J|A|C|S
COMMUNICATIONS

Published on Web 02/27/2004

Oxidation of Sulfide, Phosphine, and Benzyl Substrates Tethered to N-Donor Pyridine Ligands in Carboxylate-Bridged Diiron(II) Complexes

Emily C. Carson and Stephen J. Lippard*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02319

Received December 18, 2003; E-mail: Lippard@lippard.mit.edu

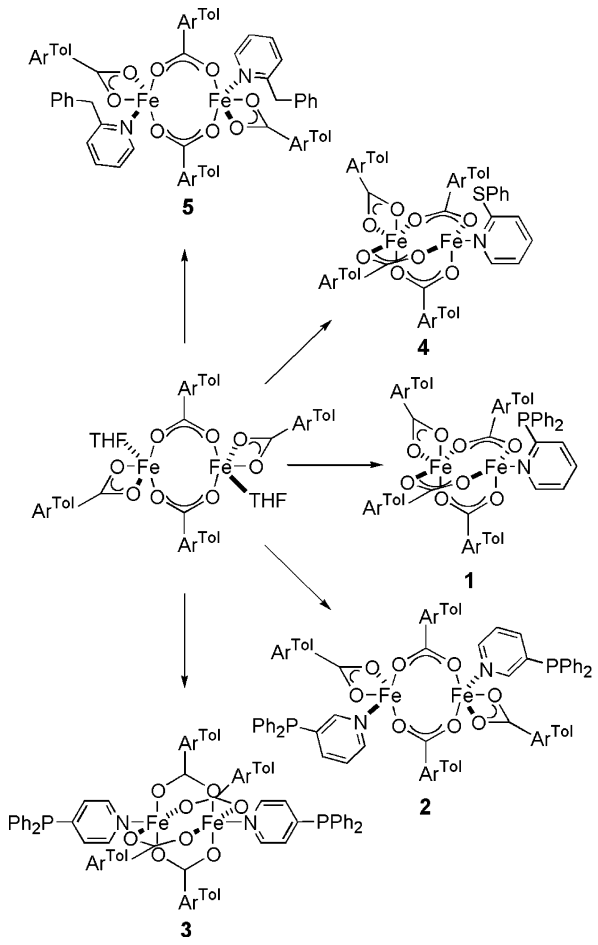
Bacterial multicomponent monooxygenases, including soluble methane monooxygenase (sMMO) and toluene/*o*-xylene monooxygenase (ToMO), catalyze the selective conversion of hydrocarbons to alcohols and can oxidize other substrates including methane derivatives, olefins, amines, and sulfides.[1,2] A carboxylate-bridged non-heme diiron active site, housed in the hydroxylase components (MMOH; ToMOH) of sMMO and ToMO, is responsible for the binding and reductive activation of dioxygen in the enzymes.[3−7] A goal of many laboratories is to create functional models of these diiron centers to provide insight into the mechanisms of their oxidation chemistry.

A successful approach to the synthesis of such biomimetic diiron(II) complexes has been to apply terphenyl-based carboxylates as ligands to assemble the desired dinuclear complexes and to mimic the protective pocket present at the protein active sites.[8−10] In the diiron(II) complexes $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(N,N\text{-}Bn_2en)_2]$[11,12] and $[Fe_2(\mu\text{-}O_2CAr^{Tol})_4(BA^{p-OMe})_2]$,[13] where $Ar^{Tol}CO_2^-$ is 2,6-di(*p*-tolyl)benzoate, *N*,*N*-Bn_2en is *N*,*N*-dibenzylethylenediamine, and BA^{p-OMe} is 4-methoxybenzylamine, the potential substrate was incorporated as part of a terminal N-donor ligand. Upon reaction with dioxygen, intramolecular benzylic oxidation resulted in N-dealkylation to afford benzaldehyde. In the present communication, we describe a significant extension of this strategy to achieve both C−H activation and oxygen atom transfer. Here, the tethered substrate is presented in the form of a phosphino-, sulfido-, or benzyl-derivatized N-donor pyridine ligand. These substrates were brought into close proximity to the carboxylate-bridged diiron(II) center through coordination of the pyridine group, the position of substitution affecting both the solid-state geometry of the starting diiron(II) complex and the subsequent chemistry following exposure to dioxygen.

The triply carboxylate-bridged diiron(II) complex, $[Fe_2(\mu\text{-}O_2CAr^{Tol})_3(O_2CAr^{Tol})(2\text{-}Ph_2Ppy)]$ (**1**) (Scheme 1), having a single 2-pyridyldiphenylphosphine (2-Ph_2Ppy) N-donor ligand, was prepared in 89% yield by treatment of $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(THF)_2]$[14] with 1 equiv of 2-$Ph_2$Ppy. Similarly, the doubly and quadruply carboxylate-bridged compounds $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(3\text{-}Ph_2Ppy)_2]$ (**2**) (Scheme 1) and $[Fe_2(\mu\text{-}O_2CAr^{Tol})_4(4\text{-}Ph_2Ppy)_2]$ (**3**) (Scheme 1) were prepared by combining 2 equiv of 3-Ph_2Ppy or 4-Ph_2Ppy with the $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(THF)_2]$ starting material. Structural characterization of **1** by X-ray crystallography revealed an Fe···Fe distance of 3.3099(6) Å, which lies between the values observed for the windmill- and paddlewheel-type geometries of **2** and **3**, 4.0372(15) Å and 2.8127(10) Å, respectively, (Figures 1 and S1−S3, Supporting Information). The distance of the phosphorus atom from the closest iron atom increases in the order ortho < meta < para, the corresponding values being 2.8321(7) Å in **1**, 5.811(3) Å in **2**, and 6.7205(15) Å in **3**.

Treatment of the $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(THF)_2]$ complex with 2-pyridylphenyl sulfide (2-PhSpy) results in the formation of $[Fe_2(\mu\text{-}O_2CAr^{Tol})_3(O_2CAr^{Tol})(2\text{-}PhSpy)]$ (**4**) (Scheme 1). The diiron

Scheme 1



core in **4** is similar to that observed for **1**, comprising three bridging carboxylate ligands, one monodentate carboxylate, and a single N-donor ligand (Figure S4). The Fe···Fe distance of 3.2714(8) Å is slightly shorter than that in **1**, and the Fe···S distance of 3.0902(19) Å is slightly longer than the Fe···P distance in **1**.

Addition of 2 equiv of 2-benzylpyridine (2-Bnpy) to $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(THF)_2]$ in CH_2Cl_2 afforded the doubly carboxylate-bridged, diiron(II) complex $[Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(2\text{-}Bnpy)_2]$ (**5**) (Scheme 1) in which the N-donor ligands are in anti positions to one another with respect to the Fe−Fe vector. Two chemically equivalent diiron(II) complexes were located in the asymmetric unit of **5** with Fe···Fe distances of 4.2385(9) Å and 4.6050(9) Å (Figure S5). The methylene carbon atoms are 3.247(3) Å and 3.219(3) Å from the closest Fe atom in **5**.

Oxidation of the substrates appended to the N-donor pyridine ligand was investigated by product analysis following introduction of dioxygen into solutions of **1**−**5** (Supporting Information). When

10.1021/ja031806c CCC: $27.50

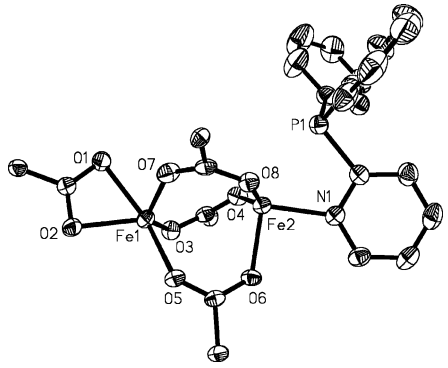


Figure 1. ORTEP diagram of $[Fe_2(\mu\text{-}O_2CAr^{Tol})_3(O_2CAr^{Tol})(2\text{-}Ph_2Ppy)]$ (**1**) with 50% probability thermal ellipsoids. For clarity, all atoms of the $Ar^{Tol}CO_2^-$ ligand, except for the carboxylate groups and the α-carbon atoms, and all hydrogen atoms were omitted. Selected distances (Å): Fe1···Fe2, 3.3099(6); Fe2···P1, 2.8321(7); Fe2−N1, 2.1311(16); Fe2−O4, 1.9907(13); Fe2−O6, 2.0568(12); Fe2−O8, 1.9990(12).

a pale yellow CH_2Cl_2 solution of **1** was allowed to react with dioxygen, the color immediately turned golden orange. Quantitative formation of 2-pyridyldiphenylphosphine oxide (2-Ph_2P(O)py) was observed by ^{31}P NMR spectroscopy. Catalytic formation of 2-Ph_2P(O)py, up to 13 turnovers, occurred when a CH_2Cl_2 solution of **1** was supplied with additional equivalents of 2-Ph_2Ppy (Table S1). Similar reactivity occurs in MeCN. Control experiments established that, in the absence of **1**, neither O_2-saturated CH_2Cl_2 nor the workup process induces ligand oxidation over the same time interval (∼1 h).

Shifting the position of the $-PPh_2$ moiety on the pyridine ligand affects the oxygenation chemistry of the resultant diiron(II) complex (Table S3). Following exposure of **2** to dioxygen for 25 min in CH_2Cl_2 at room temperature, ^{31}P NMR spectroscopy revealed the formation of 3-Ph_2P(O)py in 43% yield based on **2**, vs 95% for the analogous oxidation of **1**. Reaction of **3** with O_2 yielded only 53% conversion to 4-Ph_2P(O)py. In both cases unmodified phosphinopyridine was quantitatively recovered.

Reaction of **4** with dioxygen in CH_2Cl_2 at room temperature resulted in 29% conversion to 2-pyridylphenyl sulfoxide in 90 min as analyzed by GC-MS. The unmodified sulfido ligand was quantitatively recovered. The products formed upon exposure of a CH_2Cl_2 solution of **5** to dioxygen at ambient temperature, following analysis by GC-MS and ^{1}H NMR spectroscopy, include α-phenyl-2-pyridylmethanol, with an average yield of 80% based on **5**. This C−H oxidation product differs from that obtained from related diiron complexes having tethered benzyl groups, in which oxidation led to the elimination of benzaldehyde.[11−13] Ligand oxidation to the resultant alcohol has been frequently noted in benzyl derivatized dicopper systems, however.[15]

There are two significant differences among compounds **1**−**3** that may affect their oxygenation chemistry, the position of the substrate on the coordinated pyridine and the geometry of the diiron(II) complex. The pyridine substitution site determines the distance of the substrate from the diiron core; the carboxylate geometry modulates the steric bulk around the iron centers. After 1 h of exposure to O_2 (Table S2), the triply carboxylate-bridged complex **1** shows full conversion to the phosphine oxide, less oxidation for the windmill complex **2**, and the least for paddlewheel complex **3**. The quantity of ligand oxidized for **1**, **2**, and **3** also decreases as the $-PPh_2$ moiety moves from ortho to meta to para. Since compounds **1** and **4** have nearly identical geometries, we tentatively attribute the lower reactivity of **4** to the higher redox potential of sulfides vs phosphines.[16]

In conclusion, the present results have expanded the palette of substrates that can be oxygenated with O_2 under ambient conditions with carboxylate-rich diiron centers in synthetic models of MMOH and ToMOH. Differences in reactivity of **1**−**5**, including experiments to alter the redox potentials of the tethered moiety, to explore possible intermediates in the reaction pathway, and to distinguish intra- from intermolecular mechanisms, are under further investigation.

Acknowledgment. This work was supported by grants from the National Institute of General Medical Sciences and the National Science Foundation.

Supporting Information Available: Details of the synthetic procedures, oxidation chemistry and product analyses, X-ray crystallographic tables, physical characterization of **1**−**5**, and ORTEP diagrams for each reported structure (PDF) and X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Colby, J.; Stirling, D. I.; Dalton, H. *Biochem. J.* **1977**, *165*, 395−402.
(2) Fuse, H.; Ohta, M.; Takimura, O.; Murakami, K.; Inoue, H.; Yamaoka, Y.; Oclarit, J. M.; Omori, T. *Biosci. Biotechnol. Biochem.* **1998**, *62*, 1925−1931.
(3) Feig, A. L.; Lippard, S. J. *Chem. Rev.* **1994**, *94*, 759−805.
(4) Wallar, B. J.; Lipscomb, J. D. *Chem. Rev.* **1996**, *96*, 2625−2657.
(5) Merkx, M.; Kopp, D. A.; Sazinsky, M. H.; Blazyk, J. L.; Müller, J.; Lippard, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 2782−2807.
(6) Baik, M.-H.; Newcomb, M.; Friesner, R. A.; Lippard, S. J. *Chem. Rev.* **2003**, *103*, 2385−2419.
(7) Sazinsky, M. H.; Bard, J.; Donato, A. D.; Lippard, S. J. Submitted for publication.
(8) Lee, D.; Lippard, S. J. *Inorg. Chem.* **2002**, *41*, 2704−2719.
(9) Tolman, W. B.; Que, L., Jr. *J. Chem. Soc., Dalton Trans.* **2002**, 653−660.
(10) Tshuva, E. Y.; Lippard, S. J. *Chem. Rev.* **2004**, *104*, 987−1012.
(11) Lee, D.; Lippard, S. J. *J. Am. Chem. Soc.* **2001**, *123*, 4611−4612.
(12) Lee, D.; Lippard, S. J. *Inorg. Chem.* **2002**, *41*, 827−837.
(13) Yoon, S.; Lippard, S. J. *Inorg. Chem.* **2003**, *42*, 8606−8608.
(14) Lee, D.; Lippard, S. J. *J. Am. Chem. Soc.* **1998**, *120*, 12153−12154.
(15) Que, L., Jr.; Tolman, W. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 1114−1137.
(16) Harlan, E. W.; Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 6992−7000.

JA031806C