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at his 85th anniversary

BONDING IN FERRIC-OXO COMPLEXES

RADU SILAGHI-DUMITRESCU

Department of Chemistry, "Babeș-Bolyai" University, 11 Arany Ianos Str. Cluj-Napoca RO-400028,
Romania and *Department of Chemistry and Center for Metalloenzyme Studies,*
University of Georgia, Athens, Georgia 30602, U.S.A.,

ABSTRACT. Iron (IV) oxo complexes have been implicated in key biological oxidations with heme and non-heme enzymatic systems. Related to these, a non-heme iron (III) oxo complex has recently been described. Intriguingly, the Fe(III)-oxo interaction was proposed to consist of one σ bond, while the absence of π bonding would be compensated by three hydrogen bonds between the oxo atom and the ligand scaffold surrounding the iron. Here, we report density functional calculations unambiguously indicating that hydrogen bonding *weakens the* Fe-O bond, and Fe-O π bonding *does in fact exist* in the above-mentioned Fe(III)-oxo adduct.

INTRODUCTION

Iron (IV) oxo complexes have been implicated in key biological oxidations with heme and non-heme enzymatic systems[1-10]. Related to these, the S=5/2 iron (III) oxo complex **1** (Figure 1) has recently been described[11,12]. **1** featured a 1.81-Å Fe-O bond, which was shorter by ~0.1 Å than the Fe-OH bond in the homologous Fe(III)-OH complex[11,12]. Intriguingly, the Fe(III)-oxo interaction in **1** was proposed to consist of one σ bond, while the absence of π bonding would be compensated by three hydrogen bonds between the oxo atom and the ligand scaffold surrounding the iron[12]. Here, we report density functional calculations unambiguously indicating that, contrary to previous reports, hydrogen bonding *weakens* Fe(III)-O bonding. Additionally, we demonstrate that Fe(III)-O π bonding *does in fact exist* in the above-mentioned Fe(III)-oxo adduct.

RESULTS AND DISCUSSION

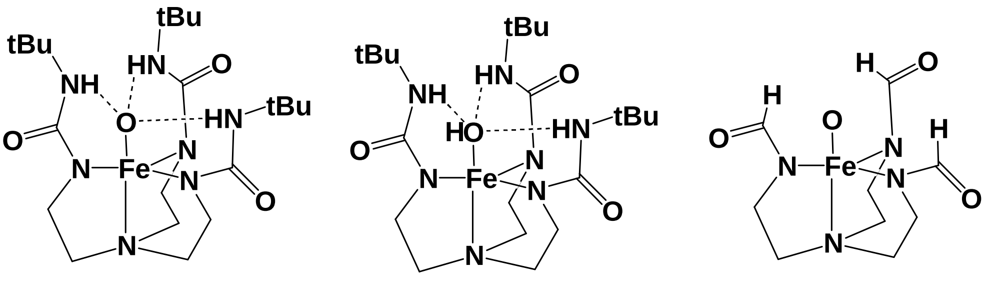
Table 1 shows key geometrical parameters for **1**, obtained from X-ray diffraction[11,12] and DFT (UBP86/6-31G**)[13-15] unconstrained geometry optimization. Also shown is data for the model **1-H**, formally obtained via protonation of the oxo atom in **1** to yield a ferric-hydroxo adduct. Additionally, since NH---O hydrogen bonding has been proposed to play a key role in iron-oxo bonding within **1**[12], we also report geometry optimization of **1-t** (cf. Figure 1), which is formally obtained from **1** by removing the three hydrogen bond-donating termini of the urea ligands. For **1** and **1-H**, the calculated Fe-O bond lengths are in good agreement with experiment and with previously reported B3LYP results[12]. In this respect, our data further supports the idea that the experimentally-observed **1** is an oxo, not a hydroxo, compound[11,12].

Table 1

Key geometrical parameters for S=5/2 **1**, **1-H** and **1-t**

	Fe-O	Fe-N_{ax}[a]	Fe-N_{eq}[b]	H···O[c]
1 (exptl)	1.81	2.27	2.06	1.91
1 (DFT)	1.82	2.14	2.09	1.69
1-H (extpl)	1.92	2.19	2.02	2.13
1-H (DFT)	1.95	2.07	2.30	2.14
1-t (DFT)	1.75	2.62	2.12	2.72

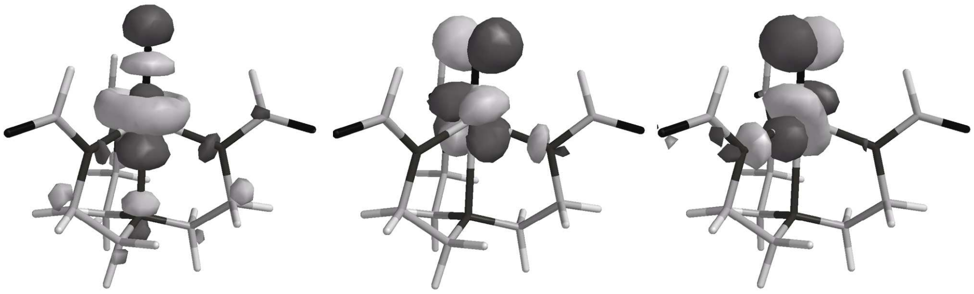
[a] nitrogen atom trans to (hydr)oxo. [b] urea nitrogens, average of three values.[c] NH---O hydrogen bonds, average of three values (cf. Figure 1). The X-ray crystal structures of **1** and **1-H** each feature two short (~ 1.75 Å) such hydrogen bonds and a longer one (elongation of the latter is due to steric clash between the hydroxo and NH protons in **1-H**). DFT-optimized **1** features three identical hydrogen bonds at ~1.7 Å; this latter result would seem to indicate the presence of a hydroxo, not oxo, ligand in the crystal structure of **1**.



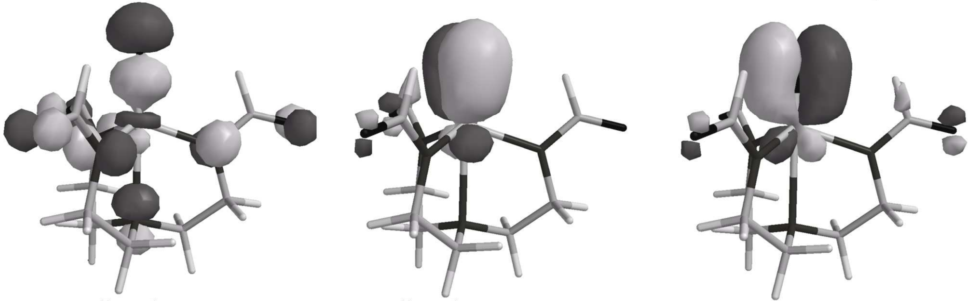
1 **1-H** **1-t**

Fig. 1. Models employed in the present study.

Figure 2 shows molecular orbitals illustrating Fe(III)-oxo bonding (orbitals shown for **1-t** rather than for **1**, for simplicity). For the σ, π_{xz} and π_{yz} interactions, the bonding orbitals are all doubly-occupied, while the antibonding orbitals are all singly-occupied. This then amounts to a formal bond order of 1.5, arising from 1/2 σ bond and two 1/2 π bonds. Similarly, for **1-H** the bond order is 1, with 1/2 σ bond and 1/2 π bond. Others have by contrast reported that the Fe-O bond order in **1** was in fact ~1, and that this arose from one single σ bond and no net π bonding[12,16]. To compensate for the absence of π bonding, a key role for NH----O hydrogen bonding in stabilizing the Fe(III)-oxo bond was proposed[12]. Table 1 instead shows that when the three hydrogen bonds are removed (i.e., in model **1-H**), the Fe-O bond shortens by 0.06 Å. This is consistent with the hydrogen bonds competing with the iron for the oxo p orbitals. Thus, the formal iron-oxo bond order in **1** is 1.5, and NH---O hydrogen bonding contributes to weakening, rather than strengthening of the iron-oxo interaction.



SOMO5 (σ*) SOMO4 (π_{xz}*) SOMO3 (π_{yz}*)

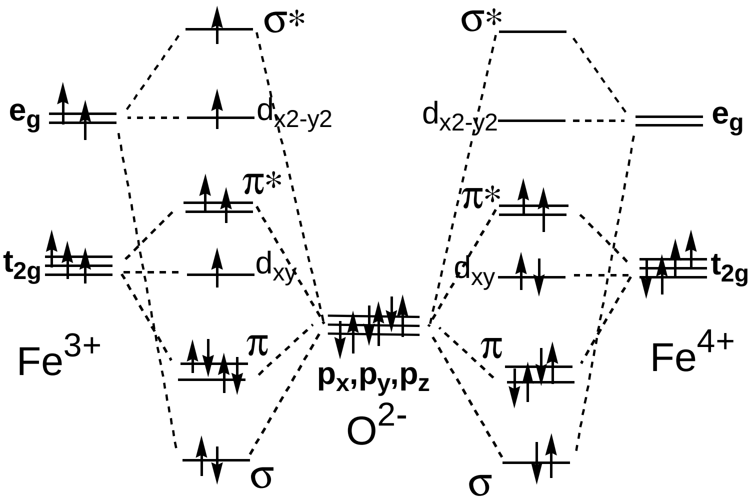


HOMO-2 (σ) HOMO-1 (π_{xz}*) HOMO (π_{yz}*)

Fig. 2. Molecular orbitals illustrating the Fe(III)-oxo interaction (isocontour 0.045). We use convention of labeling the five singly-occupied orbitals on iron as SOMO1 through SOMO5.

1 was proposed[11,12] to have relevance for the Fe(IV)-oxo complexes widely invoked in biological processes[1-8]. Scheme 1 shows a comparison of the molecular orbital diagrams for experimentally observed S=1 Fe(IV)-oxo[8,9] and S=5/2 Fe(III)-oxo complexes. Notably, S=5/2 Fe(III)-oxo contains one additional electron in a σ* orbital, compared to S=1 Fe(IV)-oxo. Thus, while the latter features one σ bond and two 1/2 π bonds (a formal bond order of 2.0), the former features 1/2 σ and two 1/2 π bonds (amounting to a formal bond order of 1.5). Consistent with this, the iron-oxygen distance in **1** is longer by ~0.1 Å than typical Fe(IV)-oxo bonds[17-19].

Notable in Fe(IV)-oxo complexes is the high covalence of the iron-oxo π interaction. Thus, within the singly-occupied π_{xz}* and π_{yz}* orbitals, 50% of each electron formally resides on the oxo atoms[17-19]. The Fe(III)-oxo interaction in **1** is less covalent, with only ~30% of the σ*, π_{xz}* and π_{yz}* electrons delocalized onto the oxygen. Fortuitously, in both Fe(IV)-oxo and Fe(III)-oxo, a total of ~one spin unit is localized on the oxygen.



Scheme 1

Thus, **1** features an iron-oxo bond even weaker than Fe(IV)-oxo bonds invoked in substrate oxygenation by highly reactive species such as cytochrome P450 Compound I (which undergoes the reaction shown in Scheme 2)[20]. **1** also features as much spin density on the oxo atom as P450 Compound I[20]. Why doesn't **1** exhibit P450 – like reactivity? It has been proposed[12] that the protecting hydrogen-bonding scaffold around the oxo atom stabilizes the oxo ligand electronically and protects it sterically. Alternatively, the more ionic character of Fe(III)-oxo bond compared to Fe(IV)-oxo, outlined above, may disfavor P450-type chemistry (which, as shown in Scheme 2 and as largely ignored in current literature[9], consists of *oxygen atom* and not an O^{2-} ion transfer).

$$[FeO]^{2+} + R\text{-}H \rightarrow R\text{-}OH + Fe^{2+}$$

Scheme 2

EXPERIMENTAL

Geometries were optimized with the BP86 functional, which uses the gradient-corrected exchange functional proposed by Becke (1988)[14], the correlation functional by Perdew (1986)[15], and the DN** numerical basis set (comparable in size to 6-31G**), as implemented in Spartan[13]. For the SCF calculations, a fine grid was used, and the convergence criteria were set to 10^{-6} (for the root-mean square of electron density) and 10^{-8} (energy), respectively. For geometry optimization, convergence criteria were set to 0.001 au (maximum gradient criterion) and 0.0003 (maximum displacement criterion). Charges and spin densities were derived from Mulliken population analyses after DFT geometry optimization.

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REFERENCES

1. D. L. Harris, *Curr. Opin. Chem. Biol*., **2001**, *5*, 724-735.

2. A. N. P. Hiner, E. L. Raven, R. N. F. Thorneley, G. Garcia-Canovas, J. N. Rodriguez-Lopez, *J. Inorg. Biochem*., **2002**, *91*, 27-34.

3. I. S. Isaac, J. H. Dawson, *Essays Biochem*., **1999,** *34*, 51-69.

[4] I. Schlichting, J. Berendzen, K. Chu, R. M. Sweet, D. Ringe, G. A. Petsko, S. G.Sligar, *Science,* **2000**, *287*, 1615-1622.

5. M. Sono, M. P. Roach, E. D. Coulter, J. H. Dawson, **Chem. Rev**., **1996**, *96*, 2841-2887.

6. E. I. Solomon, PNAS 2003, **100**, 3589-3594.

7. E. I. Solomon, T. C. Brunold, M. I. Davis, J. N. Kemsley, S.-K. Lee, N. Lehnert, F. Neese, A. J. Skulan, Y.-S. Yang, J. Zhou, *Chem. Rev*., **2000**, *100*, 235-350.

8. M. Costas, M. P. Mehn, M. P. Jensen, L. J. Que**, 2004**, DOI: 10.1021/cr020628n.

9. S. Shaik, S. Cohen, S. P. de Visser, P. K. Sharma, D. Kumar, S. Kozuch, F. Ogliaro, D.Danovich, *Eur. J. Inorg. Chem*., **2004**, 207-226.

10. J. R. Price, E. W. Barr, T. E. Glass, C. Krens, J. M. Bollinger, Jr, *J. Am. Chem. Soc*., **2003**, *125*, 13008-13009.

11. C. E. MacBeth, A. P. Golombek, V. G. Young, Jr, C. Yang, K. Kuczera, M. P. Hendrich, A. S. Borovik, *Science*, **2000**, *289*, 938-941.

12. C. E. MacBeth, R. Gupta, K. R. Mitchell-Koch, V. G. Young, Jr, G. H. Lushington, W. H. Thompson, M. P. Hendrich, A. S. Borovik*, J. Am. Chem. Soc*., **2004**, *126*, 2556-2567.

13. Spartan 5.0, Wavefunction, Inc., 18401 Von Karman Avenue Suite 18370, Irvine, CA 92612 U.S.A.

14. A. D. Becke, *Phys. Rev*., **1988**, 3098-3100.

15. J. P. Perdew*, Phys. Rev*., **1986**, B33, 8822-8824.

16. One possible source of confusion when applying automatic analyses such as NBO (used by MacBeth et al) is, in this case, the presence of two apparently non-bonding molecular orbitals with iron d_{xy} and d_{x2-y2} character, mixed with small amounts of oxygen p_x/p_y character. Taken together, and presumably due to their slight deviation from ideal symmetry, these two orbitals are likely to account for the formal cancellation of ~0.5 of the Fe-oxo bond order seen from the NBO analysis of MacBeth et al. We maintain that this cancellation cannot justify an assignement of

a formal bond order of 1. The iron-oxo s, p_{xz}* and p_{yz}* molecular orbitals still feature one unpaired electron each, and not two unpaired electrons each. To obtain a formal bond order of 1 with one s bond and no p bond, one would need to (1) have an empty iron d_{z2} orbital, and (2), have two doubly-occupied iron-oxo p* orbitals (or four singly-occupied p*), which is physically impossible.

17. H. Kuramochi, L. Noodleman, D. A. Case, *J. Am. Chem. Soc*., **1997**, *119*, 11442-11451.
18. S. Yamamoto, J. Teraoka, H. Kashiwagi, *J. Chem. Phys*., **1988**, *88*, 303-312.
19. R. Silaghi-Dumitrescu, unpublished results.
20. R. Silaghi-Dumitrescu, *J. Biol. Inorg. Chem*., **2004,** *9*, 471-476.