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A Molecular 'Double-pivot' Mechanism for Water Oxidation

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In spite of efforts to elucidate the structure and properties of the Mn center operating in the photosynthetic apparatus of green plants and catalyzing the water oxidation reaction of eqn. (1), little is known about

$$2H_2O \longrightarrow O_2 + 4H^+ + 4e^- \qquad (1)$$

the arrangement of the metal atoms, their ligation or their precise mode of action. A number of mechanistic proposals have been presented e.g. [1–4], but none have been able to satisfactorily account for all the available EXAFS [5, 6], EPR [7, 8] and UV–Vis data [9, 10]. Recent reviews of this area are available [11, 12].

The photosynthetic Mn center is capable of cycling between five distinct oxidation levels, labelled S_0 to S_4, with oxygen evolution occurring during the $S_4 \rightarrow S_0$ transition (eqn. (2)) [13]. It is

$$S_0 \longrightarrow S_1 \longrightarrow S_2 \longrightarrow S_3 \longrightarrow S_4 \xrightarrow{-O_2} S_0 \qquad (2)$$

believed that four Mn atoms per photosystem II (PSII) reaction center are essential for oxygen evolution [14]. The four Mn are apparently composed of two pools of two similar atoms [15]. EXAFS results on S_1 suggest two Mn occur in a binuclear site (Mn...Mn = 2.69(3) Å), with bridging oxide and terminal O and/or N ligands [5]. The EXAFS data can also accommodate two other Mn atoms at distances of approximately 3.3 Å from the binuclear center [5]. X-ray absorption edge studies show the edge position of the Mn in dark-adapted PSII particles ($S_0 + S_1$) to be between those of Mn(II) and Mn(III) model complexes [6]. The edge position of the S_2 state suggests a Mn(IV) center is present, and the edge position of S_3 is between that of S_1 and S_2, interpreted as evidence for a structural rearrangement [6]. The EPR spectrum of S_2 has been assigned to a site comprising 3Mn(III) + Mn(IV) [7]. Difference UV–Vis spectra suggest the $S_0 \rightarrow S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_0$ transitions involve the Mn_4 oxidation level pattern of +1:+1:+1:−3 [10]. Comparisons with the difference spectra of model complexes by Dekker *et al.* [9] and ourselves [16] indicate that individual metal oxidation state changes of Mn(II) → Mn(III) and Mn(III) → Mn(IV) could both be involved during this cycle.

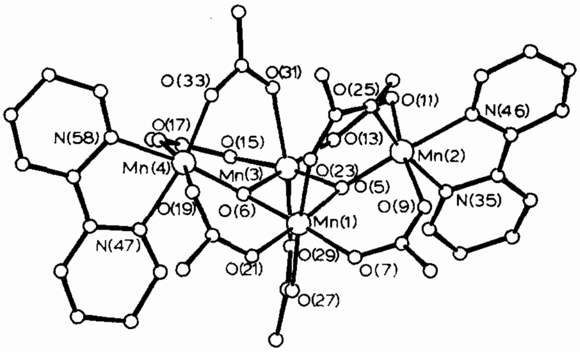

Fig. 1. The structure of $[Mn_4O_2(O_2CMe)_7(bipy)_2]^+$. Selected bond distances (Å) and angles (deg.) are: Mn(1)...Mn(3), 2.848(5); Mn(1)...Mn(2), 3.312(5); Mn(1)...Mn(4), 3.385(5); Mn(3)...Mn(4), 3.299(5); O(5)–Mn(1,2,3), 1.918(12), 1.844(13), 1.889(13), respectively; O(6)–Mn(1,3,4), 1.911(15), 1.930(15), 1.804(16), respectively; Mn(1)–O(5)–Mn(2,3), 123.3(7), 96.8(6), respectively; Mn(2)–O(5)–Mn(3), 129.1(7); Mn(1)–O(6)–Mn(3), 95.7(7); Mn(1)–O(6)–Mn(4), 131.3(9); Mn(3)–O(6)–Mn(4), 124.0(8).

The Mn_4 center is obviously able to perform the three main functions associated with facile conversion of two molecules of H_2O to one molecule of O_2: (i) stabilization and storage of oxidizing equivalents; (ii) formation of a template to hold two molecules of H_2O in close proximity to facilitate oxygen–oxygen bond formation; and (iii) making the bound H_2O molecules more acidic to facilitate H^+ loss. Wells has shown that the equilibrium constant for the reaction of eqn. (3) is at least two orders of magnitude greater for Mn(III) than for any other trivalent first row transition metal [17].

$$\mathrm{Mn(III)}{-}OH_2 + H_2O \rightleftharpoons \mathrm{Mn(III)}{-}OH + H_3O^+ \qquad (3)$$

Recently, we discovered that reaction of trinuclear $[Mn_3O(O_2CR)_6L_3]^{0,+}$ (L = pyridine, H_2O) with bipyridine (bipy) yields tetranuclear $[Mn_4O_2(O_2CR)_7(bipy)_2]^{z+}$ (R = Ph, $z = 0$; R = Me, $z = 1$). The structure of R = Me complex has been determined and is shown in Fig. 1. Pertinent bond distances and angles are given in the figure legend. The complex possesses several features which are very similar to the water oxidation Mn complex: (a) a metal nuclearity of four; (b) oxide bridges between the metal centers; (c) O- and N-based ligation; (d) two pairs of inequivalent Mn atoms; and (e) metric parameters which are reasonably consistent with the EXAFS data on the native site. We thus consider the above

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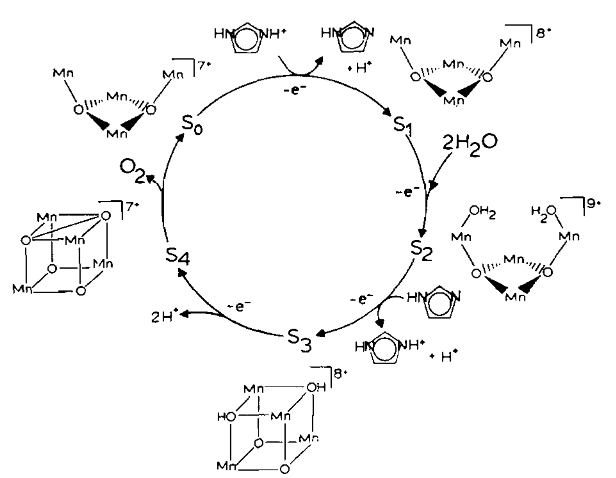

Fig. 2. Schematic representation of the proposed mechanism of water oxidation.

two complexes as potential models for the S_0 and S_1 states of the water oxidation center.

Entertaining further the possibility that models of the S_0 and S_1 states are at hand, we have sought to encompass them into a mechanistic scheme for how the water oxidation reaction is carried out, incorporating also the available biochemical data described above, and have arrived at a mechanistic scheme consistent with EXAFS, EPR and UV–Vis difference data on the native site.

The mechanism for the water oxidation cycle is depicted in schematic form in Fig. 2. For clarity, we have not shown the O- and N-based peripheral ligation, only the structural rearrangements of the core. The S_0 (Mn(II) + 3Mn(III)) and S_1 (4Mn(III)) states possess the Mn_4O_2 structure established in the model complexes, the S_1 state being obtained from S_0 by a one-electron oxidation step. On oxidation of S_1 to S_2 (3Mn(III) + Mn(IV)), the unit is EPR active and two H_2O molecules are now bound, in accord with NMR and EPR results [18–20]. Although no model complex has yet been synthesized with a structure and oxidation level analogous to that shown for S_2, it is nevertheless found as a sub-structure of a dodecanuclear mixed-valence Mn(III, IV) complex, $Mn_{12}O_{12}(O_2CMe)_{16}(H_2O)_4$ [21]. This sub-structure possesses an Mn_4O_2 unit with the same type of butterfly arrangement as seen in Fig. 1. The two 'wing-tip' Mn atoms possess bound H_2O molecules and the Mn(IV) center occupies one of the 'hinge' sites. This arrangement thus lends some feasibility to the proposed S_2 structure.

Further oxidation from S_2 to S_3 (2Mn(III) + 2Mn(IV)) now results in the structural rearrangement suggested by X-ray absorption edge studies [6]. Movement of the two 'wing-tip' Mn atoms towards each other can be accomplished by pivoting of the two Mn–O vectors about the μ_3-O atoms; this 'double-pivot' maneuver requires no movement in the Mn_2O_2 base, but merely an increase in the 'pyramidality' of the μ_3-O atoms. The two H_2O molecules will also be brought closer together, of course, and in the extreme this motion and concomitant deprotonation of H_2O molecules to OH^- allows the unit to convert into a compact cubane-like structure, possessing two μ_3-O^{2-} and two μ_3-OH^- bridges. Cubane-like Mn_4O_4 units exist as sub-structures in $Mn_{12}O_{12}(O_2CMe)_{16}(H_2O)_4$ [21], and $Mn_4(OH)_4$ cubanes are thought to be occurring in $Mn_4(OH)_4(CO)_{12}$ [22]. Further, a Mn_4 cubane with two different types of μ_3-bridging atoms has been established in $[Mn_4(CO)_{12}F_x(OH)_{4-x}]$ [23]. The proposed structure of S_3, therefore, does have indirect support and precedence.

The structural conversion of S_2 to S_3 has attractive consequences for the overall water oxidation cycle, for examination of $[Mn_4O_2(O_2CMe)_7(bipy)_2]^+$ and $Mn_{12}O_{12}(O_2CMe)_{16}(H_2O)_4$ shows that the H_2O molecules of S_2 will have a $(H_2)O...O(H_2)$ distance of approximately 4.5–5.0 Å, whereas in S_3 the (H)O...O(H) distance will be approximately 2.5 Å. The OH groups have thus been brought significantly closer together, and this can facilitate oxygen–oxygen bond formation on subsequent oxidation of S_3. Note also that Krishtalik has shown that ionization of water molecules preceding their oxidation facilitates the enzyme-catalyzed reaction [24], and we suggest that this may assist the described structural rearrangement between S_2 and S_3.

Oxidation of S_3 to S_4 (Mn(III) + 3Mn(IV)) now triggers the substrate oxidation process. The O atoms move towards each other initiating bond formation, and there is concomitant movement apart of the two Mn atoms, transfer of electrons from oxygen to Mn, and loss of the remaining two H^+. An intermediate in this concerted reaction might be a peroxide-bound form as shown in the scheme, at which point the O–O distance should be approximately 1.5–1.6 Å and a net of two electrons having been transferred to the Mn atoms. Continued approach of the O atoms, transfer of two more electrons to the Mn atoms and further movement apart of the latter by pivoting about the μ_3-O atoms leads, in the limit, to formation (and evolution) of O_2 and return of the remaining Mn_4O_2 unit to the S_0 structure and oxidation level. An attractive aspect of a peroxide-bound intermediate is that the total transfer of four electrons from $2OH^-$ groups to the Mn atoms need occur in two two-electron steps, rather than one four-electron step. Note also that structural conversion of S_3 to S_0 is a natural consequence of the approach of the O atoms so that no additional movement is necessary after O_2 evolution to return the Mn_4 unit to its initial conformation ready for recycling. The proposed scheme assumes all water oxidation takes place between S_3 and S_0, and this is supported by mass spectral studies which indicate that no intermediates in the oxidation of H_2O to O_2 are bound to S_3 or prior S_n states [25]. Also, thermoluminescence studies on PSII particles indicate a structural change to accompany conversion of S_3 to S_4; when this change is prevented, S-level advancement ceases and O_2 evolution is terminated [26].

Finally, we address the question of the H^+ release pattern, which is generally believed to be 1:0:1:2 during the S_n changes $S_0 \rightarrow S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_0$ [27]. The two H^+ lost during S_3 conversion to S_0 are already in accord with our proposed scheme. To rationalize the remaining H^+ release pattern, we invoke involvement of an amino acid side chain function such as a histidine residue and, indeed, there is evidence available to support this. Homann has shown that reactivation of Cl^--depleted particles by added anions is contingent upon protonation of membrane-bound buffering groups with apparent pK_a of approximately 6 [28], indicative of the imidazole ring of a histidine residue. Indirect evidence for the association of histidine with the Mn assembly is also mounting [29]. Thus, we depict in the scheme that the released H^+ in the S_0 to S_1 conversion originates from a protonated imidazole (imidazolium) group. This may be necessary, for instance, if the imidazole group now becomes bound to a Mn in S_1, although this is not itself essential to the proposal. The $S_2 \rightarrow S_3$ conversion of the scheme requires liberation of two H^+, one which is released and detected and the other becoming re-attached to an imidazole group. Thus, the overall pattern of H^+ release to the medium is now 1:0:1:2, perfectly in accord with experimental evidence. It should also be added, in conclusion, that the resulting changes in charges of the S_n states of the scheme are consistent with the experimental changes in charges measured by Saygin and Witt [30].

In summary, a scheme is described that is consistent with available data on the water oxidation site. The scheme has many attractive features, not least of which is the precedence provided by characterization of the Mn_4O_2 unit in $[Mn_4O_2(O_2CMe)_7(bipy)_2]^+$. To further assess the viability of this mechanism, synthetic efforts are now being directed to isolation of species having the increased oxidation level of S_2, and species containing the cubane-like structure proposed for S_3. Their isolation may even allow us to reproduce the final oxygen evolution step under laboratory conditions.

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