Thermodynamic Viability of Hydrogen Atom Transfer from Water Coordinated to the Oxygen-Evolving Complex of Photosystem II

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Photosystem II in plants and bacteria utilizes a four-manganese cluster called the oxygen-evolving complex (OEC) to catalyze the four-electron oxidation of water to molecular oxygen.[1] There are five catalytically relevant cluster oxidation states,[2] S_0–S_4. These are successively generated by electron transfer from a photochemically excited P_{680}^+ unit, mediated by a redox-active tyrosyl radical,[3] $Y_Z^•$. We have considered the thermodynamics of proton-coupled electron transfer reactions at high-valent model Mn dimers in the context of recent work on the specific role of $Y_Z^•$ in S-state advancement. It has been suggested that the potential for each transition from S_1 to S_4 must be relatively invariant,[4] a situation inconsistent with the buildup of substantial charge on the Mn cluster upon oxidation. On the basis of a 4.5 Å proximity of $Y_Z^•$ to the Mn_4 cluster,[5] its mobility properties,[6] and its lack of well-ordered hydrogen bonding,[7] a new theory[8] postulates the net transfer of a hydrogen atom from a water, terminally ligated to manganese, to $Y_Z^•$. In this insightful mechanistic proposal suggested independently by Babcock[8] and by Britt,[5] $Y_Z^•$ has the dual role of oxidizing the Mn_4 cluster *and* accepting liberated protons, neutralizing charge buildup on the Mn cluster. This may be particularly critical in higher S-state advancements where it is likely that the cluster potential is too high to be accommodated by simple electron-transfer involving a tyrosyl radical.[9]

Critical to any evaluation of the role of proton transfer in S-state advancement is understanding of proton-coupled electron transfer effects in model manganese complexes in high oxidation states. In an initial attempt to address this hypothesis through biologically relevant model complexes, our group has recently measured the homolytic bond dissociation energy (BDE_{OH}) for a bridging hydroxide ligand in $Mn^{III}Mn^{IV}(\mu\text{-}O, \mu\text{-}OH)(salpn)_2$ dimers (salpn = 1,3-bis(salicylideneamino)propane) to be 77-($\pm$3) kcal/mol.[4,10] By comparison with the BDE_{OH} for tyrosine (86 kcal/mol[11]), H-atom transfer from a bridging hydroxide to $Y_Z^•$ was deemed generally feasible. However, Babcock has suggested that hydrogen atom abstraction occurs from a *terminally ligated* water molecule coordinated to the OEC.[8] While water has a BDE_{OH} of 119 kcal/mol,[12] a water molecule terminally bound to a redox-active manganese ion exhibits substantially different thermodynamics for hydrogen atom transfer. It has been difficult to engineer high-valent multinuclear Mn complexes that can reversibly coordinate and deprotonate water in multiple oxidation states in order to test this theory with model chemistry. However, we have now shown that the alkoxide-bridged dimer $Mn_2L_2^{0,+}$ (L = 2-hydroxy-1,3-bis(3,5-X_2-salicylideneamino)propane, X = Cl, H, di-*tert*-butyl) can reversibly bind water and exhibit proton-coupled electron transfer in multiple oxidation states involving the terminally ligated water molecule. These measurements show that the BDE_{OH} value for the terminal water in our model manganese system is near 86 kcal/mol in two cluster oxidation states, optimally poised for efficient energy transfer by H-atom transfer to a tyrosyl radical.

$Mn_2L_2^{0,+}$ undergoes an alkoxide shift to accept solvating donors, breaking one manganese–alkoxide bond to give the solvent ligated forms, $Mn_2L_2OH_2^{0,+}$ (Figure 1). Tetrahydrofuran,[13a] methanol,[13b] and water[13c] adducts have been crystallographically characterized and show that a relatively minor structural shift is required in order to accommodate the solvent molecule. The bound solvent has little effect on the electronic properties of the complex as shown by the nearly identical EPR spectra[13a,14] of $Mn^{III}Mn^{IV}L_2^+$ and $Mn^{III}Mn^{IV}L_2OH_2^+$. Batch titrations of $Mn^{III}_2L_2$ and $Mn^{III}Mn^{IV}L_2^+$ complexes with water in CH_3CN were followed by UV-vis absorption difference spectroscopy between 0.0 and 20 M water concentrations, and the water-binding equilibrium constants, K_1 and K_2, were determined.[15] The more electron-deficient 3,5-Cl derivative has the highest water-binding constant, K_2, consistent with the slight stabilizing effect of the solvent donor expected for the higher-valent states. However, the reduction potentials for Mn^{III}-$Mn^{IV}L_2OH_2^+$ were measured in 16 M water/CH_3CN and found to be essentially identical to values measured for $Mn^{III}Mn^{IV}L_2^+$ in pure CH_3CN,[15] showing that water ligation to this complex has little impact on its redox potential. On the basis of this model, we conclude that, in the absence of substantial structural rearrangement, simple substrate binding or ligand exchange at the OEC should not substantially perturb the potential of the OEC in higher S-states.

In 16 M water/CH_3CN, $Mn^{III}Mn^{IV}L_2OH_2^+$ was deprotonated by incremental addition of standard tetrabutylammonium hydroxide and the change in the UV-vis absorption spectrum monitored using rapid-mixing techniques. The pK_a values (pK_4

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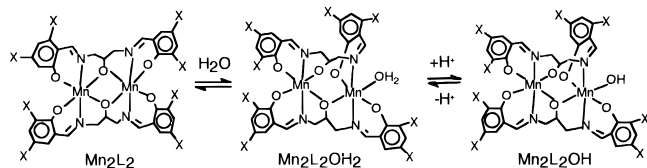(16) Gardner, K. A.; Mayer, J. M. *Science* **1995**, *269*, 1849–1851.

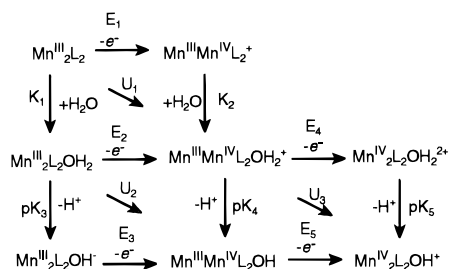**Figure 1.** Water binding to $Mn_2L_2^{0,+}$ dimers and deprotonation of $Mn_2L_2OH_2^{0,+}$.

Figure 2. Cycles showing thermodynamic parameters corresponding to Table 1.

Table 1[a]

X	E_1[b,d]	E_2[b,e]	E_3[b,d]	E_4[b,d,f]	E_5[b,g]	K_1[c]	K_2[c]	pK_3[h]	pK_4[e,i]	pK_5[h]
3,5-Cl	0.78	0.74		>1.6	0.95		0.37		10	<0
3,5-H	0.51	0.54	0.11	>1.4	0.69	0.025	0.21	19	11	<0
3,5-t-Bu	0.41	0.42	−0.14	>1.3	0.58		0.12	20	10	<0

a See Figure 2 for definition of parameters. *b* Volts *vs* aqueous NHE, uncertainties ±0.02 V. *c* In M^{-1}, uncertainties ±10%. *d* In CH$_3$CN. *e* In 16 M water/CH$_3$CN. *f* Estimated from anodic wave. *g* In CH$_3$CN at −20 °C. *h* Estimated from electrochemical data. *i* Measured by titration of OH$^-$ in 16 M water/CH$_3$CN, uncertainties ±1 unit.

in Table 1) were determined by nonlinear least-squares fitting of absorption data *vs* [OH$^-$] at multiple wavelengths.[15] Deprotonation of $Mn^{III}Mn^{IV}L_2OH_2^+$ results in an EPR shift consistent with formation of $Mn^{III}Mn^{IV}L_2OH$.[14] The reduction potential of $Mn^{III}Mn^{IV}L_2OH_2^+$ is between 0.40 and 0.80 V for all of the derivatives studied. However, in the presence of base, the potential of $Mn^{III}Mn^{IV}L_2OH$ drops to −0.14–0.11 V. A new reversible oxidation is observed between 0.55 and 0.95 V which corresponds to *oxidation* of $Mn^{III}Mn^{IV}L_2OH$ to $Mn^{IV}_2L_2OH^+$. By comparison, $Mn^{IV}_2L_2OH_2^{2+}$ is reduced at 1.3–1.6 V.[15]

Figure 2 illustrates the thermodynamic cycles relating the electrochemical, water binding, and pK_a data for the complexes in this system. Thermodynamic data for three different ring-substituted derivatives are summarized in Table 1. These data illustrate the dramatic redox stabilization of the deprotonated $Mn^{III}Mn^{IV}L_2OH$ and $Mn^{IV}_2L_2OH^+$ complexes compared to the corresponding protonated complexes $Mn^{III}Mn^{IV}L_2OH_2^+$ and $Mn^{IV}_2L_2OH_2^{2+}$. This model implies that a viable mechanism to account for S-state advancement in the OEC is to perform a proton-coupled electron transfer in which the total charge on the complex remains invariant, which in turn may facilitate cluster oxidation *without a marked increase in potential*.

The data in Table 1 can also be used to address the more specific problem of hydrogen atom abstraction by $Y_Z^{\bullet}$ from water ligated to the Mn_4 cluster. Gardner and Mayer[16] show that the energy for homolytic H-atom transfer from $HMnO_4^-$ (to give MnO_4^-) is 83 kcal/mol, calculated from its pK_a and oxidation potential. By analogy, the BDE_{OH} for our more biologically relevant water-ligated manganese dimers (eq 1) can be calculated from data in Table 1.[15]

$$Mn_2L_2OH_2 \rightarrow Mn_2L_2OH + H^{\bullet} \qquad (1)$$

The proton-coupled electron transfer potentials for the water-ligated complexes $Mn^{III}L_2OH_2$ and $Mn^{III}Mn^{IV}L_2OH_2^+$ are tabulated in Table 2, along with the corresponding BDE_{OH} value for each species. We first note that all of the BDE_{OH} values are substantially lower than those for a bulk water molecule. Also of significance is the fact that all of these values are

Table 2[a]

X	U_2[b]	U_3[b]	BDE$_{OH}$[c]	
			$Mn^{III}L_2OH_2$	$Mn^{III}Mn^{IV}L_2OH_2^+$
3,5-Cl	31	36	89	94
3,5-H	27	31	85	89
3,5-t-Bu	24	28	82	86

a See Figure 2 for definition of parameters. *b* In kcal/mol, uncertainties ±3 kcal/mol. *c* The potential for reduction of the proton, $H^+ \rightarrow \frac{1}{2}H_2$, was measured in 16 M water/CH$_3$CN and found to be 2 kcal/mol *vs* aqueous NHE. The energy for homolytic cleavage of H_2, $\frac{1}{2}H_2 \rightarrow H^{\bullet}$, is 56 kcal/mol. The BDE_{OH} values were computed by adding 58 kcal/mol to the proton-coupled potentials U_2 and U_3.

clustered between 82 and 94 kcal/mol, which closely brackets the BDE_{OH} for a tyrosyl radical, 86 kcal/mol. If 82−94 kcal/mol is a reasonable estimate for the BDE_{OH} of water bound to the OEC, then the reaction of $Y_Z^{\bullet}$ with the OEC manganese cluster is well balanced for optimum energy transfer.

The BDE_{OH} for $Mn_2L_2OH_2^{0,+}$ is between 25 and 37 kcal/mol lower than the BDE_{OH} for free water, prompting us to consider the source of this bond energy depression. The difference in pK_a between free water (pK_w = 14) and $Mn^{III}Mn^{IV}L_2OH_2^+$ (pK_a = 10) can lower the BDE_{OH} by only 5.5 kcal/mol. However, the difference in oxidation potential between OH$^-$ (2.0 V) and unsubstituted $Mn^{III}Mn^{IV}L_2OH$ (0.69 V) accounts for a nearly 30 kcal/mol lower BDE_{OH}. These data show that the primary determinant of BDE_{OH} in these manganese-ligated water complexes is not an increase in Bronsted acidity, but a substantial depression in redox potential due to the enhanced ability of the hydroxide-ligated manganese cluster to accommodate the higher oxidation state. This is also manifested among the $Mn^{III}Mn^{IV}L_2OH_2^{0,+}$ derivatives, where the pK_a is essentially invariant with ring substitution. The 7−8 kcal/mol range in BDE_{OH} values is more closely correlated with the redox potentials E_2 and E_5 which span a range of 0.35 V (8 kcal/mol), with the more electron-withdrawing 3,5-Cl derivative having the highest potential as expected.

Table 2 also shows that, for this isostructural series of Mn dimers, the BDE_{OH} value for the coordinated water increases by 4−5 kcal/mol as the oxidation level of the cluster increases. Because the overall charge on the Mn complex in both oxidation states is not changed upon hydrogen atom abstraction, the 5 kcal/mol increase in BDE_{OH} for the higher oxidation state is not driven by simple charge effects. More likely, it is driven by the intrinsically higher potential of the high-valent complex, making it a less favorable sink for the oxidizing equivalent generated by hydrogen atom transfer. If the $Y_Z^{\bullet}$ does abstract hydrogen atoms from water coordinated to Mn in the OEC, then these trends in our model system suggest that the initial redox potential of the four-manganese cluster must be precisely tuned to achieve the optimum BDE_{OH} value necessary for efficient energy transfer over all S-states.

The data presented here show that the BDE_{OH} for water directly bound to a higher-valent Mn complex is dramatically less than that for a simple bulk water. The most recent data on the structure and function of $Y_Z^{\bullet}$ combined with the model studies reported here make a circumstantial though compelling case for hydrogen atom transfer from a ligated water to $Y_Z^{\bullet}$ as the mechanism for the stepwise cluster oxidation in the OEC.

Supporting Information Available: Methods used in collection of the data in Table 1 and figures showing representative water binding data, deprotonation of ligated water, cyclic voltamgrams of $Mn^{III}_2L_2$-OH_2 and $Mn^{III}_2L_2$, and the change in cyclic voltamgram upon ligation of OH$^-$ to $Mn^{III}Mn^{IV}L_2^+$ (6 pages). See any current masthead page for ordering and Internet access instructions.