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Theoretical Investigation on the Mechanism of Oxygen Atom Transfer between Two Non-Heme Iron Centres

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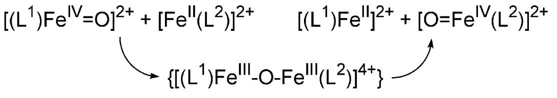
Density functional theory calculations are presented on the oxygen atom transfer reaction between two non-heme iron centres: One contains Bn–tpen [*N*-benzyl-*N*,*N′*,*N′*-tris(2-pyridylmethyl)ethane-1,2-diamine], whereas the other contains N4Py [*N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine]. The calculations show that the (Bn–tpen)Fe–O–Fe(N4Py) complex is a stable entity but considerably higher in energy than isolated species. However, a mechanism of oxygen atom transfer from one non-heme iron centre to the other will proceed via this oxido-bridged intermediate. This oxido-bridged complex has both iron atoms in oxidation state III so that in the process of the formation of the complex, an electron transfer from the Fe^{II} centre to the $Fe^{IV}(O)$ centre has taken place. Nevertheless, both metal atoms have different orbital and spin-density occupation. A large solvent effect on the reaction barriers is obtained, indicating that the reaction proceeds only in very polar environments.

Introduction

Oxido-bridged diiron complexes are found in the active sites of iron-containing enzymes that bind and activate dioxygen, such as ribonucleotide reductase (RNR) and methane monoxygenase (MMO).[1] Synthetic iron complexes have been developed to understand the chemical and physical properties of the oxido-bridged diiron active sites. In particular, biomimetics with oxido-bridged diiron units have been known for quite some time in heme and non-heme iron systems; the (μ-oxido)diiron(III) complexes of heme and non-heme ligands are thermally stable and are well characterized with various spectroscopic techniques.[2] Recently, Collins and co-workers reported the isolation and characterization of a (μ-oxido)diiron(IV) complex formed in the reaction of a non-heme iron(III) complex and O_2.[3]

It has been shown very recently that non-heme oxidoiron(IV) complexes transfer their oxygen atom to other non-heme iron(II) complexes, probably by the formation of a (μ-oxido)diiron(III) species [Equation (1)].[4] The complete intermetal oxygen atom transfer between the oxidoiron(IV) and iron(II) complexes and the failure of the isolation of the oxido-bridged diiron(III) intermediate imply that the latter species is in a thermally unstable, high energy state, which is different from what used to be reported previously.[2] The oxygen atom transfer reaction was also found to depend on the oxidizing power of the oxidoiron(IV) complexes in oxygenation reactions; $[(\text{Bn–tpen})Fe^{IV}{=}O]^{2+} > [(\text{N4Py})Fe^{IV}{=}O]^{2+} > [(\text{TMC})Fe^{IV}{=}O]^{2+}$.[4–6] Apart from the oxygen atom transfer reactions between two non-heme iron complexes, nitrogen atom transfer between manganese complexes bearing different macrocycles have also been reported.[7]



$$[(L^1)Fe^{IV}{=}O]^{2+} + [Fe^{II}(L^2)]^{2+} \rightarrow \{[(L^1)Fe^{III}\text{-O-}Fe^{III}(L^2)]^{4+}\} \rightarrow [(L^1)Fe^{II}]^{2+} + [O{=}Fe^{IV}(L^2)]^{2+} \qquad (1)$$

Although transfer of the oxygen atom formally happens in hydroxylation reactions,[8] it is still remarkable that it happens between different catalysts. In order to elucidate the mechanism by which non-heme oxidoiron(IV) complexes transfer their oxygen atom to other non-heme iron(II) systems, we present here the first density functional theory studies into a non-heme (μ-oxido)diiron(III) complex and its dissociation patterns into the respective oxidoiron(IV) and iron(II) complexes.

Results and Discussion

We chose two non-heme iron complexes bearing pentacoordinate ligands, Bn–tpen and N4Py (see Supporting Infor-

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mation for ligand structures),[6] which are known to form stable oxidoiron(IV) complexes that are efficient catalysts in arene and alkane hydroxylation reactions.[5a,9] Figure 1 displays the optimized geometries and group spin densities of the (μ-oxido)diiron complex Fe(Bn–tpen)–O–Fe(N4Py) (**BN**) in the lowest-lying septet and nonet spin states. We also calculated **BN** in the singlet and triplet spin states, but these structures are well higher in energy (see Supporting Information). In the gas phase, ^{9}**BN** is the ground state by 1.5 kcal mol^{-1} over ^{7}**BN**, but the ordering is reversed in a dielectric environment, and ^{7}**BN** is lower in energy by 3.0 kcal mol^{-1}. As follows from the structure in Figure 1, the oxygen atom is almost midway between the two iron centres in all spin states, but slightly closer to the Fe(N4Py) unit. In oxido-bridged heme systems, the crystal structure also showed the oxygen atom midway between the two iron centres.[10] The largest difference between the two Fe–O bonds is obtained in the septet spin state, where the two bonds differ by 0.044 Å. A frequency calculation, however, confirms all structures to be local minima.

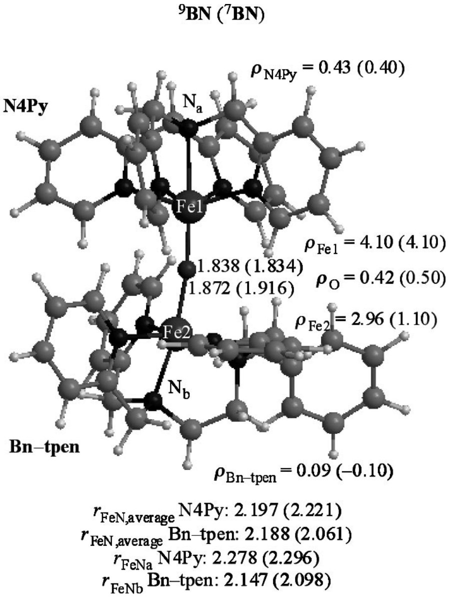

Figure 1. Optimized geometries of ^{9,7}**BN** with bond lengths [Å] and group spin densities (ρ).

The group spin densities shown in Figure 1 indicate that the complexes are either the interaction of a sextet spin state on the Fe(N4Py) moiety with a quartet (doublet) spin state on the Fe(Bn–tpen) unit in ^{9}**BN** (^{7}**BN**), respectively. Thus, the formation of a (μ-oxido)diiron complex from isolated reactants is accomplished with an electron transfer from the Fe^{II} to the Fe^{IV} centre. In other words, ^{5}Fe^{IV}=O(Bn–tpen) reacts with ^{5}Fe^{II}(N4Py) to form a (μ-oxido)diiron intermediate with both iron atoms in oxidation state III; a sextet spin Fe(N4Py) moiety is bound through a bridging oxido group to a quartet spin Fe(Bn–tpen) group in ^{9}**BN**. Further support for these oxidation state assignments follows from the molecular orbitals shown in Figure 2. The orbital occupation in **BN**, therefore, is in sharp contrast to the one observed for the diiron cluster in MMO and RNR enzymes, where the two metal atoms are antiferromagnetically coupled maximum spin states with essentially the same orbital occupation.[1a] Therefore, the unpaired electrons in the system rearrange to create a complex with an equal charge and oxidation state on each metal atom.

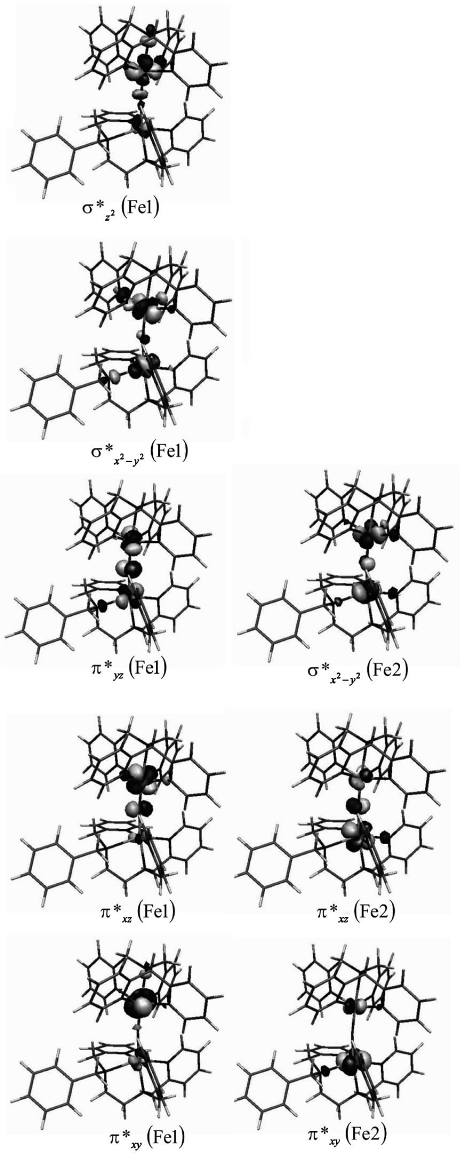

Figure 2. Singly occupied molecular orbitals of ^{9}**BN** with orbitals with dominant Fe1 contribution on the left-hand side and ones with a dominant Fe2 contribution on the right-hand side.

The singly occupied molecular orbitals of ^{9}**BN** resemble the singly occupied orbitals of the isolated species, although there are some critical differences. There are three π*-type orbitals on each metal centre; a nonbonding π^*_{xy} orbital in the plane of the four nitrogen atoms and two orbitals representing the π* antibonding interactions along the Fe–O bond (π^*_{xz}, π^*_{yz}). The highest-lying occupied orbitals represent the σ* antibonding interactions of the metal atom with the oxygen and axial nitrogen atoms ($\sigma^*_{z^2}$) and the metal atom with the four nitrogen atoms of the ligand ($\sigma^*_{x^2-y^2}$). Most orbitals are smeared out over the complete

Fe–O–Fe system. Essentially, the 3d-metal block is occupied by ten electrons of which two pair up into a nonbonding π^*_{yz} orbital mainly located on Fe2 (not shown in Figure 2). The complete metal d-block is singly occupied for the Fe(N4Py) group with occupation; $\pi^*_{xy}{}^{1}$ $\pi^*_{xz}{}^{1}$ $\pi^*_{yz}{}^{1}$ $\sigma^*_{z^2}{}^{1}$ $\sigma^*_{x^2-y^2}{}^{1}$ shown on the left-hand-side of Figure 2, while the Fe(Bn–tpen) part of ^{9}**BN** has a quartet spin with occupation $\pi^*_{yz}{}^{2}$ $\pi^*_{xz}{}^{1}$ $\pi^*_{xy}{}^{1}$ $\sigma^*_{x^2-y^2}{}^{1}$. Thus, starting from isolated reactants, formally an electron transfer from the $\sigma^*_{z^2}$ orbital in ^{5}Fe(Bn–tpen) to the $\sigma^*_{x^2-y^2}$ orbital in ^{5}Fe(N4Py) of ^{9}**BN** has taken place. In ^{5}FeO(N4Py)$^{2+}$ and ^{5}FeO(Bn–tpen)$^{2+}$, the π^*_{xz} and π^*_{yz} orbitals are equally distributed among the oxygen and iron atoms, but in ^{9}**BN** these orbitals mix and spread out over the complete Fe–O–Fe axis as expected.

To find out what the relative stability of ^{9,7}**BN** with respect to isolated reactants is, we subsequently calculated the dissociation mechanisms of ^{9,7}**BN** leading to FeO(N4Py) + Fe(Bn–tpen) products via barrier **TS1** or to Fe(N4Py) + FeO(Bn–tpen) products via barrier **TS2** on the septet and nonet spin states (Figure 3). As follows from Figure 3, the barriers and in particular the dissociation energies due to their large positive charge are extremely sensitive to a polarized environment, and even a small dielectric constant mimicking chlorobenzene lowers the exothermicity of dissociation by >100 kcal mol^{-1}. A large solvent effect on the completion of the reaction was also observed experimentally for the nitrogen atom transfer between different metal macrocycles.[7] Nevertheless, the key results are reproduced in a dielectric environment: ^{9,7}**BN** are local minima well higher in energy than isolated reactants. The dissociation barriers with respect to ^{9,7}**BN** remain the same regardless of the environmental perturbations.

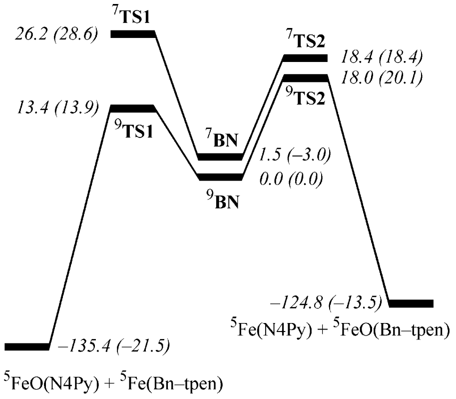

Figure 3. Potential energy profile for the dissociation of ^{9,7}**BN** into either FeO(N4Py) + Fe(Bn–tpen) or into Fe(N4Py) + FeO(Bn–tpen) products. All energies are in kcal mol^{-1} relative to ^{9}**BN**. Data in parentheses includes solvent corrections.

The thermodynamically most stable system is isolated ^{5}FeO(N4Py) + ^{5}Fe(Bn–tpen), in agreement with experimental observations that FeO(Bn–tpen) + Fe(N4Py) react to form FeO(N4Py) + Fe(Bn–tpen) products.[4] The difference in exothermicity also implies that the Fe=O bond in ^{5}FeO(N4Py) is 8.0 kcal mol^{-1} stronger than the one in ^{5}FeO(Bn–tpen). As such it is expected that FeO(Bn–tpen) will be a better catalyst of hydroxylation reactions, as indeed observed by DFT modelling by Shaik and coworkers.[11] Detailed geometry scans (see Supporting Information) for the dissociation reaction up to an Fe–O distance of 20 Å showed that ^{9}**BN** indeed dissociates into two quintet spin reactants. Moreover, the oxidation states of the metal atoms during the geometry scans changed back to Fe^{II} and Fe^{IV} from two Fe^{III} centres in ^{9,7}**BN**. Therefore, the dissociation reaction of ^{9,7}**BN** involves electronic rearrangement and electron transfer.

The height of the barriers is only marginally influenced due to the addition of a dielectric constant, since they contain the same amount of atoms and overall charge as the μ-oxido complexes (**BN**). Note that, on the nonet spin state surface **TS1** is well below **TS2**, while the ordering is reversed on the septet spin state surface. This is because the four isolated species, Fe(N4Py), FeO(N4Py), Fe(Bn–tpen) and FeO(Bn–tpen), all have different quintet-triplet energy gaps, i.e. a larger quintet-triplet energy gap was obtained for FeO(N4Py) than for FeO(Bn–tpen).[11] Thus, a collision between two quintet spin reactants should give two quintet spin products via ^{9}**BN**. However, the collision between e.g. ^{3}FeO(N4Py) with ^{5}Fe(Bn–tpen) may give rise to a mixture of quintet and triplet FeO(Bn–tpen). Therefore, spin-state scrambling may occur in all spin states except the maximum spin state. Finally, the collision between two triplet reactants will not lead to an oxygen atom transfer process as it would proceed via either ^{1}**BN** or ^{3}**BN**, which are high-lying and inaccessible intermediates. Thus, multistate reaction mechanisms occur for the oxygen atom transfer process between various non-heme iron centres.[12]

Conclusion

Theory predicts that the collision of a non-heme oxidoiron(IV) complex with a non-heme iron(II) complex can create a stable (μ-oxido)diiron non-heme complex with both iron atoms in oxidation state III. These complexes are real minima on the potential energy surface but well higher in energy than isolated reactants, which explains why they have never been detected experimentally. The calculations show that environments with a large dielectric constant should stabilize these systems considerably. The (μ-oxido)diiron complexes are shown to guide the oxygen atom transfer mechanisms between non-heme iron biomimetic complexes. In contrast to (μ-oxido)diiron complexes in enzymes, the systems studied here have different orbital and spin occupation on each iron centre although the overall oxidation state is III.

Methods Section

All calculations were performed using established procedures in our group which are briefly summarized here.[12] The initial geometry optimizations (without constraints) were performed with the Jaguar 5.5 program package[13] and utilized the unrestricted B3LYP hybrid density functional method in combination with a double-ζ quality LACVP basis set on iron and 6-31G on the rest of the atoms (basis set B1).[14,15] The optimized geometries were transferred to Gaussian 03 for a frequency analysis.[16] Subsequent, single-point calculations in the gas phase as well as in an environment with a dielectric constant of $\varepsilon = 5.7$ (probe radius of 2.7 Å) were performed in Jaguar with a triple-ζ quality LACV3P+ basis set on iron (that contains a core potential) and 6-311+G* on the rest of the atoms (basis set B2). All energies reported are obtained with basis set B2 and contain ZPE corrections with basis set B1. The oxygen transfer reaction between two non-heme iron complexes was studied using an Fe(N4Py) and Fe(Bn–tpen) complex bridged by an oxido group. The overall system has 113 atoms, a stoichiometry of $C_{50}H_{50}Fe_2N_{10}O$ and a charge of +4. We tested all low-lying spin states: nonet, septet, quintet, triplet and singlet. The quintet spin state calculations did not converge and led to high energies, so this state was not considered further.

Supporting Information (see footnote on the first page of this article): Relative energies, group spin densities and charges of all structures discussed in this work as calculated with UB3LYP/B1 and UB3LYP/B2 methods; scheme with chemical structures of Bn–tpen and N4Py.

Acknowledgments

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[6] Abbreviations used: Bn–tpen: *N*-benzyl-*N*,*N′*,*N′*-tris(2-pyridylmethyl)ethane-1,2-diamine; N4Py: *N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine; TMC: 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane.

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