A Method for Driving O-Atom Transfer: Secondary Ion Binding to a Tetraamide Macrocyclic Ligand

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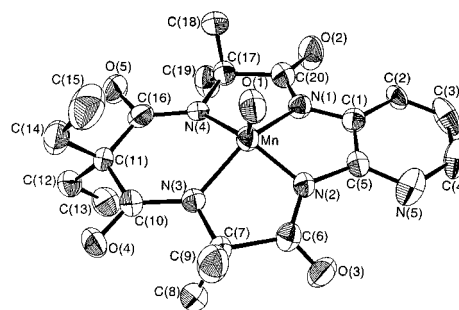Health Sciences Center at San Antonio
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Manganese−oxo complexes of salen[1,2] and porphyrin ligands[3] have been proposed as the reactive intermediates in useful O-atom transfer processes. Recently, Groves and co-workers have observed both Mn^{IV}−[3] and Mn^V−oxo porphyrins.[3,4] The Mn^V−oxo complexes **1**[5] and **2**[6] were developed as the first stable manganyls as part of our iterative design of oxidatively robust chelates aimed at expanding higher oxidation state transition-metal chemistry and oxidation chemistry.[7] Unlike the porphyrin and salen systems, these species were found not to be useful O-atom transfer agents. We assumed that the muted reactivity of **2** resulted from the higher negative charge and σ-donor capacities of the tetraamide ligands vis-à-vis the porphyrin or salen ligands. Thus, we chose to develop **3**, a system that can coordinate
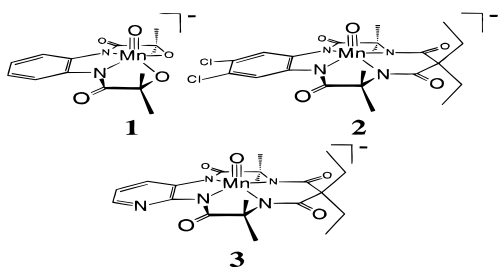
positively charged ions in the near vicinity of its Mn^V−oxo moiety to deliver an increase in O-electrophilicity over that of **2**. Here we show that **3** can be activated for O-atom transfer by the addition of secondary ions.

Complete synthetic details for producing [PPh$_4$]**3**[8] and [Et$_4$N]-**3** are given in the Supporting Information. The results of an X-ray structural study of [PPh$_4$]**3**[9] are shown in Figure 1. The reversible formation of secondary complexes of **3** was monitored in acetonitrile by UV/vis spectroscopy. Secondary ion binding was found to be significantly cation-dependent. Thus, Li$^+$ binding exhibited isosbestic behavior[10] (Figure 2) and required 2.5 equiv

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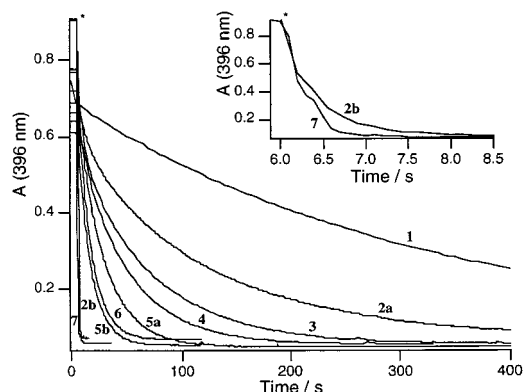(4) Groves, J. T.; Lee, J.; Marla, S. S. *J. Am. Chem. Soc.* **1997**, *119*, 6269.
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(8) Data for (C$_6$H$_5$)$_4$P[**3**]: Anal. Calcd (found) for C$_{44}$H$_{45}$MnN$_5$O$_5$P C, 65.26 (65.42); H, 5.60 (5.67); N, 8.65 (8.85); P, 3.82 (3.89). ^{1}H NMR (CDCl$_3$) δ 8.58 (m, 1 H), 8.10 (m, 1 H), 7.47−7.85 (m, 20 H), 6.86 (m, 1H), 2.05 (q, 2 H, *J* = 7.3 Hz), 1.97 (q, 2H, *J* = 7.3 Hz), 1.86 (s, 3 H), 1.85 (s, 3 H), 1.81 (s, 3 H), 1.80 (s, 3 H), 0.83 (t, 3 H, *J* = 7.7 Hz), 0.55 (t, 3 H, *J* = 7.4 Hz). ESI-MS (negative ion) *m/z* 470.1, [**3**]$^-$ (100%).

Figure 1. Molecular structure of **3**: ORTEP drawing with non-hydrogen atoms drawn to encompass 50% of electron density. The Mn atom lies 0.579 Å above the N$_4$ plane toward the oxo atom. Selected bond lengths (Å): Mn−O(1), 1.549(3); Mn−N(1), 1.884(4); Mn−N(2), 1.873(3); Mn−N(3), 1.881(3); Mn−N(4), 1.885(3).
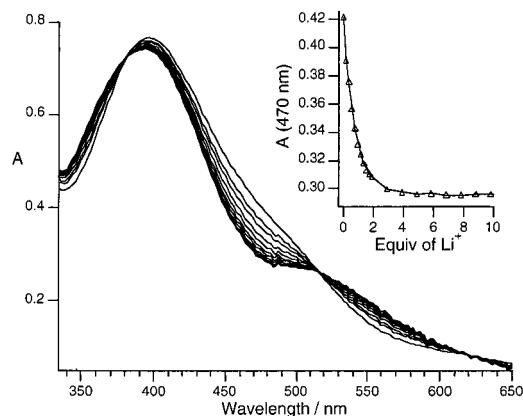
Figure 2. (A) UV/vis spectra of **3** (97.1 μM, 3 mL sample size). Aliquots of Li(SO$_3$CF$_3$) in CH$_3$CN were added (0.06 μmol in 2 μL in initial additions). (B) Mole ratio plot corrected for dilution.

of Li$^+$ for complete lithiation. In contrast, the UV/vis spectrum of **3** was unchanged on addition of K$^+$ (60 equiv). It changed nonisosbestically on addition of Ba^{2+}, Zn^{2+}, or Mg^{2+} in such a manner as to suggest that more than one **3** anion can bind to M^{2+}; the apparent endpoint was reached at 1.3 equiv of Ba^{2+}, and at 0.5 equiv for both Zn^{2+} and Mg^{2+}.[11] Similarly, Sc^{3+} binding exhibited nonisosbestic behavior; the apparent endpoint was reached at 1 equiv. As another difference, the mole ratio plot for Na$^+$ binding showed two binding processes, as evidenced by a first plateau beginning at 8 equiv of Na$^+$ and a second plateau beginning at 47 equiv. It is likely that the first binding event occurs at the bidentate site and the second binding event occurs at a monodentate amide O-atom.

(9) [PPh$_4$]**3** Crystal Data: single crystals are orthorhombic, space group *Pbca*, with *a* = 14.205(2) Å, *b* = 19.87(2) Å, *c* = 28.341(4) Å, *V* = 7999(9) Å^3 at −100 °C, and *Z* = 8 [d_{calcd} = 1.355 g·cm^{-3}; μ = 4.24 cm^{-1}]. A total of 7895 unique reflections (2° < 2θ < 52.16°) were collected using ω scans with Zr-filtered Mo *K*α X-radiation. The structure was solved by direct methods using SHELXS and was refined by full-matrix least-squares on *F*^{2} using SHELXL93 [G. M. Sheldrick, SHELXL93, *Program for Crystal Structure Refinement*, University of Göttingen, Federal Republic of Germany, 1993]. H-atoms were refined using the riding model with isotropic temperature factors set to 1.2 times that of the atom to which they were attached. Methyl hydrogens were refined as rigid groups. Refinement converged with R_1 (based on *F*) = 0.0564 for 4202 observed reflections [*I* > 2σ(*I*)].
(10) All titrations were carried out in triplicate. For Li$^+$, [**3**] = 0.30, 0.27, and 0.14 mM.
(11) Cyclic voltammograms of the **3** system are not electrochemically reversible for any secondary ion. However, CV studies of the planar, four-coordinate Co^{III} analogue of **3** show, for example, dinuclear, trinuclear, and tetranuclear species when 0.33 equiv of Ca^{2+} is present as a secondary ion, but UV/vis data indicate the presence of only one compound. Thus, CV detects differently charged species, whereas UV/vis only senses the presence of a cation in the secondary site, C. P. Horwitz and T. J. Collins, unpublished results. This suggests that binding of more than one **3** to a secondary ion leads to nonisosbestic behavior.

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Figure 3. (A) Rates of change of the UV/vis absorption of **3** at 396 nm in the presence of Ph$_3$P and different secondary ions. Normalized observed rate constants: experiment number, number of equiv of cation, cation, relative rate ± standard deviation of minimum of three runs: **1**, no cation, 0, 1; **2a**, 5, Na$^+$, 3 ± 0.1; **3**, 5, Ba^{2+}, 5 ± 0.5; 60, Ba^{2+}, 6 ± 0.1; **4**, 5, Mg^{2+}, 7 ± 0.4; 60, Mg^{2+}, 7 ± 0.8; **5a**, 5, Li$^+$, 13 ± 2.0; **6**, 5, Zn^{2+}, 24 ± 1.4; 60, Zn^{2+}, 24 ± 0.8; **5b**, 60, Li$^+$, 25 ± 0.5; **2b**, 60, Na$^+$, 506 ± 7; **7**, 5, Sc^{3+}, 1250 ± 206; 60, Sc^{3+}, 1580 ± 290. (B) Expansion of the time scale showing faster oxidations. *Addition points of Ph$_3$P.

The secondary ion binding was also monitored by ^{1}H NMR and ^{13}C NMR spectroscopy (Supporting Information). In the ^{1}H NMR spectrum on Li$^+$ addition, significant shifting was observed for all macrocycle resonances; the signals remained sharp across the entire Li$^+$ concentration gradient. In contrast, on Zn^{2+} addition, the resonances of **3** were broadened until 0.5 equiv at which point sharp resonances were again observed. The positions of the clearly defined resonances continued moving until 3 equiv had been added. The presence of several equilibrium processes is implied. A comparison of UV/vis, NMR, and electrochemical data[11] indicates that the UV/vis spectrum of **3** is sensitive to the presence of a cation in the secondary site but these changes are not influenced by more than one **3** bound to the same cation. Here UV/vis data provide apparent titration endpoints that must be augmented by analytical techniques that are more sensitive to charge and field effects from the bound cations.

Bonding within the manganyl moiety of **3** is responsive to the presence of a secondary ion as illustrated by the 15 cm^{-1} blue shift of the ν(Mn≡^{18}O)[12] IR band (from 939 to 954 cm^{-1}) that occurrs upon Li$^+$ (1 equiv) and Zn^{2+} (0.5 equiv) binding. This implies that secondary ion binding induces a drop in the donor capacity of the macrocyclic tetraamido-*N* ligand, a drop that is compensated for by an increase in donation from the oxo ligand with an implied increase in its electrophilicity.

The effects of the different activating ions on reactivity were first examined by studying a proof-of-concept oxidation, namely, Ph$_3$P to Ph$_3$PO.[13] Rates (Figure 3) normalized relative to the unactivated rate in the presence of 5 equiv of each secondary ion were: Na$^+$ = 3, Ba^{2+} = 5, Mg^{2+} = 7, Li$^+$ = 13, Zn^{2+} = 24, Sc^{3+} = 1250. As noted, K$^+$ does not bind to **3**, and Na$^+$ is unique among the activating ions studied in possessing an appreciable second binding to **3**. Thus, no increase in the rate of phosphine oxidation was found upon changing [K$^+$] from 0 to 60 equiv or upon increasing the activating ion/**3** ratio from 5:1 to 60:1 for Mg^{2+} or Zn^{2+}. Small increases were found when this ratio increase was enacted for Ba^{2+} (1.2-fold), Li$^+$ (2-fold), and Sc^{3+} (1.3-fold). In contrast, an increase in the Na$^+$/**3** ratio from 5:1 to 60:1 produced a 169-fold increase in the rate of Ph$_3$P oxidation.

The reactivity of **3** as an O-atom transfer agent for the electron-rich olefin, 2,3-dimethyl-2-butene was investigated. A mixture of [Ph$_4$P]**3** (1 equiv), ZnTf$_2$ (4.5 equiv), olefin (132 equiv), and TBHP (90%, 266 equiv) in CD$_3$CN was monitored at 50 °C via ^{13}C NMR spectroscopy until all of the olefin had been consumed (48 h). The oxygenated products observed by GC/MS were 2,3-dimethylbut-3-en-2-ol (~95%) and 2-methyl-1-butene-3-one.[14,15] The disubstituted olefin of the 2,3-dimethylbut-3-en-2-ol product is not oxidized. The 2,3-dimethylbut-3-en-2-ol, the *tert*-butyl alcohol byproduct, and the remaining TBHP had the same relative abundance as determined by ^{13}C NMR; the ketone is at a concentration too low to be observed. UV/vis analysis of the catalysis solution indicated the quantitative presence of **3** through-out and after the catalytic oxidation. A spent reaction solution in acetone-d_6 remained essentially unchanged upon standing in an NMR tube on the benchtop for nine months. After this time, it was found by ^{13}C NMR to contain 2,3-dimethylbut-3-en-2-ol, *tert*-butyl alcohol, and TBHP and its acetone adduct in the same relative ratios that were established at the end of the reaction (and presumably trace 2-methyl-1-butene-3-one). Under the above catalytic conditions, both **3**/Mg^{2+} and **3**/Sc^{3+} combinations also produce the allylic alcohol and no epoxide by ^{13}C NMR analysis. Under the catalytic conditions (50 °C, 3 days), in the absence of a secondary cation, both the allylic alcohol (74%) and the epoxide (26%) are formed (^{13}C NMR); the product ratio is essentially the same under Ar or under air. Treatment of the epoxide with Zn^{2+} in CD$_3$CN (48 h, 50 °C) under a similar concentration profile to the catalytic process produced no allylic alcohol. The epoxide does not rearrange upon prolonged standing in the presence of the Mn^{III} form of **3**. We are investigating the details of the epoxide-opening process.

Under single turnover conditions (1:11, **3**/olefin, 50 °C) without a secondary cation present, the oxidation rate is negligible under air or vacuum; after 8 days no olefin appeared to be consumed (^{1}H NMR). In contrast, with Zn^{2+} present (1:10:5.4, **3**/olefin/Zn^{2+}, 50 °C) only the allylic alcohol (>90% conversion based on 1 equiv of olefin) and unreacted olefin were observed after 24 h by ^{1}H NMR. When ^{18}O-labeled **3** was employed (~27% ^{18}O incorporation by MS), both the allylic alcohol and the ketone contain the ^{18}O label (GC/MS; ~8% ^{18}O incorporation in both products) supporting olefin oxidation through an O-atom transfer pathway.[16]

The **3**/activator combination presents a mild selective and stable catalyst for O-atom transfers. By allowing one to deliberately increase the reactivity of an otherwise slow O-atom transfer agent, the approach introduced here expands the range of controlled reactivity achievable for the relatively environmentally friendly transition metal, manganese. We are further studying the reactivity of **3** and are developing a family of conceptually related oxidation catalysts.

Supporting Information Available: Details for ligand and complex syntheses, IR and NMR data and crystallographic details including tables with atomic coordinates, bond lengths and angles, aniosotropic displacement parameters, and hydrogen coordinates and isotropic displacement parameters (17 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(12) To obtain an IR region free of macrocyclic ligand bands, the ^{18}O-labeled manganyl was examined; this was produced by stirring [Et$_4$N][**3**] in a mixture of CH$_3$CN/H$_2$^{18}O (1:1; 98% ^{18}O) for three weeks at room temperature.

(13) The reactions with different secondary ions were monitored by UV/Vis spectroscopy at 15 °C in CH$_3$CN under air employing 1 equiv of **3** and 100 equiv of Ph$_3$P, to achieve pseudo-first-order reaction conditions. A reaction with Li$^+$ as secondary ion showed the same rate under Ar and air. Secondary ions were added as the triflate salts (5 and 60 equiv); the reactions were performed at least in triplicate. Formation of Ph$_3$P=O was demonstrated by ^{1}H NMR and by IR in the ν(P=O) region.

(14) ^{13}C NMR (CD$_3$CN): 2,3-dimethylbut-3-en-2-ol, δ 19.5, 29.3, 73.3, 108.7, 153.3. Following contact with Professor Murray (ref 15), it has been agreed that the correct value is 108.7 ppm for one of the signals.

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(16) The lower ^{18}O enrichment in the organic products may arise from ^{16}O exchange with residual water in the CH$_3$CN, at a rate possibly enhanced by the Zn^{2+}. This is under investigation.