Novel dimanganese(II) complexes with (μ-H_2O)(μ-OAc)$_2$ bridges. Models for dimanganese enzymes

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We describe the syntheses and characterization of two new complexes, $Mn_2(\mu\text{-}H_2O)(\mu\text{-}OAc)_2(L)_4(OAc)_2$ 1 (L = imidazole) and 2 (L = benzimidazole), which display some novel structural features, and may have implications for the hydrolytic activity of arginase.

The cooperative action of closely coupled dinuclear or multinuclear centers is required for several manganese enzymes to carry out their biological functions.[1,2] In arginase[3] and the ribonuclease H domain of HIV-1 reverse transcriptase,[4] the coupled di-Mn^{II} center is required for the hydrolysis of substrate through activation of a water molecule. In redox-type Mn enzymes such as Mn catalase,[2,5] bacterial ribonucleotide reductase[6] and photosynthetic water oxidase,[2,7] Mn ions were also found or estimated to be assembled in very close proximity by the protein's coordinating side chains such as carboxylate groups from glutamates and/or aspartates.[1] Therefore, carboxylate bridged di- or poly-manganese centers have been attracting growing interest in both synthetic modelling and physical characterization.[8,9] Three di-Mn^{II}† model complexes with $[Mn_2(\mu\text{-}H_2O)(\mu\text{-}O_2CR)_2]^{2+}$ cores have been reported to date.[9] One of them is based on all-oxygen coordination spheres,[9a] while the other two are based on N_2O_4 coordination spheres around each Mn ion but with synthetic bidentate N-donor ligands.[9b] Our goal has been to synthesize aqua and carboxylate bridged dimetallic complexes employing monodentate N-donor ligands such as imidazole (Im) and benzimidazole (Bzim) which are truly good mimics of the histidine side chain. We chose Im and Bzim as the N-donor ligands not only to avoid the steric strains in most of the bidentate or multidentate ligands but also for utilization of the non-coordinating NH groups which can form hydrogen bonds with neighbouring molecules. Such hydrogen bonding is believed to play a very crucial role in the structural assembly and/or the function of many biological systems.[10] Here we report the syntheses, crystal structures and magnetic properties of two new di-Mn^{II} complexes with a (μ-aqua)bis(μ-carboxylate) unit, $[Mn_2(\mu\text{-}H_2O)(\mu\text{-}OAc)_2(L)_4(OAc)_2]$ (L = Im **1**, Bzim **2**), which are very good structural models for the active sites of di-Mn^{II} enzymes such as arginase and manganese catalase. Certain novel structural features in **1** and **2** provide some insight into the possible mode of enzyme action for arginase.[3a]

Complexes **1** and **2** were synthesized by mixing Im or Bzim with $Mn(OAc)_2{\cdot}4H_2O$ in 2.4 : 1 ratio, in absolute ethanol under nitrogen at room temperature. Prism-shaped, pale tan single crystals of **1** and **2** were grown from mixed solvents of absolute ethanol and diethyl ether. Their molecular structures were determined by single-crystal X-ray diffraction.‡ Both complexes are of similar structure and contain a di-Mn^{II} core bridged by an aqua and two bidentate acetates. Each of the Mn^{II} ions is further coordinated by one additional monodentate carboxylate and two N-donor ligands, forming two equivalent but slightly distorted MnN_2O_4 octahedra joined at their shared vertex by the oxygen atom of the bridging aqua ligand in a face-to-face fashion (see Fig. 1). The molecules lie on a crystallographically imposed twofold axis passing through the bridging aqua oxygen O(1). The hydrogen atoms of the bridging aqua were revealed as the highest residual electron density peak after all other atoms were included in X-ray structure elucidation. The bridging aquas were identified on the basis of the Mn–O(1) distances in **1** [2.246(2) Å] and in **2** [2.227(2) Å] which are significantly longer than those in μ-O–Mn^{III}_2 complexes (1.78–1.81 Å)[8] and those in μ-OH–Mn^{II}_2 complexes (2.05–2.09 Å).[8] The Mn···Mn distances in **1** [3.777(1) Å] and **2** [3.756(1) Å] are longer than those in **4** [3.5950(9) Å][9b] and **5** [3.621(2) Å],[9b] but very similar to that in **3** [3.739(2) Å].[9a] This is attributable to the opening up of the Mn–O(H_2)–Mn angles from *ca*. 110° in **4** and **5** to *ca*. 114° in **1**, **2** and **3**, and the elongation of Mn–O(aqua) distances from 2.182(3) Å in **4** and 2.215(5) Å in **5** to 2.228(7) Å in **3**, 2.227(2) Å in **2** and 2.246(2) Å in **1**. The N–Mn–N angles in **1** (92.6°) and **2** (92.9°) are significantly

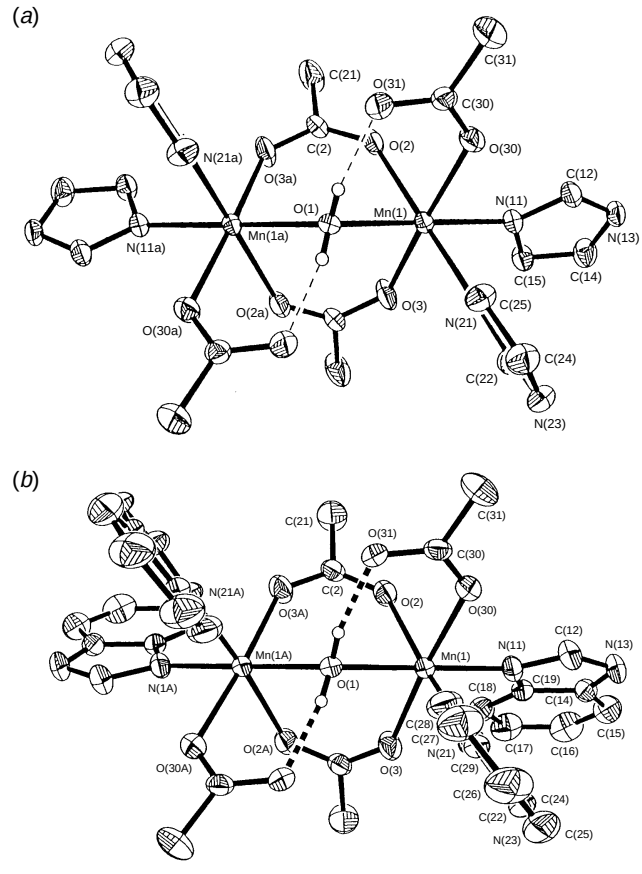

Fig. 1 Structures of **1** (*a*) and **2** (*b*), showing 40% probability thermal ellipsoids and the atom-labelling scheme. Important interatomic distances (Å) and angles (°) of **1** and **2** [in brackets] are as follows: Mn(1)···Mn(1a) 3.777(1) [3.756(1)], O(1)···O(31) 2.631(5) [2.621(3)], N(23)···O(31b) 2.741(6) [2.737(4)], N(13)···O(2c) 2.775(6) [2.808(4)], Mn(1)–O(1) 2.246(2) [2.227(2)], Mn(1)–O(2) 2.212(3) [2.206(2)], Mn(1)–O(3) 2.109(3) [2.138(2)], Mn(1)–O(30) 2.171(3) [2.183(2)], Mn(1)–N(11) 2.212(3) [2.248(2)], Mn(1)–N(21) 2.249(3) [2.269(3)], Mn(1a)–O(1) 2.246(2) [2.227(2)], C(2)–O(2) 1.252(4) [1.254(4)], C(2)–O(3a) 1.247(4) [1.242(4)], C(30)–O(30) 1.242(4) [1.252(4)], C(30)–O(31) 1.258(4) [1.262(4)]; Mn(1)-O(1)–Mn(1a) 114.4(2) [114.97(14)], O(1)–H(1)–O(31) 164.9(5) [160.6(6)].

larger than those in **4** (72°) and **5** (78°), resulting apparently from the replacement of the bidentate N-donor ligands in the latter by the two monodentate N-donor ligands. The Mn···Mn distances observed in $[Mn^{II}_2(\mu\text{-}H_2O)(\mu\text{-}O_2CR)_2]^{2+}$ cores (3.595–3.777 Å) are between those observed in the $[Mn^{II}_2(\mu\text{-}OAc)_3]^+$ core [4.034(2) Å][8] and the $[Mn^{II}_2(\mu\text{-}OH)(\mu\text{-}OAc)_2]^+$ core [3.351(3)Å].[8]

Several quite interesting structural features are noticeable in **1** and **2**. First and most important, the terminal monodentate acetate groups display an unexpected geometry. The distances of C–O(free) in **1**, 1.258(4) Å and **2**, 1.262(4) Å, are actually longer than those of their respective C–O(binding) in **1**, 1.242(4) Å and in **2**, 1.252(4) Å. Although this is only just of statistical significance based on the bond length standard deviation, this observation is contrary to the classical geometry of the terminal monodentate binding mode of a carboxylate group. Examination of over 40 related transition-metal carboxylates in the Cambridge Structural Database§ showed that the distance of C–O(free) is typically 0.03Å shorter than that of C–O(binding).[11] The reversal of C–O bond lengths is rare but has been seen, for example, in $M(CO)_5(O_2CCF_3)$ anions (M = Mo, Cr).[12] A careful examination of the structures led us to believe that the elongated C–O(free) distance may be a consequence of two hydrogen bonds, an intramolecular one with the bridging aqua ligand [O(free)···O(1) distance in **1**, 2.631(5) Å and in **2**, 2.621(3) Å] and an intermolecular one with the non-coordinating NH group from an adjacent molecule [O(free)···N in**1**, 2.741(6) Å and in **2**, 2.737(4) Å], giving rise to what may be regarded as a 'pseudo-bridging' arrangement in the terminal acetate groups.[13] The second interesting observation is that the bidentate acetate bridges are markedly asymmetric which can be attributed in part to an additional intermolecular H-bond formed between one oxygen atom of the acetate bridge and the NH group from an adjacent molecule [O(2)···N(13c) distances in**1**, 2.775(6) Å and in **2**, 2.808(4) Å], and in part to the structural *trans* effect. The significance of the observed framework of H-bonds in the formation and stabilization of **1** and **2** can therefore be envisioned. The aqua molecule bridging between two metals is stabilized by intramolecular H-bonds formed with the terminal carboxylates. This typical H-bond plays a crucial role in fixing and activating the bridging aqua or hydroxide in the process of arginine hydrolysis by arginase.[3a] Indeed, search of the CSD§ revealed *ca*. 25 other μ-aqua transition-metal complexes and in almost all cases the μ-aqua ligand was stabilized by H-bonds.

Magnetic susceptibility data for a powder sample of **1** were collected in the temperature range 5–285 K. The molar paramagnetic susceptibility increases with decreasing temperature and reaches a maximum at *ca.* 9 K with $\chi_m T = 2.129$ cm^3 mol^{-1} K, below which the susceptibility starts to decrease, indicative of antiferromagnetic coupling between the two Mn^{II} ions. A least-squares fit of the molar susceptibility by the general isotropic exchange Hamiltonian, $H = -2JS_1S_2$, $S_1 = S_2 = 5/2$, produced the best fit with $J = -1.26$ cm^{-1} and $g = 1.97$. The very small negative exchange coupling constant J in **1** is consistent with the relatively large Mn···Mn separation and the weak superexchange provided by the aqua bridge.[9a] The J value found for **1** is comparable with that deduced from EPR measurements for arginase from rat liver ($J = -2.0 \pm 0.5$ cm^{-1}),[3b] and that of **4** ($J = -2.73$ cm^{-1}) and **5** ($J = -2.952$ cm^{-1}).[9b] We also made variable temperature EPR mesurements on **1** and found the same J value as obtained from variable temperature magnetic measurements.

In summary, we have reported the syntheses, the structures and the magnetic properties of two new di-Mn^{II} complexes with (μ-aqua)bis(μ-carboxylate) bridging cores and with monodentate N-donor Im or Bzim ligands in each of the two joint MnN_2O_4 coordination spheres. This is the first symmetric di-Mn^{II} complex built up entirely with true mimics of amino acid side chains. The terminal monodentate carboxylates bind to Mn with a distinctive geometry in **1** and **2**, suggesting the possible existence of tautomeric forms of carboxylate in its coordination chemistry. Finally, we believe that the formation of strong H-bonds between the bridging aqua and the ancillary carboxylate groups in **1** and **2** provides a good mimic for arginase in which the terminal carboxylate Asp128 stabilizes and activates the bridging aqua or hydroxide, generating the basic $Mn^{II}_2(\mu\text{-}OH)^{3+}$ or superbasic $Mn^{II}_2(\mu\text{-}O)^{2+}$ by H-bond-guided proton transfer.[3a] The study of the reactivity of the title compounds and related synthetic models are currently in progress.

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Footnotes and References

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† $[Mn_2(\mu\text{-}H_2O)(\mu\text{-}O_2CC_2F_5)_2(L)_2(O_2CC_2F_5)_2(H_2O)_2]$ **3**, L = 2-ethyl-4,4,5,5-tetramethyl-3-oxo-4,5-dihydro-1H-imidazolyl-1-oxyl; $[Mn_2(\mu\text{-}H_2O)(\mu\text{-pivalate})_2(L)_2(\text{pivalate})_2]$ **4**, L = 4,4′-dimethyl-2,2′-bipyridine; $[Mn_2(\mu\text{-}H_2O)(\mu\text{-}OAc)_2(L)_2(OAc)_2]$ **5**, L = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

‡ *Crystal data* for **1** and **2** [in brackets]: $C_{20}H_{30}Mn_2N_8O_9$ [$C_{36}H_{38}Mn_2N_8O_9$], M = 636.4 [836.6], orthorhombic [orthorhombic], space group *Aba*2 [*Aba*2], a = 8.671(2) [19.043(2)], b = 19.273(2) [8.9010(10)], c = 16.789(2) [22.924(2)] Å, U = 2805.7(8) [3885.7(7)] Å^3, Z = 4 [4], D_c = 1.497 [1.430] g cm^{-3}, F(000) = 1312 [1728], λ(Mo-Kα) = 0.710 73 Å. Scan method: θ–2θ, 2θ range: 3.0 ⩽ 2θ ⩽ 55 [3 ⩽ 2θ ⩽ 60]°, μ = 0.954 [0.713] mm^{-1}, T = 198 [228] K. 1857 [2900] independent reflections were used in the refinement of which 1609 [2895] were observed. $F \geqslant 4\sigma(F)$. The final R = 0.0282 [0.0336] and R_w = 0.0322 [wR_2 = 0.0830] [$2\sigma(I) = 4\sigma(F)$]. The absolute configurations for both **1** and 2 were confirmed from anomalous scattering. CCDC 182/568.

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