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Catalytic Oxidation by a Carboxylate-Bridged Non-Heme Diiron Complex

Edit Y. Tshuva, Dongwhan Lee, Weiming Bu, and Stephen J. Lippard*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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Several enzymes featuring carboxylate-bridged non-heme diiron centers utilize dioxygen for hydrocarbon hydroxylation (eq 1).[1−5]

$$RH + O_2 + NADH + H^+ \rightarrow ROH + H_2O + NAD^+ \quad (1)$$

For example, soluble methane monooxygenase (sMMO) catalyzes the insertion of an oxygen atom from O_2 into the C−H bonds of a variety of substrates, including methane. This enzyme system also catalyzes a variety of oxo-transfer reactions, such as the conversion of sulfides to sulfoxides, amines to amine oxides, and olefins to epoxides. The fact that nature has evolved such a system has inspired chemists to attempt to reproduce its catalytic functions. Accordingly, several complexes have been described that mimic structural aspects of the active site of the hydroxylase component (MMOH) of sMMO.[6] Reproducing the reactivity of MMOH remains an elusive goal, however. In nature, introduction of NADH and dioxygen during the catalytic cycle (eq 1) occurs at two separate proteins to prevent unproductive consumption of reductant in the absence of substrate. Consequently, mimicking the enzyme oxidation reactivity with small-molecule model compounds must overcome the difficulty of reduction to the diferrous form, required for activation of dioxygen, without catalyzing autoxidation of the reductant. We present here a carboxylate-bridged diiron catalyst that achieves oxidation of several substrates by O_2 without the need to add an external reductant.

As a part of an investigation to synthesize model compounds for MMOH and related non-heme diiron enzymes, we recently introduced the sterically hindered carboxylate 2,6-di(*p*-tolyl)-benzoate ($Ar^{Tol}CO_2^-$) as a ligand to mimic the role of glutamate in the enzyme active site.[7−10] Several diiron complexes were obtained that reproduce key structural features of the enzymes. In an extension of this work we prepared the diiron(II) complex $[(Me_3TACN)_2Fe_2(\mu\text{-}O_2CAr^{Tol})_2(MeCN)_2]^{2+}$ (**1**), where Me_3TACN is *N*,*N′*,*N″*-trimethyl-1,4,7-triazacyclononane. Reaction of **1** with dioxygen affords $[(Me_3TACN)_2Fe_2(\mu\text{-}O)(\mu\text{-}O_2CAr^{Tol})_2]^{2+}$ (**2**), which in the presence of excess O_2 at atmospheric pressure catalyzes the oxidation of triphenylphosphine to the corresponding oxide with high turnover numbers of >2000.

The triflate salt of **1** (Scheme 1) was synthesized by reacting equimolar amounts of $Fe(OTf)_2{\cdot}2MeCN$, Me_3TACN, and NaO_2CAr^{Tol} in MeCN. Colorless needles of the product were obtained in 63% yield following recrystallization from CH_2Cl_2/Et_2O and analyzed by X-ray crystallography. The structure of **1** is illustrated in Figure 1. Two chemically equivalent diiron(II) complexes were located in the asymmetric unit with Fe···Fe distances of 4.713(1) and 4.679(2) Å. The octahedral iron(II) centers in **1** are coordinated by two *syn*,*syn*-bridging carboxylate ligands and the terminal sites are occupied by two facially coordinating Me_3TACN and two MeCN molecules disposed anti with respect to the Fe−Fe axis. These terminally bound solvent molecules should be readily displaced by dioxygen in solution.

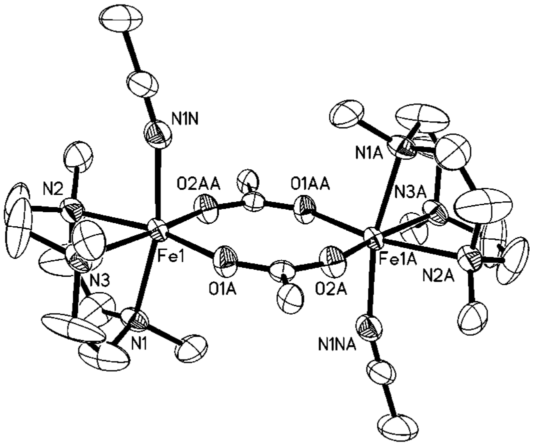
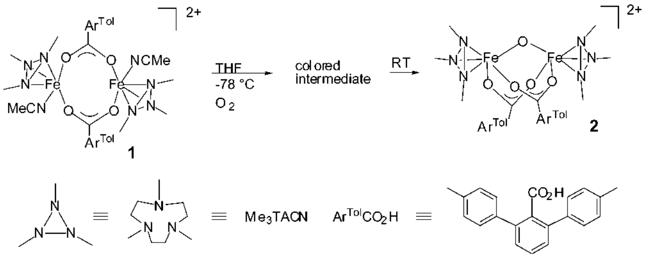


Figure 1. ORTEP diagram of $[(Me_3TACN)_2Fe_2(\mu\text{-}O_2CAr^{Tol})_2(MeCN)_2]^{2+}$ (**1**) with thermal ellipsoids at 50% probability. For clarity, all atoms of the $Ar^{Tol}CO_2^-$ ligand, except for the carboxylate groups and the α-carbon atoms, were omitted. Selected interatomic distances (Å): Fe1···Fe1A, 4.7127(13); Fe1−O1A, 2.073(3); Fe1−O2AA, 2.056(3); Fe1−N1N, 2.194(5).

Scheme 1



Cation **1** reacts with O_2 in THF at −78 °C to generate a bluish green ($\lambda_{max} = 640$ nm, $\epsilon = 2000$ M^{-1} cm^{-1}) diamagnetic intermediate (Supporting Information), which gradually decays upon warming to room temperature, giving the orange compound **2** (Scheme 1 and Supporting Information). The formation of a metastable dioxygen adduct in this chemistry prompted us to test its substrate oxidation reactivity. When the oxygenation of **1** was conducted at −78 °C in the presence of 1 equiv of Ph_3P, quantitative formation of Ph_3PO was observed, as judged by ^{31}P NMR spectroscopy. Control experiments established the orange complex **2** obtained at room temperature, and not the bluish green intermediate formed at −78 °C, to be the reactive species; addition of Ph_3P to **2** at room temperature in the presence of O_2 yielded Ph_3PO. Additional control experiments indicated the absence of any background reaction under these conditions. A THF solution of Ph_3P does not react with O_2 in the absence of **1** or **2**.

Remarkably, the reaction is catalytic in the presence of excess O_2 at atmospheric pressure. More than 2000 equiv of Ph_3P were

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* Corresponding author. E-mail address: lippard@lippard.mit.edu.

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converted to Ph_3PO when a THF solution of **2** was supplied with a phosphine solution at a rate of 10 equiv/h, by means of a syringe pump at ambient temperature (25 °C). Gradual addition is necessary since high concentrations of the substrate inhibit the reaction, presumably due to binding at an open coordination site required for O_2 activation. The catalytic reaction also proceeds to similar yields in the presence of 2,6-di-*tert*-butyl-4-methylphenol, a known radical inhibitor.[11] This result supports the notion that the chemistry does not proceed by a radical chain reaction involving molecular oxygen. When $^{18}O_2$ was employed, mass spectrometric analysis revealed the presence of $Ph_3P^{18}O$. Additional details of the mechanism are currently under investigation.

Several solvents were examined, and THF afforded the best results for the catalysis. For the solvents tested, a correlation was observed between formation of a colored species upon exposure of **1** to O_2 and oxidation reactivity. In dimethoxyethane, an orange compound formed from **1** + O_2 under ambient conditions, and within 1 h, 4 equiv of the phosphine out of the 5 introduced were converted to the oxide. Other ether solvents, such as methyl *tert*-butyl ether, isopropyl ether, and diethyl ether, gave poor results. Within 1 h, approximately 1 equiv converted out of 5 introduced. Upon exposure of **1** to O_2 in either methylene chloride or acetonitrile, the reaction mixture remained colorless and no Ph_3PO product was obtained.

Preliminary experiments indicated that **2** is also active in the oxidation of other external substrates, such as tris(pentafluorophenyl)phosphine to yield tris(pentafluorophenyl)phosphine oxide, dibenzylamine to afford benzaldehyde, and dimethyl sulfide to form dimethyl sulfoxide. No oxidation of cyclohexene, cyclohexane, toluene, adamantane, or furan has yet been observed.

Although **2** is structurally similar to other (μ-oxo)diiron(III) complexes reported in the literature,[12,13] it exhibits unusual reactivity; the acetate analogue $[(Me_3TACN)_2Fe_2(\mu\text{-}O)(\mu\text{-}O_2CCH_3)_2]^{2+}$ is significantly less reactive. This compound is, to the best of our knowledge, the first dinuclear iron complex that, in the presence of excess dioxygen at atmospheric pressure, is active in the catalytic oxidation of triphenylphosphine with high turnover numbers.[11,14-24] It thus seems that the sterically hindered carboxylate ligands play a role in the observed reactivity.

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Supporting Information Available: Details of synthetic procedures, X-ray crystallographic data, and physical measurements (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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