# Oxidative N-Dealkylation of a Carboxylate-Bridged Diiron(II) Precursor Complex by Reaction with $O_2$ Affords the Elusive $\{Fe_2(\mu\text{-}OH)_2(\mu\text{-}O_2CR)\}^{3+}$ Core of Soluble Methane Monooxygenase Hydroxylase

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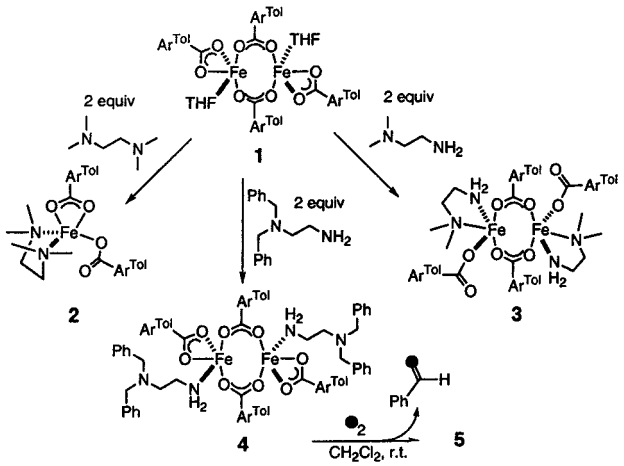
Carboxylate-bridged diiron centers occur at the active sites of several enzymes that utilize dioxygen for the selective oxidation of hydrocarbons.[1−4] The hydroxylase component of methane monooxygenase (MMOH) is one such enzyme that reduces dioxygen to afford reactive intermediate(s) that can insert one oxygen atom into a C−H bond of various substrates including $CH_4$. Efforts to unravel the molecular details of this remarkable process have until now been mainly rewarded by direct biological studies on the enzyme itself.[5,6] A complementary approach to understanding the molecular details of the C−H activation chemistry is through well-defined synthetic compounds that reproduce the architecture and reactivity of the enzyme active sites.[7,8] In this communication, we report the oxidative N-dealkylation of a substrate tethered to a carboxylate-bridged diiron(II) complex having the composition of the $MMOH_{red}$ core.[9] The reaction parallels the activation of dioxygen by non-heme diiron(II) enzymes that hydroxylate organic substrates, and, as a bonus, affords a novel diiron(III) complex with the $\{Fe_2(\mu\text{-}OH)_2(\mu\text{-}O_2CR)\}^{3+}$ core, the long-sought structural model of $MMOH_{ox}$.[9]

Previously we[10] and others[11] employed sterically hindered *m*-terphenyl-derived benzoate analogues to facilitate the assembly of diiron complexes bearing a close structural and functional resemblance to the active sites of selected non-heme diiron enzymes. The reaction of one such compound, $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(THF)_2]$ (**1**),[10a] with 2 equiv of tmeda[9] afforded the mononuclear complex $[Fe(O_2CAr^{Tol})_2(tmeda)]$ (**2**) (Figure S1), whereas alleviating steric hindrance on the diamine ligand resulted in a diiron(II) complex, $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2Ar^{Tol})_2(N,N\text{-}Me_2en)_2]$ (**3**) (Figure S2),[9] in which the terminal carboxylate ligands shift from bidentate to monodentate (Scheme 1). With this $MMOH_{red}$ analogue in hand, we envisioned the positioning of potential

**Scheme 1**




substrates as part of the terminal N-donor ligands for subsequent functional chemistry upon introduction of dioxygen. Such a strategy has been successfully implemented by us in metallohydrolase model chemistry[12] and by others in related copper oxidation chemistry.[13−15]

In pursuit of this goal, we prepared the neutral diiron(II) complex $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2Ar^{Tol})_2(N,N\text{-}Bn_2en)_2]$ (**4**) (Figure S3) in excellent yield (∼98%) following ligand substitution of **1** with 2 equiv of *N*,*N*-$Bn_2$en (Scheme 1).[9] In **4**, the terminal carboxylates are bidentate and the diamine ligands *N*,*N*-$Bn_2$en are monodentate, the opposite of the situation in **3**. This structural variation may have its origin in the steric crowding within **4**, as reflected by the significantly lengthened Fe···Fe distance of 4.3598(8) Å, compared with that in **3** (3.4245(5) Å). The composition of **4**, with four carboxylate and two N-donor ligands, is similar to that of the diiron(II) center in $MMOH_{red}$.[9,16,17]

Exposure of a colorless $CH_2Cl_2$ solution of **4** to dioxygen at room temperature rapidly afforded a brownish-yellow color. The neutral diiron(III) complex $[Fe_2(\mu\text{-}OH)_2(\mu\text{-}O_2CAr^{Tol})(O_2CAr^{Tol})_3(N,N\text{-}Bn_2en)(N\text{-}Bnen)]$ (**5**) (Figure S4)[9] was obtained in modest isolated yield (∼49%) following vapor diffusion of pentanes into the solution. As shown in Figure 1, the two iron atoms in **5** have pseudooctahedral geometry, and the metal−metal distance is 2.9788(6) Å. The di($\mu$-hydroxo)($\mu$-carboxylato)diiron(III) core of **5** is structurally analogous to the active site of $MMOH_{ox}$,[16−18] in which the Fe···Fe distances are 2.99−3.14 Å (Figure 2). Considering the frequency with which similar $\{M_2(\mu\text{-}OH)_2(\mu\text{-}O_2CR)\}^{n+}$ motifs are encountered in inorganic chemistry,[19] it is surprising that the biomimetic $\{Fe_2(\mu\text{-}OH)_2(\mu\text{-}O_2CR)\}^{3+}$ core has remained elusive in synthetic iron chemistry.[20] The three non-bridging carboxylate ligands in **5** are hydrogen-bonded to the bridging hydroxo ligands or the newly derived secondary amine

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(9) Abbreviations: $MMOH_{ox}$, MMOH in the iron(III)iron(III) oxidation state; $MMOH_{red}$, MMOH in the iron(II)iron(II) oxidation state; tmeda, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine; *N*,*N*-$Me_2$en, *N*,*N*-dimethylethylenediamine; *N*,*N*-$Bn_2$en, *N*,*N*-dibenzylethylenediamine; *N*-Bnen, *N*-benzylethylenediamine.
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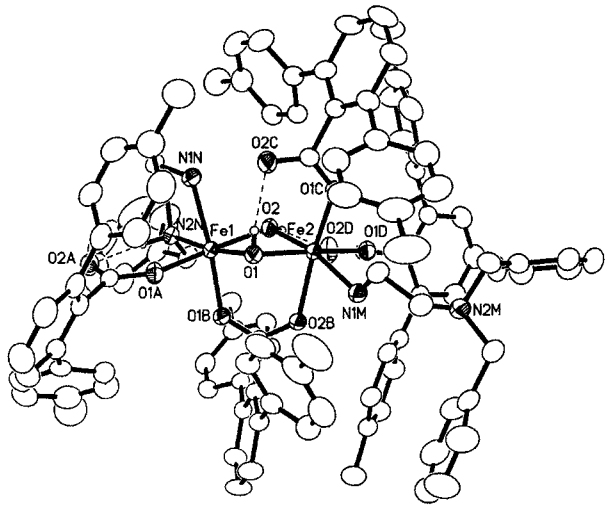


**Figure 1.** ORTEP diagram of $[Fe_2(\mu\text{-}OH)_2(\mu\text{-}O_2CAr^{Tol})(O_2CAr^{Tol})_3(N,N\text{-}Bn_2en)(N\text{-}Bnen)]$ (**5**) with thermal ellipsoids at 50% probability. Selected interatomic distances (Å) and angles (deg): Fe1···Fe1A, 2.9788(6); Fe1−O1, 1.9726(17); Fe1−O2, 1.9977(17); Fe2−O1, 1.9852(17); Fe2−O2, 1.9805(16); O1···O2C, 2.681(3); O2···O2D, 2.668(3); N2N···O2A, 2.891(3); Fe1−O1−Fe2, 97.64(7); Fe1−O2−Fe2, 96.97(7).

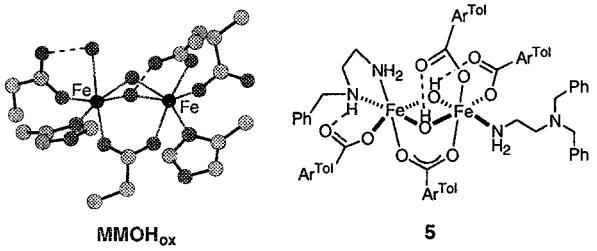


**Figure 2.** Comparison of the $MMOH_{ox}$ resting state and compound **5** structures.

group on the chelating diamine ligand, with O···H−X (X = O or N) distances of 2.668(3)−2.891(3) Å (Figure 1). Notably, the hydrogen-bonding interaction between the axial carboxylate ligand on Fe(2) and one of the bridging hydroxo ligands (O1) is analogous to that identified in a recent structural determination of $MMOH_{ox}$.[17] The Mössbauer spectrum obtained for a solid sample of **5** at 4.2 K (Figure S5) exhibits a sharp ($\Gamma$ = 0.33−0.35 mm/s) quadrupole doublet with $\delta$ = 0.48(2) mm/s and $\Delta E_Q$ = 0.61(2) mm/s. These parameters are typical for high-spin iron(III) centers with pseudooctahedral geometry.[21,22] The narrow peak width indicates that the two iron(III) centers in **5** are indistinguishable under the Mössbauer conditions.

The chemistry affording the N-dealkylated diamine ligand (*N*-Bnen)[9] in **5** was investigated by analysis of the reaction mixture following exposure of **4** to dioxygen in $CH_2Cl_2$ at room temperature. Gas chromatographic−mass spectrometric studies (Supporting Information) revealed the formation of PhCHO in an average yield of 60(5)% based on $Fe^{II}_2$. The source of the oxygen atom in the reaction product was established by use of $^{18}O_2$, which afforded $PhCH^{18}O$ as the major isotopomer (90:10 $PhCH^{18}O$/$PhCH^{16}O$) under similar conditions. This result unambiguously proves the *N*-Bnen ligand, identified in the X-ray structure of **5**, to be the product of oxidative *N*-dealkylation of **4**. Following hydroxylation of one of the benzylic positions of the *N*,*N*-$Bn_2$en ligand, the decomposition product, PhCHO, is released (Scheme 1). When an external amine substrate, such as *N*,*N*-dibenzylpropylamine, was employed in conjunction with either a mononuclear or a dinuclear iron(II) compound, however, the yield of PhCHO was significantly reduced. Under reaction conditions with 1 equiv of amine substrate per iron(II) center, the mononuclear complex **2** afforded only 1.3(3)%, and the dinuclear complex $[Fe_2(\mu\text{-}O_2CAr^{Tol})_4(4\text{-}tert\text{-}BuC_5H_4N)_2]$[10b] 13(1)%, of PhCHO. These findings indicate that reactive, dioxygen-derived species hydroxylate the tethered benzylic C−H bond with an efficiency unparalleled by analogous reactions of related complexes with external substrates. The higher oxidation efficiency of **4** most likely arises from the intramolecular nature of the chemical transformation.

Oxidative *N*-dealkylation of the metal-bound ligands has previously been observed for copper complexes in which a di($\mu$-oxo)dicopper(III) species first hydroxylates the C−H bonds $\alpha$ to the nitrogen atom, affording the corresponding aldehyde or ketone products as the final products.[13,14] This chemistry is analogous to the dealkylation of heteroatom-containing substrates effected by cytochrome P450, in which an iron(IV)−oxo porphyrin $\pi$-radical cation is invoked as the reactive intermediate.[23,24] Both stepwise oxygen "rebound" and concerted insertion of the oxygen atom into the C−H bonds have been invoked as the mechanism for such processes, although sequential one-electron oxidation of nitrogen, $\alpha$-proton abstraction, and oxygen rebound may equally well explain the product distribution. At this point, we do not have evidence to support one explanation over the other in our chemistry; however, prior work strongly suggests involvement of a high valent iron(IV)−oxo species in the key, C−H bond cleaving step.[25]

In summary, the core structure of $MMOH_{ox}$ has now been replicated following the unprecedented oxidative N-dealkylation of a diiron(II) precursor upon reaction with dioxygen. The mechanistic details of such a transformation, as well as the nature of the intermediates involved in the reaction pathway, are currently under investigation. Understanding the reaction pathway traversed by this and related well-defined non-heme diiron(II) complexes would allow us to unravel details of biological C−H activation at the molecular level.

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**Supporting Information Available:** Details of the synthetic procedures, X-ray crystallographic tables, physical characterization of **2**−**5**, and fully labeled ORTEP diagrams for each reported structure (PDF) and an X-ray crystallographic file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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