

Abstract:**Relations between non-saturated Iron coordination and electronic/geometric structures of biologically relevant molecules with $[\text{Fe}_2(\mu\text{-O})_2]^{n+}$ cores****Co-supervisor 1: Ray, Kallol, HU Berlin****Co-supervisor 2: Drieß, Matthias, TU Berlin****Co-supervisor 3: Dau, Holger; Haumann, Michael, FU Berlin**

The closed $[\text{Fe}_2\text{O}_2]$ diamond core assignment for intermediate **Q** in soluble methane monooxygenase seems to be inconsistent with previously reported X-ray absorption spectroscopy properties (large pre-edge intensity, short Fe-Fe distance of 2.46 Å). In contrast, recent studies of **Q** by employing nuclear resonance vibrational spectroscopy (NRVS) favor a closed-core description, hypothesizing unsaturated Fe coordination (i.e., 5C instead of 6C) at one or both the Fe centres as an explanation for the XAS results. In the context of this controversy (closed vs open conformation) related to the structure of **Q**, we aim at synthesizing a series of molecules with $[\text{Fe}_2(\mu\text{-O})_2]^{n+}$ cores and varying Fe coordination numbers and Fe-Fe distances. For these complexes, we will investigate how the coordination changes affect their spectroscopic and reactivity properties, e.g., in high-valent iron-oxo ($\text{Fe}^{\text{IV}}=\text{O}$) states as formed upon dioxygen exposure. This collaborative study within UniSyscat (Drieß, Dau, Haumann, Hildebrandt, Ray) may broaden the scope of models that are considered for the structure of high-valent diiron intermediates formed upon O_2 activation in biology.

Extended description version of the project:

Relations between non-saturated Iron coordination and electronic/geometric structures of biologically relevant molecules with $[\text{Fe}_2(\mu\text{-O})_2]^{n+}$ cores

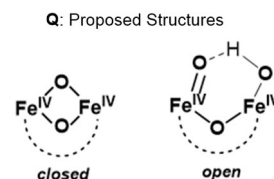
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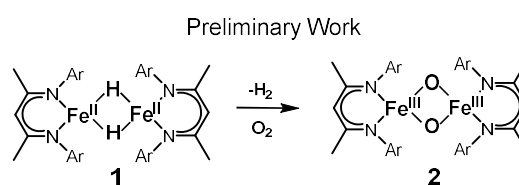
1. Overall goal of the project and state of the art

Soluble methane monooxygenases (sMMO) that are isolated from methanotrophic bacteria are non-heme diiron enzymes that carry out the chemically challenging conversion of methane to methanol (*Acc. Chem. Res.* **2011**, *44*, 280; *J. Am. Chem. Soc.* **2014**, *136*, 13942). It is proposed that the diiron(II) center in the reduced enzyme reacts with O_2 to generate a diferric-peroxo intermediate called **P** that then undergoes O–O cleavage to convert into a diiron(IV) derivative called **Q**, which carries out methane hydroxylation. Most of the spectroscopic data of **Q** accumulated by various groups to date favor the presence of an $\text{Fe}^{\text{IV}}_2(\mu\text{-O})_2$ unit with a closed diamond core (*Nature* **2015**, *518*, 431). However, an asymmetric open-core $\text{O}=\text{Fe}^{\text{IV}}\text{-O}-\text{Fe}^{\text{IV}}$ conformation containing a terminal oxoiron(IV) motif is also suggested for **Q** based on the observed large pre-edge intensity in Fe K-edge X-ray absorption spectroscopy (*J. Am. Chem. Soc.* **2017**, *139*, 18024; *J. Am. Chem. Soc.* **2018**, *140*, 16807). The discussion on the Fe–Fe distance, which is a key structural parameter that can provide insight into the core structure of **Q**, is also controversial with distances of 2.5–3.4 Å being attributed to both “open” or “closed” cores with bridging or terminal oxo groups.



The proposed involvement of $\text{Fe}^{\text{IV}}_2(\mu\text{-O})_2$ diamond core in methane oxidation reactions has made it an attractive target for biomimetic synthetic studies. One notable example is the crystallographically characterized $[\text{Fe}^{\text{IV}}_2(\mu\text{-O})_2(\text{TPA}^+)_2]^{3+}$ complex (*Faraday Discuss.*, **2022**, *234*, 109) with an Fe–Fe distance of 2.71 Å. This complex revealed a significantly diminished pre-edge intensity relative to that of **Q**, and accordingly such a structure has been refuted for the enzymatic intermediate. An increased pre-edge transition is however observed for an asymmetric open-core $\text{O}=\text{Fe}^{\text{IV}}\text{-O}-\text{Fe}^{\text{IV}}$ complex containing 6C Fe and a terminal oxoiron(IV) motif, which is presently considered as the best guess for the structure of **Q**.

In a recent study (Limberg, Braun, Drieß, Dau, Haumann, Ray *et al.*; submitted) within UniSyscat we reported the synthesis and characterization of an O_2 derived 4C $[\text{Fe}_2(\mu\text{-O})_2]^{2+}$ complex **2** supported by a β -diketiminato ligand and demonstrated that lower

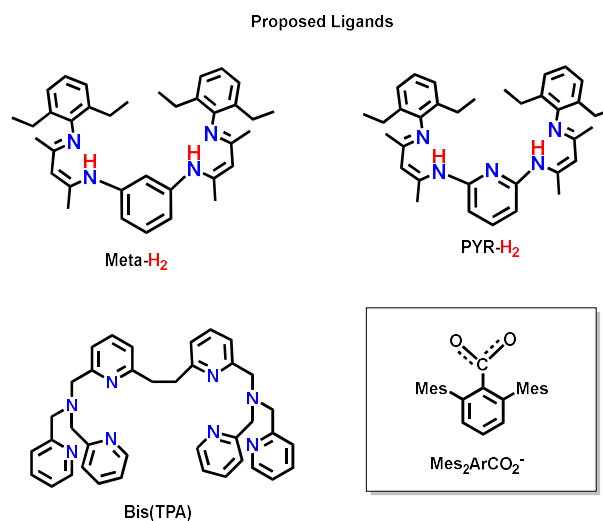


coordination number for the irons allows much more flexibility in the diamond core than proposed based on many other computational and experimental studies. In particular, an unexpected similarity in the pre-edge intensity of the closed core structure of 4C $[\text{Fe}_2(\mu\text{-O})_2]^{2+}$ complex with that of the open-core models and that of **Q** was observed, which reveals that X-ray absorption near edge spectral (XANES) data may not be a fully conclusive spectroscopic marker to discern between “open-core” and “closed-core” models for intermediate **Q**. Notably, recent studies of **Q** reported by Solomon and coworkers (*J. Am. Chem. Soc.*, **2021**, *143*, 16007) employing nuclear resonance vibrational spectroscopy, strongly favor a closed-core description for this intriguing intermediate, whereby the

large pre-edge intensity has been hypothesized to originate from lower coordination (5C instead 6C) at one or both the Fe centres. XAS measurement on 5C $\text{Fe}^{\text{IV}}_2(\mu\text{-O})_2$ cores are therefore warranted to test this hypothesis, which will be targeted in the present proposal.

3. Specific aims and how they may be reached

Dinucleating Ligands and complexes: Based on our initial success in generating 4C $[\text{Fe}_2(\mu\text{-O})_2]^{2+}$ cores supported by β -diketiminate ligands in high yield we will now employ dinucleating ligand systems containing differently bridged bis (β -diketiminate) ligand systems. The proposed ligands can be prepared in reasonable yields by a precedent two-step standard condensation route (*Organometallics* **2008**, 27, 6178) in collaboration with the group of Matthias Driess. The dinucleating ligands PYR and META will allow for a wide range of metal...metal distances. Furthermore, the PYR ligand is a potential pentadentate ligand and has been incorporated to



study the effect of additional metal coordination (moving from 4C to 5C). Since β -diketiminate is a potential non-innocent ligand, achieving the $\text{Fe}(\text{IV})$ oxidation state can be challenging, as has been observed in our preliminary study. Accordingly, redox innocent dinucleating ligand (Bis(TPA)) based on tris(pyridyl)amine ligands will be also synthesized. The β -diketiminate based ligands will be reacted with FeCl_2 in presence of KHBet_3 to obtain the corresponding $[\text{Fe}_2(\mu\text{-H})_2]$ complex, which upon reaction with O_2 should generate the $[\text{Fe}_2(\mu\text{-O})_2]^{2+}$ core. Efforts will be also made to oxidize the $[\text{Fe}_2(\mu\text{-O})_2]^{2+}$ core in presence of a bulky carboxylate ligand (2,6-dimesitylbenzoate; $\text{Mes}_2\text{ArCO}_2^-$), which may play a vital role in providing access to high-valent Fe^{IV} centres. The synthesis of the corresponding complex involving the bis(TPA) ligand will involve reaction of the ligand with iron(II) salts. The complex will then be reacted with O_2 or H_2O_2 to generate the $[\text{Fe}_2(\mu\text{-O})_2]^{n+}$ cores by precedent synthetic procedures reported for the mononuclear complex.

Spectroscopic Characterization: Efforts will be made to grow crystals of the complexes and determine their structure by single crystal X-ray diffractometer studies. Further characterization of the complexes will be performed by infrared, ^1H -nuclear magnetic resonance, electron paramagnetic resonance, Mössbauer, SQUID magnetometry (Collaboration: Limberg), X ray absorption, resonance Raman (collaboration: Hildebrandt) and UV- Vis absorption spectroscopic methods. The main target will be to examine the effects of reduced Fe coordination numbers on the Fe–Fe separation, Fe K-edge pre-edge energy and intensity, and Fe-Fe spin coupling of the $\text{Fe}_2(\mu\text{-O})_2$ core.

Reactivity Studies: Potential avenues for reactivity of these complexes to be pursued are stoichiometric C–H bond activation, C–OH bond activation, amine oxidation and oxidative group transfer reactions. Initial screens will be carried out with simple substrates like cyclohexane, cyclooctene, phosphines, sulfides, and olefins. The simplicity of the proposed ligands will allow us to vary the substituents and hence tune the steric and electronic demands of the ligands, and investigate their effect on the oxygen atom transfer and hydrogen atom transfer reactivity of the complexes