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CaMn₄O₂ model of the biological Oxygen Evolving Complex: Synthesis by cluster expansion on low symmetry ligand

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Abstract

Using a new multinucleating ligand featuring two dipyridylalkoxide and a carboxylate moiety, low symmetry tetranuclear complexes 1-M (M = Mn, Fe, and Co) have been synthesized. Complex 1-Mn was used as precursor for the synthesis of a pentanuclear CaMn₄O₂ cluster (3) with the same metal stoichiometry as the biological OEC.

Abstract

Access to model complexes that mimic the structure and function of the Oxygen Evolving Complex (OEC) in Photosystem II facilitates understanding of the mechanism of biological water oxidation.¹ The OEC consists of a CaMn₄O₅ cluster displaying a cuboidal CaMn₃O₄ subsite and a “dangling” fourth Mn (Figure 1).^{1a, 1b} The synthesis of accurate models is hampered by the low structural symmetry of the cluster, the presence of two types of metals, and the propensity of oxo moieties to form extended oligomeric structures.^{1d, 2} The nuclearity and geometry of heterometallic oxo-bridged clusters is therefore often hard to control.^{2b, 3} More recently, models of discrete Mn₃CaO_n cores have been prepared using a methodology that allows for systematic structure-function studies.⁴ Pentanuclear clusters, CaMMn₃O₄ (M = Ca,^{3f} Ag,⁵ Mn⁶) with structures closely mimicking the full OEC have been accessed by both self-assembly as well as rational, stepwise approaches. Particularly notable is the report of a CaMn₄O₄ synthetic cluster.⁶ Despite these advances, general methodologies that allow investigations of the effects of cluster structure on its properties remain very rare.

Toward rational methodologies for model compound preparation, a cluster with the complexity of the OEC requires careful consideration of synthetic strategy. We have previously established a methodology that involves the synthesis of trinuclear precursors (A,

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Fig. 1) on a suitable supporting ligand. Oxygenation in the presence of a fourth equivalent of metal results in Mn_3MO_x clusters, with cubane ($x = 4$) highlighted (**B**) in Fig. 1. Further synthetic steps have been demonstrated to provide access to $\text{CaAgMn}_3\text{O}_4$ (**C**), and hold promise for other cluster compositions. An alternative approach (2), involves a ligand framework that can directly support a Mn_4 (**D**) in a low symmetry cluster. From this tetranuclear precursor, oxygenation in the presence of a fifth equivalent of metal can provide model MMn_4O_5 (**E**). We report herein a new desymmetrized ligand that affords access to tetranuclear clusters that can be further elaborated to more oxidized pentanuclear clusters, including a heterometallic CaMn_4O_2 complex with the same metal stoichiometry as the OEC.

The nuclearity and geometry of multinuclear metal-oxo complexes can be controlled through careful ligand design. For approach 1, a series of trinuclear complexes was accessed using a pseudo- C_3 symmetric ligand based on a 1,3,5-triarylbenzene framework functionalized with three dipyriddyloxy moieties.⁷ These precursors (**A**, Fig. 1) allowed the synthesis of tetranuclear species with a variety of oxo content (for example, **B**).^{4-5, 8} Given the low symmetry of the OEC, pseudo- C_3 symmetric CaMn_3O_4 complex (**B**) was desymmetrized via ligand substitution, which facilitated binding of Ag(I) to a specific oxo moiety to generate a $\text{CaAgMn}_3\text{O}_4$ cluster (**C**).⁵ A desymmetrized version of the supporting ligand was targeted as an alternate approach, with the goals of preparing a tetranuclear, rather than trinuclear, precursor and to embed low symmetry into the Mn_4 core. Changing one of the three dipyriddyloxy moieties of the pseudo- C_3 symmetric ligand for a carboxylate group provides a more sterically open ligand precursor, **H₃L**, with lower symmetry.

The targeted proligand **H₃L** was synthesized in four steps from 1,3,5-tris(2-bromophenyl)benzene (**L0**, Scheme 1), previously used for the synthesis of the pseudo- C_3 symmetric ligand.^{7b} Lithium-halogen exchange using 1 equiv. of *n*-BuLi followed by addition of DMF gives the monoaldehyde-dibromide **L1** as a major product. **L1** was separated from minor amounts of starting material as well as the dialdehyde species via silica flash column chromatography. The aldehyde moiety in **L1** was then protected by conversion to an acetal upon condensation with ethylene glycol, giving **L2**. The conversion to **L2** is quantitative and the product can be used without further purification. Treatment of **L2** with 4 equiv. of *t*-BuLi followed by addition of 2 equiv. of di(2-pyridyl)ketone gives the aldehyde precursor **L3** upon acidic workup. Conversion of the aldehyde moiety in **L3** to the carboxylic acid was achieved via Pinnick oxidation using NaClO_2 .⁹ Without optimization, **H₃L** can be obtained on multigram scale (> 20 g) in 46% overall yield from **L0**.

Metalation reactions were performed with Mn(II) (Scheme 2). Treatment of **H₃L** with Mn(OAc)_2 in THF/ H_2O results in the formation of a tetranuclear complex as indicated by a prominent peak at $M/Z = 1128$ in the ESI-MS corresponding to the mass of $[\text{LMn}_4\text{O(OAc)}_3]^+$. Single crystals suitable for X-ray diffraction could not be obtained to date. Treatment of **H₃L** with a different Mn(II) carboxylate precursor (benzoate, OBz) gives rise to ESI-MS peaks at $M/Z = 1543$ and 1724 , corresponding to the masses of $[\text{LMn}_4\text{O(OBz)}_3]^+$ and $[\text{LMn}_4\text{O(OBz)}_4]^+$, respectively. Colorless single crystals of **1-Mn** were obtained from DCM/ Et_2O vapor diffusion (Fig. 2b). Structural parameters and charge

balance are consistent with the $\text{LMn}_4(\text{OH})(\text{OBz})_4$ formulation. Both alkoxide moieties of **H₃L** serve as bridging ligands between Mn(1) and Mn(2) through O(1), and between Mn(1) and Mn(3) through O(2). The binding mode of the dipyriddy alkoxide moieties in **1-Mn** is identical to that in the trimetallic complex.^{7a} In contrast, a fourth Mn center is incorporated in **1-Mn** supported by the carboxylate moiety of **H₃L**, bridging Mn(3) and Mn(4), and by a water derived $\mu^3\text{-O}(3)$ ligand bridging Mn(2), Mn(3), and Mn(4). Notably, the $\mu^3\text{-O}(3)$ ligand occupies the position that an alkoxide moiety occupies in the trimetallic complex geometrically and in terms of bridging two metals that are also coordinated by alkoxides. Although the trinuclear $[\text{Mn}_3(\mu^3\text{-OH})]$ subunit in **1-Mn** is reminiscent of the numerous examples of carboxylate bridged $[\text{Mn}_3\text{O}]^{6+/7+}$ complexes, comparison of Mn-O(3) bond distances in **1-Mn** suggests that O(3) is a hydroxide.¹⁰ Bond metrics within the $[\text{Mn}^{\text{II}}_3(\mu^3\text{-OH})]$ core are consistent with known Mn(II) complexes.¹¹

To test the versatility of **L³⁻** in supporting tetranuclear clusters, other first row transition metals were tested. Fe and Co complexes structurally analogous to **1-Mn** were targeted. Treatment of **H₃L** with $\text{Fe}(\text{OAc})_2$ or $\text{Co}(\text{OAc})_2$ in the presence of organic bases such as Et_3N or py leads to the formation of tetranuclear complexes **1-Fe** and **1-Co**, respectively. For both compounds, single crystals suitable for X-ray crystallography were obtained from py/ Et_2O vapor diffusion (Fig. 2). The structures are consistent with the $\text{LM}_4(\text{OH})(\text{OAc})_4(\text{py})$ formulation. **1-Fe** and **1-Co** are isostructural, and the binding mode of **H₃L** is essentially analogous to **1-Mn**. Bond metrics within the $[\text{M}^{\text{II}}_3(\mu^3\text{-OH})]$ core are consistent with known Fe and Co complexes.¹² A pyridine molecule is bound to the six-coordinate Fe(4) and Co(4) centers, in contrast to the five-coordinate Mn(4) center in **1-Mn**. Such difference in coordination geometry is accompanied by structural changes in the $[\text{M}_3(\mu^3\text{-OH})]$ core. Mn(2)–Mn(4) and Mn(3)–Mn(4) distances are shorter than the corresponding Fe–Fe and Co–Co distances, whereas the Mn(2)–Mn(3) distance is longer. Mn(2)–O(3)–Mn(4) and Mn(3)–O(3)–Mn(4) angles are more acute than the corresponding Fe–O(3)–Fe and Co–O(3)–Co angles, whereas the Mn(2)–O(3)–Mn(3) angle is more obtuse. Aside from these differences, the overall topology of the three **1-M** complexes is highly analogous.

Tetranuclear Mn clusters with varying oxo content have been obtained from the higher symmetry trinuclear analogs of **1-Mn**.^{8b} For instance, treatment with $\text{Mn}(\text{OAc})_2$ and KO_2 results in the formation of a Mn_4O_2 cluster featuring $\mu^4\text{-O}$ and $\mu^2\text{-O}$ moieties. Similar incorporation of an additional metal center is observed upon treatment of **1-Mn** with $\text{Mn}(\text{O}_2\text{CR})_2$ and PhIO or $\text{Mn}(\text{OTf})_2$, KO_2 , and 2-phenylbenzoic acid (Scheme 2), as indicated by a prominent ESI-MS peak at 1810 that corresponds to the mass of $[\text{LMn}_5\text{O}_2(\text{OBz})_4]^+$. The solid-state structure of product **2** is consistent with the $\text{LMn}_5\text{O}_2(\text{OBz})_5(\text{THF})$ formulation (Fig. 2e). While the binding mode of the dipyriddy alkoxide moieties remains unchanged compared to the higher symmetry ligand, the incorporation of a carboxylate moiety in **L** facilitates binding of Mn(5). Based on Mn–oxo distances, the oxidation states of Mn(1), Mn(2), and Mn(5) are assigned to Mn(II), and those of Mn(3) and Mn(4) to Mn(III). The $[\text{Mn}_5\text{O}_2]^{8+}$ core of **2** is reminiscent of an incomplete $[\text{Mn}_6(\mu^4\text{-O})_2]^{10+}$ core of pseudo- D_{2h} symmetric $[\text{Mn}_6(\mu^4\text{-O})_2(\text{OAc})_{10}]$ complexes, missing one of the metal centers.^{10b}

Toward the synthesis of a Ca-Mn cluster, treatment of **1-Mn** with $\text{Ca}(\text{OTf})_2$, KO_2 , and 2-phenylbenzoic acid (Scheme 2) results instead in the formation of product **3** consistent with the $\text{LCaMn}_4\text{O}_2(\text{OBz})_5(\text{THF})$ formulation. The structure of **3** (Fig. 2d) is analogous to **2** and shows a CaMn_4O_2 cluster with the same metal stoichiometry as the OEC. Based on Mn-oxo distances, the oxidation states of Mn(1) and Mn(2) are assigned to Mn(II), and those of Mn(3) and Mn(4) to Mn(III). Among reported discrete CaMn_4 clusters,^{3c, 3h, 6, 13} there are only two reports of clusters that display oxo bridges CaMn_4O_x ($x = 1$ or 4).^{3c, 6} To our knowledge, the $[\text{Mn}_5(\mu^4\text{-O})(\mu^3\text{-O})]^{8+}$ and $[\text{CaMn}_4(\mu^4\text{-O})(\mu^3\text{-O})]^{8+}$ clusters have not been described, underscoring the utility of low-symmetry multinucleating ligands such as **H₃L** in the synthesis of hitherto unobserved oxo-bridged multimetallic core geometries related to the OEC. Furthermore, addition of $\text{Mn}(\text{OTf})_2$ to **3** results in the formation of **2**, providing a modular approach to the synthesis of other pentametallic complexes.

In summary, low symmetry tetranuclear complexes **1-M** ($M = \text{Mn, Fe, Co}$) have been synthesized and structurally characterized. The feasibility of using **1-Mn** as a precursor for the synthesis of novel pentanuclear clusters has been demonstrated with the synthesis of **2** and **3** featuring more oxidized $[\text{Mn}_5\text{O}_2]^{8+}$ and $[\text{CaMn}_4\text{O}_2]^{8+}$ cores. Compound **3** is notable as a rare example of cluster of same metal composition, with oxo bridges, as the OEC. Synthesis of pentanuclear complexes with higher oxo content toward more accurate models of the OEC is currently being pursued.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Notes and references

1. (a) Yano J, Yachandra V. Chem. Rev. 2014; 114:4175–4205. [PubMed: 24684576] (b) Shen JR. Annu. Rev. Plant Biol. 2015; 66:23–48. [PubMed: 25746448] (c) Blakemore JD, Crabtree RH, Brudvig GW. Chem. Rev. 2015; 115:12974–13005. [PubMed: 26151088] (d) Tsui EY, Kanady JS, Agapie T. Inorg. Chem. 2013; 52:13833–13848. [PubMed: 24328344] (e) Dismukes GC, Brimblecombe R, Felton GAN, Pryadun RS, Sheats JE, Spiccia L, Swiegers GF. Acc. Chem. Res. 2009; 42:1935–1943. [PubMed: 19908827]
2. (a) Mukhopadhyay S, Mandal SK, Bhaduri S, Armstrong WH. Chem. Rev. 2004; 104:3981–4026. [PubMed: 15352784] (b) Gerey B, Gouré E, Fortage J, Pécaut J, Collomb M-N. Coord. Chem. Rev. 2016; 319:1–24.
3. (a) Mishra A, Wernsdorfer W, Abboud KA, Christou G. Chem. Commun. 2005:54–56. (b) Mishra A, Yano J, Pushkar Y, Yachandra VK, Abboud KA, Christou G. Chem. Commun. 2007:1538–1540. (c) Hewitt IJ, Tang J-K, Madhu NT, Clerac R, Buth G, Anson CE, Powell AK. Chem. Commun. 2006:2650–2652. (d) Nayak S, Nayek HP, Dehnen S, Powell AK, Reedijk J. Dalton Trans. 2011; 40:2699–2702. [PubMed: 21327234] (e) Park YJ, Ziller JW, Borovik AS. J. Am. Chem. Soc. 2011; 133:9258–9261. [PubMed: 21595481] (f) Mukherjee S, Stull JA, Yano J, Stamatatos TC, Pringouri K, Stich TA, Abboud KA, Britt RD, Yachandra VK, Christou G. Proc. Nat. Acad. Sci. 2012; 109:2257–2262. [PubMed: 22308383] (g) Park YJ, Cook SA, Sickerman NS, Sano Y, Ziller JW, Borovik AS. Chem. Sci. 2013; 4:717–726. [PubMed: 24058726] (h) Koumoussi ES, Mukherjee S, Beavers CM, Teat SJ, Christou G, Stamatatos TC. Chem. Commun. 2011; 47:11128–11130. (i) Azar

- MR, Boron TT, Lutter JC, Daly CI, Zegalia KA, Nimthong R, Ferrence GM, Zeller M, Kampf JW, Pecoraro VL, Zaleski CM. *Inorg. Chem.* 2014; 53:1729–1742. [PubMed: 24417545] (j) Gerey B, Gennari M, Goure E, Pecaut J, Blackman A, Pantazis DA, Neese F, Molton F, Fortage J, Duboc C, Collomb M-N. *Dalton Trans.* 2015; 44:12757–12770. [PubMed: 26089197]
4. (a) Kanady JS, Tsui EY, Day MW, Agapie T. *Science*. 2011; 333:733. [PubMed: 21817047] (b) Tsui EY, Agapie T. *Proc. Nat. Acad. Sci.* 2013; 110:10084–10088. [PubMed: 23744039] (c) Kanady JS, Mendoza-Cortes JL, Tsui EY, Nielsen RJ, Goddard WA, Agapie T. *J. Am. Chem. Soc.* 2013; 135:1073–1082. [PubMed: 23241061] (d) Tsui EY, Tran R, Yano J, Agapie T. *Nat Chem.* 2013; 5:293–299. [PubMed: 23511417]
5. Kanady JS, Lin P-H, Carsch KM, Nielsen RJ, Takase MK, Goddard WA, Agapie T. *J. Am. Chem. Soc.* 2014; 136:14373–14376. [PubMed: 25241826]
6. Zhang C, Chen C, Dong H, Shen J-R, Dau H, Zhao J. *Science*. 2015; 348:690–693. [PubMed: 25954008]
7. (a) Tsui EY, Kanady JS, Day MW, Agapie T. *Chem. Commun.* 2011; 47:4189–4191. (b) Tsui EY, Day MW, Agapie T. *Angew. Chem. Int. Ed.* 2011; 50:1668–1672.
8. (a) Herbert DE, Lionetti D, Rittle J, Agapie T. *J. Am. Chem. Soc.* 2013; 135:19075–19078. [PubMed: 24304416] (b) Kanady JS, Tran R, Stull JA, Lu L, Stich TA, Day MW, Yano J, Britt RD, Agapie T. *Chem. Sci.* 2013; 4:3986–3996. [PubMed: 24163730]
9. Bal BS, Childers WE, Pinnick HW. *Tetrahedron*. 1981; 37:2091–2096.
10. (a) Vincent JB, Chang HR, Folting K, Huffman JC, Christou G, Hendrickson DN. *J. Am. Chem. Soc.* 1987; 109:5703–5711. (b) Christou G. *Acc. Chem. Res.* 1989; 22:328–335.
11. (a) Canada-Vilalta C, Pink M, Christou G. *Dalton Trans.* 2003:1121–1125. (b) Reynolds RA, Yu WO, Dunham WR, Coucouvanis D. *Inorg. Chem.* 1996; 35:2721–2722.
12. (a) Aromí G, Batsanov AS, Christian P, Helliwell M, Parkin A, Parsons S, Smith AA, Timco GA, Winpenny REP. *Chem. Eur. J.* 2003; 9:5142–5161. [PubMed: 14562332] (b) Kiskin MA, Fomina IG, Aleksandrov GG, Sidorov AA, Novotortsev VM, Shvedenkov YG, Eremenko IL, Moiseev II. *Inorg. Chem. Commun.* 2004; 7:734–736. (c) Lachicotte RJ, Hagen KS. *Inorg. Chim. Acta.* 1997; 263:407–414.
13. Alaimo AA, Takahashi D, Cunha-Silva L, Christou G, Stamatatos TC. *Inorg. Chem.* 2015; 54:2137–2151. [PubMed: 25478943]

Previous synthetic approach (1):

Approach targeted here (2):

Figure 1.

Representation of the OEC and an overlay of the OEC and a synthetic CaAgMn₃O₄ cluster core (top); previously reported synthetic strategy to OEC models (middle); synthetic strategy to OEC models targeted here (bottom).

Figure 2.

Crystal structures: **a)** Structure of **1-Co**. **b, c)** Truncated cores of the **1-Mn** and **1-Fe**, respectively. Bolded bonds highlight metal-alkoxide and metal-hydroxide bonds. **d, e)** Truncated cores of the **2** and **3**, respectively. Bolded bonds highlight Mn-oxo bonds. Selected bond distances (Å) and angles (°): **a) 1-Co** Co(2)–O(3) 2.041(2), Co(3)–O(3) 2.016(2), Co(4)–O(3) 2.124(3), Co(1)–Co(2) 3.4670(5), Co(1)–Co(3) 3.2410(6), Co(2)–Co(3) 3.7139(5), Co(2)–Co(4) 3.4186(6), Co(3)–Co(4) 3.4001(6), Co(2)–O(3)–Co(4) 113.3(1), Co(3)–O(3)–Co(4) 109.4(1), Co(2)–O(3)–Co(3) 132.5(1); **b) 1-Mn** Mn(2)–O(3) 2.179(3), Mn(3)–O(3) 2.187(3), Mn(4)–O(3) 2.102(3), Mn(1)–Mn(2) 3.328(1), Mn(1)–Mn(3) 3.223(1), Mn(2)–Mn(3) 4.099(1), Mn(2)–Mn(4) 3.289(1), Mn(3)–Mn(4) 3.275(1), Mn(2)–O(3)–Mn(3) 139.6(2), Mn(2)–O(3)–Mn(4) 100.2(1), Mn(3)–O(3)–Mn(4) 99.4(1); **c) 1-Fe** Fe(2)–O(3) 2.097(5), Fe(3)–O(3) 2.029(5), Fe(4)–O(3) 2.187(7), Fe(1)–Fe(2) 3.254(2), Fe(1)–Fe(3) 3.486(2), Fe(2)–Fe(3) 3.823(1), Fe(2)–Fe(4) 3.429(2), Fe(3)–Fe(4) 3.464(2), Fe(2)–O(3)–Fe(4) 106.8(2), Fe(3)–O(3)–Fe(4) 110.7(2), Fe(2)–O(3)–Fe(3) 135.3(3); **d) 3** Mn(1)–O(1) 2.128(2), Mn(2)–O(1) 2.147(2), Mn(3)–O(1) 1.906(2), Mn(4)–O(1) 1.862(2), Mn(3)–O(2) 1.821(2), Mn(4)–O(2) 1.853(2), Ca(1)–O(2) 2.200(2). **e) 2** Mn(1)–O(1) 2.122(1), Mn(2)–O(1) 2.140(1), Mn(3)–O(1) 1.910(1), Mn(4)–O(1) 1.857(1), Mn(3)–O(2) 1.825(1), Mn(4)–O(2) 1.860(1), Mn(5)–O(2) 2.077(1). Hydrogen atoms omitted for clarity.

Scheme 1.

Synthesis of **H₃L**. a) 1.1 equiv *n*-BuLi, 2 equiv DMF, THF; b) ethylene glycol, 10 mol% TsOH, C₆H₆; c) 4.1 equiv *t*-BuLi, 2 equiv di(2-pyridyl)ketone, THF; d) 3 equiv NaClO₂, 3 equiv NaHPO₄, THF/H₂O/DMSO. Red circle emphasizes the carboxylic acid moiety that replaced a dipyridyl alcohol moiety from the pseudo-*C*₃ symmetric system.^{7b}

Scheme 2.

Synthesis of tetra- and pentanuclear clusters supported by L^{3-} .