A DFT/B3LYP study of the mechanisms of the O₂ formation reaction catalyzed by the [(terpy)(H₂O)Mn^{III}(O)₂Mn^{IV}(OH₂)(terpy)](NO₃)₃ complex: A paradigm for photosystem II

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ABSTRACT

We present a theoretical study of the reaction pathway for dioxygen molecular formation catalyzed by the [(terpy)(H₂O)Mn^{III}(O)₂Mn^{IV}(OH₂)(terpy)](NO₃)₃ (terpy = 2,2':6',2''-terpyridine) complex based on DFT-B3LYP calculations. In the initial state of the reaction, a partial oxido radical (0.44 spins) is formed ligated to Mn. This radical is involved in a nucleophilic attack by bulk water in the O—O bond reaction formation step, in which the oxido fractional unpaired electron is delocalized toward the outermost Mn of the μ-oxo bridge, instead of the ligated Mn center. The reaction then follows with a series of proton-coupled electron transfer steps, in which the oxidation state, as well as the bond strength of the OO moiety increase, while the OO—Mn(1) bond gets weaker until O₂ is released. In this model, basic acetate ions from the buffer solution capture protons in the proton-transfer steps. In each step there is reduction of the OO—Mn(1) binding strength, with concomitant increase of the O—O bond strength, which culminates with the release of O₂ in the last step. This last step is entropy driven, while formation of hydroperoxide and superoxide moieties is enthalpy driven. According with experiments, the rate-limiting step is the double oxidation of Mn(IV,III) or peroxyoxymonosulfate binding, which occur prior to the O—O bond formation step. This supports our findings that the barriers of all intermediate steps are below the experimental barrier of 19–21 kcal/mol. The implications of these findings for understanding photosynthetic water-splitting catalysis are also discussed.

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1. Introduction

The oxygen-evolving complex (OEC) of photosystem II (PSII), is a Mn₄Ca cofactor that catalyzes the oxidation of water to dioxygen in the thylakoid membrane of green plant chloroplasts and internal membranes of cyanobacteria, during the light period of photosynthesis [1,2]. Besides its biological significance, the OEC is a paradigm system for engineering direct solar fuel production catalysts since it is based on inexpensive metals and achieves an overall catalytic efficiency of water splitting that is yet to be matched by artificial systems [3]. Elucidating the mechanisms of the O—O bond reaction formation is, therefore, central for understanding the catalytic mechanism of photosynthetic water oxidation as well as for the development of biomimetic catalysts for oxidation chemistry.

Bioinorganic model chemistry has provided important insights into the mechanism of photosynthetic water oxidation, in particular by inspiring the idea of a Mn—O species as a key intermediate in the O—O bond formation, created by the abstraction of H-atoms from a water ligated to manganese [4–6].

Although many complexes have been considered as structural models for the OEC [7–16], only a few act also as functional models [17–26].

Barely four classes of metal complexes are known to catalyze homogeneous water oxidation. These involve Ru dimers [19,27–30], Mn-bound porphyrin dimers [18,21,31], a carboxylate-bridged MnII/II 2 dimer [23], and a complex containing a Mn—(μ-O)₂—Mn moiety [6].

Among these complexes, only the latter show clear structural resemblances with the actual OEC. Extended X-ray absorption fine structure (EXAFS) studies of PS II samples at the Mn K-edge reveal at least two 2.7-Å Mn—Mn backscattering distances that are characteristic of Mn—(μ-O)₂—Mn moieties [32–35]. The recent 1.95- and 1.9-Å-resolution [36,37] X-ray crystal structures of the PS II, isotropic [38,39] and polarized [40,41] EXAFS [42], as well as DFT-B3LYP [43–45], and Quantum Mechanics/Molecular Mechanics (QM/MM) studies [46] revealed that the Mn atoms in the OEC are also linked via μ-O bridges. Due to the structural and functional similarities the manganese complex [(terpy)(H₂O)Mn^{III}(O)₂Mn^{IV}(OH₂)(terpy)](NO₃)₃ (terpy = 2,2':6',2''-terpyridine) [5,6,47] (**1**), the “terpy” complex (Fig. 1), has been considered to be the only functional model of the OEC [5,6,48].

The biomimetic complex **1** evolves O₂ in aqueous solution, using only oxygen transfer oxidants, such as NaClO, or KHSO₅ (potassium peroxyoxymonosulfate or oxone). While some authors advocate water-oxidation [5,6,49,50], others have debated about the source of oxygen evolution [22,51]. Using isotope labels, Brudvig *et al.* conducted an investigation of the identity of the reactant species involved in the oxygen

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Fig. 1. The “terpy” complex **1**: [(terpy)(H₂O)Mn^{III}(μ-O)₂Mn^{IV}(CH₃CO₂)(terpy)](NO₃)₃ (terpy = 2,2′:6′,2″-terpyridine).

evolution reaction catalyzed by the terpy complex [6]. One of the reactants for the O—O formation reaction is the terpy complex in a high spin Mn^V(1)—Mn^{IV}(2) state. For the other reactant, several species involved were identified, including two oxygen atoms from bulk water, one oxygen atom from water and the second from oxone, or both oxygen atoms from oxone. This observation alone does not prove the atoms of O₂ can come solely from water, as O atoms of water may exchange with other oxygen-containing species in the system. Therefore, it was additionally established that in systems using oxone as oxidant, water does not undergo O atom exchange with the oxidant HSO₅[−], the SO₄^{2−} ions present alongside with HSO₅[−], or with the NO₃[−] counterions of **1** [48].

A common way to avoid the use of oxygen transfer oxidants is using the Ce^{IV} oxidant. It has been shown that **1** catalyze the oxidation of water with the Ce^{IV} oxidant, if attached to kaolin clay [22,52]. In a further work, the photocatalytic activity of **1** was also confirmed, when the complex was adsorbed onto a heterogeneous matrix in a three components system with **1** as catalyst, [Ru^{II}(bpy)₃]²⁺ as photosensitizer, and Na₂S₂O₈ as sacrificial electron acceptor [53]. However, the experiments with **1**/clay adsorbate have been questioned by findings that show that when **1** is supported on montmorillonite clay and using Ce^{IV} as the chemical oxidant, the actual water oxidation catalyst are layered type Mn-oxide particles [54].

Electrochemical studies of **1** in the presence of acetate buffer show that the potential for oxidation of **1** can be decreased compared with experiments in aqueous solution. It also reveals proton-coupled electron-transfer reactivity analogous to the OEC. When the electrochemical oxidation of **1** is carried out in aqueous solution, appearance of a tetramer is observed, via formation of a mono-μ-oxo bridge, preventing **1** to function as a catalyst [51]. However, almost all published procedures for oxygen evolution catalysis with **1** are done in the presence of acetate buffer [5,47,55]. Besides, the tetramer has been suggested to evolve O₂ electrochemically by reaction with water [56].

Ultimately, the oxygen transfer agent is required in the peroxymonosulfate binding step, which occurs prior to the O—O formation. The first oxidation does not require an oxygen transfer agent, as it was observed to occur electrochemically [57]. The second oxidation was only observed with oxygen transfer agents. The highest oxidized species becomes the actual catalyst that undergoes water splitting. From this point, it can be considered as a functional model of the OEC. This is the

portion of the reaction that is analyzed in this investigation. As the natural water splitting system PSII generates molecular di-oxygen from water, the most relevant mechanism related to the natural process is one in which both reactant oxygen atoms come from water. Hence, in this investigation we will concentrate only in the catalytic mechanism of water splitting.

The mechanisms of the O₂-evolving reaction catalyzed by **1** described by Limburg *et al.* are mainly based on observations in which HSO₅[−] is used as the oxidant [6]. In those cases, the pH of the solution was kept at 4.5, using an AcOH/AcO[−] buffer. The concentrations of the acetate species at this pH are [AcO[−]] = 4 · 10^{−5} M, and [AcOH] = 7 · 10^{−5} M, which makes both species available along the whole reaction process.

Water was commonly assumed to be ligated to both Mn centers [58–60]. However, aside from pH regulation, the presence of acetate plays a key role in the catalyzed reaction of oxygen formation [5,47,55]. Using electrochemistry, Brudvig *et al.* concluded that acetate displaces one of the water Mn ligands. In particular, acetate is proposed to bind to Mn^{IV}, blocking the ligand-binding site at the highest oxidation state metal [57]. Acetate binding to only one Mn was also reproduced by computational models [61,62]. The ligand at the other Mn center can be either oxone or water. In this report we will only consider the case of a water ligand, to allow a closer parallelism with PSII.

The experimental reaction rate for the O—O formation corresponds to a barrier of 19–21 kcal/mol. This barrier actually impose an upper limit to this investigation, as the rate-determining step during turnover was established to be the formation of the highest oxidation state [6,50], or peroxymonosulfate binding [63], occurring prior to the O—O bond formation. Several theoretical studies examined the mechanism of the O—O bond formation [60,64,65]. Among these studies, P. Siegbahn and coworkers address the analysis of the catalytic properties of the terpy complex (**1**) for this reaction [59,66]. In that study, the calculated barrier for O—O formation turns out to be higher than 23 kcal/mol, being probably too high compared with the experimental value.

In this report we present a plausible pathway for water oxidation in the terpy complex based on DFT-B3LYP calculations. The proposed reaction pathway follows several steps that give place to the formation of an O₂H[−] peroxide intermediate species, and molecular bi-oxygen. This calculation involves a spin rearrangement during the O—O bond formation step, which reduces the barrier in >15 kcal/mol [67], as compared with previously published results [59,66].

The paper is organized as follows. Section 2 introduces the theoretical background for the calculation of stationary point configurations and free energies. It also includes the electronic structure of selected species present in the O₂ reaction. Section 3 includes results of the mechanistic aspects of the triplet-oxygen formation catalyzed by the terpy complex, with emphasis on the relation with the related process in the natural system PSII. Section 4 contains a discussion of the relation between the energetic and electronic structure results presented in the previous sections. Conclusions are presented in Section 5.

2. Methods

2.1. Molecular models

The X-ray atomic coordinates of the Mn complexes were obtained from the Cambridge Crystallographic Data Center (CCDC) with reference codes FIQFIU [5]. Fully optimized molecular structures were obtained through minimum- or transition state (TS)-geometry optimizations in a broken symmetry (BS) state [68,69]. In this state the α and β densities are allowed to localize on different atomic centers providing a multiconfigurational character to the spin state. Each step of the above protocol is checked for stability of the Density Functional Theory (DFT) wavefunction. The ionic spin states were characterized according to the analysis of Mulliken atomic spin density populations. Preparation of the models was subject to the constraints of total charge

and total spin multiplicity, consistent with experimental data. Different arrangements of individual spin states were analyzed by relaxing the molecular structures from appropriate initial-guess spin-electronic states, based on ligand field theory [70].

All steps of the catalytic cycle and the O₂ formation reaction are calculated in water solvent, using the Polarizable Continuum Model (PCM) with the integral equation formalism variant [71]. Frequency calculations are used to characterize the structures as local minima (all real frequencies), or first-order saddle points, *i.e.* transition states (one single imaginary frequency for the correct mode). Transition states are located by initially running a stepwise geometry scan between two local minima by varying the reaction coordinate in a full geometry optimization with one degree of freedom fixed. The maximum point of these geometry scans is used as a starting point for transition state optimizations via Synchronous Transit-guided Quasi-Newton (STQN) methods [72,73]. This approach ensures that the transition state indeed connects the minima at each side of the barrier. Further confirmation is achieved analyzing the normal mode associated with the imaginary frequency. These methods have been shown to accurately reproduce structures and free energies of activation of reaction processes of metal-oxo reactions [74].

Optimizations are done with the unrestricted B3LYP [75,76] density functional method with a basis set constructed as a combination of LACVP on Mn and 6–31+G(d) on the rest of the atoms. This functional is known to perform well in the study of catalytic properties of the oxygen-evolving complex of PSII [77,78], as well as in related inorganic complexes [43,60,61,79]. Geometry optimizations and single point calculations use the Gaussian 09 software package [80]. Spin and electronic densities were generated using Gaussian 09 cube files, and plotted with Visual Molecular Dynamics (VMD) visualization computer program [81,82].

2.2. Free energies

All optimizations are carried out in liquid phase to avoid artifacts that may arise from eventually different protonation states in the gas and liquid phases, or when stationary points present in liquid solution may not exist in the gas phase [83–85]. One problem with this approach is that optimizations and single point calculations in solvent require longer computational times, and this is aggravated by the number of trial calculations usually necessary to find stationary point configurations, combined with several possible protonation and spin states.

Calculations of solution equilibrium free energies make use of Eq. (1) where G_{soln} is the solution Gibbs free energy change of the reaction [86]. The values of G_{soln} of each reactant and product are obtained according with the standard Born-Haber thermodynamic cycle, by adding the thermal correction to the Gibbs free energy ($G_{corr-soln}$), the total energy calculated without temperature correction (E_{soln}), and the solvation free energy G_{solv} as indicated in Eq. (1).

$$G_{soln} = E_{gas} + G_{corr-soln} + G_{solv} \quad (1)$$

In this case, ΔG_{soln} can be calculated from the difference in G_{soln} of the products and reactants:

$$\Delta G_{soln} = \sum G_{soln}(\text{products}) - \sum G_{soln}(\text{reactants}) \quad (2)$$

The electronic energy contributions were computed by single-point calculations in gas phase (E_{gas}). The free energy corrections ($G_{corr-soln}$), which include enthalpic and entropic terms, and zero point energy (ZPE) corrections, are determined within the rigid rotor-harmonic oscillator approximation (RRHO) from frequency calculations at the B3LYP/6-31G(d) level on aqueous-phase optimized structures.

The solvating effect of the aqueous medium was taken into account through the SMD (Solvation Model D, where the “D” stands for “density”, to denote that the full solute electron density is used without defining

partial atomic charges) polarizable continuum model (G_{solv}) [87] (see Section SI.1 in SI).

The energy differences of intermediates and transition states are sometimes very small, particularly TS associated with proton transfers. These differences usually lie within the error of the DFT methodology. For that reason, we will use enthalpy differences through the text, and present free energies only when they predict a different reaction step. This will allow us to corroborate the actual course of the reaction, as predicted by Gibbs free energies.

3. Results

We are interested in the mechanistic aspects of the triplet-oxygen evolution relevant to the similar process in the natural system PSII. A proposal for the whole catalytic cycle based on the findings of Limburg *et al.* [6] is shown in Fig. 2. As the oxidant (oxone or hypochlorite) has not been observed as a radical, it follows that each step of the cycle consists of a double oxidation.

In the following subsections, we will separate the reaction in three step sequences, each of which describing basically an oxidation event. The first is the sequence that involves the O–O bond formation step, which goes from the first reactant to the first product, dubbed **R1** to **P1** (Section 3.1.3). The second is the sequence that starts from hydroperoxo to give the superoxide ion, **R2** to **P2** (Section 3.1.4). The third is the formation of paramagnetic dioxygen from the superoxide radical, named **R3** to **P3** (Section 3.1.5).

3.1. Triplet di-oxygen evolution

3.1.1. Oxidation state of the catalyst and reactants at the beginning of the reaction

A high-valent Mn(III,IV) state is confirmed by calculations to be the most stable state of the catalyst dimer. From this state, a double oxidation of the Mn complex concerted with deprotonation of one water ligand gives a state with the two manganese centers in oxidation state IV and a stripped-water oxygen in a partial radical state ligated to Mn(1). After exchange with the chemical oxidant, the system undergoes several oxidant-driven oxidation steps along the catalytic cycle, and reaches the highest oxidation state achieved in the cycle, which is formally described as Mn(1)^V-Mn(2)^{IV}. Every attempt to isolate a manganese in oxidation state V by DFT calculations fails, due to the absence of ligands strong enough to keep such high

Fig. 2. Proposed mechanism for the reaction between **1** and water. Terpy ligands are omitted for clarity. The figure has been adapted from Limburg *et al.* [6], with updated findings from Cadý *et al.* [57].

Table 1
Binding energies of AcOOH and H₂O hydrogen bonded to μ -O ligands.

Reaction state ^a	Mn oxidation state	Binding energy [kcal/mol]			
		AcOOH		H ₂ O	
		O(3)	O(4)	O(3)	O(4)
R1	Mn(IV,IV)	10.72	10.96	11.00	8.77
P1/R2	Mn(IV,III)	12.84	11.96	10.29	12.07
P2/R3	Mn(III,III)	15.58	15.84	13.66	12.44

^a See Figs. 3 and 4 for the different reaction states.

oxidation state [88]. This state is the initial step of the di-oxygen evolution reaction. As reported elsewhere [41,59,66,89], the oxidation at position (1) is ligand centered rather than metal centered. In those previous reports, the oxidation state is best described as O(5)¹—Mn(1)^{IV}—Mn(2)^{IV}, including O(5) as an oxyl radical. However, although both high- and low-spin Mn^V-oxo species are known experimentally, support for the Mn^{IV}-oxyl comes exclusively from DFT calculations. In our investigation, we found unpaired spin density associated with the oxido ligand of Mn(1) (0.44 spins), yet the density is less than what is expected from an oxyl radical (one spin).

3.1.2. Molecular environment around the catalyst

The reaction environment includes proton donor species such as AcOOH and H₂O, which can form hydrogen bonds among themselves, as well as with the oxo-bridge ligands. Assuming a simple model based on the Boltzmann distribution, we found that there is 98% probability of finding AcOOH at O(4) compared with water in the initial step of the reaction (Table 1). Conversely, at O(3) there is a slight preference for water. The increased water affinity to O(3) compared to O(4) arises from the water molecule having an additional stabilizing electrostatic interaction with the acetate ligand of Mn(2), which is not present in the O(4) position (see Fig. S1 in SI). The binding energy of AcOOH to the oxo-bridge ligands in the Mn^{IV}—Mn^{IV} state is >10 kcal/mol, which is considerably higher than the typical O—H...O interaction of 5.0 kcal/mol among solvent molecules. This energy difference suggests that an AcOOH molecule will usually be hydrogen bonded to an oxo-bridge ligand in the first step of the O—O bond formation reaction.

3.1.3. O—O bond formation

In this stage, a water molecule from the bulk approaches the water ligand of Mn(1), which at this stage is a completely deprotonated oxido ligand (**R1**, Fig. 3). After deprotonation of the approaching water molecule and spin rearrangement, hydrogen peroxide is formed (**P1**). Mechanistically, deprotonation and O—O bond formation can occur either in a concerted or in a stepwise mechanism. The latter imposes a less stringent arrangement, and hence suggests lower energy barriers.

Different molecular species can serve as the base responsible for proton abstraction of the water molecule, including the μ -oxo ligands, acetate ion from the solution, or a bulk water molecule. Direct proton transfer to the oxo-bridge ligands is impeded, as the bridging ligand position is capped by an AcOOH from the solution, which decreases the probability of direct proton transfer to the oxo-bridge ligands.* Among the other two proton abstractor candidates, AcOO[−] is better base than water, which makes a bulk acetate ion the best candidate for proton abstraction, as established by previous results [62].

3.1.3.1. Alternative O—O bond formation mechanism with protonation of the μ -O bridging ligand. Although proton transfer to an AcOO[−] in solution is the mechanism maximally consistent with the surrounding conditions of the catalyst (AcOOH capping the oxo ligand), this mechanism

is qualitatively different to some recent proposals of water splitting in PSII based on real time X-ray laser spectroscopy, in which protonation of a μ -O bridging ligand is proposed as part of the O—O bond formation step [90,91].

To further analyze this option, alternative approaches that entail protonation of the μ -oxo ligand O(4) are also considered. This protonation can be achieved in two different ways. One is direct transfer from the attacking water molecule to O(4). The product of this alternative mechanism is approximately 11 kcal/mol less stable than transfer to a bulk acetate anion. The second is an indirect transfer, and involves proton transfer of the attacking water molecule to an AcOO[−] ion H-bonded to O(4), and proton transfer from acetate to O(4). In this alternative arrangement, one of the oxygens of the AcOO[−] is proton acceptor of two simultaneous hydrogen bonds, one from the OOH[−] peroxide ligand and the second from the OH bridging ligand (Fig. S2 in SI). For this reason, each proton forms a weaker hydrogen bond, and it does not extract the proton from the OH bridging ligand, as is the case with single H-bonded acetate.

This arrangement is approximately 10 kcal/mol less stable than a setup in which acetic acid is hydrogen bonded to O(4), and has no interactions with the hydroperoxo ligand. Hence, from an energetic perspective, the bridging ligand must be deprotonated at this stage of the reaction.

3.1.4. Formation of superoxide

This step involves reduction of Mn(IV,III) to Mn(III,III) (**R2** to **P2**), and deprotonation of the OOH peroxo formed in the previous **R1** to **P1** step (Fig. 4).

The 11.96 kcal/mol binding enthalpy of AcOOH to O(4) in the Mn(IV,III) oxidation state of **R2** is higher than in the Mn(IV,IV) state in **R1**. Similarly, the 12.84 kcal/mol binding affinity of AcOOH to O(3) in **R2** is also higher than in **R1** (Table 1). This suggests that AcOOH remains H-bonded to the μ -O ligand in the current step. The reduction of the manganese centers in going from **R1** to **R2** decreases charge transfer from the oxo-bridge ligands to the metals, which contributes to the concentration of electron density on the bridging moieties. This effect contributes to raise the affinity of proton donor species to the μ -O ligands.

Two molecular groups can act as bases that grab the transferred proton from the OOH peroxo, the oxo-bridge ligands, or acetate from the solution. DFT computations confirm that the final oxidation state Mn(III,III) of **P2** is either consistent with a single-protonated bridge [62], or a non-protonated bridge (Table 2). When the AcOOH is hydrogen bonded to O(4), the configuration with the protonated acetate is 1 kcal/mol more stable than the AcOO[−]/HO(4) hydrogen-bond arrangement. However, the enthalpy barrier of proton transfer from AcOOH to the O(4) bridging ligand is 1.33 kcal/mol, while the inverse transfer from μ -OH to AcOO[−] is only 0.33 kcal/mol. This means that at room temperature, the proton can be transferred from the bridge to the AcOO[−], while proton transfer in the opposite direction will be hindered.

It is also feasible to consider an alternative protonation mechanism of the bridge in which the AcOOH hydrogen bonded to O(3) protonates the bridge. Once O(3) is protonated, the AcOO[−] ligand of Mn(2) will form a H-bond with the protonated O(3), preventing the proton to be transferred back to the solution. The configuration with AcOOH hydrogen bonded to O(3) is only 1 kcal/mol more stable than the hydrogen bond pair AcOO[−]/O(3)H. However, as in the case of O(4), the barrier to proton transfer from AcOOH to O(3) is 1.15 kcal/mol, while the reverse transfer is much smaller at 0.20 kcal/mol. We will hence consider only the more stable configuration of AcOOH hydrogen bonded to O(3). An unprotonated O(3) is consistent with previous studies [62].

From a strictly energetic point of view, proton transfer to a bulk AcOO[−] is 4.75 kcal/mol more stable than proton transfer from the attacking water to O(4). In addition, direct protonation of μ -O ligands in the current step is additionally hindered, as it incurs an energy

* An indirect protonation is also possible in which the AcOOH molecule receives a proton from the reactant water molecule, and transfers its proton to the μ -O ligand, in a concerted mechanism (see Section 3.2.3.1).

Fig. 3. Proposed mechanism for the first reaction sequence (**R1** to **P1**), corresponding to the O–O bond formation starting with two water molecules. Non-integer approximate spin densities are indicated with fractional numbers, while integer spin densities are indicated with several “1” symbols, following the standard convention of spin up (α) and down (β). Selected distances that vary along the reaction pathway are also specified. Blue highlighted moieties show the atom groups involved in changes in the following step, while red highlighted atom groups indicate moieties that changed with respect to the previous step. Terpy ligands are omitted for clarity.

penalty of >10 kcal/mol. This energy is required to break the H-bond between AcOOH and μ -O, prior to proton transfer. Besides, if proton transfer to O(4) occurs, the proton will be captured back by a bulk AcOO $^-$, thus in both mechanisms the proton transferred from the OOH will end up being in a solution acetate.

All these considerations show that direct proton transfer from the attacking OOH to a bulk AcOO $^-$ is the most straightforward and energetically more favorable mechanism for this reaction step. After proton transfer, a superoxide radical ($O_2^{\bullet-}$, with spin densities 0.47 and 0.57 associated with each oxygen atom) is formed, ligated to Mn(1) (Fig. 5).

Fig. 4. Proposed mechanism for the second reaction sequence (**R2** to **P2**), corresponding to the second oxidation event that leads to superoxide anion formation. Non-integer approximate spin densities are indicated with fractional numbers, while integer spin densities are indicated with several “1” symbols, following the standard convention of spin up (α) and down (β). Selected distances that vary along the reaction are also specified. Blue highlighted moieties show the atom groups involved in changes in the following step, while red highlighted atom groups indicate moieties that changed with respect to the previous step. Terpy ligands are omitted for clarity, as well as acetate, which has a passive role in this sequence.

3.1.5. Molecular di-oxygen formation (3O_2)

In this step, the Mn(1) superoxide radical ligand is oxidized, with concomitant reduction of manganese (from Mn(III,III) in **R3** to Mn(II,III) in **P3**, to release the molecular paramagnetic dioxygen final product (3O_2) (see Table 3).

Whereas the Mn(III,III) oxidation state in **R3** does not require protonation of the bridge, a reduced Mn(II,III) state requires the bridge to be double protonated (single protonation is not consistent with this reduced state). As the reaction progresses, there is a reduction of the oxidation state of the metals, and a concomitant increase of the binding enthalpy of proton donor groups hydrogen bonded to the μ -O bridging ligands (Table 1). This increase ultimately creates a covalent bond between the hydrogen and the oxo-bridging ligands in the final Mn(II,III) state (**P3**).

The proton transfer can be achieved with both protons transferred from AcOOH to the oxo bridging ligands with a concerted mechanism, or in a stepwise mechanism. The latter can be done in two different ways, according to the order in which the proton is transferred to each oxo-bridge ligand. Protonation of the oxo-bridge ligands is essentially

Table 2

Spin densities consistent with different protonation states of the μ -O ligands.

Protonation state of bridging ligands	Spin density	
	Mn(1)	Mn(2)
O(3), O(4)	−3.85	3.84
HO(3), O(4)	−3.91	3.83
O(3), HO(4)	−3.95	3.83
HO(3), HO(4)	−4.81	3.86

Fig. 5. Proposed mechanism for the third reaction sequence (**R3** to **P3**), corresponding to the last OO oxidation, and formation of diamagnetic O_2 from the superoxide ion. Non-integer approximate spin densities are indicated with fractional numbers, while integer spin densities are indicated with several "1" symbols, following the standard convention of spin up (α) and down (β). Selected distances that vary along the reaction are also specified. Blue highlighted moieties show the atom groups involved in changes in the following step, while red highlighted areas indicate moieties that changed with respect to the previous step. Terpy ligands are omitted for clarity.

barrier-less for both oxo-bridge ligands; showing that both mechanisms can be simultaneously operative.

Enthalpy differences in this oxidation-reduction step are very small, and do not entail reduction of the energy along the reaction path. The corresponding free energies are close together, but they give a definite lower value for the final product (Table S1 in SI). This is due to the weakening of the Mn(1)— O_2 bond induced by the trans-standing hydroxo groups renders the final desorption step to be entropy driven. It is clear that, from an entropic point of view, the Mn—O—O subunit benefits significantly by acquiring a quasi-degenerate rotational degree of freedom.

3.2. Electronic structure properties along the reaction pathway

The analysis of the topology of spin and electron density surfaces helps to understand more clearly the details of spin transfer between

different molecular moieties. In this sub section, differences of spin and electron densities with respect to an initial state are plotted for selected reaction steps. Due to changes in the molecular structure associated with the charge transfer events, the corresponding spin-density differences are only approximate. We adopt the convention of taking the alpha spin as positive, and beta spin negative.

In an octahedral environment, the five d orbitals of manganese are split into a three-fold degenerate t_{2g} set (d_{xy}, d_{yz}, d_{xz}) and a two-fold degenerate e_g set ($d_{z^2}, d_{x^2-y^2}$). In a distorted octahedral environment, the degeneracies are lifted, but the symmetries of the t_{2g} and e_g sets remain. The t_{2g} orbitals mediate π interactions with the ligands, whereas e_g orbitals mediate σ interactions. In the high-spin ground-state of Mn^{III} and Mn^{IV}, all α 3d orbitals are empty, and can contribute to σ and π bonding. In high-spin Mn^{III}, β electrons have electron configuration $[t_{2g}]^3 [e_g]^1$, with only one unoccupied e_g function available. In Mn^{IV}, the three β electrons occupy t_{2g} orbitals, so there are two unoccupied e_g functions available. Hence, β -spin MOs can only contribute to σ bonding (e_g).

Table 3

Spin populations of stationary states along the O_2 evolution reaction.

Reaction state	Mulliken spin density				
	Mn(1)	Mn(2)	O(5)	O(6)	O(3)
R1	−2.64	2.69	0.44	0.30	0.26
TS1	−2.59	2.67	0.25	0.43	0.29
Int1	−2.50	2.64	−0.03	0.61	0.32
TS2	−2.26	2.63	−0.12	0.44	0.33
P1^a	−2.67	3.87	−0.00	−0.00	−0.18
TS3	−3.27	3.85	0.28	0.19	−
P2^a	−3.83	3.84	0.47	0.57	−
TS4	−3.94	3.85	0.47	0.66	−
Int2	−3.96	3.84	0.48	0.67	−
TS43	−4.79	3.85	1.00	1.00	−
P3^a	−4.81	3.86	1.00	1.00	−
TS4'	−3.89	3.84	0.45	0.64	−0.00
Int2'	−3.95	3.84	0.47	0.67	−0.00
TS34	−4.81	3.86	1.00	1.00	−0.02
P3	−4.81	3.86	1.00	1.00	−0.02

^a Densities correspond to the product. Reactant values of the following step differ in <1%.

3.2.1. R1-TS1-Int1 reaction sequence

The half spin associated with O(5) (0.44 spins) represents an intermediate situation between the stronger double bond with the non-radical oxygen in $O=Mn^V$, and the weaker single bond with the oxyl radical in $O^{\bullet}-Mn^{IV}$. The orbital bonding contributions to the HOO—Mn(1) bond in **R1** include p_z orbitals of the oxido ligand, and d_{xz} orbitals of manganese in 189a MO (Fig. 6), indicating a π -donor bonding interaction via $p_z + d_{xz}$ orbital components (Table 4). Similarly, the $p_y + d_{xy}$ orbital components of the 186a MO form a second π -donor interaction. The resulting bonding orbitals have 7% manganese and 21% oxygen character (189a MO), and 8% manganese and 17% oxygen character (186a MO), indicating a very covalent π -donor ligand-to-metal bond. There are additional alpha contributions to the O—Mn(1)^{IV} bond, from 189a, 186a, 192a, 175a and 169a MOs, with metal admixtures of 7%, 8%, 5%, 4% and 5%, respectively. Beta orbitals contribute small σ donor interactions to the empty β e_g orbitals from 173b, 168b, and 160b MOs.

Fig. 6. Boundary surface plots of α -spin orbitals that contribute to O—Mn(1) bonding in **R1**. x-axis along the Mn(1)—O(3) bond, y-axis along the Mn(1)—N bond, and z-axis along the Mn(1)—O(4) bond.

Deprotonation of the water molecule triggers electronic redistribution, with accumulation of negative charge on the formed OH^- . This moiety is stabilized by hydrogen bonds with bulk acetate, including the acetate H-bonded to $\mu\text{-O}$. The O ligand of Mn(1) is highly electrophilic, and attracts charge from the incoming OH^- . There is redistribution of β -spin from the OH^- to O(5), which gives an increase of alpha spin associated with the OH^- (0.2 spins in **TS1**, and another 0.2 spins in **Int1**), and a reduction of the net spin in O(5) in this reaction step (Table 3).

Spin density differences in the **R1-TS1-Int1** reaction sequence, shows that the net positive spin transfer from O(6) to O(5) entails p orbitals localized on both oxygen atoms, along the O—O axis at the O(6) end, and perpendicular to this axis on O(5); as well as orbitals of d symmetry localized on Mn(1), perpendicular to the μ -oxo plane (Fig. 7). Although the net spin transfer is positive, there are no α orbital transitions with the described symmetry in **R1**. On the other hand, the β -spin HOMO-LUMO transition involves charge transfer from the attacking water to the oxide ligand. This transfer has both the correct symmetry and spin transfer direction (Fig. 8). The transition corresponds to the 199b, 201b MO pair (200b MO is localized on bulk acetate). The spin transfer in this transition contributes to add β density around O(5), which tends to compensate the excess α density localized around this center at the beginning of the reaction, contributing to the O—O bond formation. The Mn(1) center also plays a role in the spin redistribution, as it acquires positive spin density along the transition to **Int1** (0.05 spins in **TS1**, and 0.10 in **Int1**).

3.2.2. Int1-TS2-P1 reaction sequence, the O—O bond formation step

In **Int1**, the main contribution to the O5—Mn(1) bond comes from the α orbitals. The two most important contributions arise from 201a, and 172a MOs (Table 5), which are essentially π - and

σ -type bonding orbitals, respectively (Fig. 9). In the 201a MO, the α -spin HOMO, the bonding contribution comes from the $p_y + d_{xy}$ and $p_z + d_{xz}$ orbital bonding combinations; while in 172a MO, it arises from the $p_x + d_{x^2-y^2}$ orbital bonding combination. The resulting bonding orbitals have 12% manganese and 27% oxygen character (201a MO), and 11% manganese and 14% oxygen character (172a MO), indicating a very covalent σ, π -donor ligand-to-metal bond contribution from

Fig. 7. Spin density differences at different stages of the O—O bond formation reaction. The densities at different configurations are obtained via subtraction of the last state minus the initial state. Green isosurfaces correspond to more positive spin with respect to the initial state, while orange isosurfaces correspond to a decrease of spin density.

Table 4
Charge contributions of important MOs to the Mn(1)—O(oxide) bond in **R1**.

MO ^a	Orbital components (O—Mn)	Symmetry	Mn(1)		O(5)	
			s + p	d	s	p
173b	$p_x - d_{x^2-y^2}$	σ	1	1	0	6
168b	$p_x - d_{x^2-y^2}$	σ	1	2	1	12
160b	$p_x - d_{z^2}$	σ	2	7	1	6
192a	$p_y - d_{xz} + d_{xy}$	π	1	5	0	15
189a	$p_y + p_z - d_{xz} + d_{yz}$	π	1	7	0	21
186a	$p_y + p_z - d_{yz} + d_{xy}$	π	1	8	0	17
175a	$p_x + p_y + p_z - d_{xz} + d_{yz}$	π	0	4	0	10
169a	$p_y + p_x + p_z - d_{xy} + d_{x^2-y^2}$	σ, π	1	5	1	20

^a α -HOMO, α -LUMO: 201a, 202a MO; β -HOMO, β -LUMO: 199b, 201b MO.

Fig. 8. Boundary surface plots of the β -spin HOMO (199b MO) and LUMO (201b MO) orbitals in **R1**. x-axis along the Mn(1)—O(3) bond, y-axis along the Mn(1)—N bond, and z-axis along the Mn(1)—O(4) bond.

Table 5

Charge contributions of important MOs to the Mn(1)—O(oxide) bond in **Int1**.

MO ^a	Orbital components (O—Mn)	Symmetry	Mn(1)		O(5)	
			s	p	s	p
184b	$p_x - d_{x^2-y^2}$	σ	0	1	0	8
175b	$p_x - d_{x^2-y^2}$	σ	1	1	0	7
169b	$p_x - d_{x^2-y^2}$	σ	0	2	0	10
164b	$p_x - d_{x^2-y^2}$	σ	0	6	0	5
201a	$p_y + p_z - d_{x^2-y^2} + d_{xz} + d_{xy}$	π	1	12	0	27
196a	$p_x + p_y + p_z - d_{xy}$	π	1	3	0	11
193a	$p_y + p_z - d_{xz}$	π	0	4	0	10
191a	$p_y + p_z - d_{xz} + d_{xy}$	π	1	6	0	18
172a	$p_x + p_y + p_z - d_{xz} + d_{xy} + d_{x^2-y^2}$	σ	1	10	0	14

^a α -HOMO, α -LUMO = 201, 202 MO; β -HOMO, β -LUMO = 200, 201 MO.

the α -spin manifold. Other smaller contributions of α orbitals come from π bonding interactions in 196a, 193a, and 191a MOs. Other minor contributions arise from interactions to the two empty β e_g orbitals, and are mainly σ -type donor interactions in 184b, 175b, 169b, and 164b MOs.

The delocalization of α spin density from O(5) to Mn(1) can be associated with the overall increase of the O(5)—Mn(1) bond order in going from **R1** to **Int1**, which is mainly represented by the α -spin O—Mn bonding orbitals. From an energetic point of view, the extra bond strength acquired in this reaction step contributes to stabilize the system, relative to **R1**.

Transfer of β -spin density from O(6) to O(5) in the previous **R1** to **Int1** steps, left O(6) with excess alpha spin. This will prompt the

approach to O(5), with transfer of α -spin density, and O—O bond formation. The excess of α spin accumulated in the previous reaction steps on O(6), O(3) and Mn(1) find their way in the **Int1-TS2-P1** reaction sequence to Mn(2) (Table 3 and Fig. 7). Basically, this sequence starts with spin transfer of ~ 0.3 spins from O—O to the directly ligated Mn(1) in the **Int1-TS2** step, followed by a net transfer of approximately 1.2 spins from several moieties to Mn(2) in the **TS2-P1** step, distributed as ~ 0.4 spins coming from Mn(1), ~ 0.5 from O(3), and ~ 0.3 from the O—O pair. The preference for migration of the positive spin density to Mn(2) is consistent with the tendency of manganese in a weak field environment to adopt high spin states.

The most significant spin rearrangement in the **Int1-TS2-P1** sequence occurs in the **TS2-P1** step. According with the isodensity plots, the density is mostly modified around O(5), O(6), Mn(1), Mn(2), and O(3), and to a lesser extent, around O(4), affecting oxygen orbitals of p symmetry, and orbitals of d symmetry around the manganese centers (Fig. 7). The spin density increases around Mn(2), and O(5), while it decreases around O(6), O(4), and to a lesser extent around O(3). Mn(1) shows increase and decrease of spin density, with a net increase of spin, due to the Mn 3d orbitals participating in both the donor and acceptor MOs, and also due to induced polarization from Mn(2), via superexchange interactions. This spatial redistribution is consistent with a transition between the α -HOMO (201a MO) and the α -LUMO (202a MO) orbitals in **TS2** (Fig. 10).

The exchange coupling constant $J = -300 \text{ cm}^{-1}$ is indicative of moderately strong antiferromagnetic exchange among manganese centers [43]. Spin transfer to Mn(2) occurs from non-directly attached groups via several mechanisms. The effectiveness of the Mn(1) d-based

Fig. 9. Boundary surface plots of MOs that contribute to the O—Mn(1) bonding in **Int1**. x-axis along the Mn(1)—O(3) bond, y-axis along the Mn(1)—N bond, and z-axis along the Mn(1)—O(4) bond.

Fig. 10. Boundary surface plots of the α -spin HOMO (201a MO) and LUMO (202a MO) orbitals in **TS2**. x -axis along the Mn(1)—O(3) bond, y -axis along the Mn(1)—N bond, and z -axis along the Mn(1)—O(4) bond.

MOs for superexchange is given by the extent of orbital contributions from the bridging oxide and the second manganese. Antiferromagnetic contributions to J arise from delocalization of the excess spin-down electron density localized on Mn(1) onto Mn(2)-centered d orbitals whose spin-up counterparts are occupied. Inspection of the corresponding orbitals [92,93] (COs) in **TS2** (Fig. 11) shows that the superexchange interaction is mediated through two π pathways, Mn(1)(d_{yz})—O(4)(p_z)—Mn(2)(d_{xz}) (199 CO, $S = 0.201$), and Mn(1)(d_{xy})—O(3)(p_z)—Mn(2)(d_{yz}) (200 CO, $S = 0.094$), which involves oxygen p orbitals perpendicular to the Mn_2O_2 plane.

π^* orbitals of the hydroperoxo ligand (see Fig. S4 in SI) give the most important donor interactions with Mn d orbitals, and contribute to the Mn—OOH bonding in the product **P1**. The in-plane π_h^* alpha orbital of the hydroperoxo interacts with the d_{xz} orbital of Mn(1), via π donation (Table 6). The resulting bonding orbital, $\pi_h^* + d_{xz}$, 196a MO, has 3% manganese and 20% hydroperoxo character, indicating a covalent π -donor bond [94]. The second π^* orbital of the hydroperoxo (the out-of-plane π_v^*) interacts with the Mn d_z^2 to form a σ -type bonding $\pi_v^* + d_z^2$ orbital (199b MO) [95], which has 2% manganese and 58% hydroperoxo character (Fig. 12).

An additional bonding contribution within the alpha manifold comes from the out of plane π_v^b orbital of the hydroperoxo, which interacts with the $d_{x^2-y^2}$ orbital of manganese, via π donation. The resulting orbital $\pi_v^b - d_{x^2-y^2}$ contributes through two MOs, with 2% manganese and 24% hydroperoxo character in 150a MO, and 2% manganese and 18% hydroperoxo character in 151a MO. The 197a, 194a, 190a, and 169a have negligible contributions to bonding as they include bonding and antibonding interactions.

Within the beta manifold, there are also small contributions from σ -type donating orbitals from π_v^* , π_v^b , and σ^{b*} hydroperoxo orbitals, through 199b, 150b, and 149b MOs, respectively.

The net effect is a bonding interaction, in which the π^* orbitals of hydroperoxo are the most important contributors to bonding. These two orbitals are also responsible for binding in a mono Fe complex, but with significantly higher bonding strength contribution [96]. Among the several bonding contributions to Mn(1)—OO, 196a MO is the most important, with 3% metal admixture. The other interactions have 2% or less manganese contributions from 150a, 151a, and 199b MOs. Hence the O(5)—Mn(1) bond strength is estimated to be smaller in **P1** than **R1**.

3.2.3. R2-TS3-P2 reaction sequence

PCET in going from **R2** to **TS3** reduces the β -spin HOMO-LUMO energy gap in 18.2 kcal/mol. Direct examination of spin differences between

Fig. 11. Boundary surface plots of corresponding orbitals (COs) in **TS2**.

Table 6
Charge contributions of important MOs to the Mn(1)—O(oxide) bond in **P1**.

MO ^a	Orbital components (O—Mn)	Symmetry	Mn(1)		O(5)		O(6)	
			s + p	d	s	p	s	p
199b	$\pi_v^* - d_z^2 + d_x^2 - y^2$	σ	1	$1(d_x^2 - y^2), 1(d_z^2)$	0	25(p_x)	0	20(p_x)
150b	$\pi_v^b - d_x^2 - y^2$	σ	0	$2(d_x^2 - y^2)$	0	2(p_x)	0	3(p_x)
149b	$\sigma^{b*} - d_x^2 - y^2$	σ	0	$4(d_x^2 - y^2)$	0	2(p_x)	0	0(p_x)
197a	$\pi_h^* - d_{xz} + d_{xy}$	π	2	4	0	18	0	3
196a	$\pi_h^* - d_{xz}$	π	0	3	0	17	0	3
194a	$\pi_v^* + \pi_h^* - d_{xz}$	π	0	3	0	8	0	3
190a	$\pi_v^* + \pi_h^* - d_{xz}/d_{xy}$	π	1	11	0	10	0	2
169a	$\pi_v^b - d_z^2$	π	1	3	0	6	0	3
151a	$\pi_v^b - d_x^2 - y^2$	π	0	2	1	11	0	12
150a	$\pi_v^b - d_x^2 - y^2$	π	1	2	0	9	0	9

^a α -HOMO, α -LUMO = 201a, 202a MO; β -HOMO, β -LUMO = 200b, 201b MO.

Fig. 12. Boundary surface plots of MOs that contribute to the HOO—Mn(1) bonding in **P1**. x-axis along the Mn(1)—O(3) bond, y-axis along the Mn(1)—N bond, and z-axis along the Mn(1)—O(4) bond.

the **R2** and **TS3** shows a decrease of spin density of similar shape to the out-of-plane π^* hydroperoxo orbital (the main component of the **R2** β -HOMO), and a density increase of the Mn(1) d_z^2 , the main component of the **R2** β -LUMO (Figs. 13 and 14). This confirms that the reduction of the HOMO-LUMO gap facilitates the preconditions for electron transfer between these two moieties.

The most important contribution to the Mn(1)—OO bonding in **R3** (equivalent to **P2**) comes from the 180a MO, in which the π_v^* orbital[†] from the O—O superoxide (Section SI.6 in SI) radical interacts with Mn $d_{xz} + d_{yz}$ orbitals. 180a MO has 5% manganese and 40% superoxo character, indicating a covalent σ -donor bond (Table 7). Other contributions from the alpha manifold have 2% or less Mn contributions. Within the beta manifold, 183b MO has a very high contribution of d_z^2 (29%), but the covalency of the Mn(1)—OO bond is very low, indicating that d_z^2 is the e_g filled orbital. The β -spin HOMO (184b MO) contributes to Mn—OO bonding, which includes the in-plane π_h^* orbital of the superoxo ligand that interacts with the $d_x^2 - y^2$ and d_z^2 orbitals of Mn(1), in a σ -type bonding interaction. 184b MO has 2.1% $d_x^2 - y^2$, and 1.3% d_z^2 contributions, and 21% p_x superoxo character, indicating a covalent σ -donor bond (Table 7). 137b MO has only 1% Mn contribution. No other significant contribution from the beta manifold is observed.

The bond strength in this case has only one significant contribution from the 180a MO, with 5% manganese. This indicates that the bond

strength is weaker than **P1**, which clearly gets the ligand ready to be cleaved in the following step.

3.2.4. R3-TS4-Int2-TS34/43-P3 reaction sequence

The major spin rearrangement within this sequence occurs between the **Int2** and **TS34** steps, in which there is spin transfer between O—O and Mn(1). Spin density isosurfaces show that the involved orbitals have π symmetry in the region of O—O ($\pi^*(OO)$), and d symmetry in the μ -O plane around Mn(1) (Fig. 15). The region around Mn(2) shows redistribution of spin, without net change.

The O—O superoxide radical ligand in **Int2** has a π^* orbital (200b MO, the β -spin HOMO) that has donor interactions with Mn d orbitals and contributes to the Mn—OO bonding. The in-plane π_h^* orbital of the superoxo ligand interacts with the $d_x^2 - y^2$ orbital of Mn(1), resulting in a σ -type bonding molecular orbital $\pi_h^* + d_x^2 - y^2$ (Fig. 16). This component of 200b MO has 7% $d_x^2 - y^2$ and 55% superoxo character from the p_x orbitals, indicating a covalent σ -donor bond. There are additional small contributions to OO—Mn(1) bonding from 200a, 194a, and 192a MOs (Table 8).

Electron transfer initiates with HOMO-LUMO transition. The β -spin LUMO (201b MO) is formed by the antibonding combination $\pi_h^*(OO) - d_x^2 - y^2$ (Mn(1) orbital; while, the β -spin HOMO (201b MO) is the main contributor to the OO—Mn(1) bond. The HOMO-LUMO transition therefore facilitates charge transfer from the OO—Mn(1) bond to the Mn center. In this way, electron transfer assists OO—Mn(1) bond cleavage, by weakening the metal ligand bond strength. From a spatial perspective, both donor and acceptor MOs are partially localized on

[†] The v (“vertical”) subscript is relative to this particular arrangement, and indicates the orbital lobes are perpendicular to the O—O—Mn(1) plane. Concomitantly, the h (“horizontal”) subscript indicates the orbital lobes are parallel to the mentioned plane.

Fig. 13. Boundary surface plots of the β -spin HOMO (215b MO) and LUMO (217b MO) orbitals in **R2**. x-axis along the Mn(1)–O(3) bond, y-axis along the Mn(1)–N bond, and z-axis along the Mn(1)–O(4) bond.

O–O and Mn(1), which facilitates electron transfer. Release of the O–O moiety in the last reaction step gives room to the return of another water ligand during the following catalytic cycle.

A comparison between configurations with the AcOOH hydrogen bonded and not hydrogen bonded to μ -O in **R3**, shows there is an increase of the contribution of the β -spin HOMO $d_{x^2-y^2}$ component from 2% to 3% in going from the non-bonded to the hydrogen bonded configuration, and this contribution increases even further when the proton is transferred from AcOOH to μ -O (7% of $d_{x^2-y^2}$, see Table 9). Along the same series, the p_x component decreases from 21%, to 20%, to 17%, respectively. This tendency shows charge shift from the ligand to the metal, which will facilitate the reduction of Mn(1). This suggests that the catalyst takes advantage of proton donor groups coordinated to the oxo bridge ligands, to facilitate OO–Mn bond rupture, and Mn reduction via a fine-tuned HOMO–LUMO transition.

4. Discussion

As the reaction advances, the approaching water oxido ligand combination in **R1** evolves to hydroperoxo in **P1**, to superoxo in **P2**, and finally dioxygen in **P3**, with oxygen formal oxidation states associated with the (O,O) pair increasing from (–2,–1) to (–1,–1), (–1/2,–1/2) and (0,0), respectively. In all these steps, the redox

partner is manganese. In the first step, there is β -spin transfer from O(6) to O(5), which compensates the initial excess alpha spin on O(5), and prepares for the O–O singlet bond formation. The following spin transfer occurs from the O–O system to the outer-most Mn(2) center. The last two oxidation steps include spin transfer from the O–O to the directly attached Mn(1). In each step there is reduction of the OO–Mn(1) binding strength, with concomitant increase of the O–O bond strength, which culminates with the release of O₂ in the last step. The HOMO in the last step is localized in the OO–Mn(1) bond, which means that charge transfer contributes directly to OO–Mn(1) bond cleavage. This last step is entropy driven, while formation of hydroperoxide and superoxide moieties is enthalpy driven.

Along the reaction, the spin density associated with the O–O pair takes the approximate values (rounded to the nearest integer) 1, 0, 1, and 2 spins. Only the first transition is alpha transfer, while the other two are beta spin transfers. Spin transfer in the steps **R2** to **P3** is required to increase the number of unpaired electrons of the O–O bond, as well as weakening of the OO–Mn(1) bond, which ultimately will allow the entropy-driven release of O₂. Beta spin transfer from OO is more efficient as it involves the adjacent nucleus Mn(1), and is observed in most of the reaction steps.

The first step (**R1** to **P1**) requires spin transfer of the opposite spin (alpha) to aid in the O–O bond formation, which requires both alpha and beta spin rearrangements within the OO moiety to form the O–O bond. Alpha spin transfer also assists in keeping closer the oxidation states of both metal centers. The weak field manganese ligands create a small t_{2g} – e_g gap, making the high spin state the most stable. The transfer of spin to the outermost manganese center in the O–O formation is therefore to conserve the manganese high spin state.

The strength of the hydrogen bond between AcOOH and the μ -O bridging ligands also increases along the reaction path, with proton

Fig. 14. Spin density differences at different stages of the hydroperoxo to superoxo ion formation reaction sequence. The densities at different configurations are obtained via subtraction of the last state minus the previous state. Green isosurfaces correspond to more positive spin with respect to the initial state, while orange isosurfaces correspond to a decrease of spin density.

Table 7

Charge contributions of important MOs to the Mn(1)–OO(superoxo) bond in **R3**.

MO ^a	Orbital components (O–Mn)	Symmetry	Mn(1)		O(5)		O(6)	
			s + p	d	s	p	s	p
184b	$\pi_h^* - d_{x^2-y^2} + d_z^2$	σ	1	3.5	0	21(p_x)	0	41(p_x)
183b	$\pi_h^* - d_z^2$	σ	2	29	0	0.4(p_x)	0	4(p_x)
137b	$\pi_h^* - d_{x^2-y^2}$	σ	1	1	1	11(p_x)	0	12(p_x)
183a	$\pi_v^* - d_{yz}$	π	0	2	0	18	0	19
180a	$\pi_v^* - d_{xz} + d_{yz}$	π	0	5	0	18	0	22
137a	$\pi_h^* - d_z^2 + d_{x^2-y^2}$	σ	1	1	2	38	1	25
126a	$\pi_v^* - d_{xz}$	π	2	1	0	31	0	26
116a	$\sigma^b - d_{xy} + d_{x^2-y^2}$	σ, π	2	1	0	11	2	10

^a α -HOMO, α -LUMO = 185a, 186a MO, β -HOMO, β -LUMO = 184b, 185b MO.

Int2 to TS34

Fig. 15. Spin density differences at the **Int2** to **TS34** step of the superoxo to paramagnetic di-oxygen formation reaction sequence. The densities at different configurations are obtained via subtraction of the last state minus the previous state. Green isosurfaces correspond to more positive spin with respect to the initial state, while orange isosurfaces correspond to a decrease of spin density.

transfer to the μ -O ligands in the last Mn^{II} — Mn^{III} step. This property is correlated with charge transfer from the OO —Mn bond to Mn, facilitating the OO —Mn bond rupture, and reduction of Mn, via HOMO—LUMO interactions.

One of the findings of this investigation is that in the initial state **R1**, the oxygen ligand has an intermediate spin between zero (non radical) and one (oxyl radical). From a methodological point of view, it suggests that broken symmetry DFT, and particularly the inclusion of solvent in the calculations gives a particularly realistic description of the experimental process.

From a mechanistic perspective, the attacking water molecule plays an active role in the O — O formation (beyond being merely attracted by the oxido ligand). It requires to be properly oriented and retained in place, to proceed with the O — O bond formation reaction. Also, it

Table 8

Charge contributions of important MOs to the $\text{Mn}(1)$ — OO (superoxide) bond in **Int2**.

MO ^a	Orbital components (O —Mn)	Symmetry	Mn(1)		O(5)		O(6)	
			s + p	d	s	p	s	p
200b	$\pi_{\text{H}}^* - d_{x^2-y^2}$	σ/B	0	7	0	17(p_x)	0	38(p_x)
200a	$\pi_{\text{H}}^* - d_{xy} + d_{x^2-y^2}$	π/B	0	1	0	13	0	20
194a	$\pi_{\text{V}}^* - d_{xz}$	π/B	1	3	0	6	0	6
192a	$\pi_{\text{V}}^* - d_{yz}$	π/B	0	3	0	26	0	31

^a α -spin HOMO, LUMO: 201a, 202a MO; β -spin HOMO, LUMO: 200b, 201b MO.

presents electrophilic properties, in addition to those present in the water molecule ligated to Mn. From a PSII perspective, this suggests that positioning of the attacking water molecule is a key step, and that the electrophilic properties may not be only present in the water molecule ligated to Mn, but also on the attacking water molecule.

Although the μ -O ligands were proposed as reactants in some models of the OEC of PSII [37,97,98], the results of the present report suggest that the oxo bridging ligands do not act as reactants. We found that the oxo-bridging ligands have the following functions and characteristics along the reaction:

- 1) provision of the appropriate strength to the ligand metal field in different reaction steps,
- 2) anchor molecular species, such as AcOOH . This species aids in the positioning of reactive groups, particularly the orientation and positioning of the attacking water molecule at the beginning of the reaction,
- 3) hold p-orbitals that provide support for super-exchange spin interaction pathways.
- 4) bind protons that stabilize manganese in low oxidation states,
- 5) assistance in charge shifting from the OO —Mn bond to Mn in the last reaction step (after μ -O protonation), which contributes to OO —Mn cleavage via HOMO—LUMO interactions.

Energy differences between intermediates and transition states during proton transfers to AcOO^- are very small (≤ 1 kcal/mol, usually within the error of the DFT methodology). This is due to AcOO^- is a very good base (e.g., $\text{pK}_{\text{b}} = 9.25$ in CH_3COONa), and hence these steps are basically barrier-less.

Barriers along the catalytic reaction of water oxidation analyzed in the preceding sections are always lower than the 19–21 kcal/mol experimental value. However, according with the experimental results, the rate-limiting step is the formation of the highest oxidized species

Fig. 16. Boundary surface plots of MOs that contribute to the OO — $\text{Mn}(1)$ bonding in **Int2**. x-axis along the $\text{Mn}(1)$ — $\text{O}(3)$ bond, y-axis along the $\text{Mn}(1)$ —N bond, and z-axis along the $\text{Mn}(1)$ — $\text{O}(4)$ bond.

Table 9

Mn(1) 3d, and O(5) 2p components of the β -spin HOMO in **R3** (Mn oxidation state Mn(III,III)) for several AcOOH–O(4) bonding modes.

Center	Orbital	H–O(4) bond type		
		No bond	H-bond	Covalent bond
Mn(1)	d_z^2	1	1	0
	d_{xz}	0	0	0
	d_{yz}	4	4	3
	$d_{x^2-y^2}$	2	3	7
	d_{xy}	0	0	0
O(5)	p_x	21	20	17
	p_y	5	4	3
	p_z	1	2	2

(**R1** in our nomenclature) by oxidation of Mn(1)^{IV}–Mn(2)^{III} [6,50], or peroxymonosulfate binding [63], both of which occur prior to the O–O formation. Hence, the fact that the O–O bond formation and dioxygen O₂ evolution reaction does not include the rate-limiting step, support the experimental findings.

Water splitting catalyzed by **1** is a paradigm for PSII. It oxidizes bulk water to give molecular dioxygen. The whole process relies in several key factors.

- 1) the presence of a strong base (AcOO[−]), which acts as a proton abstractor in all proton transfer processes;
- 2) the availability of at least two metal centers to interchange spin and act as redox partners of the OO moiety;
- 3) the accessibility of nearby groups to help accommodate/orient the reactant species, as well as provide protons necessary to achieve a low metal oxidation state (Mn^{II}–Mn^{III}). This role is also performed by solution AcOOH.

The role of AcOO[−] is remarkable, as AcOO[−] is not an integral part of the catalyst, and only belongs to the solution buffer. The parallelism with PSII is compelling, as the natural system also requires a proton acceptor group to trap the exiting protons from the water splitting reaction. This role can be played by either D1-Asp170, or O5 (the μ -O bridging ligand between Mn(3) and Mn(4) in the OEC), according with current X-ray models [37].

Proposals for the mechanism of O–O bond formation in PSII can be grouped into two major categories based on the nature of the bound substrate water molecules. The first group involves coupling reactions of an oxyl radical [34,99–101]. The second category of mechanisms for water oxidation involve nucleophilic attack of a calcium-bound water (or hydroxide) ligand on the electrophilic oxygen atom of an Mn^V=O intermediate in the O–O bond-forming step [55,102–104]. The finding of a partial oxidation state, with a magnitude intermediate between an oxyl radical (Mn^{IV}–O^I) and an oxo ligand (Mn^V=O) in the **R1** state of the reaction catalyzed by **1** may reconcile the two most accepted proposals for the mechanism of O–O bond formation in PSII. Gupta *et al.* also present an intermediate alternative, by providing spectroscopic evidence for O radical character in a complex containing a formal Mn(V) ion [105–107].

After the S₃ state of the PSII Kok cycle, several spectroscopic studies, including time-resolved ultraviolet–visible [108,109], electron paramagnetic resonance [110], infrared spectroscopy [111], Mn K-edge XAS [112], and femtosecond X-ray diffraction [113], suggest the presence of a transient state S₃Y₂^{OX}, also referred to as S₃' [109,111]. This intermediate state hints to deprotonation occurs prior to the onset of Mn redox chemistry. One of the reasons of the delay in starting the Mn redox chemistry in going from S₃ to S₄ in PSII was postulated to be the restructuration of the hydrogen bond network [109]. In line with this findings, after O(5) in **1** is oxidized in **R1**, a delay may occur due to reprotonation of the AcCOOH directed ligated to the reactant water molecule, or due to substitution with a protonated acetate in the second solvation shell.

Although Rivalta *et al.* discuss the same catalyst in a similar experimental setup [62]; there are differences with the catalytic process explained in this investigation:

- 1) O–O bond formation (**R1** to **P1**): We showed a systematic analysis showing that AcOH is hydrogen bonded to the oxo bridge ligands. This poise a difference on where the substrate water anchors during the first step of the reaction. In our case, it is the oxygen of the AcOH H-bonded to the oxo-bridge ligand, whereas Rivalta *et al.* proposes an oxo-bridge ligand. There is consistency in both investigations that bulk acetate is the base that captures the leaving proton. The spin rearrangement is similar in both investigations.
- 2) Formation of superoxide (**R2** to **P2**): In our case there is proton transfer from the hydroperoxo to a bulk acetate and electron transfer from the hydroperoxo to the adjacent Mn(1); whereas in Rivalta *et al.* the proton transfer is to an oxo bridge ligand, with electron transfer from the HOO to the adjacent Mn(1). As a result, the bridge is protonated in their model, at difference with our model.
- 3) Molecular di-oxygen formation (³O₂) (**R3** to **P3**): In our case there is proton transfer from the two H-bonded acetates to the oxo bridges, and electron transfer from the superoxo to the adjacent Mn(1); whereas in Rivalta *et al.* there is only one proton transfer, which is from bulk acetate to the unprotonated oxo bridge.
- 4) The methodology is also different, with different basis sets (ours is larger), and different ways of including the solvent in the calculations. In particular, our optimizations in solvent are closer to the experimental conditions.

Early works of Lundberg *et al.* also addressed the mechanisms of the reaction catalyzed by **1** [59,66]. In these studies only the O–O bond formation step was analyzed (**R1** to **P1**). There is no acetate involved in the reaction, *i.e.*, the base capturing protons is one of the oxo-bridge ligands, instead of acetate in our approach. The spin transfer is also different than in our approach, *i.e.*, the spin from the HOO moiety in the last step of the **R1** to **P1** sequence is transferred to the directly attached Mn(1) center in the Lundberg *et al.* model, whereas the transfer is to the outermost Mn(2) in our approach. This different spin rearrangement lowers the barrier in this step.

5. Summary and Conclusions

In summary, we have shown that the terpy complex (**1**) catalyzes the oxidation of water to give oxygen, with a process that signals several possible similarities with the equivalent process in PSII. The model includes high spin manganese centers in the III and IV oxidation states in a μ -oxo bridge arrangement, and a partial oxido radical, as reactants. This radical becomes an electrophile, and reacts with a bulk water molecule. We proposed a mechanism in which the manganese center not directly attached to the reactant oxido species is not a simple spectator, but a key factor in the O–O bond formation reaction. It participates in spin density transfer during the O–O bond formation reaction. In consistency with the OEC, in which proton acceptor groups are implicated in trapping the exiting protons from the water splitting reaction, the reaction catalyzed by **1** uses the AcOO[−] base from the buffer solution as proton receptor, which makes the reaction less energetically stringent than oxo bridge ligands as proton acceptors.

The rate-limiting step does not belong to the molecular paramagnetic dioxygen formation reaction, concomitant with experimental findings in which the rate-limiting step is the oxidation of Mn(IV,III) to the formal Mn(IV,V) oxidation state. Our findings establish that there is unpaired spin density associated with the oxido ligand in O–Mn(1), at the beginning of the O–O bond formation reaction, yet the density is less than what is expected for an oxyl radical. This result suggests the possibility that a high-spin Mn^V-oxo center could be operative within the S₄ state of the OEC. This might be a remarkable property, as despite the suggestion that Mn^V may be a key component

of S4, presently there are no crystallographically characterized small molecule complexes containing Mn^V as dinuclear or higher nuclearity structures [8].

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Appendix A. Supplementary data

Methodology used to include the solvent in the calculations; arrangement of H₂O hydrogen bonded to the μ -O(3) ligand instead of AcOOH with Mn oxidation state Mn(IV,IV); configuration corresponding to alternate mechanism of proton transfer to μ -O(4) ligand in the O—O bond formation step; comparison of different levels of theory of calculated free energies along the reaction pathway; description of spin redistribution along the O—O bond formation step in the **R1-P1** reaction sequence; electronic structure of the hydroperoxo and superoxo ion ligands. This material is available free of charge via the Internet. Supplementary data associated with this article can be found in the online version, at <http://dx.doi.org/10.1016/j.jinorgbio.2017.02.014>.

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