme 3). This is consistent with the slow rate of scrambling in Mn3O4 complexes and in another Mn4O4 cubane system.33 We found that complex 2 did not incorporate 18O under the same reaction conditions, showing that the Mn4O4 product did not further exchange once fully formed. These experiments taken together suggest that an intermediate species in the conversion of 2 to 3 is responsible for the incorporation of any additional 18O from water. Attempts to isolate intermediate species, for example, a singly oxidized, singly protonated
Mn^{16}Mn^{18}O(OH) species, have been unsuccessful thus far. The Mn_2CaO_4 and Mn_2ScO_4 cubanes 4 and 5 were also subjected to excess H_2^{18}O and showed no exchange over 1 h.

Complex 2* was subjected to an excess of PMe_3 in C_6H_6, producing 3* as major product in mixture with isotopologues (Figure 7b; Scheme 3).^{32a} Labeled Me_3P^{18}O was observed at 95.1 m/z along with natural abundance Me_3P^{16}O at 93.1 m/z in a ratio of ca. 3:1 Me_3P^{16}O/Me_3P^{18}O. To test for the generation of lower nuclearity manganese-oxido species capable of isotopic scrambling, we mixed 3* and 2* in various solvents and found no isotopic scrambling. Additionally we treated a mixture of 3 (5 equiv) and 2* with substoichiometric amounts of PMe_3 (0.5 equiv) in benzene to test for lower nuclearity species under oxygen atom transfer conditions. Less than 10% increase of 2* was observed by ESI-MS (close to our detection limit). These results are consistent with clusters 2 and 3 being robust in solution supporting the direct oxygen atom transfer conditions. Less than 10% increase of 2* in benzene to test for lower nuclearity species under oxygen atom transfer conditions. Less than 10% increase of 2* was observed by ESI-MS (close to our detection limit). These results are consistent with clusters 2 and 3 being robust in solution supporting the direct oxygen atom transfer conditions.

We analyzed the isotopologue distribution of 3* and 3 in the context of various mechanistic possibilities for water incorporation and oxygen atom removal (Scheme 4). In the first step of the study, water could be incorporated at the bottom, the top, or both positions. These incorporation mechanisms give the isotopomers 2^{B, B}, 2^{T, T}, or a mixture of the two. In the second step—oxygen atom transfer—an oxygen atom could hypothetically be removed from top, bottom, or both sites. These removal mechanisms afford a ratio of 3/3* and 16OP-Me_3/16OPMe_3 that is correlated to the mechanism of the first step: incorporation (Scheme 4, bottom).

The deceivingly simple mechanism of selective ^18O incorporation at the bottom position, which is open, followed by selective removal by PMe_3 from the bottom would be consistent with the observed products/starting materials. However this would give solely unlabeled, natural abundance 3 and fully labeled Me_3P^{18}O, which is not observed (Scheme 3). If the water were incorporated solely at the top and the bottom oxygen atom was transferred to phosphine, the label location would be opposite: 100% mono-^{18}O labeled 3* and natural abundance Me_3P^{16}O. Because mixtures of 3 and 3* were observed as well as Me_3PO and Me_3P^{15}O, these two mechanisms can be ruled out, in agreement with the top selective mechanism for oxygen atom transfer to phosphine suggested by the QM studies.^{32b} Another mechanism inconsistent with experiment involves water incorporation at the bottom position, followed by selective removal of any of the top three oxides by PMe_3. This mechanism could be plausible if the lower site were accessible by water and not PMe_3. However, this mechanism would lead to solely 3* after cluster rearrangement and natural abundance Me_3P^{16}O, which again is not observed (Scheme 4, right-hand pathway).^{32b}

A number of mechanisms are consistent with the experimental distributions. If water is selectively incorporated into the top positions, 2^T is the sole isotopomer of 2^* formed. Selective transfer from the top oxygen sites would then give a 2:1 mixture of 3^*/3. If the water incorporation is not selective, then a 3:1 mixture of 2^T/2^B is expected. Any mechanism of oxygen atom transfer would then give a 3:1 mixture of 3^*/3 (Scheme S1). Both mechanisms are roughly consistent with the experimental ratio of ca. 2:1. Intramolecular scrambling after incorporation also predicts isotopologue mixtures for both 3 and Me_3PO and cannot be distinguished based on the present data.

Given the steric constraints of the ligand framework, the phosphine cannot access directly the bottom oxido of compound 2, as supported by the high-energy barriers calculated above. Hence, the observed mixture of Me_3P^{16}O and Me_3P^{18}O upon treatment of 2* with Me_3P suggests that a significant amount of 2^T must be generated upon ^18O incorporation from H_2^{18}O. Isotopomer 2^T may be generated by direct ^18O incorporation at the top position upon

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Figure 7. Positive ion ESI mass spectrum of labeled and unlabeled 2 (a) and 3 (b). Both fly as cations with one lost acetate.

Scheme 4. Mechanistic Possibilities of Water Incorporation and Removal

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**Ligand framework L is below Mn_6O_n units as drawn in Scheme 2.**
isomerization of 3 to transfer an oxido to the bottom position or migration within 2. Either mechanism for $\text{^{18}O}$ incorporation at the top position involves intramolecular migration of oxido moieties in 2 or 3. Intermolecular versions of this scrambling process are not supported by our control experiments. Hence, although there is more than one mechanism consistent with the present studies, all pathways involve migration of oxido ligands within the clusters during the process of oxidative water incorporation.

Interestingly, recent computational work suggests that the OEC interconverts between two “sub-state” structures in both the S$_{1/2}$ and S$_2$ states.$^{12c}$ Both studies involve $\mu$-O-migration: a $\mu_2$-oxido or hydroxido bond more strongly to either a Mn in the cubane subsite or the dangling Mn to form the open-cuboidal structure mentioned above. One report posits that this fluxionality could engender a higher exchange rate to this oxygen consistent with one of the substrate waters as observed in experimental kinetics studies$^{34}$ and $^{17}$O electron–electron double resonance-detected NMR spectroscopy$^{6}$ studies.

3. SUMMARY

Oxygen atom transfer reactivity and incorporation was explored for cuboidal Mn$_3$MO$_4$ complexes (M = Mn, Ca, Sc; n = 3, 4) displaying $\mu_2$-oxido moieties relevant to the OEC in PSII. High-oxidation state heterometallic cubanes Mn$_{\text{III}}$CaO$_4$ and Mn$_{\text{III}}$ScO$_4$ did not show oxygen atom transfer to trimethylphosphine. In contrast, the Mn$_{\text{III}}$Sc$_2$O$_4$ cubane reacts with this phosphine within minutes to generate a novel Mn$_{\text{III}}$O$_3$ partial cubane and trimethylphosphine oxide. Reaction paths were interrogated by QM for oxygen atom transfer from Mn$_{\text{III}}$Sc$_2$O$_4$ and Mn$_{\text{III}}$CaO$_4$. We found that the preferred mechanism involves partial CH$_3$COO$^-$ ligand dissociation and coordination with PMe$_3$. This leads to a five-coordinated phosphorus transition state that is 5–10 kcal/mol lower than when all CH$_3$COO$^-$ ligands are attached. This partial dissociation of the CH$_3$COO$^-$ ligand is accessible only when Mn(III) is present. Experimentally, the rate of exchange between metal-bound acetates and CD$_3$COO$^-$ was highest for Mn$_{\text{III}}$Sc$_2$O$_4$ in agreement with the QM. These results indicate that even with a strong oxygen atom acceptor, such as trimethylphosphine, the oxygen atom transfer chemistry from Mn$_3$MO$_4$ cubanes is controlled by ligand lability, with the Mn$_{\text{III}}$CaO$_4$ OEC model being unreactive.

The Mn$_{\text{III}}$$_4$O$_3$ partial cubane, 3, was isolated cleanly upon oxygen atom transfer, without overreduction. This species was converted back to the full cubane Mn$_{\text{III}}$$_2$Mn$_{\text{IV}}$O$_4$ with water as oxygen source, base, and oxidant, mimicking the biological incorporation of an oxido ligand in the OEC. $^{18}$O-labeling experiments were performed via two-step conversions, from Mn$_{\text{III}}$$_4$O$_3$ to Mn$_{\text{III}}$$_2$Mn$_{\text{IV}}$O$_4$ (with H$_2$O) and back to Mn$_{\text{III}}$$_4$O$_3$ (with phosphine). Following the extent of $^{18}$O/$^{16}$O distribution in the products provided mechanistic insight into this two-electron, two-proton process with respect to the position of incorporation into the partial cubane structure. These isotopic labeling experiments support reaction mechanisms involving migration of oxido moieties within the cluster and are not consistent with selective oxide incorporation at the site available in the starting species, thus supporting the possibility of such migration processes during water incorporation into the OEC during photoactivation and turnover. Further studies of multinuclear Mn and Mn/Ca complexes are ongoing toward gaining a better understanding of mechanistic details of oxygen evolution at heteronuclear metal oxide sites such as the one in photosystem II or heterogeneous catalysts.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, computational methodology, isotopologue distribution, and crystallographic details. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

agapi@caltech.edu; wag@wag.caltech.edu

Author Contributions

$^1$These authors contributed equally.

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