Communications

Density Functional Calculations

Models of High-Valent Intermediates of Non-Heme Diiron Alkane Monoxygenases: Electronic Structure of a Bis(µ-oxo) diiron(IV) Complex with Locally Low-Spin Metal Centers**

Abhik Ghosh,* Espen Tangen, Emmanuel Gonzalez, and Lawrence Que, Jr.*

Long known as a common structural unit in inorganic chemistry, the bis(µ-chalcogeno)dimetal “diamond” core is increasingly recognized as important in a biological context.[1,2] Thus, a variety of clusters based on [Fe₂(µ-S₂)] complexes occur in iron–sulfur proteins and are involved in redox reactions, while intermediates with [M₂(µ-O₂)] cores have been implicated more recently for non-heme metalloenzymes involved in oxygen metabolism.[1,2] For example, [M₂(µ-O₂)] units have been identified as components of the tetramanganese cluster involved in photosynthetic oxygen evolution,[3] while [Cu₃(µ-O₂)] intermediates have been recently synthesized and postulated as intermediates in the catalytic cycles of copper oxigenases such as particulate methane monoxygenase.[2,4] Strong evidence for a high-valent {FeIV₂(µ-O₂)} core has also been found for the key methane-hydroxylating intermediate Q of soluble methane monoxygenase (SMO).[5] A related Fe₃III–FeIV species called middle X can be catalytically essential tyrosyl radical in the R2 protein of ribonucleotide reductase to initiate the process of ribonucleotide reduction in DNA biosynthesis.[6] By analogy, high-valent {FeIV₂(µ-O₂)} intermediates are also proposed for other non-heme diiron alkane-oxidizing enzymes such as fatty acid desaturases[7] and the membrane-bound α-hydroxylase AlkB[8].

In recent years, a number of synthetic complexes with [Fe₂(µ-O₂)]ⁿ⁺ (n = 3 or 4) cores and tetradentate N₄ capping ligands have been isolated and characterized; these serve as models of the enzymatic intermediates Q and X. With the tpa ligand (tpa = tris(2-pyridylmethyl)amine) and its 5-alkyl derivatives, the complexes with an [Fe₂(µ-O₂)]⁺ core exhibit an S = 3/2 ground state (S is the total spin angular momentum).[9] Mössbauer spectroscopy indicated that the two iron centers in these species are electronically identical, thus suggesting a valence-delocalized diiron(III)ν4 description for the dinuclear center.[10] Density-functional theory (DFT) calculations further indicated that the individual iron centers in these complexes could be described as locally low-spin.[12]

More recently, the first synthetic [FeIV₂(µ-O₂)] intermediate has been reported[13] which provides the closest synthetic model so far of Q. However, while Q has a carboxylate-rich ligand environment and antiferromagnetically coupled, locally high-spin FeIV centers,[14] the synthetic model is paramagnetic (S = 1), features relatively strong-field N,N'-bis(2-pyridylmethyl)-N,N'-dimethyl-trans-1,2-diaminocyclohexane (bpmcn) terminal ligands and presumably low-spin FeIV centers.[13] Such an [FeIV₂(µ-O₂)] intermediate with locally low-spin iron centers may actually be involved in the catalytic cycle of the alkane α-hydroxylase AlkB, which has thought to have a histidine-rich ligand environment.[15] Because of its importance, the catalytic cycle of SMMO has been the subject of several quantum-chemical studies.[16,17,18]

To complement these efforts, we have undertaken a DFT study of an [FeIV₂(µ-O₂)] model complex with locally low-spin iron centers.

By using nonlocal DFT[19,20] as implemented in the ADF[21] program system, the VWN local exchange-correlation functional, PW91 gradient corrections for both exchange and correlation, triple-ζ plus polarization Slater-type basis sets, and a fine mesh for numerical integrations of matrix elements, we carried out full geometry optimizations of [(bipy)Fe(µ-O₂)Fe(bipy)]⁺ (bipy = 2,2'-bipyridyl) for the lowest-energy S = 1 and 2 electronic states and also of [(bipy)Fe(µ-O₂)Fe(bipy)]²⁺ for its S = 3/2 ground state. Use of the bipy ligand instead of the bpmcn ligand used in the synthetic modeling studies permitted us to exploit D₂ symmetry in each of these calculations. We also carried out similar calculations with D₄d symmetry constraints on the high-valent nitrido-bridged heme dimer complexes [(por)Fe]N (S = 1/2)[22] and [(por)Fe]²⁺N⁺ (S = 0)[23] (por = porphyrinato) which feature the same formal metal oxidation states as [(bipy)Fe(µ-O₂)Fe(bipy)]⁺ and [(bipy)Fe(µ-O₂)Fe(bipy)]²⁺, respectively. A spin-restricted formalism was used for [(por)Fe]²⁺N⁺, a closed-shell species,[24] while spin-unrestricted calculations were used for all the other complexes.

Figure 1 presents the Kohn–Sham molecular orbital (MO) energy levels in the Fe 3d “band” of each of the three [Fe₂(µ-O₂)]₅ species studied. Figure 2 provides pictorial representations of some of these MOs. Figure 1 reveals a substantial energy separation between the t₂g and e_g bands, with only the t₂g band populated, thus indicating the low-spin nature of the iron centers in the species studied. Note also that the e_g band is fairly densely spaced, which provides a simple explanation for the S = 3/2 ground state of [(bipy)Fe(µ-O₂)Fe(bipy)]²⁺ in terms of filling six MOs with nine 3d electrons according to Hund’s rules.[25] Not surprisingly, the S = 1 and S = 2 states of
of these MOs pictorially. The linear Fe-N-Fe arrangement in [{(por)Fe}2N] and [{(por)Fe}2N] provided by these calculations. The density of the MOs is slightly larger than that in [{(bipy)Fe(μ-O)}Fe(bipy)]4+, in agreement with a similar expansion observed for [{FeIV(μ-O)Fe(bipy)}2]4+. Without elaborating too much, we also note that the optimized geometry parameters for the nitrido-bridged heme dimers studied are also in excellent agreement with relevant crystallographic results. For example, the calculated Fe–Nmin distances in [(por)Fe(N)] of 1.645 Å and in [(por)Fe(μ-O)] of 1.619 Å agree closely with the corresponding distances of 1.662 and 1.628 Å in the crystal structures of [FeIV(μ-O)Fe(bipy)]4+ (TTP = mesotetraakis(p-tolyl)porphyrin), respectively.[23] The overall excellent agreement between the calculated and observed geometry parameters constitutes powerful evidence that these calculations correctly describe the electronic structures of FeIV(μ-O)Fe(bipy)]4+ intermediates and, specifically, that the canonical MOs presented in Figure 1 and Figure 2 provide a correct description (although, of course, not a unique description) of the electron distributions in the relevant experimentally studied species.
density and presumably also positive charge away from high-valent iron centers.

An examination of the Mulliken charges of the three [Fe₂(µ-O₂)₂Fe(bipy)]³⁺ species studied (Figure 5) provided further insights into this issue. The charges on the Fe, O, Nₐxial, and Nₑquatorial atoms are +0.890, −0.632, −0.428 and −0.359 for [(por)Fe₂(µ-N)]⁺ (S = 0).

**Figure 3.** MO energy level diagrams for the nitrido-bridged heme dimers studied. The energy scale is in eV. The numerical values of the orbital energies are listed in the Supporting Information.

**Figure 4.** Some primarily d-orbital-based MOs of [(por)Fe₂(µ-N)]⁺ (S = 0).
expected from the fact that Fe–N_{equatorial} bonds are longer than the Fe–N_{axial} bonds. The overall molecular charge density profiles of the +3 and +4 species are not radically different, which is consistent with the electroneutrality principle and reflects the ability of the bipy ligands to delocalize the high positive charges of these ionic species. That said, the total Mulliken electronic charge on the [Fe_{2}(\mu-O)]_4 unit is about 30–40% higher in the [Fe_{2}(\mu-O)]_4^+ species, relative to the [Fe_{2}(\mu-O)]_4^+ species, which is a significant difference. Accordingly, the oxygen atoms in the [Fe_{2}(\mu-O)]_4^+ species may be expected to be much more electrophilic relative to the [Fe_{2}(\mu-O)]_4^+ species. This has indeed been observed to be the case. Thus, in the context of C–H activation, while [Fe_{2}(\mu-O)]_4(tpa)$_2$ only reacts with substrates with activated C–H bonds such as ethylbenzene and cumene, [Fe_{2}(\mu-O)]_4(bpmcn)$_2$ was found to react with adamantane at −40°C under Ar, affording 1-adamantanol and 2-adamantanone in 56% and 20% yield, respectively.[13]

In summary, DFT calculations have provided a framework for understanding the electronic structures of [Fe_{2}(\mu-O)]_4 intermediates with locally low-spin metal centers, species that may actually occur in Nature as reactive intermediates of non-heme diiron alkane monooxygenases such as AlkB. The calculations also explain why these intermediates exhibit different ground spin states relative to high-valent \mu-nitrido/ carbido heme dimers, despite the same formal metal oxidation states. The close agreement between theory and experiment with respect to key geometry parameters provides strong evidence that the calculations presented here faithfully describe the actual electronic structures of the relevant synthetic [Fe_{2}(\mu-O)]_4 intermediates.

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For additional technical details, the reader is referred to the ADP program manual, available from: Scientific Computing and Modeling, Department of Theoretical Chemistry, Vrije Universiteit, 1081 HV Amsterdam, The Netherlands.


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