The Linear Mn^{II} Complex $Mn_3(5\text{-}NO_2\text{-}salimH)_2(OAc)_4$ provides an Alternative Structure Type for the Carboxylate Shift in Proteins

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The title complex {where 5-NO_2-salimH_2 = 4-[2-(5-NO_2-salicylideneimine)ethyl]imidazole} has been structurally characterized and is the first μ-phenolato, μ-carboxylato-*O*, μ-carboxylato-*O,O'* type model for the 'carboxylate shift' in polymanganese and polyiron enzymes.

Carboxylates, when acting as ligands in the metal-containing active sites of metalloproteins, take on a variety of binding modes. The most common motifs for carboxylate binding in these sites are as terminal oxygen donor ligands and, in polynuclear sites, as triatomic bridges. The diiron(III) site of the oxidized forms of the oxygen transport protein haemerythrin has been shown to contain two triatomic carboxylate bridges (μ-carboxylato-*O,O'*) and a μ-oxo bridge.[1] The identity of the bridging ligands in the reduced diiron(II) site of this protein is uncertain, but is known to be different based on magnetic susceptibility and other spectroscopic studies.[2] Similarly, the oxidized form of the diiron ribonucleotide reductase has recently been shown to contain a μ-oxo, μ-carboxylato-*O,O'* bridging set, as well as mono- and bi-dentate terminal carboxylates,[3] while the Mn^{II}-substituted Fe ribonucleotide reductase contains a bis(μ-carboxylato-*O,O'*) bridging set as well as terminal carboxylates.[4] Structurally related active sites have been proposed for dimanganese proteins such as the Mn catalase[5] and Mn ribonucleotide reductase.[6]

Lippard and coworkers have proposed that a carboxylate shift between various binding modes of carboxylate ligands, including the monatomic μ-carboxylato-*O* mode, may be important to the reactivity of a variety of metal-containing biological systems.[7,8] While a monatomic carboxylate bridging motif has been shown for a handful of Mn^{II}[7-10] and Fe^{II}[7,8,10,11] complexes, until very recently the only biological system in which this carboxylate bridging mode has been shown to exist is the Mn^{II}, Ca^{II} site of the carbohydrate-binding jackbean lectin concanavalin A.[12] However, a μ-catecholate, μ-carboxylato-*O*, μ-carboxylato-*O,O'* bridging set was recently discussed for the Fe ribonucleotide reductase mutant R2 F208Y.[13,14] In addition, two variations of the carboxylate shift have been suggested by Atta, *et al.*[4] to occur in ribonucleotide reductase, see below. To date, all examples of monatomic μ-carboxylato-*O* binding modes in Mn and Fe complexes have contained three bridging carboxylates and no additional bridges. [The only previous examples of μ_2-carboxylato-*O*, μ_2-carboxylato-*O,O'*, μ_2-O(R) bridging sets are in Cu[15] and Ru[16] complexes, both of which have significantly different

bridging geometries, class I (see below), from the complex reported here.] The best characterized biological structural motif, however, is a bis (μ-carboxylato), μ-oxo (or hydroxo, alkoxo, or phenolato) bridging set. Herein, we report the first such structurally characterized bridging unit with a monatomic carboxylate bridge in a Mn or Fe model complex.

The centrosymmetric, linear Mn^{II} trimer, $Mn_3(5\text{-}NO_2\text{-}salimH)_2(OAc)_4$ {5-NO_2-salimH$_2$ = 4-[2-(5-NO_2-salicylideneimine)ethyl]imidazole}, **1**, shown in Fig. 1, was prepared by dissolving 3 equiv. of $Mn(OAc)_2 \cdot 4\,H_2O$, 2 equiv. of 5-NO_2-salimH$_2$ (from the Schiff base condensation of 5-NO_2-salicylaldehyde and histamine), and excess NaOAc in methanol or acetonitrile and recrystallization from methanol. This structure provides the first example of a $[M_2(\mu\text{-}RCO_2)_2\{\mu\text{-}O(R)\}]$ (M = Mn, Fe) environment using a μ-phenolato, μ-carboxylato-*O*, μ-carboxylato-*O*,*O*′ bridging set.† All previously described Mn and Fe complexes with the monatomic carboxylate bridging mode have three carboxylate bridges and no additional non-carboxylate bridge. From a strictly structural viewpoint, this results in a conversion of a corner-shared to an edge-shared octahedron for the Mn ions in **1**, and a correspondingly shorter M–M distance in **1** (3.270 Å) than has been seen for any other Mn or Fe complexes with a monatomic carboxylate bridge (3.325 to > 3.7 Å).[8]

Lippard has shown[8] that the existing Mn and Fe structures represent a virtual continuum of bridging geometries between the symmetric, triatomic μ-carboxylato-*O*,*O*′ geometry and the strictly monatomic μ-carboxylato-*O* geometry and divides the μ-carboxylato-*O* structures into different classes ('I'–'III')

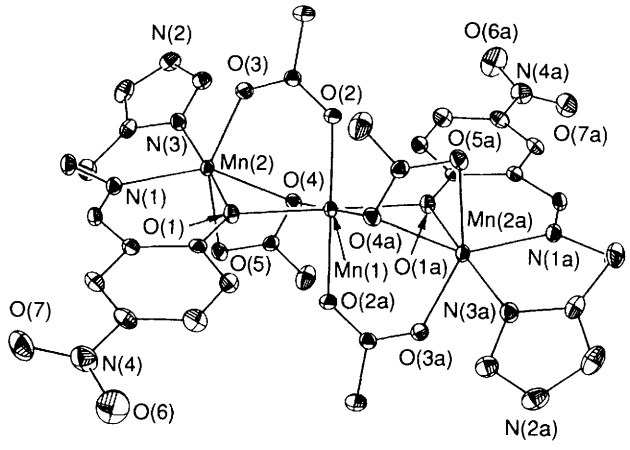


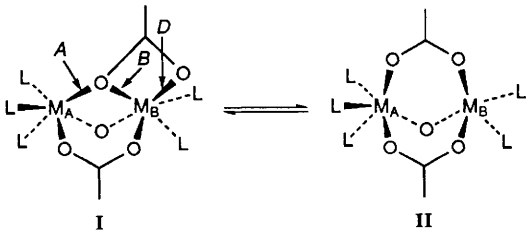
Fig. 1 ORTEP diagram of **1**. Distances in Å (Letters in parentheses refer to labels in Scheme 1): Mn(1)–Mn(2), 3.270; Mn(2)–O(1), 2.124(2); Mn(2)–O(3), 2.102(2); Mn(2)–O(4) (*B*), 2.309(2); Mn(2)–O(5) (*D*), 2.371(2); Mn(2)–N(1), 2.232(2); Mn(2)–N(3), 2.159(2); Mn(1)–O(1), 2.261(2); Mn(1)–O(2), 2.100(2); Mn(1)–O(4) (*A*), 2.264(2); O(2)–C(13), 1.262(4); O(3)–C(13), 1.273(4); O(4)–C(15), 1.288(4); O(5)–C(15), 1.268(3).

† *Crystal data*: $C_{32}H_{34}N_8O_{14}Mn_3$, amber rectangular block, monoclinic, space group $P2_1/n$ (No. 14), a = 8.258(1), b = 18.607(6), c = 12.506(4) Å, β = 95.42(2)°, V = 1913.2(9) Å^3, Z = 2, D_c = 1.595 g cm^{-3}, T = 183 K, crystal dimensions 0.20 × 0.22 × 0.32 mm^3. Data collected using a Siemens R3m/v with LT-2, Mo-Kα radiation, λ = 0.71073 Å, Lp corrected, graphite monochromator, 2θ = 5–50°, Octants used: +*h*, +*k*, +*l* (*h*: 0/10; *k*: 0/23; *l*: −15/15), at 3–6° per minute, variable, scan width 0.8° below $K\alpha_1$ to 0.8° above $K\alpha_2$, background/scan ratio 0.5, 3 standard reflections measured every 97 reflections, random variation <2%, 3818 data collected 3309 unique reflections, R_{int} = 0.0174, no absorption correction. Solution and refinement done on a Siemens SHELXTL PLUS, VAXStation. 3500, Direct methods and full-matrix least-squares analysis, respectively, $\Sigma w(|F_o|-|F_c|)^2$ function minimised, hydrogen atoms individually isotropically refined, refined reflections 2866, 328 parameters refined, Data/parameter ratio 8.7, R = 0.0407, R_w = 0.0368.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

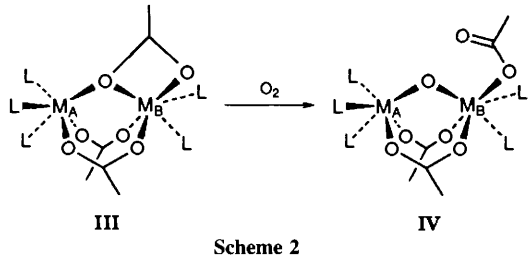
depending on the strength or lack of interaction of the non-bridging or 'dangling' carboxylate oxygen (O_d in Scheme 1) with one of the pair of metal ions (Mn_B in Scheme 1). Class I indicates no or little interaction and class III indicates strong interaction. Complex **1** adds a new structural type, analogous to the known μ-oxo (or μ-OR), bis μ-carboxylato bridging sets, to this series of compounds. The distance *D* in **1**, identified in Scheme 1, is neither long enough (> 2.5 Å) to define this complex as class I nor short enough (< distance *A* or *B*) to define it as class III. It must therefore be defined as Class II. The M–M distance is 0.1 Å shorter, at 3.270 Å, than in any other class II complex owing to the presence of the phenolate bridge, and the distances *A*, *B*, and *D* are far more symmetric than any class II complexes with M–M distances less than 3.65 Å.[8] These structural distinctions indicate that differences in the set of bridging ligands, which are not represented in the previously defined monatomic carboxylate-bridged complexes, may cause deviations from the approximately linear correlation between *B* and *D* noted for the tris-(μ-carboxylato) complexes.

There are several possible chemical contributions to reactivity at metal sites in biological systems, which may be derived from the changes in carboxylate binding mode mediated by the 'carboxylate shift'. The simplest is a change in coordination number for one of the bridged metals, as shown in Scheme 1. A shift from structure **I** to structure **II** involves a shift from a monatomic to a triatomic bridge, eliminating ligation by one of the carboxylate oxygens to M_B and consequently opening up a coordination site for exogenous ligand binding. Structure **II** has a ligand set equivalent to the previously reported complex $Mn^{II}Mn^{III}_2(saladhp)_2(OAc)_4(MeOH)_2$ which has tridentate ligands, like **1**, but which is more oxidized and has 'open' coordination sites, owing to the different carboxylate bridging mode as in **II**, which are occupied by solvent molecules.[17] A second contribution comes from the possibility of tuning the potential of the metal ions, and thus activating or deactivating the site for reactivity. The monatomic carboxylate bridge has been found only in model complexes with divalent metals,[8] and may therefore be expected to raise the reduction potential of the metal centre. A shift from structure **III** to structure **IV** in Scheme 2 (in which a monatomic carboxylate bridge shifts to a terminal, monodentate binding mode with addition of a μ-oxo bridge upon oxidation of the metal centre) has been shown by Tolman, *et al.*[18] to occur in a binuclear iron complex. Finally, comparison of the structure of the iron(III) site of Fe ribonucleotide reductase (**V** in Scheme 3) to the reduced (M^{II}_2) site in Mn-substituted Fe ribonucleotide reductase (**VI** in Scheme 3) has shown that two carboxylate shifts occur upon this metal substitution and has been suggested to occur upon reduction to the diferrous site.[4] One involves a shift from a terminal bidentate to a terminal monodentate mode while the other involves a shift from a terminal monodentate to a triatomic bridging (μ-carboxylato-*O*,*O*′) mode. Thus, the μ-phenolato, μ-carboxylato-*O*, μ-carboxylato-*O*,*O*′ complex **1** is the first structural model for the reduced structure **I** in systems which undergo the carboxylate shift indicated in Scheme 1, and is a direct analogue for the suggested bridging structure of the diiron site in the R2 F208Y ribonucleotide reductase mutant. In contrast, the previous μ-carboxylato-*O*, bis μ-carboxylato-*O*,*O*′ complexes are structural models for



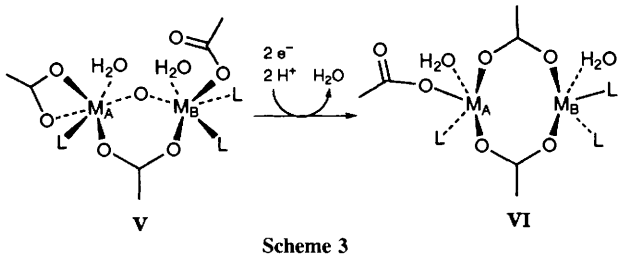
I II

Scheme 1



III IV

Scheme 2



V VI

Scheme 3

the reduced structure **III** in systems which undergo the carboxylate shift indicated in Scheme 2, and the ribonucleotide reductase carboxylate shift involves the significantly different structures in Scheme 3. Any or all of these types of 'carboxylate shift' may be important in the reactivity of polynuclear carboxylate-bridged metal sites in biological systems.

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