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Dioxygen Reactivity of Fully Reduced [LFe^{II}···Cu^{I}]$^+$ Complexes Utilizing Tethered Tetraarylporphyrinates: Active Site Models for Heme-Copper Oxidases

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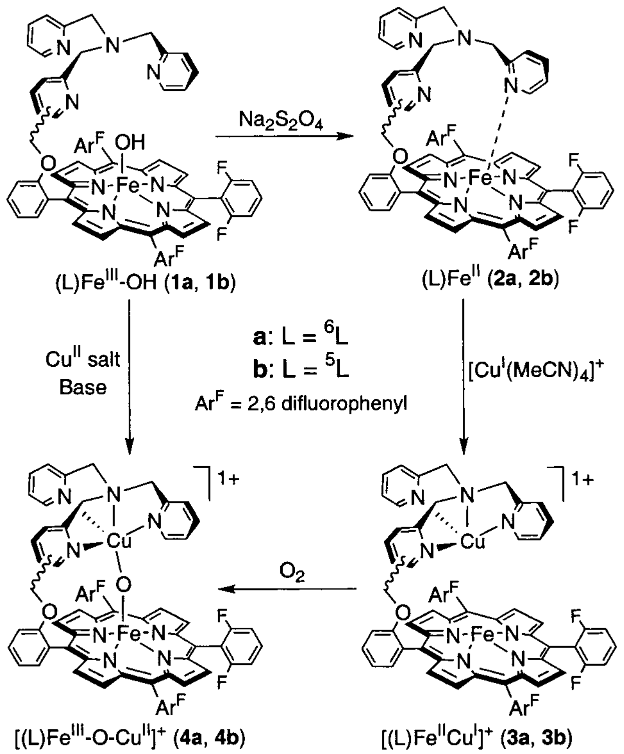
In aerobic organisms, the heme a_3−Cu$_B$ binuclear active center in heme-copper oxidases is responsible for O_2 binding, O−O reductive cleavage, and protonation to give H_2O.[1] The enzyme couples this $4e^-/4H^+$ O_2 reduction to the translocation of protons, creating the membrane potential used to drive ATP synthesis. There is considerable interest in developing structural, spectroscopic, and functional active site models,[2−4] but only a few discrete heterobinuclear Fe^{II}···Cu^{I} species have been well characterized and employed for critical O_2-reactivity studies.[3,5−8]

We wish to study systems where the (porphyrinate)Fe^{II}/LCu^{I}/O_2 chemistry (L = copper ligand) may be controlled (but also systematically varied), in situations where intramolecular reactions are favored. Here, we report such chemistry with heterobinucleating ligands, the constitutional isomers ^{6}L and ^{5}L, where a tetradentate TMPA[9] ligating moiety is covalently attached to the periphery of a porphryin, through either the 6-position (^{6}L) or the 5-position (^{5}L) of one pyridine arm (Scheme 1). ^{6}L and ^{5}L take advantage by employing a Cu ligand with an established (TMPA)Cu^{I}/O_2 chemistry with known kinetics, thermodynamics, structures, and spectroscopy.[10] In addition to the description of new Fe^{II} (with "empty tether") and Fe^{II}···Cu^{I} complexes with ^{6}L and ^{5}L, we report biomimetic reactions where μ-oxo Fe^{III}−O−Cu^{II} cores are generated directly from O_2 reduction;[11] a crystal structure of the ^{6}L oxygenation product is described.

Scheme 1



The complexes described herein (Scheme 1) are characterized by multinuclear NMR[12] and UV−visible spectroscopies, and supported by MALDI-TOF mass spectrometry on isolated solids.[13] Metalation begins with addition of excess $FeCl_2$ to either the ^{6}L or ^{5}L ligands, followed by air oxidation. This procedure yields

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(9) Abbreviations used: TMPA, tris(2-pyridylmethyl)amine; F_8-TPP, tetrakis-(2,6-difluorophenyl)porphyrinate; MALDI-TOF-MS, matrix-assisted laser desorption ionization time-of-flight mass spectrometry; BAr^F, tetrakis-(3,5-bis(trifluoromethyl)phenyl)borate; THF, tetrahydrofuran; EXAFS, extended X-ray absorption fine structure.

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(11) (a) With separate mononuclear reduced heme and copper(I) complexes, we have previously[11b,c] described details of the reaction of (F_8-TPP)Fe^{II} plus [(TMPA)Cu^{I}(RCN)]$^+$ with O_2, which produces the μ-oxo complex [(F_8-TPP)Fe^{III}−O−Cu^{II}(TMPA)]$^+$ (**5**). Isotope labeling showed that the oxo atom in **5** is derived from O_2, and the reaction stoichiometry (unpublished results) is Fe:Cu:O_2 = 2:2:1. (b) Karlin, K. D.; Nanthakumar, A.; Fox, S.; Murthy, N. N.; Ravi, N.; Huynh, B. H.; Orosz, R. D.; Day, E. P. *J. Am. Chem. Soc.* **1994**, *116*, 4753−4763. (c) Nanthakumar, A.; Nasir, M. S.; Karlin, K. D.; Ravi, N.; Huynh, B. H. *J. Am. Chem. Soc.* **1992**, *114*, 6564−6566.

(12) ^{1}H NMR spectra, particularly pyrrole resonances, are useful as a criterion for compound purity, since most of the compounds (including impurities) possess paramagnetically shifted and distinctive (i.e., highly sensitive to spin and oxidation states) resonances.

(13) See Supporting Information.

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Table 1. ^{1}H NMR (300 MHz) Pyrrole Resonances of Reduced Complexes (295 K)

solvent	*^{6}LFe(II)* (**2a**)	*^{5}LFe(II)* (**2b**)	*[(^{6}L)FeCu]$^+$* (**3a**)	*[(^{5}L)FeCu]$^+$* (**3b**)
THF-d_8	52.9 (s), 54.2 (s), 57.8 (s), 58.6 (s)	55.0 (s), 56.3(s), 57.5 (s), 58.3 (s)	53.5 (s, br), 54.6 (s, br), 55.7 (s, br), 56.8 (s, br)	54.9 (s), 55.6 (s), 56.8 (s, br), 57.9 (s, br)
non-coordinating[a]	43.0 (s), 44.6 (s), 46.3 (s), 47.1 (s)	38.7 (s, br)	diam[c,d]	diam[c]
pyridine-d_5	8.7 (s)[b]	diam[c]	8.7 (s)[b]	diam[c]

[a] Noncoordinating: CD_2Cl_2 (**2a**, **2b**), toluene-d_8 (**3a**, **3b**). [b] ^{2}H NMR. [c] All signals in the diamagnetic region. [d] Low concentrations.

μ-oxo-heme/non-heme diiron(III) complexes [(L)Fe^{III}−O−Fe^{III}-(Cl)]$^+$;[14] treatment with base (to "rust" out the iron bound to TMPA) or chlorotrimethylsilane and subsequent purification via column chromatography gives (L)Fe^{III}−OH, **1a**, and **1b** {1112 m/z (M + H)$^+$}. Sodium dithionite reduction of **1a** or **1b** under an inert atmosphere yields the (L)Fe^{II} "empty-tether" complexes **2a** and **2b**, both with characteristic UV−visible (424 (Soret), 544 nm) and ^{1}H NMR (see Table 1) features.[15] Addition of a copper(I) source, usually [Cu(CH$_3$CN)$_4$](BAr^F), gives the desired Fe^{II}···Cu^I complexes **3a** and **3b** with similar UV−vis spectra (424 nm, 544 nm).[16]

For [(L)Fe^{II}Cu^I](BAr^F) complexes **3a** and **3b**, high-spin ferrous ^{1}H NMR split pyrrole signatures (45−55 ppm) are generated in weakly to moderately coordinating solvents ((CD$_3$)$_2$C(O), THF-d_8).[17] Owing to the lack of up- or downfield-shifted peaks, we attribute the high-spin state of the iron(II) center to fifth-ligand solvent coordination; the pyridine arms of the TMPA moiety are unavailable for iron(II) ligation due to coordination by copper(I). An intermediate $S = 1$ spin state is generated in a noncoordinating solvent such as toluene: (i) the ^{1}H NMR spectrum is further upfield shifted (Table 1) compared to that of a high-spin ferrous center, and (ii) the UV−vis spectrum of [(L)Fe^{II}Cu^I](BAr^F) in toluene is distinctive (424 (Soret), 528, 558 (sh) nm) and identical to that of the parent compound, (F$_8$-TPP)Fe^{II}, with known planar $S = 1$ four-coordination.[4c] Again, pyridine-d_5 solvent gives an iron(II) species with low-spin configuration.

Exposure of **3a** or **3b** to dioxygen at room temperature results in clean reaction to give oxidized products, the μ-oxo complexes [(L)Fe^{III}−O−Cu^{II}](BAr^F), **4a** or **4b**, Scheme 1.[18] Oxygenation in acetonitrile with $^{18}O_2$ results in the incorporation of the ^{18}O label into **4a** or **4b**, as confirmed by MALDI-TOF-MS. These reactions point to a crudely biomimetic process, in that the dioxygen O−O bond is reductively cleaved and an oxo atom at the oxidation state level of water is incorporated into the final product.[11]

Crystals of **4a** suitable for X-ray diffraction were isolated;[13] its overall structure (Figure 1) is very similar to that of the untethered parent compound, [(F$_8$-TPP)Fe^{III}−O−Cu^{II}(TMPA)]$^+$, **5**, with a near-linear Fe−O−Cu moiety, similar very short Cu−O, Fe−O, and Fe···Cu distances, and a typical high-spin structure with Fe out of the porphyrin plane (0.46 Å).[11b] The distortion giving ∠Fe−O−Cu = 171.1°, vs 178.2° for **5**, could represent an imposed ^{6}L ligand constraint. In support of this, and illustrating the influence of ligand architecture, an EXAFS spectroscopy structural study of [(^{5}L)Fe^{III}−O−Cu^{II}](BAr^F) (**4b**) reveals that the different ligand architecture of ^{5}L causes a severe bending, ∠Fe−O−Cu ≅ 140°.[4a] Such distortions (going from **5** to **4a** to **4b**) lead to increased basicity (i.e., oxo protonation) or diminished stability of the Fe^{III}−O−Cu^{II} core.[4a] These changes in structure and reactivity are of significance given that μ-oxo and μ-hydroxo cores have been suggested as possible models for resting-state heme-copper oxidases, or as turnover intermediates in the catalytic cycle.[19]

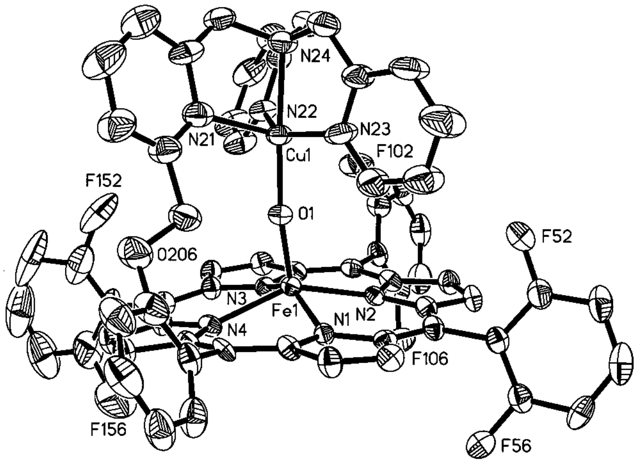

Figure 1. Perspective view (30% ellipsoids) of the structure of **4a**. Selected bond lengths (Å) and angles (deg): Fe1−O1 1.750(4), Fe1−N (N1−N4) 2.092(5)−2.114(4), Fe−N$_{4(plane)}$ 0.46, Cu−O1 1.848(4), Cu1−N24 2.074(5), Cu1−N21 2.316(6), Cu1−N22 2.015(5), Cu1−N23 1.948(7); Fe...Cu 3.586; Fe−O−Cu 171.1(3), N24−Cu1−O1 175.7(2), N22−Cu1−N23 143.8(3).

In summary, discrete fully reduced Fe^{II}···Cu^I complexes can be prepared using heterobinucleating tethered tetraarylporphryinate ligands ^{6}L and ^{5}L, where NMR spectroscopic inquiry reveals that their structure and iron(II) spin states are diverse and can be manipulated. In both ^{6}L and ^{5}L, a biomimetic reaction results in the formation of stable μ-oxo Fe^{III}−O−Cu^{II} complexes. Future directions for study include low-temperature manipulation and inquiry, in order to try to stabilize and characterize O$_2$ intermediates, as well as mechanistic investigations of these observed reductive O−O splitting reactions.

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Supporting Information Available: Synthesis and characterization of new compounds and X-ray structure details for [(^{6}L)Fe^{III}−O−Cu^{II}]-(BAr^F) (**4a**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Compounds **2a**, **2b**,^{19}F NMR (376 MHz; THF-d_8, trifluorotoluene external reference): −115 ppm (s). MALDI-TOF-MS: parent ion at 1095 {m/z (M + H)$^+$}, a loss of 17 (hydroxide) from the (L)Fe^{III}−OH precursor.

(16) Consistent with compound identity and purity, ^{19}F NMR spectra of **3a** and **3b** show only two sets of peaks: (a) TPP fluorines (δ −113 to −114 ppm, multiple peaks), and (b) BAr^F counterion (δ −65.3 ppm), with an integration of 6:24 (F$_6$-TPP:BAr^F) ratio. MALDI-TOF-MS: parent peak at 1159 {m/z (M−BAr^{F-})$^+$}, corresponding to the [(L)Fe^{II}Cu^I]$^+$ cation.

(17) The ^{1}H NMR spectrum of (F$_8$-TPP)Fe^{II} in THF exhibits a high-spin pyrrole resonance at 56.9 ppm; unpublished results.

(18) (a) Acid−base syntheses of **4a** and **4b**, from Fe(III) and Cu(II) precursors, have been described.[4a] (b) Complexes **4** behave as antiferromagnetically coupled $S = 2$ systems and exhibit novel ^{1}H NMR properties, with upfield paramagnetically shifted TMPA H resonances, and downfield-shifted pyrrole peaks.[4a]

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