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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 \( \text{[Mn}_2(\mu-\text{OH})_2(\mu-\text{O}_2\text{CR})]^{1-} \) unit, were described. 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**

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 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*,\(^6\) *Bacillus subtilis* class Ib ribonucleotide reductase,\(^8\) and arginase\(^9\) have been revealed by crystallographic studies. 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 effort has been devoted to reproducing the structures of the active sites by synthetic model complexes and correlating the structures 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,\(^{14,15}\) very few of the models to date have 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 the existence of a water-related dynamic equilibrium in the manganese(II) carboxylate core.

![Scheme 1. Dimanganese active sites. Left: L. plantarum catalase; Middle: B. subtilis Mn
\( \mu \)-NdF; Right: arginase.](image)

The preparation of carboxylate-rich Mn complexes introduces synthetic complications, owing to the kinetic lability of 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 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 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 \( \text{Mn(OTf)}_2.2\text{CH}_3\text{CN} \) with sodium 2,6-di-(4-fluorophenyl)benzoate\( (\text{NaO}_2\text{Ca}_4\text{F}_2\text{Ph}_2) \) (2 equiv) in anhydrous THF afforded colorless crystals of the neutral bis(\( \mu \)-carboxylato)dimanganese(II) complex, \( \text{[Mn}_2(\mu-\text{O}_2\text{Ca}_4\text{F}_2\text{Ph}_2)(\text{THF})_2] } \) (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 trigonal bipyramidal manganese(II) centers with a Mn\( \cdots\)Mn
The same synthetic procedure carried out under hydrous conditions resulted in the formation of colorless block crystals of [Mn₂(µ-OH₂)₂(µ-O₂CAr⁴FPh)₆(O₂CAr⁴FPh)₄(THF)₆] (2). The coordinated water molecule resulted from the moisture present in the THF solvent used for the reaction. Alternatively, the dissolution of I in THF containing 4 equiv water, followed by recrystallization under N₂, resulted in the identical complex. Fig. 2 displays the severely distorted octahedral manganese(II) centers, with a Mn···O separation of 3.529(2) Å. (The selected bond lengths and bond angles are presented in Fig. 3 and Table S3, respectively. Two octahedral hexaqua manganese(II) units with a Mn···Mn separation of 5.676(7) Å were present in the unit cell, with Mn···O bond lengths ranging from 2.190(5) to 2.262(5) Å. The charge of the hexaqua manganese(II) cation was balanced by two carboxylate groups, and there were also two THF molecules in the asymmetric unit. The dramatic difference in the Mn···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 water incorporation.

By treating the [Mn₂(µ-O₂CAr⁴FPh)₆] core of I with varying amounts of water, the di-water bound form, the [Mn₂(µ-OH₂)₂(µ-O₂CAr⁴FPh)₆(THF)₆] core of 2, and the completely disrupted form, the [Mn(OH₂)₆] motif of 3, were isolated. The synthetic pathway, shown in Scheme 3, clearly reveals the existence of a dynamic equilibrium between water and the carboxylate-bridged dimanganese(II) complexes.

Furthermore, the dissolution of [Mn₂(µ-O₂CAr⁴FPh)₆(O₂CAr⁴FPh)₄(THF)₆] (I) in THF containing 20 equiv water, followed by pentane diffusion into the solution, resulted in the formation of long needle-shaped colorless crystals of [Mn(OH₂)₆]₂O₂CAr⁴FPh)₂2THF(3), for which the structure and selected bond lengths and bond angles are presented in Fig. 3 and Table S3, respectively. Two octahedral hexaqua manganese(II) units with a Mn···Mn separation of 5.676(7) Å were present in the unit cell, with Mn···O bond lengths ranging from 2.190(5) to 2.262(5) Å. The charge of the hexaqua manganese(II) cation was balanced by two carboxylate groups, and there were also two THF molecules in the asymmetric unit. The dramatic difference in the Mn···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 water incorporation.

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. 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.

Figure 3. Left: ORTEP/space filling overlayed view of [Mn₂(OH₂)₂(µ-O₂CAr⁴FPh)₆(O₂CAr⁴FPh)₄(THF)₆] (3) showing 50% probability thermal ellipsoids. Right: View of the structure with the aromatic rings of Ar⁴FPhCO₂ ligands omitted for clarity.

Scheme 3. Speculative mechanism for inter-conversion of manganese (II) compounds exhibiting the water dependent equilibria between the structures 1, 2 and 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$_2$Cl$_2$ 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 3422 cm$^{-1}$ indicates that compound 2 and at least more than one species with the [Mn$_2$(OH)$_x$]$_2$($x = 1 - 9$) 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$_2$Cl$_2$; (C) 2 in KBr; (D) 1 upon addition of 4 equiv water in CH$_2$Cl$_2$; (E) 3 in KBr; (F) 1 upon addition of 20 equiv water in CH$_2$Cl$_2$.

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 coordination sphere of a metalloenzyme, as suggested by the model complexes, which would further alter the redox catalytic behavior.

Notes and references

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Crystal structure determination of 1, 2 and 3

complex 1: C₆₄H₄₀F₄M₂O₁₀, M = 1491.20, triclinic, space group P-T, a = 10.7747(6), b = 13.2190(7), c = 14.0466(8), α = 67.7730(10)°, β = 68.4860(10), γ = 76.3580(16)°, V = 1711.98(16) Å³, Z = 1, T = 223(2)K, d = 1.446 Mg/m³, 12810 reflections measured, 8377 unique [R(int) = 0.0270], R₁ = 0.0633, wR₁ = 0.1007 for (I>2σ(I)), R₁ = 0.1179, wR₂ = 0.1564 (all data), GOF = 1.162. CCDC no. 778666.

complex 2: C₆₀H₄₆Cl₄F₈M₆O₁₂, M = 1697.08, triclinic, space group P-T, a = 12.3313(3), b = 14.072(3), c = 14.127(3), α = 97.27(3)°, β = 114.67(3), γ = 111.21(3), V = 1616.8(7) Å³, Z = 1, T = 293(2) K, d = 1.436 Mg/m³, 12360 reflections measured, 8706 unique [R(int) = 0.051], R₁ = 0.0480, wR₁ = 0.1225 (all data), GOF = 0.952. CCDC no. 923655.

complex 3: C₆₀H₄₆F₆M₄O₁₂, M = 925.80, triclinic, space group P-T, a = 11.321(2), b = 13.7116(2), c = 15.3645(3), α = 109.2440(10), β = 90.1040(10), γ = 100.7220(10), V = 2207.48(7) Å³, Z = 2, T = 296 (2)K, d = 1.393 Mg/m³, 39434 reflections measured, 10882 unique [R(int) = 0.0142], R₁ = 0.0443, wR₁ = 0.1256 for (I>2σ(I)), R₁ = 0.0519, wR₂ = 0.1324 (all data), GOF = 1.037. CCDC no. 923654.

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