Role of Trans Ligands in the Reductive Cleavage of the μ-Oxo−Diiron Bridge

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The μ-oxo bridge is a common structural component of non-heme iron proteins,[1] but information about its reactivity is limited.[1,2] Here we demonstrate control of the rate of reductive μ-oxo bridge cleavage on the basis of obligatory ligation within one and only one of the two cyclophane-like[3] cavities trans to the oxo bridge in $[Fe((DMG)BPh_2)_2]_2O$, **1**[4] (Figure 1).

Three ligated forms of **1** (eqs 1 and 2; L = amines, imidazoles, pyridines, nitriles, etc.) have been characterized[4a] and the X-ray structures for **1** and **1-(BuNH$_2$)$_2$** reported.[4b] The

$$FeN_4{-}O{-}FeN_4 + L \overset{K_1}{\rightleftharpoons} LFeN_4{-}O{-}FeN_4 \quad (1)$$

$$LFeN_4{-}O{-}FeN_4 + L \overset{K_2}{\rightleftharpoons} LFeN_4{-}O{-}FeN_4L \quad (2)$$

unligated dimer, **1**, is diamagnetic with a bent oxo bridge (166°), and the iron atoms lie 0.3 Å out of the N_4 planes with the shortest known Fe−O bond (1.71 Å). The **1-(BuNH$_2$)$_2$** complex is paramagnetic (μ = 2.9 μ_B, Fe−O 1.76 Å, Fe−O−Fe 178.6°) with the iron atoms in the N_4 planes. A significant rearrangement of the BPh_2 superstructure accompanies ligation and gives rise to a negative cooperativity in the binding of some ligands,[4a] thus permitting a direct study of the intermediate monoligated form.

Studies[5,6] of reaction 3 or 4 were carried out in CH_2Cl_2 using the substrate 4-*tert*-butylcatechol (H_2Q). The kinetics obey the rate law given in eq 5 with the parameter K_2 reflective of the

$$LFeN_4{-}O{-}FeN_4L + H_2Q \xrightarrow[(+2L)]{} 2FeN_4L_2 + H_2O + Q \quad (3)$$

$$LFeN_4{-}O{-}FeN_4 + H_2Q \xrightarrow[(+3L)]{k_{red}} 2FeN_4L_2 + Q + H_2O \quad (4)$$

$$-d[Fe_2O]/dt = +^1/_2 d[Fe(II)]/dt = k_{obs}[Fe_2O]$$

$$k_{obs} = k_{red}[H_2Q]/(1 + K_2[L]) \quad (5)$$

independently verified speciation of the μ-oxo complex.

These results are compelling evidence that in the reaction with 4-*tert*-butylcatechol, the **monoligated species is the redox-active form**. In the terminology appropriate to linked functions,[7] the ligand serves as a heterotropic effector when it binds once but an allosteric inhibitor when bound twice. Data are summarized in Table 1. The constant k_{net} provides a direct measure of the relative rate of reaction 3 for the different ligands. The true reactivity (k_{red}) of the active form is revealed when the preequilibrium step (K_2) is factored out.

The magnitude of K_2 provides one control on the rate. For TCNE and NPT, attractive interactions between electron-

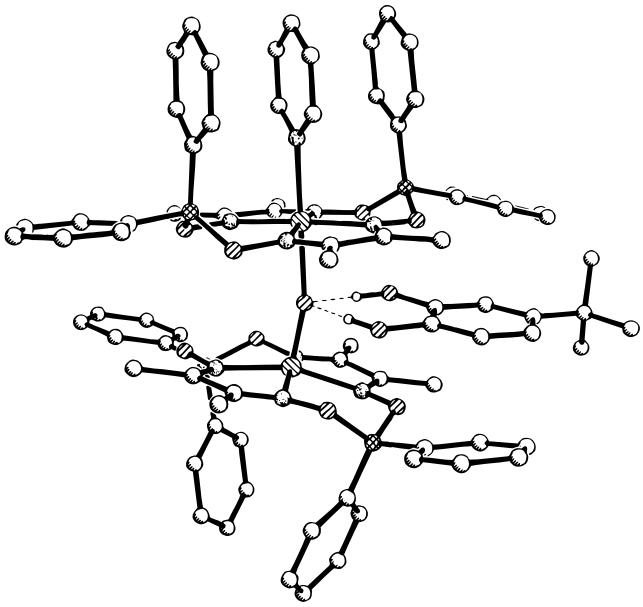

Figure 1. Proposed geometry of the precursor complex for reduction of a PY adduct of $[Fe((DMG)BPh_2)_2]_2O$ with 4-*tert*-butylcatechol. Geometries for the halves of the μ-oxo species are based on X-ray coordinates[4b] for **1** and **1-(BuNH$_2$)$_2$**.[16]

Table 1. Ligand-Binding Data and Rate Constants for Reduction of $[LFe((DMG)BPh_2)_2]_2O$ with 4-*tert*-Butylcatechol[a]

L	log K_2[b]	log k_{net}[c]	log k_{red}[c]	E_L,[d] V
CH_3CN	1.6	−2.36	−0.76	0.34
PhCN	0.3	−1.51	−1.21	0.38
NPT	2.3	−3.66	−1.36	0.45
TCNE	3.7	e		0.78
1-MeIM	3.8	−3.15	+0.62	0.08
4-NMe_2PY	1.7	−2.5	−0.8	0.15
PY	−0.7	−0.74[f]	−1.44	0.25
2,6-Me_2PZ	0.6	−2.3[f]	−1.70	0.29
4-CNPY	0.6	−2.4[f]	−1.80	0.32

[a] CH_2Cl_2, 25 °C. [b] From spectrophotometric titration (eq 2). [c] log k_{red} = log K_2 + log k_{net}. [d] ligand electrochemical parameter,[14] more positive values indicate preferential stabilization of the lower oxidation state. [e] A direct reaction between TCNE and H_2Q occurs. [f] Calculated from k_{red} and K_2.

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(5) Abbreviations: 4-nitrophthalonitrile, NPT; pyridine, PY; tetracyanoethylene, TCNE; 1-methylimidazole, 1-MeIM; pyrazine, PZ; N_4 = bis((dimethylglyoximato)diphenylborate). Typical conditions: $[Fe_2O]$ = 0.05 mM, $[H_2Q]$ = 0.01−0.1 M, [L] = 0.001−0.1 M except for nitriles, where [L] = 0.1−1 M. For CH_3CN, NPT, PhCN, and 1-MeIM, eq 3 was studied (K_2[L] ≫ 1). For pyridines and 2,6-Me_2PZ, eq 4 was studied (1 ≫ K_2[L]), giving rates independent of [L].

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deficient regions of the ligand and the negative π face of the surrounding phenyls[8] result in enhanced binding in the BPh_2 system. The PhCN experiences repulsive contacts within the cyclophane-like binding cavities and shows reduced affinity. Pyridines and pyrazines show reduced values for K_2 (compared to BF_2 analogues[4a]) associated with repulsive interfacial contacts which are introduced only when both cavities are occupied. The constant k_{net} shows that these peripheral contacts are a source of allosteric control of the reactivity at the remote oxo site.

The redox step is proposed to involve attack on the oxo group as shown in Figure 1, leading directly to the quinone and Fe(II) products. This mechanism avoids complications associated with proton-coupled electron transfer,[9] which would accompany electron transfer from the trans site. The obligatory nature of the site-differentiated[10] monoligated species is thought to be a result of both conformational[11] and electronic factors.

Barriers toward bending and substrate access are expected to be reduced in a monoligated species favoring the formation of the hydrogen-bonded precursor complex. The displacement of the iron toward the oxo ligand in **1** (Figure 1) expands the size of the oxo cavity (interplanar distances are 3.983 Å in **1** vs 3.588 Å in **1-(BuNH$_2$)$_2$**). Bending opens the oxo cavity along precisely that edge appropriate for hydrogen-bond interactions[12] with the approaching substrate.

The asymmetry generated in the Fe−O−Fe bridge by ligation to only one of the two trans sites appears to be crucial. Monoligation may be considered to increase the contribution from a $L-Fe^{IV}-O-Fe^{II}$ resonance form.[13] This would explain the peculiar trend seen in k_{red}. Trans ligands which stabilize the **higher oxidation state** (on the basis of Lever's parameters[14]) increase the rate of **reduction**!

Electronic effects of the cis N_4 ligand are in the direction expected on the basis of E_L parameters and opposite to that found for the trans ligand. The analogous $[LFe((DMG)BF_2)_2]_2O$ complexes are stronger oxidants and react much faster than the BPh_2 analogue (10^5 times for L = CH_3CN; less for ligands which experience significant steric reductions in K_2 in the BPh_2 system).[15]

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Supporting Information Available: Figures showing visible spectral changes with time for reactions 3 and 4 and plots of k_{obs} vs 1/[L] for L = 1-MeIm, PY, and 2,6-Me_2PZ and a plot of log k_{red} vs E_L (1 page). Ordering information is given on any current masthead page.

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(12) Barriers for hydrogen-bond formation are analogous to those associated with protonation of the μ-oxo group.[2]

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(14) Lever, A. B. P. *Inorg. Chem.* **1990**, *29*, 1271−1285. E_L's for 2,6-Me_2PZ, and 4-NMe_2PY are estimated on the basis of Hammett or pK_a correlations. Values for NPT and TCNE are calculated from data in ref 8c. E_L (V) for the N_4 ligand: 0.44 (BF_2), 0.18 (BPh_2).

(15) For the BF_2 system: L = CH_3CN, log K_2 = 2.3, log k_{net} = +2.34; L = PhCN, log K_2 = 2.3, log k_{net} = 2.42; L = 1-MeIM, log K_2 > 5, log k_{net} = −1.1.

(16) In the bent geometry of **1**, equatorial phenyls flanking the open edge of the oxo cavity lie nearly perpendicular to the N_4 plane and were rotated to the orientation shown.