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Oxygen Activation and Intramolecular C−H Bond Activation by an Amidate-Bridged Diiron(II) Complex

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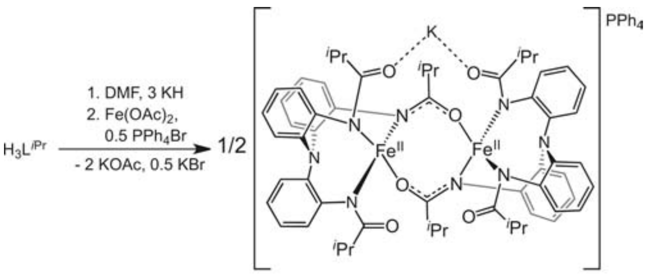
Supporting Information

ABSTRACT: A diiron(II) complex containing two μ-1,3-(κN:κO)-amidate linkages has been synthesized using the 2,2′,2′′-tris(isobutyrylamido)triphenylamine (H_3L^{iPr}) ligand. The resulting diiron complex, **1**, reacts with dioxygen (or iodosylbenzene) to effect intramolecular C−H bond activation at the methine position of the ligand isopropyl group. The ligand-activated product, **2**, has been isolated and characterized by a variety of methods including X-ray crystallography. Electrospray ionization mass spectroscopy of **2** prepared from $^{18}O_2$ was used to confirm that the oxygen atom incorporated into the ligand framework is derived from molecular oxygen.

Bacterial multicomponent monooxygenases (BMMs) react with dioxygen to form intermediates capable of cleaving C−H bonds in hydrocarbon substrates.[1,2] Within the BMM family, the hydroxylase components of soluble methane monooxygenase[3] and toluene/*o*-xylene monooxygenase[4] both contain structurally similar nonheme, diiron active sites that incorporate bridging carboxylate ligands.[5] Consequently, synthetic carboxylate-bridged diiron(II) complexes have been extensively studied as both structural and functional models of these active sites.[5−13] These synthetic studies have illustrated the importance of ligand design in the assembly of diiron complexes that display biomimetic reactivity.[5] Recently, a diiron(IV) complex, $[(Fe^{IV})_2(\mu\text{-O})(L)_2]^{2+}$ [where L = *N*,*N*-bis(3′,5′-dimethyl-4′-methoxypyridyl-2′-methyl)-*N*′-acetyl-1,2-diaminoethane], containing a (μ-oxo)bis(μ-1,3-(κN:κO)-amidate)diiron(IV) core was prepared by bulk electrolysis.[14] This complex was shown to be a very reactive dehydrogenating agent, attacking strong C−H and O−H bonds. These results suggested to us that diiron(II) complexes incorporating bridging amidate ligands could be promising synthetic candidates for creating functional models of diiron(II) hydroxylases. With this goal in mind, we set out to explore the reactivity of a diiron(II) complex that incorporates bridging μ-1,3-(κN:κO)-amidate ligands. Herein, we describe the reactivity of one such complex and demonstrate that these species can react directly with dioxygen or oxygen-atom-transfer reagents to afford intramolecular aliphatic C−H oxygenation.

The target diiron(II) complex was prepared using the tris(isobutyrylamido)triphenylamine (H_3L^{iPr}) ligand[15] by the route shown in Scheme 1. Treatment of an *N*,*N*-dimethylformamide (DMF) solution of H_3L^{iPr} with 3 equiv of potassium hydride, 1 equiv of iron(II) acetate, and 0.5 equiv of tetraphenylphosphonium bromide yields $PPh_4[KFe_2(L^{iPr})_2]$ (**1**) as a bright-yellow solid in 78% yield. This route is similar to the route reported by Stavropoulos and co-workers[16] for the preparation of a related multinuclear iron(II) complex from the H_3L^{iPr} ligand with one important difference: the route presented here incorporates a noncoordinating countercation (PPh_4^+) that leads to the formation of a single asymmetric diiron(II) core structure upon crystallization that is soluble in a variety of organic solvents. The alternative route, which incorporates only coordinating potassium ions, results in the formation of a dimer of diiron(II) cores (i.e., a dimer of dimers) upon crystallization.[16] Crystals of **1** suitable for single-crystal X-ray diffraction studies were grown by vapor diffusion of diethyl ether into a DMF solution of the complex.

Scheme 1



[1]

The solid-state structure of **1** is shown in Figure 1 and reveals an asymmetric diiron(II) core supported by two bridging μ-1,3-(κN:κO)-amidate ligands. One amidate arm from each ligand adopts the bridging coordination mode. The remaining amidate ligands bind to the iron centers in a monodentate, *N*-amidate coordination mode[17] with average $Fe-N_{amidate}$ bond lengths of 2.108 Å for Fe1 and 2.102 Å for Fe2. Both Fe1 and Fe2 exhibit slightly distorted tetrahedral coordination geometries, with τ_4 values of 0.94 and 0.99, respectively.[18] The tertiary nitrogen atoms (N1 and N5) of the ligand backbone are effectively noncoordinating because each is positioned ca. 2.5 Å from their respective iron center. The iron(II) centers in **1** are separated by 4.138 Å. A potassium ion is also situated near the diiron(II) core and is coordinated by three carbonyl groups [two from the diiron(II) core and one from a neighboring molecule in the unit cell (Figure S1 in the Supporting Information)]. This potassium ion is positioned equidistant from the iron(II) centers (ca. 4.13 Å).

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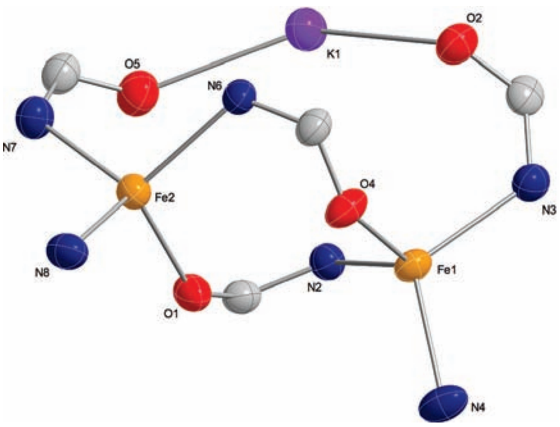
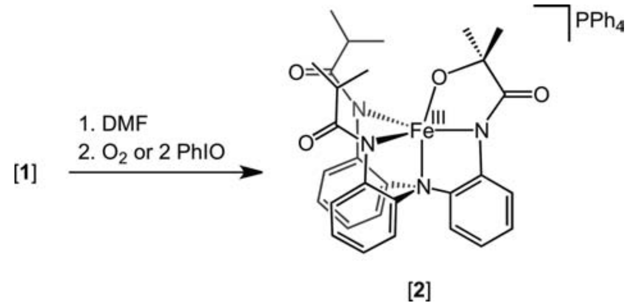


Figure 1. Molecular structure of **1** illustrated by thermal ellipsoids drawn at 50% probability. Hydrogen atoms, PPh$_4^+$ counterion and solvents of crystallization have been removed for clarity. Selected bond lengths (Å) and angles (deg): Fe1−N2 2.116(3); Fe1−N3 2.110(4); Fe1−N4 2.099(4); Fe1−O4 1.985(3); Fe2−N6 2.120(3); Fe2−N7 2.084(4); Fe2−N8 2.102(4); Fe2−O1 1.999(3); K1−O2 2.604(3); K1−O5 2.568(3); N2−Fe1−N4 111.92(15); N2−Fe1−N3 104.46(13); N2−Fe1−O4 110.40(13); N3−Fe1−N4 115.21(15); N3−Fe1−O4 109.80(14); N4−Fe1−O4 105.13(14); N6−Fe2−N7 108.65(15); N6−Fe2−N8 109.60(14); N6−Fe2−O1 109.39(13); N7−Fe2−N8 109.09(15); N7−Fe2−O1 110.36(14); N8−Fe2−O1 109.74(14); O5−K1−O1 141.02(11).

Scheme 2



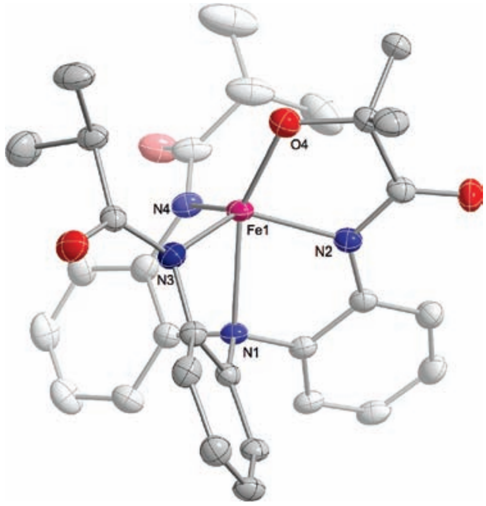


Figure 2. Molecular structure of **2** depicted with thermal ellipsoids drawn at 50% probability. Hydrogen atoms and the counterion are removed for clarity. Selected bond lengths (Å) and angles (deg): Fe1−N1 2.274(3); Fe1−N2 1.994(3); Fe1−N3 1.992(3); Fe1−N4 1.998(3); Fe1−O4 1.882(3); O4−Fe1−N1 155.13(11); O4−Fe1−N2 81.86(11); O4−Fe1−N3 104.86(12); O4−Fe1−N4 122.02(12); N2−Fe1−N3 122.28(11); N3−Fe1−N4 111.00(12); N1−Fe1−N2 76.42(10); N1−Fe1−N3 77.42(10); N1−Fe1−N4 78.18(11).

In coordinating solvents (e.g., DMSO-d_6 and CD$_3$CN), the ^{1}H NMR spectrum of **1** exhibits a complex pattern of paramagnetically broadened peaks consistent with a structure of low symmetry. The electrospray ionization mass spectroscopy (ESI-MS) spectrum of a tetrahydrofuran solution of **1** displays peaks and an isotope pattern consistent with the $[\mathrm{K}(\mathrm{Fe}^{\mathrm{II}})_2(\mathrm{L}^{i\mathrm{Pr}})_2]^-$ formulation (m/z 1145.34). The magnetic moment of **1** was determined to be 7.3(2) μ_B (Evans' method, DMSO-d_6, 298 K). This value is comparable to the μ_eff values measured for carboxylate-bridged diiron(II) complexes that exhibit similar Fe−Fe distances.[19,20]

To explore the reactivity of **1** with oxygen-atom-transfer reagents, a DMF solution of the complex was treated with 2 equiv of iodosylbenzene (PhIO; Scheme 2). The reaction color changed from bright yellow to dark red within 5 min. The crude product of this reaction was investigated by ESI-MS, and a strong molecular ion peak was observed at a mass-to-charge ratio (m/z = 568.18) consistent with a mononuclear iron complex containing a modified ligand. To unambiguously identify the reaction product, the crude reaction mixture was crystallized by vapor diffusion of diethyl ether into a concentrated DMF solution of the product. This procedure affords analytically pure **2** in 43% yield as a tetraphenylphosphonium salt. The molecular structure of **2** was determined by single-crystal X-ray crystallography and is shown in Figure 2. The structure confirms that the product of this reaction is a mononuclear iron(III) complex containing a modified ligand in which an oxygen atom has replaced a methine proton on one of the isopropyl groups. This type of intramolecular isopropyl group activation has been observed before in synthetic cobalt[21] and copper complexes.[22,23] The five-coordinate iron(III) center in **2** displays a coordination geometry intermediate between trigonal-bipyramidal and square-pyramidal (τ_5 = 0.55).[24] Its coordination sphere is made up of three *N*-amidate donors, an alkoxide from the ligand modification site, and the tertiary nitrogen of the ligand backbone. Complex **2** displays an average Fe−N$_{\mathrm{amidate}}$ bond length of 1.995(3) Å, which is ~0.1 Å shorter than the average Fe−N$_{\mathrm{amidate}}$ bond lengths in **1**. Complex **2** also displays a Fe1−O4 (iron alkoxide) bond distance of 1.882(3) Å, which is comparable to other iron(III) terminal alkoxide species[25,26] and shorter than typical Fe$^{\mathrm{II/III}}$−O(H)R (alcohol) bond lengths (ca. 2.1 Å).[27] In solution, **2** is dark red and exhibits a charge-transfer band at 450 nm (ε = 3000 M^{-1} cm^{-1}, DMF) in its electronic absorbance spectrum. The solution-state magnetic moment of **2** was measured to be 5.9(2) μ_B (DMF-d_7, 298 K), consistent with a high-spin iron(III) center (S = $^5/_2$). Analysis of **2** by cyclic voltammetry (25 °C, DMF, 0.2 M TBAPF$_6$) revealed a single, reversible event at $E_{1/2}$ = −1.53 (ΔE_p = 0.080 V; $i_{\mathrm{pc}}/i_{\mathrm{pa}}$ = 0.99) versus the ferrocene/ferrocenium (Figure S6 in the Supporting Information) that is tentatively assigned to the Fe$^{\mathrm{II}}$/Fe$^{\mathrm{III}}$ couple.

In order to probe the reactivity of **1** with dioxygen, an anaerobic DMF solution of **1** was reacted with an excess of dry dioxygen gas. After 15 min, the solution had changed from yellow to dark red. The reaction mixture was stirred for a additional 2 h

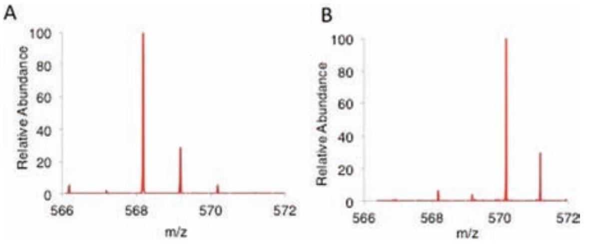


Figure 3. (A) HR-ESI mass spectrum of **[2]** prepared from $^{16}O_2$ (m/z 568.1778 obsd (568.1773 calcd)); and (B) HR-ESI mass spectrum of **[2]** prepared from $^{18}O_2$ (m/z = 570.1823 obsd (570.1815 calcd)).

and then concentrated to dryness. The crude product was then recrystallized under an inert atmosphere. The product of this reaction displayed spectroscopic (^{1}H NMR, IR, ESI-MS, and UV−vis) characteristics identical with those observed for **2**. To verify that dioxygen was the source of the oxygen atom incorporated in **2** prepared by this route, the reaction was repeated using $^{18}O_2$ (98%) as the oxidant. High-resolution ESI-MS of the product isolated from this reaction confirms that the oxygen atom inserted into the ligand backbone is derived from dioxygen because the mass-to-charge ratio for **2** prepared from $^{18}O_2$ (m/z 570.1815) is two units greater than the mass-to-charge ratio observed for **2** prepared from $^{16}O_2$ (Figure 3). The reaction of **1** with dioxygen at room temperature was followed using electronic absorption spectroscopy to estimate the yield of **2** formed during this reaction (Figure S5 in the Supporting Information). These experiments suggest that **2** is formed in ∼47% yield during this reaction. The maximum yield of **2** obtained by either route does not appear to exceed 50%. Attempts to completely characterize the other byproduct of these reactions have not been successful, but mass spectroscopy of the reaction mixtures suggests that at least one of the byproducts is the protonated (uncoordinated) H_3L^{iPr} ligand. Studies addressing the mechanisms of these transformations are ongoing. At this point, the intermediates involved in the formation of **2** from the diiron(II) complex **1** are unknown. We speculate, however, that this reaction may proceed via high-valent diiron intermediates that contain μ-oxo, μ-hydroxo, or, in the case of the dioxygen reaction, μ-peroxo bridging ligands because both PhIO (an oxygen-atom-transfer reagent) and dioxygen can be used as oxidants in this C−H activation reaction.

In summary, we have shown that a diiron(II) complex containing bridging amidate ligands can promote intramolecular aliphatic C−H activation of an isopropyl group. We have demonstrated that both an oxygen-atom-transfer reagent and dioxygen can be used as oxidants in this reaction. This study supports the idea that chelating ligand scaffolds that incorporate amidate ligands are promising candidates for the development of functional models of diiron(II) hydroxylase enzymes. Future studies will focus on identifying the intermediates involved in these reactions and exploring ligand scaffolds that are resistant to intramolecular oxidation reactions so that intermolecular, catalytic hydroxylation reactions may be realized.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Complete experimental details and CIF files for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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