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ARTICLE TYPE

Water is a Key Factor to Alter the Structure and Electrochemical Properties of Carboxylate-bridged Dimanganese(II) Complexes

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Synthesis and physical properties of dimanganese(II) compounds with varying numbers of water ligands housed in the four bulky carboxylate motif, including the first complex with a parallelogram core $\{Mn_2(\mu\text{-}OH_2)_2(\mu\text{-}O_2CR)\}^{3+}$ unit, were described. 10 **The isolation of these complexes revealed how water could alter the structural and electrochemical properties of similar carboxylate-bridged dimanganese(II) cores that may occur in a variety of the active sites of Mn-containing metalloenzymes. These studies support the notion that water molecules in coordination spheres of active site of metalloproteins are not a simple spectator medium but the modulation factor of structures and functions.**
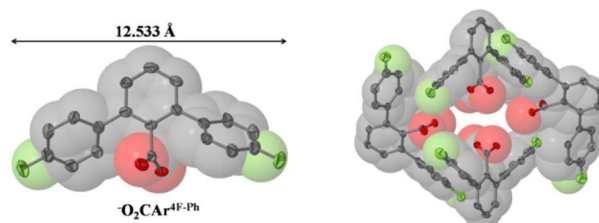
Introduction

15 Dinuclear manganese-containing cores function as important cofactors in enzymes which play pivotal roles in the protection of living cells against oxidative stress by the disproportionation of hydrogen peroxide, the biosynthesis of the nitroaryl-substituted 20 metabolite aureothin, and the cleavage of L-arginine to L-ornithine in mammalian nitrogen metabolism.[1-5] Recently, structures of the active sites of the manganese in *Lactobacillus plantarum*,[6,7] *Bacillus subtilis* class Ib ribonucleotide reductase,[8] and arginase[9] have been revealed by crystallographic studies. 25 These active site structures contain carboxylate-based ligands derived from glutamate or aspartate (bridging two manganese atoms), and water-derived ligands (Scheme 1). It is quite intriguing that the functions of the shared motif vary, though the differences in the structures of the active sites are small. Much 30 effort has been devoted to reproducing the structures of the active sites by synthetic model complexes and correlating the structures
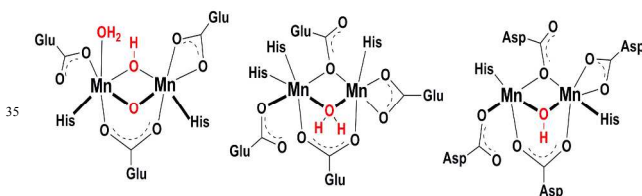
Scheme 1. Dimanganes active sites. Left: *L. plantarum* catalase:[6] Middle: 40 *B. subtilis* Mn[II]$_2$-NrdF:[8] Right: arginase[9]

and functions of the enzymes at the molecular level.[10-13] Although the carboxylate and water in the coordination sphere have been proposed as key participants in the chemistry of these Mn-containing enzymes,[1,14,15] very few of the models to date have 45 addressed the effects of these ligands on the reactions of the carboxylate-rich manganese centers. Herein, we describe our initial effort to address this issue through modeling chemistry, via

the designed synthesis of novel manganese(II) complexes with varying numbers of ligated water molecules. These studies reveal 50 the existence of a water-related dynamic equilibrium in the manganese(II) carboxylate core.

Scheme 2. The pocket derived from sterically hindered *m*-terphenyl-based 55 carboxylates

The preparation of carboxylate-rich Mn complexes introduces synthetic complications, owing both to the kinetic lability of 60 Mn(II) ions and the multiple binding modes of carboxylate ligands.[16,17] Significant problems include the generation of mono-, tri-, or polynuclear complexes, commonly encountered products in Mn-carboxylate chemistry.[18,19] Successful preparations of dinuclear Mn complexes with only carboxylate ligands and water 65 molecules, rather than elaborate ligand moieties, have not yet been reported, indicating that the synthesis of dinuclear manganese complexes with O-rich coordination environments is a difficult task to achieve. Interestingly, the fact that the pocket derived from four sterically hindered *m*-terphenyl-based 70 carboxylates[20-25] could nicely accommodate a dimetal(II) core, as shown in Scheme 2, led us to utilize these carboxylates in the synthesis of the model complexes. The reaction of Mn(OTf)$_2$.2CH$_3$CN with sodium 2,6-di-(4-fluorophenyl)benzoate(NaO$_2$CAr$^{4F\text{-}Ph}$,2 equiv) in anhydrous THF 75 afforded colorless crystals of the neutral bis(μ-carboxylato)dimanganese(II) complex, [Mn$_2$(μ-O$_2$CAr$^{4F\text{-}Ph}$)$_2$(O$_2$CAr$^{4F\text{-}Ph}$)$_2$(THF)$_2$] (**1**) in modest yield (11 %). The crystal structure of **1** is shown in Fig. 1(The selected bond lengths and bond angles can be found in Table S1), comprising two distorted 80 trigonal bipyramidal manganese(II) centers with a Mn···Mn

separation of 4.299(13) Å. The coordination sites were occupied by two μ-1,3-bridging carboxylate ligands, one oxygen atom of THF, and a terminal bidentate carboxylate ligand, thus forming two five-coordinate Mn(II) centers. A crystallographic inversion
5 center in **1** requires the two manganese and four oxygen atoms of the μ-1,3 carboxylates to lie in the same plane. The two THF molecules and two terminal bidentate carboxylate ligands were disposed anti to each other across this $\{Mn_2(\mu-O_2CR)_2\}$ plane.
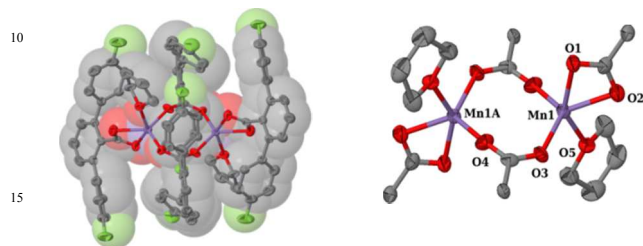

Figure 1. Left: ORTEP/space filling overlayed diagram of $[Mn_2(\mu-O_2CAr^{4F-Ph})_2(O_2CAr^{4-FPh})_2(THF)_2]$ (**1**), showing 50% probability thermal
20 ellipsoids for all non-hydrogen atoms. Right: The aromatic rings of $^-O_2CAr^{4-FPh}$ ligands are omitted for clarity

The same synthetic procedure carried out under hydrous conditions resulted in the formation of colorless block crystals of
25 $[Mn_2(\mu-OH_2)_2(\mu-O_2CAr^{4F-Ph})_2(O_2CAr^{4F-Ph})_2(THF)_2]$ (**2**). The coordinated water molecule resulted from the moisture present in the THF solvent used for the reaction. Alternatively, the dissolution of **1** in THF containing 4 equiv water, followed by recrystallization under N_2, resulted in the identical complex. Fig.
30 2 displays the severely distorted octahedral manganese(II) centers, with a Mn$\cdots$Mn separation of 3.529(2) Å. (The selected bond lengths and bond angles can be found in Table S2) The coordination sites were occupied by two bridging carboxylate ligands and the oxygen atoms of the THF, water, and a
35 monodentate terminal carboxylate group. The water molecule coordinated to Mn(1) with a Mn$\cdots$O bond length of 2.214 Å was 3.153 Å from Mn(1A), thus bridging the two manganese atoms in an asymmetric fashion. A THF molecule was located *trans* to the water ligand. Strong intramolecular hydrogen bonding
40 interactions were present between the terminal metal-bound carboxylates and the water molecules, with O$\cdots$O distances of 2.627 Å, possibly stabilizing a $\{Mn_2(\mu-OH_2)_2(\mu-O_2CR)_2\}$ core fragment.
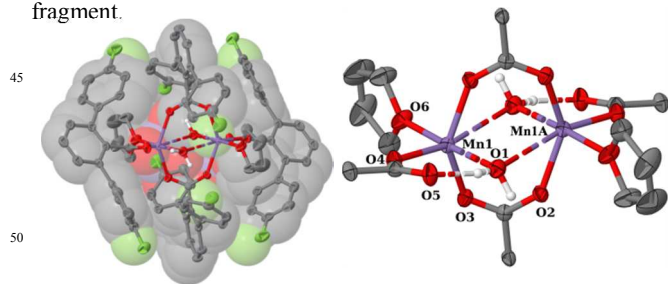
Figure 2. Left: ORTEP/space filling overlayed view of $[Mn_2(OH_2)_2(\mu-O_2CAr^{4F-Ph})_2(O_2CAr^{4F-Ph})_2(THF)_2]$ (**2**) showing 50% probability thermal
55 ellipsoids for all non-hydrogen atoms. Right: View of the structure with the aromatic rings of $Ar^{4F-Ph}CO_2^-$ ligands omitted for clarity.

Furthermore, the dissolution of $[Mn_2(\mu-O_2CAr^{4-FPh})_2(O_2CAr^{4F-Ph})_2(THF)_2]$ (**1**) in THF containing 20 equiv water,
60 followed by pentane diffusion into the solution, resulted in the formation of long needle-shaped colorless crystals of $[Mn(OH_2)_6](O_2CAr^{4F-Ph})_2 \cdot 2THF$(**3**), for which the structure and

selected bond lengths and bond angles are presented in Fig. 3 and
65 Table S3, respectively. Two octahedral hexaaquamanganese(II) units with a Mn$\cdots$Mn separation of 5.676(7) Å were present in the unit cell, with Mn$\cdots$O bond lengths ranging from 2.190(5) to 2.262(5) Å. The charge of the hexaaquamanganese(II) cation was balanced by two carboxylate groups, and there were also two
70 THF molecules in the asymmetric unit. The dramatic difference in the Mn$\cdots$Mn distance between **1**, **2**, and **3**, from 3.50 Å to 5.70 Å, illustrates the flexible nature of dimanganese(II) complexes with a four carboxylate ligand framework, which was imposed by the capability of the carboxylate ligands to undergo shifts upon
75 water incorporation.

By treating the $\{Mn_2(\mu-O_2CR)_2\}$ core of **1** with varying amounts of water, the di-water bound form, the $\{Mn_2(\mu-OH_2)_2(\mu-O_2CR)_2\}$ core of **2**, and the completely disrupted form, the $[Mn(OH_2)_6]$ motif of **3**, were isolated. The synthetic pathway,
80 shown in Scheme 3, clearly reveals the existence of a dynamic equilibrium between water and the carboxylate-bridged dimanganese(II) complexes.
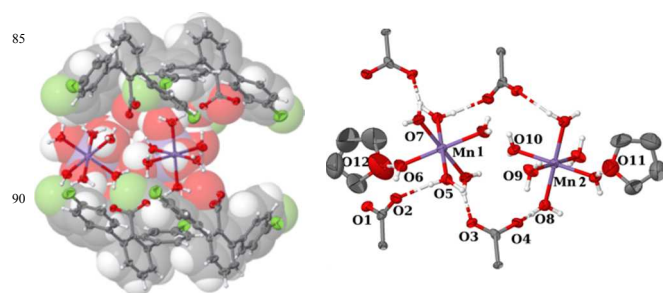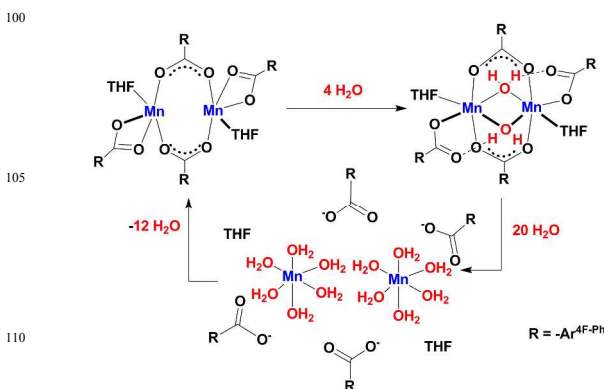

95 **Figure 3.** Left: ORTEP/space filling overlayed view of $[Mn_2(OH_2)_{12}(O_2CAr^{4F-Ph})_4(THF)_2]$ (**3**) showing 50% probability thermal ellipsoids. Right: View of the structure with the aromatic rings of $Ar^{4F-Ph}CO_2^-$ ligands omitted for clarity.

Scheme 3. Speculative mechanism for inter-conversion of manganese (II)
115 compounds exhibiting the water dependent equilibria between the structures **1**, **2** and **3**.

The IR spectra of compounds **1**, **2**, and **3** in the range of the OH-stretch vibrations are shown in Fig. 4A, 4C and 4E, respectively.
120 The peak at 3612 cm^{-1}(Fig 4C) is attributed to free OH stretch of coordinated water molecules in **2**. Meanwhile, the broad band at 3458 cm^{-1} (Fig 4E) is assigned to H-bonded OH stretch coordinated water molecules in **3**.

To expand the proposed water-related equilibrium in the solid state, the alteration of chemical species upon addition of water molecule is probed by IR spectroscopy in CH_2Cl_2 as shown in Fig. 4B, 4D, and 4F. Upon the addition of 4 equiv water in the solution of **1**, the characteristic OH vibration at 3614 cm^{-1} is observed as those in the solid sample of **2** in Fig. 4C. Interestingly, existence of additional peaks at 3524 and 3422cm^{-1} indicates that compound **2** and at least more than one species with the $\{Mn_2(OH_2)_x\}$ (x = 1 - 9) motif coexist in solution. Meanwhile, the broad band at 3458 cm^{-1} (Fig. 4E & Fig. S2) is assigned to H-bonded OH stretching of coordinated water molecules in **3**. Upon the addition of 20 equiv water, the peak at 3614 cm^{-1} disappears, suggesting that **3** may be the major species. It reiterates that the proposed dynamic equilibrium between water and the carboxylate-bridged dimanganese(II) complexes exists.
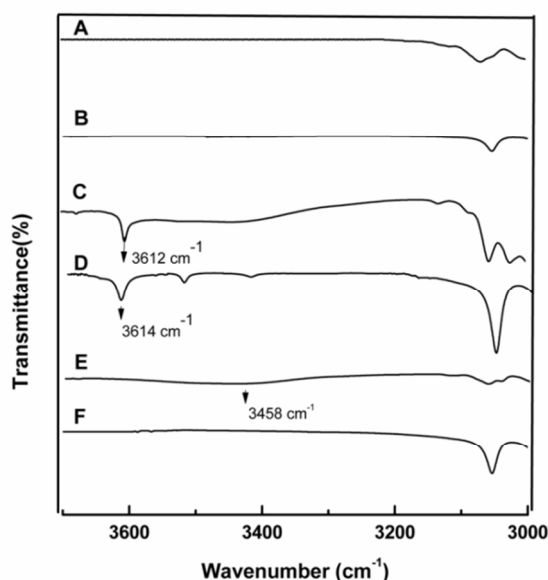

Figure 4. IR spectra of; (A) **1** in KBr; (B) **1** in CH_2Cl_2; (C) **2** in KBr; (D) **1** upon addition of 4 equiv water in CH_2Cl_2; (E) **3** in KBr; (F) **1** upon addition of 20equiv water in CH_2Cl_2.

To check the influence of water coordination in the $\{Mn_2(\mu-O_2CR)_2\}$ core on electrochemical properties, **1** was investigated by cyclic voltammetry upon the addition of sequentially increasing amounts of H_2O (Fig. 5). The cyclic voltammogram of compound **1** in CH_2Cl_2 (Fig. 5 (plain line)) exhibited one irreversible oxidation wave at $E_{pa} = 0.52$ V vs. Fc$^+$/Fc, which may correspond to the oxidation of the Mn_2(II,II) to the Mn_2(II,III) species. Similar redox properties have also been reported for other dinuclear Mn(II) and Fe(II) complexes.[26] (the detailed analysis of redox potential of **1**, together with the Fe(II) analogue compound, is available in Fig S1) Interestingly, upon addition of 4 equiv water, distinct irreversible oxidation peak at 0.664 V vs. Fc/Fc$^+$ was observed with increased current flow(Fig. 5(dash-dot line)) and this anodic peak was attributed to Mn_2(II,III) species of **2**, in addition, one quasi-irreversible peak appears at 1.30 V. Upon the addition of 20 equiv water, voltammograms with a quasi-reversible couple at 1.19 V vs. Fc/Fc$^+$ were observed, which corresponded to the oxidation of $[Mn(II)(H_2O)_6]$ to $[Mn(III)(H_2O)_6]$.[27] Previously, the oxidation potential decreases from 1.18 V for Mn_{aq}^{II} to less positive values(0.52V- 0.69V) upon formation of Mn complexes with carboxylates are

reported.[28] These results clearly indicate that once the Mn(II) site ligates more water molecules, the oxidation potential shifts to more positive values. Combined with the described crystallographic data, these results emphasize that the redox properties of $\{Mn_2(\mu-O_2CR)_2\}$ cores are dramatically altered depending on the availability of water molecules in the environment.

The function of metalloproteins with carboxylate-bridged Mn(II) cations in the active site is believed to be related to the structure of the metal core, which, in turn, is governed by the binding mode of the carboxylate ligands.[29,30] In addition, based on the results presented in this paper, the structure of the core may also be altered severely by the availability of non-acidic ligands such as water from the protein medium. A Mn(II) active site in a metalloprotein with different numbers of water ligands may exhibit altered redox properties, as suggested by the model complexes, which would further alter the redox catalytic behavior. This may be clear evidence that the number of water molecules in the coordination sphere of a metalloenzyme is a vital element in determining the catalytic function of the protein.
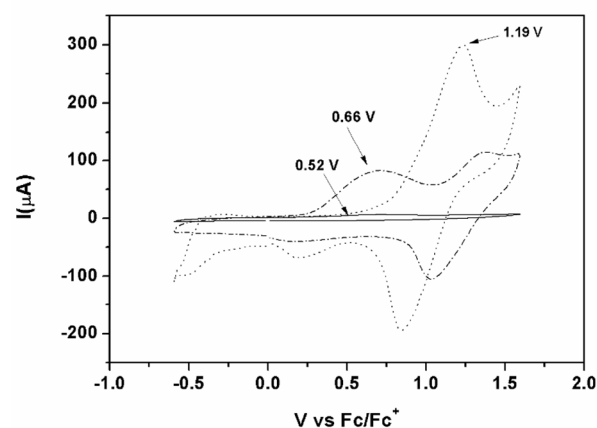

Figure 5. Cyclic voltammograms of $[Mn_2(\mu-O_2CAr^{4F-Ph})_2(O_2CAr^{4F-Phi})_2(THF)_2]$(**1**) in CH_2Cl_2 and with 4 and 20 equivalents of H_2O. Supporting electrolyte 0.5 M $(Bu_4N)PF_6$ and a scan rate 100 mV/s. 5 mM of **1** in CH_2Cl_2 (plain line), 4 equivalents of H_2O (dash-dot line) and 20 equivalents of H_2O (dot line).

In summary, this work provides an efficient synthesis of carboxylate-rich dimanganese(II) complexes. It also highlights the ability of carboxylate ligands to undergo shifts upon the incorporation of water, leading to water-bound complexes. The Mn(II) motifs with varying numbers of coordinated water molecules presented much different redox behaviors, such as occur in the various active sites of Mn-containing metalloenzymes. In addition to the isolation of proposed species with the $\{Mn_2(OH_2)_x\}$ (x = 1, and 3-9) motif, a more quantitative treatment and understanding of the influence of water, including a detailed analysis of the magnetic properties and the chemical and electrochemical oxidations of the dimanganese(II) complexes, will be subjects of further studies

Notes and references

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^{b}*Clean Energy Research Center Korea Institute of Science and Technology, Hwarangno 14-gil 5, Seongbuk-gu, Seoul, 136-791, Republic of Korea*

‡**Crystal structure determination of 1, 2 and 3**

complex 1: $C_{84} H_{60} F_8 Mn_2 O_{10}$, $M = 1491.20$, triclinic, space group $P\bar{1}$, $a = 10.7747(6)$ Å, $b = 13.2190(7)$ Å, $c = 14.0466(8)$ Å, $\alpha = 67.7730(10)°$, $\beta = 68.4860(10)°$, $\gamma = 76.3580(10)°$, $V = 1711.98(16)$ Å^3, $Z = 1$, $T = 223(2)$K, $d = 1.446$ Mg/m^3, 12810 reflections measured, 8377 unique [R(int) = 0.0270], $R_1 = 0.0633$, w$R_2 = 0.1007$ for (I>2σ(I)), $R_1 = 0.1179$, w$R_2 = 0.1564$ (all data), GOF = 1.162. CCDC no. 778666.

complex 2: $C_{86} H_{68} Cl_4 F_8 Mn_2 O_{12}$, $M = 1697.08$, triclinic, space group $P\bar{1}$, $a = 12.331(3)$ Å, $b = 14.072(3)$ Å, $c = 14.127(3)$ Å, $\alpha = 97.27(3)°$, $\beta = 114.67(3)°$, $\gamma = 111.21(3)°$, $V = 1961.8(7)$ Å^3, $Z = 1$, $T = 293(2)$ K, $d = 1.436$ Mg/m^3, 12360 reflections measured, 8706 unique [R(int) = 0.051], $R_1 = 0.0480$, w$R_2 = 0.1225$ (all data), GOF = 0.952. CCDC no. 923655.
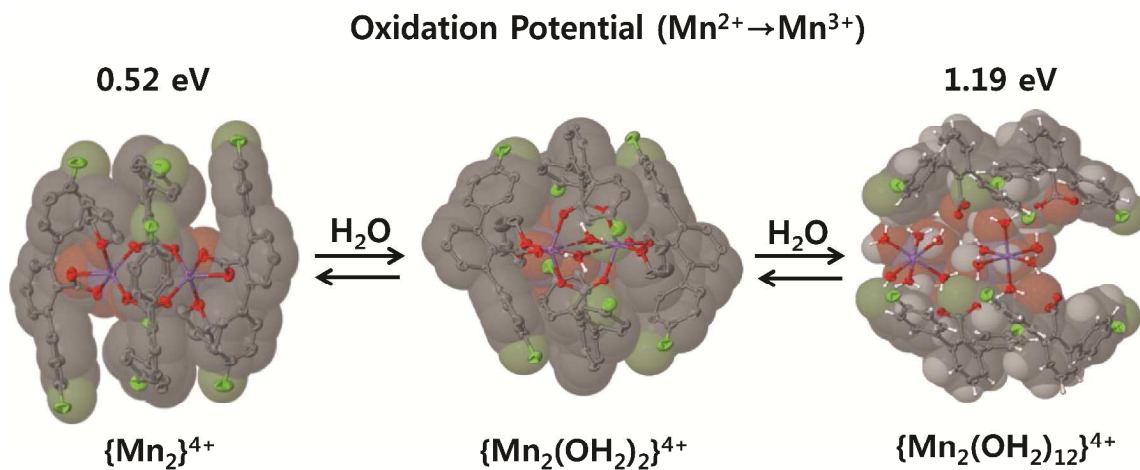
complex 3: $C_{46} H_{50} F_4 Mn O_{12}$, $M = 925.80$, triclinic, space group $P\bar{1}$, $a = 11.3219(2)$ Å, $b = 13.7116(2)$ Å, $c = 15.3645(3)$ Å, $\alpha = 109.2440(10)°$, $\beta = 90.1040(10)°$, $\gamma = 100.7220(10)°$, $V = 2207.48(7)$ Å^3, $Z = 2$, $T = 296(2)$K, $d = 1.393$ Mg/m^3, 39434 reflections measured, 10882 unique [R(int) = 0.0142], $R_1 = 0.0443$, w$R_2 = 0.1256$ for (I>2σ(I)), $R_1 = 0.0519$, w$R_2 = 0.1324$ (all data), GOF = 1.037. CCDC no. 923654.

References

1. G. C. Dismukes, *Chem. Rev.* 1996, **96**, 2909-2926.
2. C. F. Yocum and V. L. Pecoraro, *Curr. Opin. Chem. Biol.* 1999, **3**, 182-187.
3. H. Okawa and H. Sakiyama, *Pure & Appl. Chem.* 1995, **67**, 273-280.
4. A. J. Wu, J. E. Penner-Hahn and V. L. Pecoraro, *Chem. Rev.* 2004, **104**, 903–938.
5. J. W. De Boer, W. R. Browne, B. L. Feringa and R. Hage, *C. R. Chimie,* 2007, **10**, 341-354.
6. V. V. Barynin, M. M. Whittaker, S. V. Antonyuk, V. S. Lamzin, P. M. Harrison, P. J. Artymiuk and J. W. Whittaker, *Structure* 2001, **9**, 725-738.
7. T. L. Stemmler, B. E. Sturgeon, D. W. Randall, R. D. Britt and J. E. Penner-Hahn, *J. Am. Chem. Soc.* 1997, **119**, 9215-9225.
8. A. K. Boal, Jr, J. A. Cotruvo, J. Stubbe and A. C. Rosenzweig, *Biochemistry* 2012, **51**, 3861−3871.
9. Z, F. Kanyo, L. R. Scolnick, D. E. Ash and D. W. Christianson, Nature 1996, **383**, 554-557.
10. P. J. Pessiki, S. V. Khangulov, D. M. Ho and G. C. Dismukes, *J. Am. Chem. Soc.* 1994, **116**, 891-897.
11. J. Gao and S. H. Zhong, *Journal of Molecular Catalysis A: Chemical.* 2002, **186**, 25–32.
12. M. U. Triller, W.–Y. Hsieh, V. L. Pecoraro, A. Rompel, B. Krebs, *Inorg. Chem.* 2002, **41**, 5544-5554.
13. L. Dubois, J. Pécaut, M-F. Charlot, C. Baffert, M-N. Collomb, A. Deronzier and J-M. Latour, *Chem. Eur. J.* 2008, **14**, 3013–3025.
14. a) V. K. Yachandra, K. Sauer and M. P. Klein, *Chem. Rev.* 1996, **96**, 2927−2950; b) S. V. Khangulov, P. J. Pessiki, V. V. Barynin, D. E. Ash and G. C. Dismukes, *Biochemistry* 1995, **34**, 2015-2025.
15. T. M. Raschke, *Curr. Opin. Struct. Biol,* 2006, **16**, 152-159.
16. V. Madhu, B. Ekambaram, L. J. W. Shimon, Y. Diskin, G. Leitus and R. Neumann, *Dalton Trans.* 2010, **39**, 7266-7275.
17. R. A. Reynolds III, W. R. Dunham and D. Coucouvanis, *Inorg. Chem.* 1998, **37**, 1232-1241.
18. S. Mukhopadhyay and W. H. Armstrong, *J. Am. Chem. Soc.* 2003, **125**, 13010-13011.
19. S. Mukhopadhyay, B. A. Gandhi, M. L. Kirk and W. H. Armstrong, *Inorg. Chem.* 2003, **42**, 8171-8180.
20. D. Lee and S. J. Lippard, *J. Am. Chem. Soc.* 1998, **120**, 12153-12154.
21. D. Lee, S. Krebs, B. H. Huynh, M. P. Hendrich and S. J. Lippard, *J. Am. Chem. Soc.* 2000, **122**, 5000-5001.
22. D. Lee, P.–L. Hung, B. Spingler and S. J. Lippard, *Inorg. Chem.* 2002, **41**, 521-531.
23. J. R. Hagadorn, Jr. L. Que and W. B. Tolman, *J. Am. Chem. Soc.* 1998, **120**, 13531-13532.
24. J. R. Hagadorn, Jr. L. Que, W. B. Tolman, I. Prisecaru, E. Münck, *J. Am. Chem. Soc.* 1999, **121**, 9760-9761.
25. S. Yoon and S. J. Lippard, *J. Am. Chem. Soc.* 2004, **126,** 16692-16693.
26. A. E. M. Boelrijk, S. V. Khangulov and G. C Dismukes, *Inorg. Chem.* 2000, **39**, 3009-3019.
27. J. Dasgupta, A. M. Tyryshkin, Y. N. Kozlov, V. V. Klimov and G. C. Dismukes. *J. Phys. Chem. B.* 2006, **110**, 5099-5111.
28. Y. N. Kozlov, S. K. Zharmukhamedov, K. G. Tikhonov, J. Dasgupta, A. A. Kazakova, G. C. Dismukes and V. V. Klimov, *Phys. Chem. Chem. Phys.* 2004, **6**, 4905-4911.
29. M. Högbom, M. E. Andersson and P. Nordlund, *J. Biol. Inorg, Chem.* 2001, **16**, 315-323.
30. R. L. Rardin, A. Bino, P. Poganiuch, W. B. Tolman, S. Liu and S. J. Lippard, *Angew. Chem. Int. Ed.* 1990, **29**, 812-814.

Oxidation Potential (Mn^{2+}→Mn^{3+})

0.52 eV　　　　　　　　　　　　　　　　　　　　1.19 eV

$\{Mn_2\}^{4+}$　　　　　$\{Mn_2(OH_2)_2\}^{4+}$　　　　　$\{Mn_2(OH_2)_{12}\}^{4+}$

The three manganese complexes with the $\{Mn_2(\mu\text{-}O_2CR)\}^{3+}$, $\{Mn_2(\mu\text{-}OH_2)_2(\mu\text{-}O_2CR)\}^{3+}$, and $\{Mn_2(OH_6)_2(O_2CR)\}^{3+}$ motifs are in dynamic equilibrium, displaying significantly different electrochemical properties ranged from 0.52 V to 1.19 V vs. Fc/Fc$^+$.