



Kinetic studies on oxidation of L-cysteine and 2-mercaptoethanol by a trinuclear Mn(IV) species in aqueous acidic media

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ABSTRACT

In aqueous media, the trinuclear Mn^{IV} complex, [Mn^{IV}₃(μ-O)₄(phen)₄(H₂O)₂]⁴⁺ (phen = 1,10-phenanthroline) (**1**) behaves like a monobasic acid, equilibrates with its deprotonated conjugate base (**2**) (**1** ⇌ **2** + H⁺, pK_a = 4.00 (± 0.15) at 25.0 °C, I = 1.0 M, maintained with NaNO₃). An aqueous solution of **1** in the pH range 2.2–4.0 smoothly oxidizes 2-mercaptoethanol (mercap) and L-cysteine (cys) to their respective disulfides; itself being reduced to [Mn(phen)₃]²⁺ in presence of excess 1,10-phenanthroline which also masks Cu²⁺, if any, present in the reaction media as impurity as well as acting as a buffer that controls pH range during the reaction. The observed rate constants in H₂O media were found to be considerably lowered in media enriched with D₂O and a proton-coupled single electron transfer rate step is proposed. Interestingly, we found that deprotonated oxidant (**2**) reacts faster than the protonated species (**1**) in oxidizing both the thiols.

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1. Introduction

Many synthetic models of higher valent oxo-bridged multinuclear manganese complexes have structural resemblance to the water oxidation center (WOC) in photosystem II. Structural, magnetic and spectroscopic aspects of these models are well-studied [1]. Moreover, during recently, the literature is becoming richer in the mechanistic aspects of redox reactions of some of these selected species in aqueous solution [2] along with their catalytic water oxidation capabilities [3]. The trinuclear Mn^{IV} species, [Mn^{IV}₃(μ-O)₄(phen)₄(H₂O)₂]⁴⁺ (**1**, Fig. 1) is one of such representative models. Recent X-ray crystallographic data supports the S₁ state of WOC contains a CaMn₃O₄ cubane linked to a fourth Mn atom with a μ-oxo [1a,1b,1d,4], EPR/ENDOR studies also suggest a “3 + 1” structural arrangement for the four Mn atoms [5].

The Mn^{IV}₃ species **1** is structurally well-characterized [6]. In relevance to the WOC in PS II, [7] **1** has oxo-bridged high valent Mn ion; two sets of Mn···Mn contacts, (viz. 2.7 and 3.33 Å) identical to the Mn···Mn distances in the Mn₄Ca clusters in PS II and two fully protonated water molecules coordinated to two different Mn^{IV} centers [1c,4d]. The key step in the mechanism of water oxidation in PS II is believed to involve water molecules binding at two neighboring Mn sites followed by deprotonation and O–O bond formation [8].

Based on the above-mentioned observations and on the fact that **1** is fairly soluble in water and the UV–Vis spectra of these solutions in the pH range 2–4 do not change within at least 10 h illustrating the kinetic stability of the Mn species in spite of the high valence state of Mn atoms (+4), particularly in water, media where PS II acts, it is becoming kineticists' choice to study the reactions of **1**. Oxidation reactions of thiols by metal-centered oxidants are catalyzed by metals ions, especially by Cu²⁺ [9]. Even, small quantity Cu²⁺ ions that might be present as impurities in the solution dramatically affect the kinetics. However, the catalytic path can be completely suppressed [10] using suitable masking agent effective for Cu²⁺. We here describe our kinetic observations on its reactions with two representative thiols, viz. L-cysteine and 2-mercaptoethanol. In the entire study we used excess 1,10-phenanthroline in the reaction media to suppress any Cu²⁺ catalyzed path. Furthermore, we show that the title redox is associated with proton coupled electron transfer (PCET), a key element in the S-state transitions in PS II [1a–c]. Occurrence of PCET in redox reactions of multinuclear high-valent Mn complexes has been documented in the literature [2a,11].

2. Experimental

2.1. Materials

The Mn trimer [Mn₃(μ-O)₄(phen)₄(H₂O)₂](NO₃)₄·2.5H₂O was prepared following the literature procedure [6] which involves oxidation of Mn^{II} acetate by Ce⁴⁺ in ca. 1.6 M HNO₃ containing 1,10-

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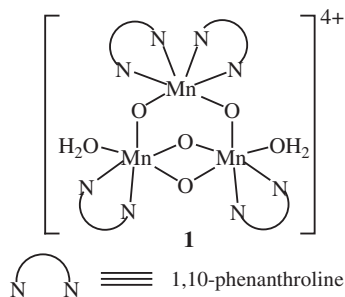


Fig. 1. Schematic drawing of $[\text{Mn}_3(\mu\text{-O})_4(\text{phen})_4(\text{H}_2\text{O})_2]^{4+}$.

phenanthroline. The purity of the product was confirmed from the elemental (CHN) analysis result: *Anal. Calc.* for $\text{C}_{48}\text{H}_{41}\text{N}_{12}\text{O}_{20.5}$: C, 44.2; H, 3.20; N, 13.0. Found: C 43.9, H 3.35, N 12.9%. 2-Mercaptoethanol (Aldrich) and L-cysteine (SRL, India) solutions were prepared with 99% reagent grade thiols. Thiols were dissolved just prior to the kinetic studies and fresh solutions were always used. NaNO_3 solution for the maintenance of ionic strength in kinetic measurements was standardized using cation exchange resin in the acid form [12]. 1,10-Phenanthroline (Sigma) was used as received. D_2O (99.9 atom%) was of Sigma or E. Merck grade. All other chemicals were of reagent grade. Doubly distilled, deionized and then freshly boiled water was used throughout.

2.2. Stoichiometric experiments

The stoichiometries of the reactions were determined under excess of reducing agent concentrations over **1**. Unreacted L-cysteine or 2-mercaptoethanol was quantified spectrophotometrically [13] after the completion of the reactions. For reactions with cysteine, the unreacted cysteine along with cystine sulfinic acid was additionally determined by titration of the product mixture with aqueous sodium nitrite [14]. By difference, cystine sulfinic acid, produced if any, was estimated. No attempt was made to determine sulfinic acid for mercap oxidations.

2.3. Physical measurements and kinetics

All absorbance or optical spectra were recorded with a Shimadzu (UV-1700) Spectrophotometer using 1.00 cm quartz cells. The kinetic runs were taken *in situ* in the “kinetic mode” of the instrument at 420 nm in the electrically controlled thermostated ($25.0 \pm 0.1^\circ\text{C}$) CPS – 240A cell housing. The ionic strength of the reaction media was normally maintained at 1.0 M using NaNO_3 . The pH values of the solutions were measured with calibrated [15] Orion–Ross combined electrode system (model 81–02). Presence of excess 1,10-phenanthroline (pK_a of $\text{Hphen}^+ = 5.12$ [16]) nicely buffers the reaction within a maximum of 0.06 pH unit. For reactions carried out in D_2O , pD was calculated as $\text{pH}_{\text{measured}} + 0.40$ [17].

3. Results and discussion

3.1. Suppression of catalytic effect of Cu^{2+}

We observed that either of the thiols, present in excess, reduce **1** almost instantaneously either in absence of added 1,10-phenanthroline or in presence of externally added Cu^{2+} . Atomic absorption spectroscopy (AAS) quantified an impurity level of $[\text{Cu}^{2+}] = 2.2 \times 10^{-6}\text{ M}$ in the blank reaction media. Such an impurity level of Cu^{2+} ion catalyzes the conversion of L-cysteine and 2-mercaptoethanol in such an extent that the catalyzed reaction interferes with

the study of direct reaction. 1,10-phenanthroline is a good chelating agent for Cu^{2+} [18] ion and it can effectively mask the catalysis.

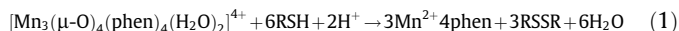
3.2. Equilibrium studies

The trinuclear Mn complex has $\text{pK}_1 = 4.00 (\pm 0.15)$ in H_2O and $\text{pK}_1 = 4.70 (\pm 0.20)$ in 95% D_2O –5% H_2O mixed-media [19a]. To the best of our knowledge, only one more example is known so far among the multinuclear Mn species, viz. $[(\text{terpy})_2\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\mu\text{-O})_2(\text{H}_2\text{O})_2]^{3+}$ that deprotonates at physiological pH [19b] (terpy = 2,2′:6′,2′′-terpyridine). The acid dissociation constants of the thiols in pure H_2O and in 95% D_2O –5% H_2O media were recently determined by us [2b] and we have used these values (Table 1) for the determination of rate constants. The reported ionization constants of thiols in H_2O media [20,21] nicely match with our observed values.

3.3. Stoichiometric analysis

Measurements of the amount of unreacted reducing agents, L-cysteine and 2-mercaptoethanol suggested a consumption ratio, $\Delta[1^{4+}]/\Delta[\text{thiol}] = 1:6$ (Table S1) that indicates both the thiols are quantitatively oxidized to their respective disulfides. Moreover, titration of the cys reaction product with aqueous sodium nitrite [14] gave no indication of formation of cystine sulfinic acid. The likely Mn^{II} species under the experimental condition are $\text{Mn}^{\text{II}}\text{-phen}$ complexes [18]. Optical spectra for the product solutions were superimposable on that of a mixture of $\text{Mn}(\text{NO}_3)_2$ and 1,10-phenanthroline under similar experimental conditions.

Eq. (1) thus represents the overall stoichiometric reaction.



3.4. Kinetics

Under the condition that the concentration of either of the reducing agent is greater than at least 10 times of $[\text{Mn}^{\text{IV}}_3]$, the decay in absorbance of the Mn-trimer could be well-fitted to a standard first-order decay at least up to four half lives and the observed rate constants (k_0) were evaluated in the usual way. Average of at least three measurements was taken for each k_0 reported, coefficient of variation (CV) [22] was within 3%. First-order rate constants were invariant to a range of wavelengths (380–490 nm) and dissolved oxygen concentration. At the entire pH range, k_0 versus T_R (T_R = total reducing agent concentration) plots were found to be linear (Fig. S1) with essentially insignificant intercept and no rate saturation was observed at higher T_R for both cys and mercap reactions.

Excess of 1,10-phenanthroline was used in all the kinetic runs because of several reasons: acting as a pH buffer (pK_a of $\text{Hphen}^+ = 5.12$) [16], necessary for the quantitative formation of the reduced product $[\text{Mn}(\text{phen})_3]^{2+}$ [18] and for effective masking of Cu^{2+} thus blocking Cu-catalyzed reactions [23]. We, however, observed that the observed k_0 values were unaltered in presence of varying amount of added phen (5.0–20.0 mM) indicating no

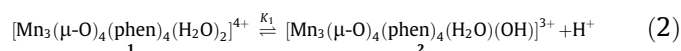
Table 1

Proton dissociation constants of the thiols in H_2O and D_2O medium at 25.0°C , $I = 1.0\text{ M}$ (NaNO_3) (maximum deviation ± 0.10).

| Thiols | Medium | pK_{a1} | pK_{a2} | pK_{a3} |
|------------------|----------------------------|------------------|------------------|------------------|
| L-Cysteine | H_2O | 2.05 | 8.07 | 9.95 |
| | D_2O (95%) | 2.52 | 8.42 | 10.38 |
| Mercapto ethanol | H_2O | 9.61 | | |
| | D_2O (95%) | 9.96 | | |

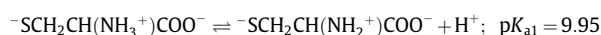
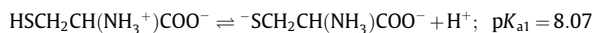
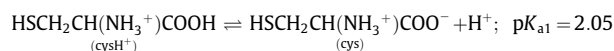
ligand (phen) dissociation pre-equilibrium exists prior to electron transfer. In this context, it might be noted that the bipy (bipy = 2,2'-bipyridine) analog of **1**, viz. $[\text{Mn}^{\text{IV}}_3(\mu\text{-O})_4(\text{bipy})_4(\text{H}_2\text{-O})]^{4+}$ experienced ligand (bipy) dependence on rate when it reacts with ascorbic acid [24] although $\text{d}^3 \text{Mn}^{\text{IV}}$ is inert to substitution reactions [25]. The observed ligand (bipy) dependency clearly indicates a bipy releasing pre-equilibrium exists in aqueous solution of the bipy analog. Structural rigidity between phen and bipy ligands [26] may be responsible for this observed difference, and, in fact, the methods of preparation of these trinuclear Mn complexes differ depending on the ligand (phen or bipy) [6,27]. Bipy is known to open up to result in monodentate forms and in aqueous acidic media bipy can be entirely replaced. Bipyridine can rotate around the 2,2' single bond to go to its monodentate form, phen compounds can't do so [26].

Despite its preparation from highly acidic media, protonated oxo-bridge could not be detected in the solid-state structure of **1** [6] and thus it is believed that one of the H₂O molecules bound to Mn(IV) dissociates (Eq. (2)).

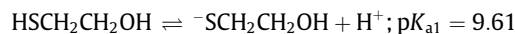


The reducing thiols show following protic equilibria in aqueous media:

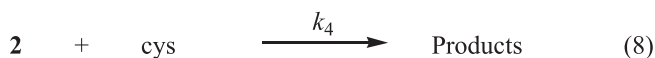
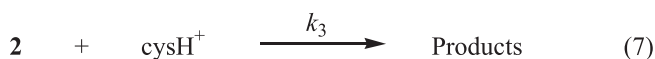
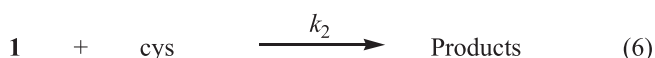
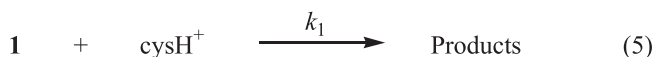
Cysteine:



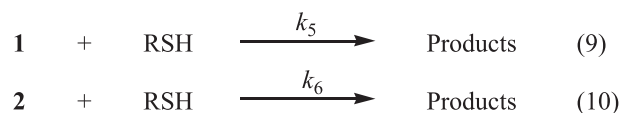
2-Mercapto ethanol:



Tables S2 and S3 collect the k_0 values for the oxidation of cysteine and 2-mercaptoethanol, respectively. For both the reactions, increase in pH of the reaction media increased the redox rate. It appears from the protic dissociation of the thiols that both cysH^+ and cys could be the reactive species whereas only the conjugate acid of anionic 2-mercaptoethanol, viz. $\text{HSCH}_2\text{CH}_2\text{OH}$ be reactive in the experimental pH range, 2.2–4.0, reacting with both **1** and **2**. Neutral thiols (RSH) are extremely weak bases when protonation



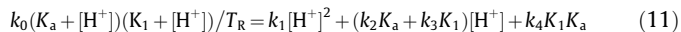
Scheme 1.



Scheme 2. (RSH = mercap)

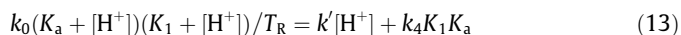
on S is considered ($\text{pK}_a \sim -7$) [28] and thus is unable to accept proton to form RSH_2^+ . We propose [Scheme 1](#) and [Scheme 2](#) for the oxidations of cys and 2-mercaptoethanol, respectively.

Scheme 1 and **Scheme 2** described above leads to the rate laws (11) and (12), respectively, for cys and mercap oxidations, where T_R refers to the total concentration of the respective thiol.



When left hand side of the Eq. (11) is plotted against $[H^+]$, it results in a good linear fit (Fig. 2, $r > 0.98$) instead of a second order polynomial. So, it is clear k_1 path has no contribution to the overall rate indicating $cysH^+$ is not reactive towards **1**.

However, with this information we cannot predict whether k_3 path (reaction of cysH^+ with **2**) is absent or not. Eq. (11) can be re-written as (assuming k_1 path is absent):



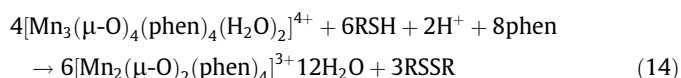
where k' refers to the composite $(k_2K_a + k_3K_1)$.

k' and k_4 were evaluated from the slope and intercept of the straight line shown in Fig. 2 (Table 2). Solution of Eq. (12) yielded k_5 and k_6 (Fig. 3, Table 3). These rate constants and their composites, thus evaluated, regenerate all the experimental k_0 values quite satisfactory (within 8%) for both the redox studied.

Assuming cysH^+ is not reactive toward **2** (that is, if k_3 path is absent), we get $k_{2(\text{max})} \approx 1.31 \text{ M}^{-1} \text{ s}^{-1}$, much lower than k_4 (Table 2). This suggests **2** reacts faster than **1**. Kinetic data for mercap oxidation further concludes more reactivity of the deprotonated oxidant **2**. This observation appears uncommon as generally protonated oxidant reacts faster than their conjugated bases [2a,2d,29] although very recently we observed the same situation in the reaction of this trinuclear Mn oxidant with NH_3OH^+ [2c].

3.5. Mechanism

An overall six-electron transaction in these redox must proceed through several steps. To detect the formation of any intermediate, we mixed separately slightly less ($1: T_R = 1:4$) and slightly more ($1: T_R = 1:8$) than stoichiometric amount of the redox partners and consequent spectral change was recorded with time. A progressive growth and decay of a narrow band at 684 nm with a shoulder at 555 nm was observed. Both these bands are indicative of the formation of a mixed valent dimer $[(\text{phen})_2\text{Mn}^{\text{III}}(\mu\text{-O})_2\text{Mn}^{\text{IV}}(\text{phen})_2]^{3+}$ [30]. Moreover, reaction of stoichiometric amount of the reagents ($1: T_R = 4:6$, Eq. (14)) resulted nearly quantitative [30] ($95\% \pm 2\%$) generation of the mixed-valent species (Fig. 4). Intervention of the mixed valent $\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}$ dimer as an intermediate in these redox reactions is thus established.



The conversion of trinuclear Mn^{IV} oxidant to the $\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}$ also depends on the media pH and buffer used [31] (phen/phenH⁺), where the free phen ligand acts as a reducing agent [6]. This transformation is prominent at pH ≥ 4.5 , when after the 48 h, 95% conversion to the $\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}$ dimer have been noticed [6]. However, we have found that the conversion is not more than 5% after 12 h in the pH region 2.0–4.1, even in presence of large excess of 1,10-

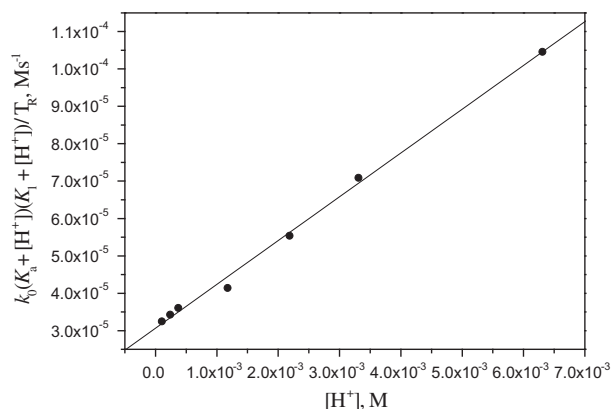


Fig. 2. Plot of left hand side of Eq. (13) vs. $[H^+]$, $[complex] = 0.1$ mM, $[cys] = 5.0$ mM, $C_{phen} = 5.0$ mM, $T = 25.0$ °C, $I = 1.0$ M ($NaNO_3$). Points in circles are calculated from experimentally observed first-order rate constants while the solid curvature is the best fit of the left hand side of Eq. (13) vs. $[H^+]$.

Table 2

Second-order rate constants for the oxidation of L-cysteine by the trinuclear Mn oxidant at $[1] = 0.1$ mM, $T = 25.0$ °C, $[phen] = 100$ mM, $I = 1.0$ M ($NaNO_3$).

| Media | k' (s^{-1}) | k_4 ($M^{-1} s^{-1}$) |
|--|---------------------------------|---------------------------|
| H ₂ O medium | $(11.7 \pm 0.6) \times 10^{-3}$ | 34.4 ± 1.2 |
| 95% D ₂ O–5% H ₂ O | $(3.79 \pm 0.4) \times 10^{-3}$ | 28.4 ± 1.4 |

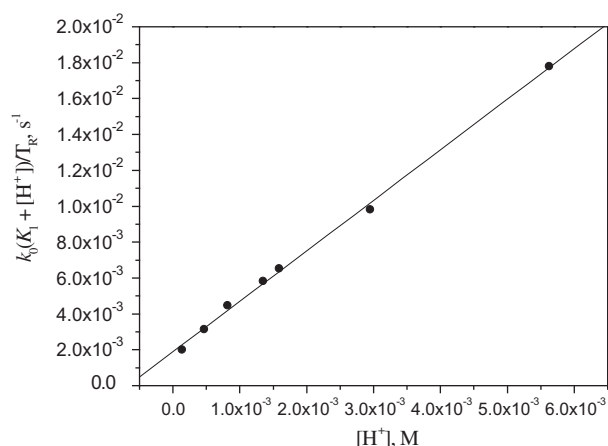


Fig. 3. Plot of left hand side of Eq. (12) vs. $[H^+]$, $[complex] = 0.1$ mM, $[mercap] = 2.0$ mM, $C_{phen} = 5.0$ mM, $T = 25.0$ °C, $I = 1.0$ M ($NaNO_3$). Points in circles are calculated from experimentally observed first-order rate constants while the solid curvature is the best fit of the left hand side of Eq. (12) vs. $[H^+]$.

Table 3

Second-order rate constants for the oxidation of 2-mercaptoethanol by the trinuclear Mn oxidant at $[1] = 0.1$ mM, $T = 25.0$ °C, $[phen] = 5.0$ mM, $I = 1.0$ M ($NaNO_3$).

| Media | k_5 ($M^{-1} s^{-1}$) | k_6 ($M^{-1} s^{-1}$) |
|--|---------------------------|---------------------------|
| H ₂ O medium | 2.81 ± 0.06 | 18.9 ± 1.48 |
| 95% D ₂ O–5% H ₂ O | 1.81 ± 0.04 | 15.8 ± 0.4 |

phenanthroline [19a]. Thus, the disproportionation of Mn^{IV} to binuclear $Mn^{III}Mn^{IV}$ had no contribution to the observed kinetics we present here.

The reactions between the trinuclear Mn^{IV} and thiols yielded good first order decay. Moreover, we noticed that under the same experimental conditions, the mixed valent manganese dimer $[Mn_2(\mu-O)_2(phen)_4]^{3+}$ reacts much faster (too fast to be measured)

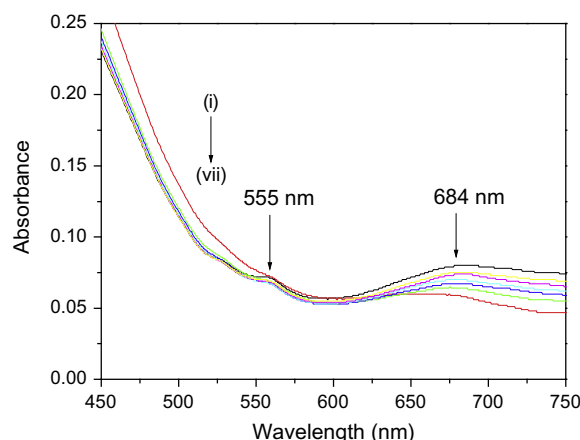


Fig. 4. Spectrum (i), shown in red is obtained immediately after mixing 0.15 mM cysteine with 0.1 mM Mn^{IV}_3 (1) at pH 3.9, $C_{phen} = 5.0$ mM, $I = 1.0$ M ($NaNO_3$) spectra (ii)–(vii) show change of (i) at 5, 10, 20, 25, and 30 min, respectively. Spectrum (vii), shown in black, did not change after 2 h indicating almost quantitative formation (>97%) of dinuclear $Mn^{III}Mn^{IV}$ (see the text). Mercap reaction showed a similar result.

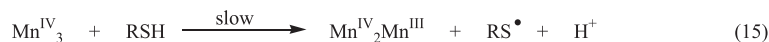
than the title trinuclear Mn^{IV} oxidant with both of the reducing agents. It can thus be concluded that the intermediate dinuclear species decays in the non rate limiting step. It might be possible that the intermediate species formed first is not $[Mn_2(\mu-O)_2(phen)_4]^{3+}$, but rather a bis(phenanthroline) species $[Mn_2(\mu-O)_2(phen)_2(H_2O)_4]^{3+}$, which can change to an equilibrium mixture of corresponding tris(phenanthroline) and tetrakis(phenanthroline) complexes. These hydrolytic species are more aquated than $[Mn_2(\mu-O)_2(phen)_4]^{3+}$ and are expected to be kinetically more reactive [2f,31,32] to its reduction. These species have similar spectra [30,32b] and inter-conversions are likely to be rapid on the time-scale for spectral measurements. $[Mn_2(\mu-O)_2(L)_4]^{3+}$ equilibrates with its tris(L) species $[Mn_2(\mu-O)_2(L)_3(H_2O)_2]^{3+}$ in ligand buffer (pH 4–5) and this aquation is acid catalyzed ($L = 1,10$ -phenanthroline or 2,2'-bipyridyl) [6]. More acidic environment employed in the present study may result in further aquation leading to more reactive bis(phenanthroline) complexes. The trend that aquated species are more reactive, however, is not a specialty for the binuclear Mn complexes; it is also well-documented in the chemistry of higher-valent mononuclear manganese complexes [33]. We propose Scheme 3 that reflects our kinetic observations stated above.

In scheme 3, the first electron transfer is assumed to be the rate step and all subsequent steps are rapid that involve one-electron transfer with retention of nuclearity ($\{Mn_3O_4\}$ core) until Eq. (18) where the dinuclear mixed-valent $Mn^{III}Mn^{IV}$ is generated. One may also propose alternative routes for formation of mixed-valent dinuclear species.



It might be noted here that generation of Mn^{III}_3 in reaction (17) in lieu of $Mn^{IV}Mn^{III}Mn^{II}$ is also probable. Stable compounds of trinuclear Mn(III) could be isolated or electrochemically generated [34].

It is well-established that the comproportionation reaction $2Mn^{III} + 2Mn^{IV} \rightarrow 2Mn^{III}Mn^{IV}$ has high driving force (equilibrium constant $10^{15.6}$) [30] and is expected to be fast too. Reactions shown in Eqs. (20) and (21) should thus be rapid. Moreover, in acidic media clusters containing Mn^{II} are not kinetically stable and they quickly release Mn^{II} [27,35]. Reactions (20) and (21) are thus distinctively preferred over reaction (18) for the formation of the mixed valent $Mn^{III}Mn^{IV}$ dimer intermediate.



Scheme 3.

Stepwise one-electron transfer and retention of nuclearity as proposed in Scheme 3 are supported by the fact that different oxidation levels of the binuclear catalase enzyme models preserve nuclearity, [36] the S-state of the Mn cluster in PS II also apparently retain bond connectivity [1c,4b,37] and high valent Mn has a tendency to form (μ -oxo) complexes in weakly acidic media [37]. Trinuclear species proposed in Scheme 3 is further supported by the experimental (kinetic) evidence of formation of a trinuclear $\text{Mn}^{\text{IV}}_2\text{Mn}^{\text{III}}$ intermediate during dismutation of H_2O_2 by a $\{\text{Mn}_2\text{O}_2\}^{3+}$ core [38]. Synthetic complexes of $\text{Mn}^{\text{III}}_2\text{Mn}^{\text{IV}}$ and $\text{Mn}^{\text{IV}}\text{Mn}^{\text{III}}\text{Mn}^{\text{II}}$ are also reported [39].

The redox decay of $\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}$ to Mn^{II} is also expressed to proceed through a series of one-electron transfers like the electrochemical reduction of $[(\text{bipy})_2\text{Mn}^{\text{IV}}(\mu\text{-O})_2\text{Mn}^{\text{III}}(\text{bipy})_2]^{3+}$ and similar complexes with a $\{\text{Mn}_2\text{O}_2\}^{3+}$ core to produce an Mn^{III}_2 dimer [30,40]. The sequence $\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}} \rightarrow \text{Mn}^{\text{III}}_2 \rightarrow \text{Mn}^{\text{II}}\text{Mn}^{\text{III}} \rightarrow 2\text{Mn}^{\text{II}}$ is also suggested earlier [21].

The second order rate constants in D_2O enriched media (95% D_2O –5% H_2O) were evaluated in the same way as in pure H_2O that clearly show the presence of kinetic isotope effect. Rate retardation in D_2O suggests the reduction process involves simultaneous proton transfer. Furthermore, k_0 varied linearly (Fig. S2) with D_2O content of the H_2O – D_2O mixed media for both the reactions suggesting a single proton transfer at the rate step. An increase in the basicity of the oxo-bridges of the one-electron reduced species formed in the rate step (Eq. (15)) should invite a simultaneous proton transfer from the bulk solvent to the oxo-bridge [41]. Two thiol radicals generally combine quickly to form disulfide [42]. The thiol radical so generated can also react with thiol rapidly to form the corresponding well-known disulfide radical anion [43], as in Eq. (23). Further oxidation of the disulfide radical anion yields final product disulfide at fast steps; thus, it could not affect the kinetics.



A few reactions were studied in presence of 6% (v/v) acrylonitrile where we observed polymerization indicating generation of free radicals in these reactions. Moreover, as suggested by a reviewer, we used TEMPO to trap the radicals during the reactions but we found that TEMPO itself reacted with the title Mn trimer. Also, the literature reports that TEMPO can be reduced by $-\text{SH}$ groups of thiols [44].

In the electrochemical reduction of the bipy analog of **1**, Thorp and co-workers [27] proposed an initial one-electron proton coupled reduction of the trimer as an intermediate. The Mn^{IV} shown at the top of Fig. 1 differs with the two other similar ones in terms of their ligand environment. Ease of electron acceptance is expected to be higher at this top Mn^{IV} because it is bonded to lesser number of electron donating oxo ligands as well as more in numbers of π -accepting phen ligands. Our recent DFT studies [2c] firmly support the fact that the top Mn^{IV} is reduced first.

Contrary to a general expectation that protonated metal centered oxidants reacts quicker than their conjugated bases, [2a,2d,29] we found here just the reverse, that is, **2** reacts faster than **1**. In some model systems, it was shown that enhancement of reactivity of hosts appear due to coordination of water molecules [9,2f,31,32]. This argument, however, does not hold here as only protonation/deprotonation state of a Mn^{IV} bound H_2O molecule differs in **1** and **2**. Charge calculations show that the top Mn^{IV} in **2** has a bit more positive charge than that in **1** due to a stronger non-classical C–H \cdots O interaction in **2** and that may be a reason for higher reactivity of **2** [2c].

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ica.2012.12.015>.

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