Manganese Carboxylate Chemistry and Its Biological Relevance

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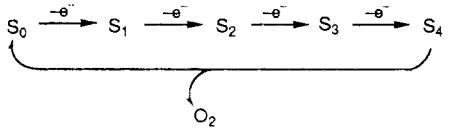
The most important role in nature identified to date for the metal manganese (Mn) is its involvement at the water oxidation/oxygen evolution center (WOC) within the photosynthetic apparatus of green plants and cyanobacteria.[1] A variety of studies have shown the Mn to be the site of substrate binding and oxidation (eq 1).

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \quad (1)$$

Although no crystallographic data are yet available, our knowledge of this site has, nevertheless, been growing; four Mn are needed for activity, Mn···Mn separations are of two types (2.72 (3) Å and ~3.3 Å), the metals are bridged by oxides (O^{2-}) (or hydroxides), and ligation is by O- and/or N-based groups from amino acid side chains (tyrosine phenoxide, histidine imidazole, aspartate/glutamate carboxylate).[1,2] Based on available evidence, the four Mn are located in one of the following: a single, asymmetric tetranuclear aggregate, two closely spaced dinuclear aggregates, or a trinuclear aggregate close to a mononuclear unit. Different workers prefer different possibilities at the present time; I favor the tetranuclear possibility. This aggregate can adopt various oxidation levels during turnover (the S_n states, n = 0–4), involving metal oxidation states in the range II–IV, with S_4 being unstable and relaxing back to S_0 with evolution of O_2.



The catalytic cycle thus involves four one-electron oxidations of the Mn aggregate, and the latter can be thought of as a biological capacitor, storing not charge but oxidizing equivalents, with "discharge" of the capacitor occurring during the $S_4 \rightarrow S_0$ transition on oxidation of substrate to O_2. Many additional studies, designed to probe the structure and properties of the Mn aggregate, have been reported. It is beyond the scope of this Account to review this literature; the interested reader is directed elsewhere.[1,2] Some points will be relevant to later discussion, however, and are briefly mentioned. First, the S_2 state is EPR active, displaying a Mn hyperfine-structured "multiline" signal at $g \sim 2.0$, and also a $g \sim 4.1$ signal under certain conditions. The multiline signal (17–19 lines) has been suggested, on the basis of simulations, to be arising from $Mn^{III}Mn^{IV}$ or $Mn_3^{III}Mn^{IV}$ mixed valence aggregates.[1] Second, water oxidation activity has an absolute requirement for Cl^-, although other small anions (Br^-, NO_3^-, I^-, and HCO_3^-) can substitute for the Cl^- with varying efficiencies.[1] It has often been suggested that Cl^- may be serving as a ligand to Mn; EXAFS data show no clear evidence for Mn–Cl linkages, but it has been noted that Cl^- ligation at the level of 1 Cl^-/4 Mn cannot be ruled out.[2] Third, peripheral ligation to the Mn aggregate is predominantly O-based (carboxylate and/or phenoxide). This conclusion is based on the results of several attempts to detect N-based (histidine) ligation. Some reports conclude there is some N-ligation at the level of 1 or 2 N/4 Mn,[3a] while other reports conclude there is no N-ligation at all.[3b,c] The true situation is thus unclear, but it appears safe to say the ligation is predominantly O-based.

Our own involvement in this area began in 1984. It was recognized that the WOC was a prime candidate for the synthetic analogue or model approach,[4] in which it is assumed that the Mn unit is a thermodynamically stable entity capable of independent existence outside its protein environment. If this is entertained, then means should be available for its synthesis in the laboratory in its various oxidation levels to allow detailed structural, physicochemical, and reactivity studies. Only then could one possibly hope to understand this site at a detailed level with respect to any structural changes during the S_n state advancement and the overall mechanism by which two H_2O molecules are bound, deprotonated, oxidatively coupled and eliminated as O_2. This Account offers a brief summary of the necessarily first stage of the model approach, the synthetic investigations designed to provide higher oxidation state (≥II) Mn complexes reproducing the

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(3) (a) Tamura, N.; Ikeuchi, M.; Inoue, Y. *Biochim. Biophys. Acta* **1989**, *973*, 281. (b) Britt, R. D.; Sauer, K.; Klein, M. P. In *Progress in Photosynthesis Research*; Biggins, J., Ed.; Nijhoff: Dordrecht, 1987; Vol. I, pp 573–576. (c) Andreasson, L.-E. *Biochim. Biophys. Acta* **1989**, *973*, 465.

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known structural and other properties of the Mn aggregate. We have employed simple carboxylates, phenoxides, and aromatic amines (pyridine, bipyridine, occasionally imidazole) as "substitutes" for amino acid side groups, with primary concentration on carboxylates given the carboxylate-rich nature of the polypeptide sequences known to bind the metal ions[5] and the absence of significant amounts of N-based ligands.[3] The resulting synthetic efforts have unearthed a large variety of products, and they are all included in the discussion, not just those of potential biological relevance. The latter will then be indicated, however, together with any potential insights they might provide into the nature of the enzyme site.

Syntheses and Structures

The first task was to develop new synthetic procedures into higher oxidation state Mn chemistry. One reagent found useful for this objective was $NBu^n_4MnO_4$. This easily prepared material is soluble and stable in a variety of organic solvents and has been shown to be an efficient oxidant in organic chemistry.[6] We suspected it might also be a useful new reagent for inorganic syntheses in organic solvents, and this has proven to be the case.[7,8] Particularly relevant to this Account is its use in a convenient, one-pot procedure to produce $[Mn_3O(O_2CR)_6L_3]^{z+}$ complexes (R = various; z = 0 or 1; L = a neutral donor molecule).[8] Thus, the comproportionation between $NBu^n_4MnO_4$ and a Mn^{II} salt in organic solvents in the presence of excess L and carboxylic acid leads directly to good yields (>60%) of pure, highly crystalline products, the oxidation level (z) governed by the Mn^{VII}:Mn^{II} ratio. The procedure is thus readily amenable to variation in z, L and R, and this fact, together with the one-step nature of the reaction, is the main advantage of this procedure to produce $[Mn_3O]$ complexes over previous ones. A few such complexes were already known, but they were limited to the R = Me derivative and synthetic procedures almost invariably employed polymeric "Mn^{III} acetate", $[Mn_3O(O_2CMe)_6{\cdot}O_2CMe{\cdot}HO_2CMe]_n$, which requires prior preparation from $KMnO_4$.[9] The $[Mn_3O]$ complexes are either $3Mn^{III}$ (z = 1) or Mn^{II}, $2Mn^{III}$ (z = 0) and possess the triangular oxide-centered structure of the venerable "basic metal carboxylates".[9a] The representative structure of one such complex is shown in Figure 1; this complex,[8] $Mn_3O(O_2CPh)_6(py)_2(H_2O)$, showing a unique asymmetry in the terminal ligands, has proven of particular utility (vide infra).

The availability of large amounts of $[Mn_3O(O_2CR)_6L_3]^{z+}$ complexes prompted us, in early 1986, to initiate a systematic investigation of their reactivity characteristics. It was, of course, hoped that one spinoff of this study would be attainment of the desired complexes with the appropriate properties to suggest that models of Mn biomolecules had been obtained; this did indeed turn out to be the case, as will be detailed below. The $[Mn_3O]$ complexes were particularly attractive for use as reagents, given their availability in large amounts and purity, their readily adjustable R and L groups, their availability in two oxidation states, and their high solubility in organic solvents such as MeCN or CH_2Cl_2, our preferred choices for reaction media.

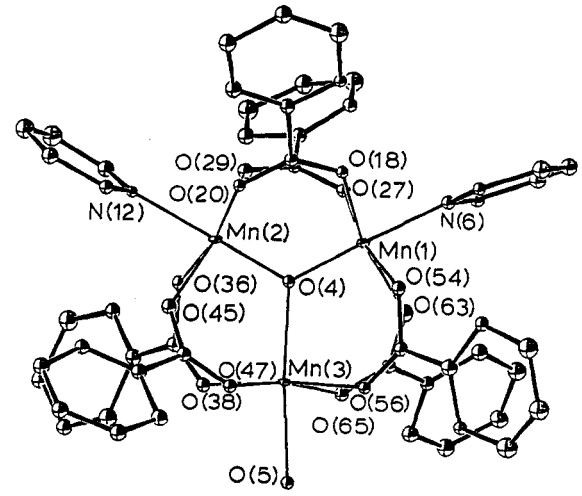

Figure 1. The structure of $Mn_3O(O_2CPh)_6(py)_2(H_2O)$. Mn(3) is the Mn^{II} center, and O(5) is the H_2O molecule. Mn(1)···Mn(2), 3.218 (4) Å; Mn(1)···Mn(3), 3.418 (5) Å; Mn(2)···Mn(3), 3.396 (5) Å.

Figure 2 conveniently summarizes the current status of our investigation. Immediately evident is the rich variety of products obtainable, with Mn nuclearities in the range 1–12 and oxidation levels in the range II–IV. In some cases, alternative and even preferable methods of preparation have since been developed, but this detracts little from the obvious versatility of the $[Mn_3O]$ starting materials as reagents for synthesis. In future reference to the products in Figure 2, they shall be numbered according to their method of preparation.

Reactions 1–3 with bipy were the only ones in Figure 2 that yielded, if not the obvious or expected product, nevertheless precisely the desired product. Our approach was based on the recognition that chelating bipy could not bind to the $[Mn_3O]$ complex without causing a serious structural perturbation. By keeping the bipy:Mn ratio low (1:1) to prevent formation of mononuclear Mn/bipy products, it was hoped that tetranuclear products would be obtained that would be structurally akin to $Fe_4O_2(O_2CF_3)_8(H_2O)_6$[10a] and $Fe_4O_2(O_2CPh)_7(H_2B(pz)_2)_2^-$;[10b] these types of complexes were unknown in Mn chemistry at the time, the only oxide-bridged tetranuclear complex then known being $Mn_4O_6(TACN)^{4+}$ (TACN = 1,4,7-triazacyclononane) prepared by Wieghardt and co-workers in 1983[11] and possessing an adamantane-like $[Mn_4(\mu\text{-}O)_6]^{4+}$ core.[12]

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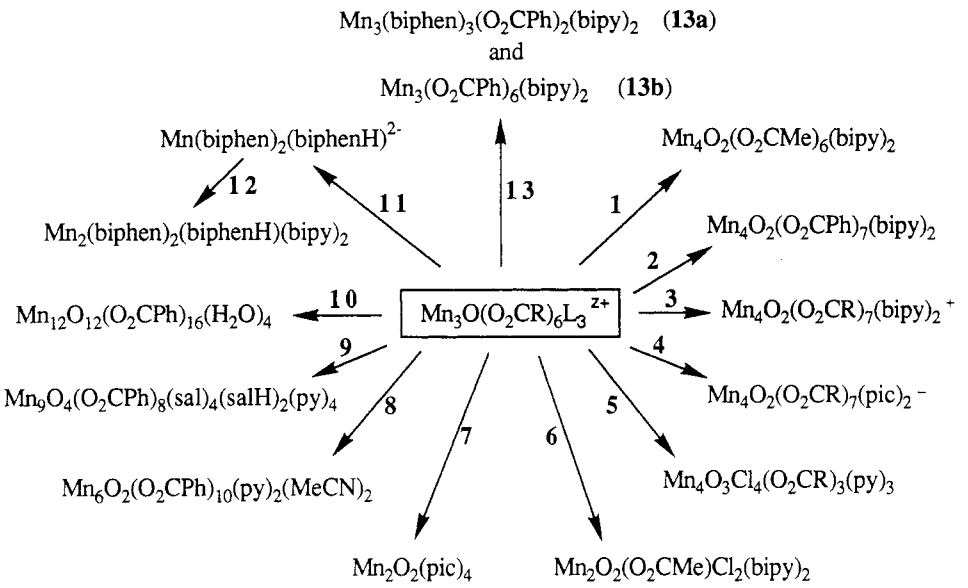

Figure 2. The established transformations of $[Mn_3O]$ starting materials. Conditions: 1, $z = 0$, bipy; 2, $z = 0$, bipy; 3, R = Me, Et, or Ph, $z = 1$, bipy; 4, R = Me or Ph, $z = 1$, Na(pic); 5, R = Me or Et, $z = 1$, Me_3SiCl; 6, $z = 1$, Me_3SiCl, bipy; 7, R = Me, $z = 1$, Me_3SiCl, Na(pic); 8, $z = 0$, phenol or NaACN; 9, $z = 0$, $salH_2$; 10, $z = 1$, N-*n*-Bu_4MnO_4, py, $PhCO_2H$; 11, R = Ph, $z = 1$, $biphenH_2$, NEt_3; 12, bipy; 13, $z = 0$, $biphenH_2$, NEt_3, bipy. For reactions 1, 3–7, 10, and 11, $L_3 = (py)_3$; for reactions 2, 8, 9, and 13, $L_3 = (py)_2(H_2O)$. The identity of R is not specified when obvious from the product. The reaction solvent is MeCN unless otherwise stated.

The strategy proved successful, and subsequent investigation demonstrated that the precise structure and oxidation state of the product depends on both the carboxylate (R) and oxidation level (z) of the $[Mn_3O(O_2CR)_6L_3]^{z+}$ reagent. Thus, use of $[Mn_3O(O_2CR)_6(py)_3](ClO_4)$ (R = Me, Et, Ph), containing three Mn^{III} ions, leads to high yields of the ClO_4^- salts of cation **3**, possessing four Mn^{III} ions.[13]

The structure of the R = Me cation is shown in Figure 3 (bottom). The four Mn ions are disposed in a "butterfly" arrangement with Mn(1) and Mn(3) occupying the "hinge" or "backbone" positions and Mn(2) and Mn(4) occupying "wing-tip" positions. (Note the unique carboxylate (O(27) and O(29)) bridging the two "hinge" Mn ions.) In contrast to reaction 3, reaction of bipy with the lower oxidation state (Mn^{II}, $2Mn^{III}$) complexes, $Mn_3O(O_2CR)_6L_3$, leads to lower oxidation state products, but their *precise* identity depends on the identity of R. Thus, for R = Me the product is complex **1** ($2Mn^{II}$, $2Mn^{III}$),[13,14] whereas for R = Ph the product is complex **2**.[13] The structure of complex **1**, $Mn_4O_2(O_2CMe)_6(bipy)_2$, is shown in Figure 3 (top). The major differences with cation **3** are the now-planar disposition of the four Mn ions and the absence of the unique carboxylate bridging the central two Mn ions. Complex **2**, $Mn_4O_2(O_2CPh)_7(bipy)_2$, has hitherto thwarted innumerable attempts at obtaining its crystal structure, but a variety of analytical and spectroscopic data are consistent with its formulation and its Mn^{II}, $3Mn^{III}$ oxidation level; these include EPR activity and a one-electron electrochemical oxidation at a potential

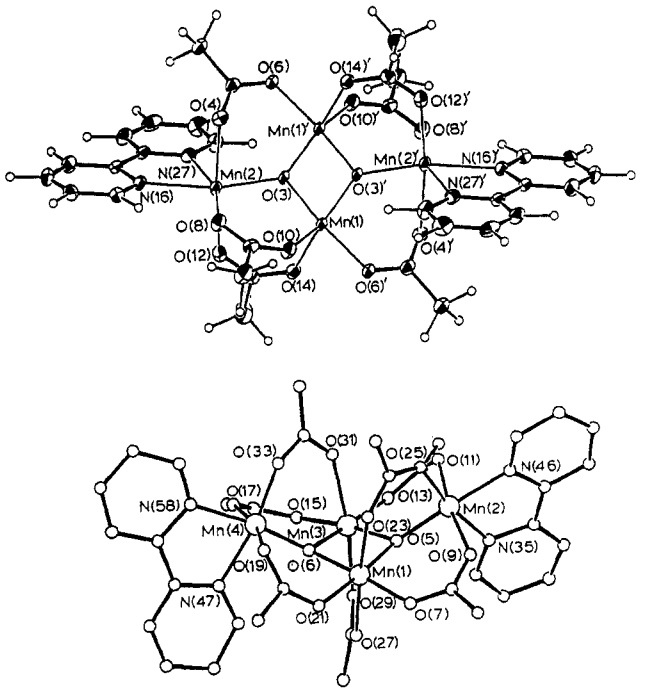

Figure 3. The structures of complexes **1** (top) and **3** (bottom). For **1**: Mn(1)···Mn(1)′, 2.779 (1) Å; Mn(1)···Mn(2), 3.288 (1) Å; Mn(1)···Mn(2)′, 3.481 (1) Å. For **3**: Mn(1)···Mn(3), 2.848 (5) Å; Mn(1)···Mn(2), 3.312 (5) Å; Mn(2)···Mn(3), 3.371 (5) Å; Mn(3)···Mn(4), 3.299 (5) Å; Mn(1)···Mn(4), 3.385 (5) Å.

identical with that for the reduction of the R = Ph version of **3**.[13b]

In an attempt to lower the total nitrogen ligation in cation **3**,[3] the corresponding reactions with Na(pic) in place of bipy have been investigated, and procedures have now been developed for the isolation of anion **4** as Na^+ or $NBu^n_4{}^+$ salts.[16] Its structure (not shown) is

(12) The monoprotonated version is also now known: Hagen, K. S.; Westmoreland, T. D.; Scott, M. J.; Armstrong, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 1907. Also reported here is the 1,1,1-tris(aminomethyl)ethane complex.

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(14) Christmas, C.; Vincent, J. B.; Huffman, J. C.; Christou, G.; Chang, H.-R.; Hendrickson, D. N. *J. Chem. Soc., Chem. Commun.* **1987**, 1303.

(15) A second planar Mn_4O_2 complex at this oxidation level has now been reported: Kulawiec, R. J.; Crabtree, R. H.; Brudvig, G. W.; Schulte, G. K. *Inorg. Chem.* **1988**, *27*, 1309.

(16) Libby, E.; Huffman, J. C.; Christou, G.; Hendrickson, D. N., manuscript in preparation.

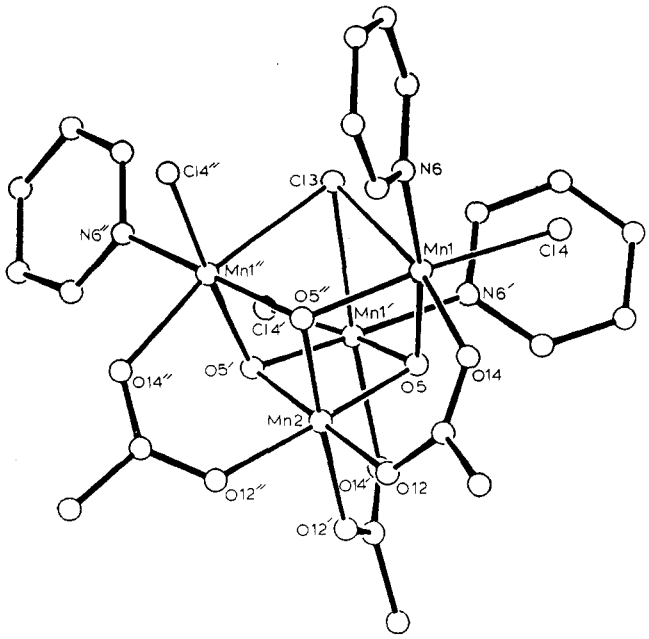


Figure 4. The structure of complex **5** (R = Me): Mn(1)···Mn(2), 2.815 (2) Å; Mn(1)···Mn(1)′, 3.272 (2) Å. (Reprinted with permission from ref 19. Copyright 1988 VCH (Weinheim).)

essentially identical with that of cation **3**, with the picolinate carboxylate replacing the bipy pyridine ring trans to the μ_3-O^{2-} ions.

Reactions 5–7 are all related and form part of an investigation into the reactivity of $[Mn_3O]$ complexes with Me_3SiCl. The latter had been shown to be an effective abstractor of carboxylate groups,[17] substituting chlorides in their place. Our thinking when planning reaction 5 was that removal of some carboxylates would force a structural perturbation akin to that in reactions 1–4. This indeed turned out to be the case, but what we could not have anticipated was a disproportionation also occurring. Thus, charge considerations show that complex **5**, $Mn_4O_3Cl_4(O_2CR)_3(py)_3$, possesses $3Mn^{III}$, Mn^{IV}. The structure of the R = Me derivative is shown in Figure 4.[19] The core consists of a Mn_4O_3 "partial cubane" with the vacant apex occupied by a μ_3-Cl^- ion. On the basis of structural parameters, Mn(2) is assigned as the Mn^{IV} site.

Reaction 5 has been further investigated. The Me_3SiCl:Mn_3O ratio has been varied from 8:1 to 1:1, but this merely affects the yield of **5** without affecting its identity, the optimum yields (30–40% based on *total* available Mn) are obtained at a ~5.5:1 ratio. Addition of imidazole (HIm) to the R = Me reaction mixture after addition of Me_3SiCl leads to the crystallization of $Mn_4O_3Cl_4(O_2CMe)_3(HIm)_3$, whose structure is identical with that of **5** except for the py/HIm substitution.[16]

Subsequent investigation of reaction 5 has involved perturbing it by addition of bidentate ligands. In reaction 6, the presence of added bipy leads instead to

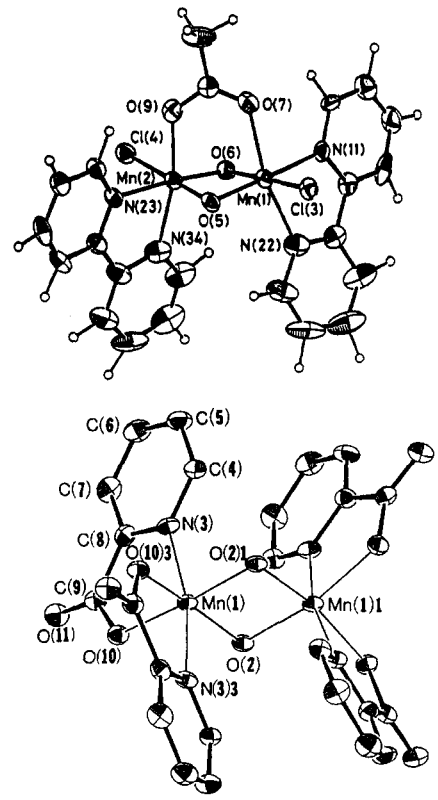


Figure 5. The structures of complex **6** (top) and complex **7** (bottom). For **6**: Mn(1)···Mn(2), 2.667 (2) Å. For **7**: Mn(1)···Mn(1)1, 2.747 (2) Å. (Reprinted with permission from ref 20a. Copyright 1988 Royal Society of Chemistry.)

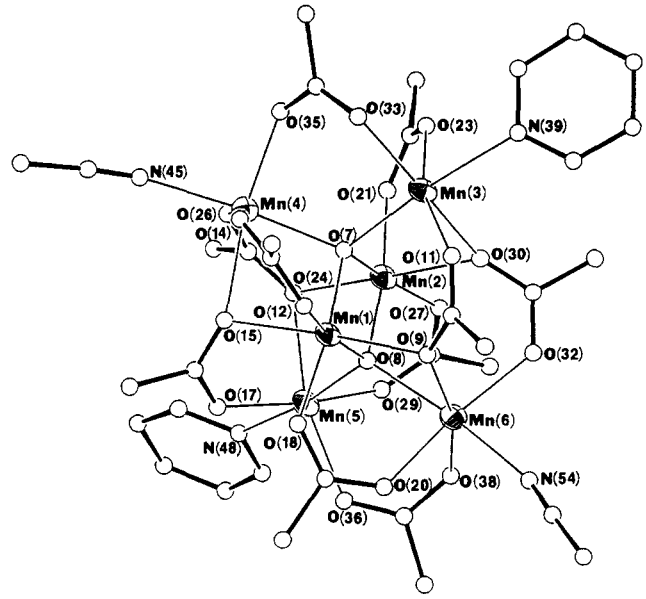


Figure 6. The structure of complex **8**. Mn(1)···Mn(2), 2.820 (3) Å; Mn(1)···Mn(3,4,5,6), 3.139–3.543 Å; Mn(2)···Mn(3,4,5,6), 3.159–3.507 Å; Mn(3)···Mn(4), 3.732 (3) Å; Mn(5)···Mn(6), 3.824 (3) Å.

dinuclear complex **6**, containing Mn^{III}, Mn^{IV}, whose structure is shown in Figure 5 (top).[20a] The two Mn ions are bridged by two O^{2-} and one acetate group. In contrast, the addition of Na(pic) (reaction 7) yields the

(17) (a) Green, M. L. H.; Parkin, G.; Bashkin, J.; Fail, J.; Prout, K. *J. Chem. Soc., Dalton Trans.* **1982**, 2519. (b) McCarley, R. E.; Ryan, T. R.; Torardi, C. C. *ACS Symp. Ser.* **1981**, *155*, 41.

(18) The first product was actually $[Mn_4O_3Cl_6(O_2CMe)_3(HIm)]^{2-}$ (HIm = imidazole): Bashkin, J. S.; Chang, H.-R.; Streib, W. E.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. *J. Am. Chem. Soc.* **1987**, *109*, 6502. This reaction employed polymeric "Mn^{III} acetate".

(19) Li, Q.; Vincent, J. B.; Libby, E.; Chang, H.-R.; Huffman, J. C.; Boyd, P. D. W.; Christou, G.; Hendrickson, D. N. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1731.

(20) (a) Bashkin, J. S.; Schake, A. R.; Vincent, J. B.; Chang, H.-R.; Li, Q.; Huffman, J. C.; Christou, G.; Hendrickson, D. N. *J. Chem. Soc., Chem. Commun.* **1988**, 700. (b) Libby, E.; Webb, R. J.; Streib, W. E.; Folting, K.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. *Inorg. Chem.*, in press.

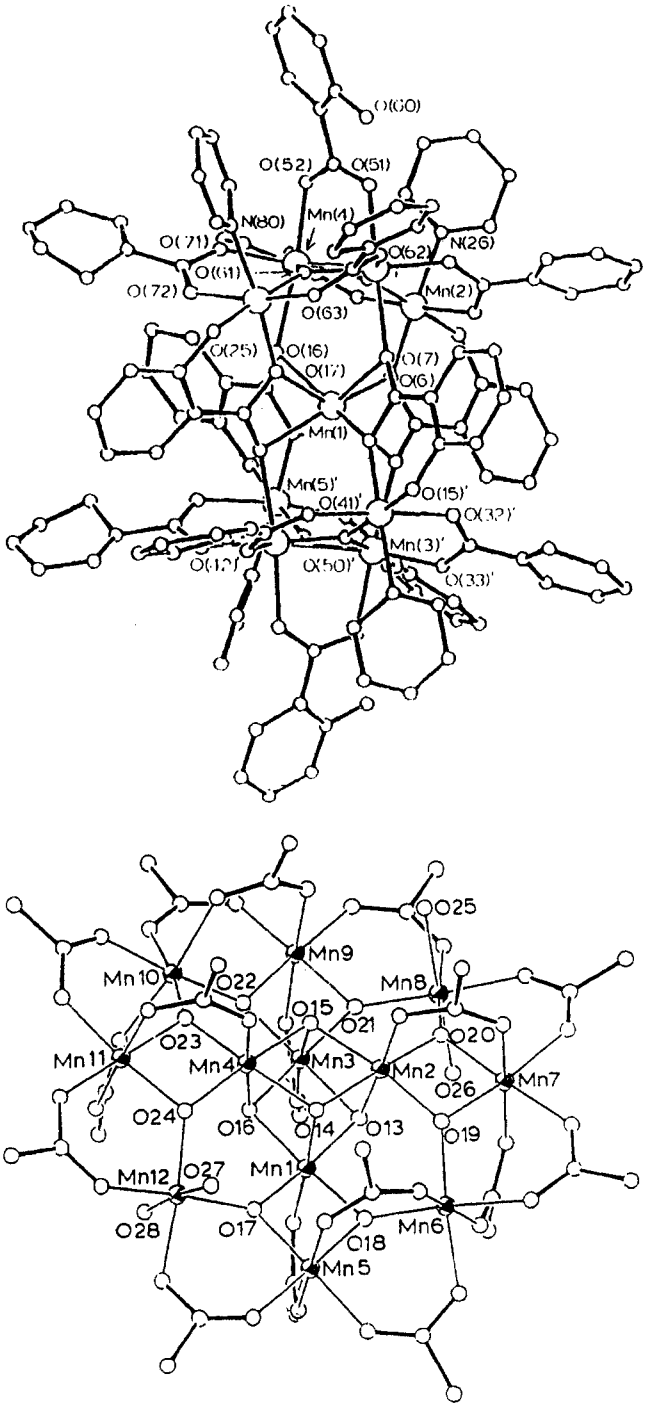


Figure 7. The structures of complex **9** (top) and **10** (bottom). For **9**: Mn(1)···Mn(2,3,4,5), 3.814–3.983 Å; Mn(2)···Mn(3), 3.406 (6) Å; Mn(2)···Mn(4), 3.443 (6) Å; Mn(3)···Mn(5), 3.408 (6) Å; Mn(4)···Mn(5), 3.425 (6) Å; Mn(3)···Mn(4), 2.817 (6) Å. For **10**: Mn···Mn distances in the central cube, 2.817–2.981 Å; Mn(1)···Mn(5), 2.809 (7) Å; Mn(2)···Mn(7), 2.775 (7) Å; Mn(3)···Mn(9), 2.803 (7) Å; Mn(4)···Mn(11), 2.813 (7) Å.

Mn_2^{IV} complex **7** shown in Figure 5 (bottom); in this case, the Mn ions are bridged by only two O^{2-} ions.[20b] It is noteworthy that in every case to date the reactions with Me_3SiCl have yielded a product containing at least some Mn^{IV}. Disproportionation of Mn^{III} is by no means rare, and while we could not have predicted it, the attainment of the Mn^{IV}-containing products was most welcome and beneficial to our biological modeling studies (vide infra).

Reaction 8 represents the most rationalizable transformation of Figure 2. Reduction of the $[Mn_3O]^{6+}$ unit

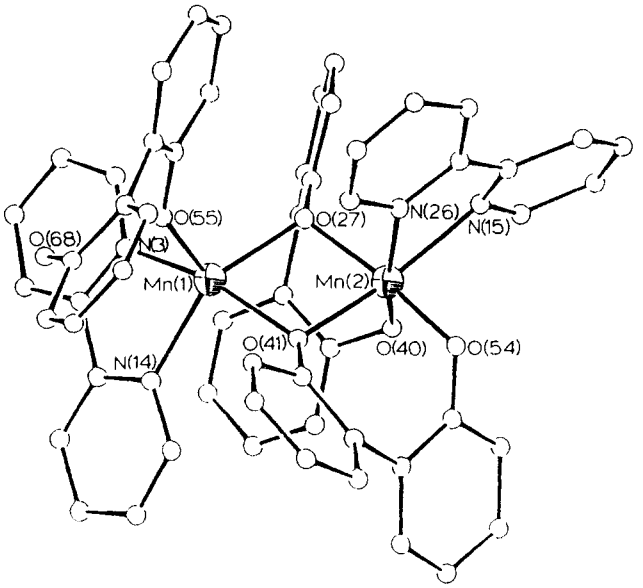


Figure 8. The structure of complex **12**: Mn(1)···Mn(2), 3.182 (6) Å. (Reprinted with permission from ref 20a. Copyright 1988 Royal Society of Chemistry.)

leads to a reductive dimerization to the $[Mn_6O_2]^{10+}$ complex **8** (eq 2).[21] A variety of reducing agents are

$$[Mn_3O]^{6+} + e^- \rightarrow [Mn_3O]^{5+} \rightarrow \tfrac{1}{2}[Mn_6O_2]^{10+} \quad (2)$$

suitable, including phenol, tyrosine, biphenol, cresols, 8-hydroxyquinoline, and sodium acenaphthylenide. The structure of the product is shown in Figure 6. Complex **8** represents somewhat of a thermodynamic "sink" for the $[Mn_3O]$ complexes under reducing conditions and will also form from brief refluxing of $Mn_3O(O_2CPh)_6(py)_2(H_2O)$ in PhCN (188 °C).[21]

An even higher nuclearity product is obtained from reaction 9. This reaction stemmed from an attempt to make complex **3**, but with salicylate in place of bipy, and thus provide completely O-based ligation. While the reaction did yield Mn_4O_2 units, two of them were held together by a central Mn^{II} and four sal^{2-} groups (Figure 7 (top)). The resulting product was, therefore, enneanuclear ($8Mn^{III}$, Mn^{II}).[22] The highest nuclearity complex obtained to date was obtained from reaction 10, the oxidation of $[Mn_3O]$ prepared in situ with $NBu^n_4MnO_4$.[23] This dodecanuclear complex ($8Mn^{III}$, $4Mn^{IV}$) is shown in Figure 7 (bottom) and comprises an Mn_4O_4 cubane held within a nonplanar ring of eight Mn^{III} ions by eight μ_3-O^{2-} ions. Inspection of the structure indicates the central cubane to be the location of the Mn^{IV} ions.

Finally, reactions 11–13 form part of an investigation of the reactions of $[Mn_3O]$ with biphenoxide (protonated biphenol undergoes reaction 8). The product of reaction 11 was originally thought to be a Mn^{IV} system based on its analysis as a tris(biphen) dianion, but the crystal structure (not shown) consists of a five-coordi-

(21) Schake, A. R.; Vincent, J. B.; Li, Q.; Boyd, P. D. W.; Folting, K.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. *Inorg. Chem.* **1989**, *28*, 1915.

(22) Christmas, C.; Vincent, J. B.; Chang, H.-R.; Huffman, J. C.; Christou, G.; Hendrickson, D. N. *J. Am. Chem. Soc.* **1988**, *110*, 823.

(23) (a) Boyd, P. D. W.; Li, Q.; Vincent, J. B.; Folting, K.; Chang, H.-R.; Streib, W. E.; Huffman, J. C.; Christou, G.; Hendrickson, D. N. *J. Am. Chem. Soc.* **1988**, *110*, 8537. (b) The structure is similar to but not identical with that reported for the AcO^- version by Lis: Lis, T. *Acta Crystallogr., Sect. B* **1980**, *B36*, 2042.

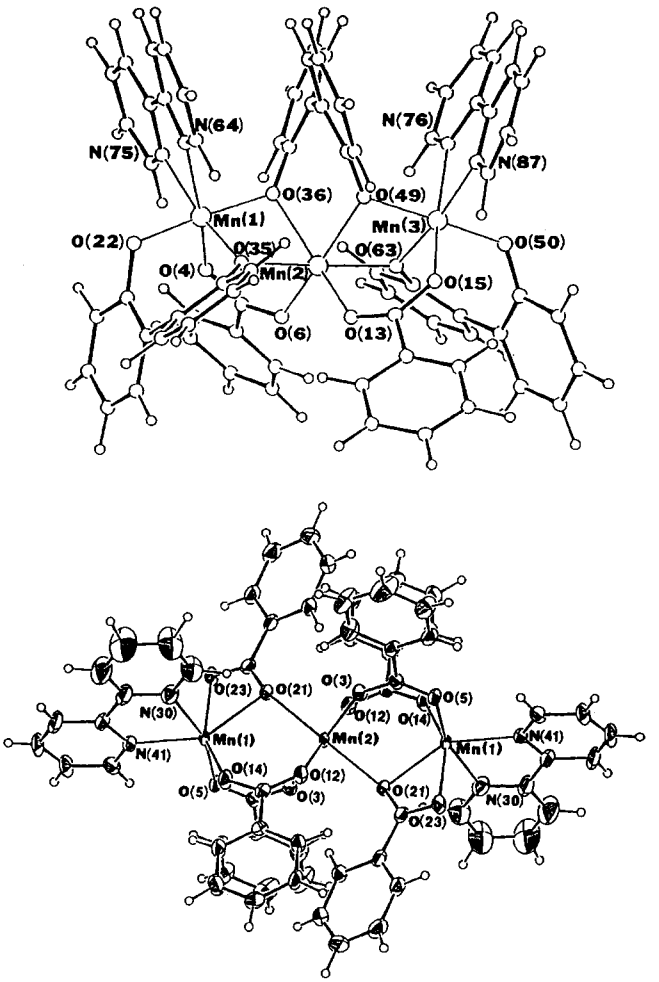


Figure 9. The structures of complex **13a** (top) and complex **13b** (bottom). For **13a**: Mn(1)···Mn(2), 3.143 (3) Å; Mn(2)···Mn(3), 3.139 (3) Å. For **13b**: Mn(1)···Mn(2), 3.588 (2) Å.

nate Mn^{III} with the sixth biphenoxide oxygen protonated and not bound.[24] Mononuclear complex **11** has itself proven a useful reagent, and treatment with bipy converts it to the mixed-valence (II, III) complex **12** (Figure 8).[20a] In contrast, reaction 13 yields two products, which have been successfully separated by solubility differences. Both products are trinuclear, but **13a** is Mn^{II}, $2Mn^{III}$, whereas **13b** is $3Mn^{II}$; both structures are shown in Figure 9; note the unique μ_3-biphen bridging mode in the structure of **13a**.[24] One immediately evident difference between the biphenoxide reactions (11–13) and the others in Figure 2 is the nonretainment of any oxide bridges in the former products. We believe this to be due to the propensity of biphen to bridge (in contrast to bipy, for example), leading to displacement of oxides. Complex **13b** can be more conveniently prepared from $Mn(O_2CPh)_2$ and bipy (eq 3).

$$3Mn(O_2CPh)_2 + 2bipy \xrightarrow{MeCN} Mn_3(O_2CPh)_6(bipy)_2 \quad (3)$$

Although the reactions of $[Mn_3O(O_2CR)_6L_3]^{z+}$ have been used as a unifying theme for this discussion, this is by no means our only investigated synthetic approach. For reasons that will become apparent below, we describe one additional structural type; to date, its

(24) Schake, A. R.; Huffman, J. C.; Chang, H.-R.; Hendrickson, D. N.; Christou, G., manuscript in preparation.

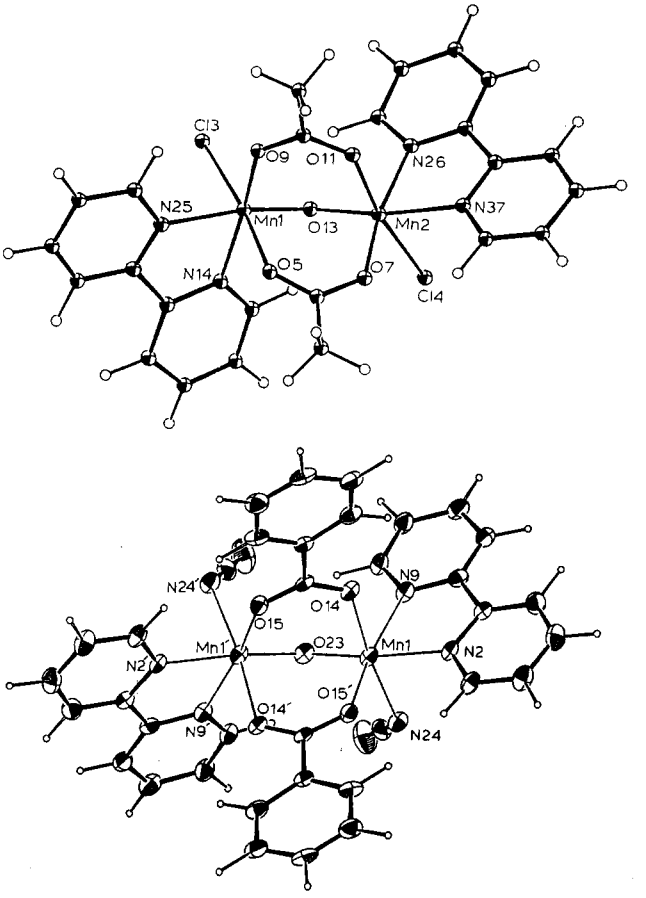


Figure 10. The structures of complex **14** (top) and complex **15** (bottom). For **14**: Mn(1)···Mn(2), 3.153 (3) Å. For **15**: Mn(1)···Mn(1)′, 3.153 (4) Å.

synthesis from $[Mn_3O]$ sources has not been accomplished. As part of our investigation into the utility of $NBu^n_4MnO_4$, we found that reaction with $Mn(OAc)_2$, benzoic acid, and bipy in pyridine leads to good (60%) yields of complex **3** (R = Ph), thus avoiding the need to use preformed $[Mn_3O]$ materials. However, in the presence of Cl^- or N_3^- the products are instead $Mn_2O(O_2CR)_2Cl_2(bipy)_2$ (**14**) and $Mn_2O(O_2CR)_2(N_3)_2(bipy)_2$ (**15**), respectively.[25] The structures of **14** (R = Me) and **15** (R = Ph) are shown in Figure 10. Complex **14** differs from **6** in possessing a $(\mu\text{-}O^{2-})(\mu\text{-}O_2CMe^-)_2$ bridge rather than $(\mu\text{-}O^{2-})_2(\mu\text{-}O_2CMe^-)$ and a $2Mn^{III}$ oxidation level rather than Mn^{III}, Mn^{IV}.

Magnetic Properties

In collaboration with D. N. Hendrickson and coworkers, we have investigated the magnitude of magnetic exchange interactions within, and the electronic structures of, the complexes described above. Results available at the time of writing are listed in Table I. Also shown are the obtained ground-state spin values. Briefly, in all cases the Mn centers are high-spin and the exchange interactions are relatively small and, in most cases, antiferromagnetic (negative J). Complexes **6** and **7** show the strongest interactions, as found for other similar III,IV and IV,IV dinuclear systems and consistent with the bis(μ_2-oxide) nature of their bridging region. Some interactions have been found to be fer-

(25) (a) Vincent, J. B.; Folting, K.; Huffman, J. C.; Christou, G. *Biochem. Soc. Trans.* **1988**, *16*, 822. (b) Vincent, J. B.; Li, Q.; Boyd, P. D. W.; Folting, K.; Huffman, J. C.; Hendrickson, D. N.; Christou, G., to be submitted.

Table I
Exchange Interactions (J)[a] and Ground-State Spin Values (S)

complex	interaction	J/cm^{-1}	S	ref
$Mn_3O(O_2CPh)_6(py)_2(H_2O)$	II–III	−7.3	$^1/_2$	8
	III–III	−10.9		
$Mn_3O(O_2CMe)_6(py)_3^+$	III–III	−10.2	0	8
1	II–III	−2.0	2[b]	13
	III–III	−3.1		
3	III–III	−7.8	3[b]	13
	III–III	−23.5		
5	III–III	+12.1	$^9/_2$[b]	19
	III–IV	−26.8		
6	III–IV	−114.0	$^1/_2$	20a
7	IV–IV	−86.5	0	20b
8	II–II	−2.4	0	21
	II–III	−0.8		
	III–III	−42.0		
9	II–III	−1.0	$^3/_2$	22
	III–III	−26.2		
	III–III	−11.2		
10		na[c]	14[b]	23a
12	II–III	+0.9	$^9/_2$[b]	20a
14	III–III	−4.1	0	25
15	III–III	+3.4	4[b]	25

[a] Based on the spin Hamiltonian $\hat{H} = -2\sum J_{ij}\hat{S}_i\cdot\hat{S}_j$. [b] Confirmed by magnetization versus magnetic field dependence studies. [c] Not available.

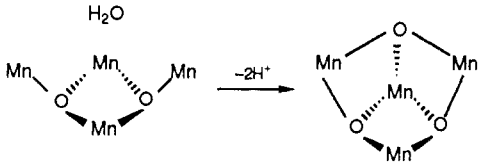
romagnetic (positive J), and this has led to rare examples of large spin ground states in complexes **5**, **12**, and **15**. Most noteworthy is the remarkable spin ground state of $S = 14$ for complex **10**! The exchange parameters have yet to be calculated; the ground state was determined by magnetization versus magnetic field dependence studies. A value of $S = 14$ is the highest yet observed for a discrete molecule,[26] and attempts are in progress to link such Mn_{12} clusters together via some suitably chosen ligands and investigate the possible onset of bulk ferromagnetism.

Biological Relevance

The initial impetus for this work was the search for tetranuclear models of the water oxidation enzyme, and the work described above has indeed unearthed a group of complexes important in this regard, namely, complexes **1**–**5**. The complexes differ by three oxidation levels and are attractive as potential models for several reasons: (i) they contain four Mn atoms which are oxide-bridged; (ii) they possess two distinct types of Mn···Mn separations (~2.8 Å and ~3.3 Å);[27] (iii) their oxidation levels are appropriate for the S_n levels; and (iv) their ligands are substitutes for histidine and aspartate/glutamate ligation. With respect to iii, current thinking is that S_1 has four Mn^{III} centers, so the S_n state correspondence would be as shown below:

S_{-1}	S_0	S_1	S_2
complex **1**	complex **2**	complexes **3**, **4**	complex **5**
$2Mn^{II}$, $2Mn^{III}$	Mn^{II}, $3Mn^{III}$	$4Mn^{III}$	$3Mn^{III}$, Mn^{IV}

The S_{-1} state does not participate in the water oxidation cycle, although it can be adopted under certain conditions.[28] The structures of complexes **1**–**4** are sufficiently similar to be appropriate (assuming **2** to be isostructural with **3**) for near neighbors in a catalytic cycle, but is not the Mn_4O_3 core of **5** too different from the Mn_4O_2 cores of **1**–**4** for consideration of the former as a model for S_2? The answer is no, for the Mn_4O_2 and Mn_4O_3 cores are more closely related than might at first seem apparent; the Mn_4O_3 core can be obtained by merely adding a third μ_3-O^{2-} to a "butterfly" unit, as depicted below:



This third O^{2-} could originate, for example, from a deprotonated substrate (H_2O) molecule, as shown. These arguments are more fully detailed in our published mechanistic proposal for the water oxidation cycle based on complexes **1**–**5**, so we refrain from further discussion here.[29] Therein is also described our proposed structure for S_3, an Mn_4O_4 cubane[30,31] obtained from the Mn_4O_3 "partial cubane" by addition of a fourth μ_3-O^{2-}. A second mechanistic proposal we have offered for consideration differs only in the identity of S_2; S_2 is now formulated as an Mn_4O_2-containing unit (as in complexes **3** or **4**) but with a $3Mn^{III}$, Mn^{IV} oxidation level, then converting directly to Mn_4O_4 at S_3 by incorporation of two deprotonated H_2O molecules. We have yet to isolate such an oxidation level for the Mn_4O_2 species, but the cyclic voltammograms of **3** and **4** do show a reversible one-electron oxidation to the $3Mn^{III}$, Mn^{IV} level; attempts to isolate these materials are in progress.

Two additional properties of complex **5** are worthy of mention. Firstly, it is EPR active, showing a 16-line hyperfine-structured signal at $g \sim 2$, in addition to features at $g \sim 6$ and 9.[18,19] Although not identical with the S_2 spectrum, it is satisfying that a synthetic $3Mn^{III}$, Mn^{IV} model complex can at least reproduce the main feature of the S_2 spectrum. Signal-to-noise is currently too poor to allow observation of any additional hyperfine lines, if present. Secondly, the μ_3-Cl^- is intriguing. We have tried but have failed, to date, to obtain a Cl^--free version of **5**. Remembering the Cl^- requirement for water oxidation, it can be speculated that a μ_3-Cl^- within a Mn aggregate as seen in complex **5** may be needed to stabilize the S_2 oxidation level. The need for a μ_3-Cl^- may thus be the origin of, or at least a contribution to, the Cl^- requirement for enzyme activity.

Should the WOC possess two closely space dinuclear units rather than a tetranuclear unit, then the dinuclear complexes **6**, **7**, **14**, and **15** would be the more biologically relevant. The $2Mn^{III}$ complexes **14** and **15** would presumably correspond to S_1. Complexes containing

(26) The next largest is $S = 12$: Caneschi, A.; Gatteschi, D.; Laugier, J.; Rey, P.; Sessol, R.; Zanchini, C. *J. Am. Chem. Soc.* **1988**, *110*, 2795.

(27) The number of ~3.3-Å vectors in **1**–**5** is greater than or equal to the number of 2.7-Å vectors. For S_1, the situation is reversed (~1 and 2, respectively). However, it is difficult to know how accurate the latter figures are, and we note that the number of Mn–O,N linkages in ref 2b is less than reasonable, as the authors themselves state.

(28) (a) Pistorius, E. K.; Schmid, G. H. *Biochim. Biophys. Acta* **1987**, *890*, 352. (b) Bader, K. P.; Thibault, P.; Schmid, G. H. *Z. Naturforsch., C: Biosci.* **1983**, *38C*, 778. (c) Velthuys, B.; Kok, B. *Biochim. Biophys. Acta* **1978**, *502*, 211.

(29) Christou, G.; Vincent, J. B. *Biochim. Biophys. Acta* **1988**, *895*, 259.

(30) Such a cubane is to be seen within complex **10**. In discrete form, it is only known, to date, at lower Mn oxidation levels.[31]

(31) (a) Herbehold, M.; Wehrmann, F.; Neugebauer, D.; Huttner, G. *J. Organomet. Chem.* **1978**, *152*, 329. (b) Brooker, S.; McKee, V.; Shepard, W. B.; Pannell, L. *J. Chem. Soc., Dalton Trans.* **1987**, 2555. (c) Horn, E.; Snow, M. R.; Zeleny, P. C. *Aust. J. Chem.* **1980**, *33*, 1659.

this $[Mn(\mu\text{-}O)(\mu O_2CR)_2Mn]^{2+}$ core had, in fact, been reported previously,[32] so **14** and **15** represent recent additions to this pool. Complexes **14** and **15**, and the related complex $Mn_2O(OAc)_2(H_2O)_2(bipy)_2$,[32b] do provide some advantage in possessing bidentate rather than tridentate terminal chelates, allowing exogenous ligands (H_2O, Cl^-, N_3^-) to be attached to the available sixth site. This is important for future reactivity studies. The Mn^{III}, Mn^{IV} and $2Mn^{IV}$ complexes **6** and **7** would then correspond to S_2 and S_3, respectively. Other dinuclear complexes at these oxidation states have been long known and many structurally characterized.[33] The Mn^{III}, Mn^{IV} systems, including **6**, are all known to give 16-line EPR signals at $g \sim 2$, again consistent with the S_2 multiline spectrum.

It was stated earlier that I favor the tetranuclear possibility for the WOC, based on currently available evidence at least. Nevertheless, we have actively pursued the synthesis and full characterization of any dinuclear products we have come across. This is partially due to the possibility that this nuclearity may yet prove to be the more relevant to the WOC, but also due to the recent identification of Mn enzymes that apparently possess dinuclear sites. The Mn catalase[34] possibly possesses a $[Mn_2O(O_2CR)_2]^{2+}$ core akin to that in complexes **14** and **15** and in the Fe protein hemerythrin.[35] Similarly, the recent identification of a Mn ribonucleotide reductase containing two Mn suggests another possible occurrence of this same bridged unit.[36]

Conclusions and Further Work

The systematic investigations described above have provided the hoped-for entry point into potential models for the WOC and even possibly for other Mn biomolecules. Certainly they have yielded, in addition, a variety of other products with interesting properties and relevance to nonbiological areas that will also continue to occupy our attention. The momentum of our modeling studies is now built up, but important objectives remain. The most important in the WOC work is that a model for S_3 is now imperative. This state represents the immediate precursor to S_4 (and O_2 evolution). Attainment of an S_3 model would make feasible the all-important reductive elimination of O_2 from bridging oxides on chemical or electrochemical oxidation of the model complex under controlled laboratory conditions.

The accumulated synthetic expertise on Mn carboxylates can now be channeled into additional areas. The Mn catalase, Mn ribonucleotide reductase, and the growing family of Fe_2 biomolecules[37] are immediate candidates, and preliminary work has been reported.[37,38] Given the variety and fundamental importance of the functions these Mn and Fe enzymes accomplish (i.e., water oxidation, methane hydroxylation, etc.), the greater understanding a model approach promises to deliver would make the invested time and effort well worthwhile.

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(32) (a) Wieghardt, K.; Bossek, U.; Nuber, B.; Weiss, J.; Bonvoisin, J.; Corbella, M.; Vitrols, S. E.; Girerd, J. J. *J. Am. Chem. Soc.* **1988**, *110*, 7398. (b) Menage, S.; Girerd, J. J.; Gleizes, A. *J. Chem. Soc., Chem. Commun.* **1988**, 431. (c) Sheats, J. E.; Czernuszewicz, R. S.; Dismukes, G. C.; Rheingold, A. L.; Petrouleas, V.; Stubbe, J.; Armstrong, W. H.; Beer, R. H.; Lippard, S. J. *J. Am. Chem. Soc.* **1987**, *109*, 1435. (d) Wieghardt, K.; Bossek, V.; Ventur, D.; Weiss, J. *J. Chem. Soc., Chem. Commun.* **1985**, 347.

(33) Tabulations are available in ref 20b and the following: Christou, G.; Vincent, J. B. In *Metal Clusters in Proteins*; Que, L., Jr., Ed.; ACS Symposium Series 372; American Chemical Society: Washington, DC, 1988; pp 238–255.

(34) (a) Beyer, W. F., Jr.; Fridovich, I. *Biochemistry* **1985**, *24*, 6460. (b) Fronko, R. M.; Penner-Hahn, J. E.; Bender, C. J. *J. Am. Chem. Soc.* **1988**, *110*, 7554. (c) Barynin, V. V.; Vagin, A. A.; Melik-Adamyan, V. R.; Grebenko, A. I.; Khangulov, S. V.; Popov, A. N.; Andrianova, M. E.; Vainshtein, B. *Dokl. Akad. Nauk SSSR* **1987**, *288*, 877.

(35) (a) Stenkamp, R. E.; Sieker, L. C.; Jensen, L. H.; McCallum, J. D.; Sanders-Loehr, J. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 713. (b) Wilkins, P. C.; Wilkins, R. G. *Coord. Chem. Rev.* **1987**, *79*, 195.

(36) Willing, A.; Follmann, H.; Anling, G. *Eur. J. Biochem.* **1988**, *170*, 603 and *175*, 167.

(37) Vincent, J. B.; Huffman, J. C.; Christou, G.; Li, Q.; Nanny, M. A.; Hendrickson, D. N.; Fong, R. H.; Fish, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 6898 and references therein to Fe biomolecules.

(38) Fish, R. H.; Fong, R. H.; Vincent, J. B.; Christou, G. *J. Chem. Soc., Chem. Commun.* **1988**, 1504.