Characterization of a Six-Coordinate Ferrous High-Spin Heme with Both Intramolecular Axial Carboxylic Acid and Pyridine

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Abstract: Synthesis of a bis-strapped porphyrin with a pyridyl residue on one side and a malonic acid on the other side gives after iron(II) insertion a six-coordinate complex in which both apical groups are the two axial ligands of the iron atom. Unexpectedly, this six-coordinate iron(II) complex proves to be high-spin, likely due to some stabilization of the axial metal−ligand antibonding orbitals.

Dioxygen transport and storage are the first two steps of all aerobic life and are performed by hemoproteins in vertebrates.[1] In these hemoproteins, Myoglobin (Mb)[2] and Hemoglobin (Hb),[3] the coordination site is composed of a single heme buried in a hydrophobic pocket. In Mb and Hb the bound dioxygen interacts with the histidine residue E7, positioned above the iron atom, to establish a hydrogen bond with the superoxo complex (Pauling hypothesis, confirmed by neutron diffusion).[4] This hydrogen bond increases the affinity of the ferrous heme for dioxygen. Therefore, the construction of superstructures bearing such hydrogen bond donors is of immediate interest for better understanding of the structure and function of hemoproteins. For this purpose, the synthesis and dioxygen binding studies of various strapped iron(II) porphyrins bearing hanging malonic ester and malonic acid groups (Scheme 1) were recently described.[5] Our rationale was to provide at least one carboxylic acid above the coordination site of dioxygen to (i) verify the increase of dioxygen affinity and (ii) structurally characterize the superoxo complex stabilized by hydrogen bonds.

Scheme 1. Synthesis of Six-Coordinate Complex **2Fe**^{II} and Five-Coordinate **3Fe**^{III}
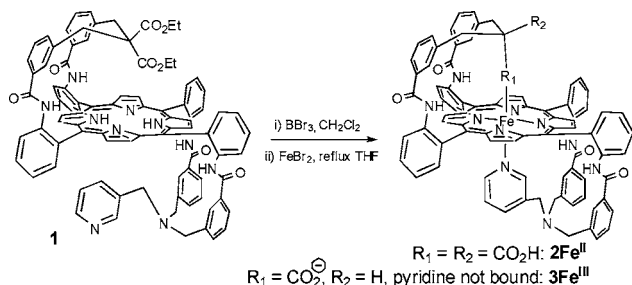
During our investigation, an unprecedented paramagnetic six-coordinate iron(II) complex was discovered for porphyrin **2Fe**^{II}. In this complex both the pyridyl base and the malonic acid axially coordinate to the iron(II) atom inside the porphyrin; therefore the complex is expected to be diamagnetic. As a reference, iron(II) insertion into **1** leads unambiguously to a five-coordinate complex **1Fe**^{II} in which the pyridyl ring acts as the fifth ligand of iron, as shown by X-ray crystallography.[5]

Treatment of **1** with 20 equiv of BBr_3 in methylene chloride afforded porphyrin **2** in which a malonic acid hangs over the coordination site. Subsequent iron insertion into **2** was performed with $FeBr_2$ in refluxing THF in a glovebox to afford **2Fe**^{II} (Figure 1) in 92% yield. The monodecarboxylated compound **3Fe**^{III} (Figure 2) was isolated as a minor product. **2Fe**^{II} exhibits a peculiar proton NMR spectrum with paramagnetic signals (Figure 7, Supporting Information (SI)). Single crystals suitable for X-ray diffraction were grown by slow evaporation of a solution of **2Fe**^{II} in a mixture of chloroform/pentane. Although porphyrin **2** was designed with the aim of preparing a five-coordinate ferrous complex leaving a coordination site vacant for dioxygen, surprisingly, **2Fe**^{II} is six-coordinate (Figure 1).

The strap in **2Fe**^{II} is apparently flexible enough to allow the strong axial coordination of one carboxylic acid to the iron center, with a short Fe−O1 bond length of 2.017 Å. The O3 and O2 atoms are 2.478 Å apart, indicating a strong hydrogen bond between the two carboxylic acids. Whereas a five-coordinate ferrous heme complex with an axially bound carboxylato group has been reported,[6] a six-coordinate iron(II) with both an axially bound carboxylic acid group and a pyridine ligand has never been observed.
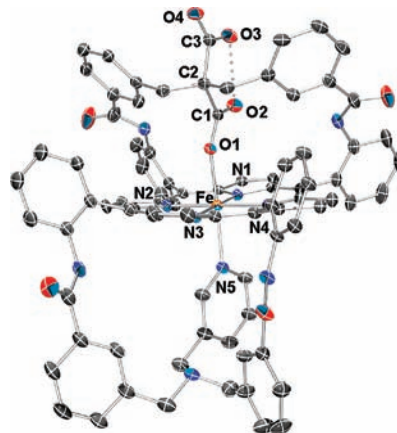

Figure 1. X-ray structure of six-coordinate **2Fe**^{II}. The dashed line represents a hydrogen bond.

Based on the bond lengths, the O4−C3−O3 group is the hydrogen bond donor; the C3−O3 bond is longer (1.311 Å) than the C3−O4 bond (1.199 Å). For the Fe-bound carboxylic acid group O1−C1−O2, the lengths of the two C−O bonds are almost identical (1.242 and 1.259 Å for C1−O2 and C1−O1, respectively). Thus, O2 is the hydrogen bond acceptor site, and O3 the donor site. The C1−O1 bond is elongated due to its coordination to iron. Both O2 and O3 should be considered as protonated (Figure 3).

In this complex, the iron atom exhibits an octahedral geometry with the four porphyrin nitrogen atoms in equatorial positions and

an average N−Fe distance of 2.055 Å. The iron atom is displaced 0.080 Å out of the 24-atom mean porphyrin plane toward the pyridyl axial ligand (Figure 4, SI). Furthermore, the two aromatic rings tethered to the strap bearing the pyridine are located out of the mean plane of the porphyrin. Contrary to an analogous low-spin ferrous complex with mixed imidazole-thioether ligation,[7] the very long axial Fe−N5 bond (2.250 Å) and the radial expansion (Figure 5, SI) favor a high-spin complex. The very short axial Fe−O1 bond (2.017 Å) is particularly intriguing when compared to that described for related complexes.[8,9] The unusually short distance between the iron atom and O1 is probably due to both the flexibility of the strap that is bent over the iron atom and the strong hydrogen bond between the O2 and O3 atoms. The structurally characterized octahedral **2Fe^{II}** complex, with a combination of carboxylic acid/pyridine axial ligands, is unprecedented. Indeed, high-spin octahedral iron(II) complexes are extremely scarce. With its rather short axial Fe−O bond and long Fe−N(py) bond, **2Fe^{II}** represents a novel high-spin iron(II) porphyrin complex and opens a new route for the synthesis of related compounds.
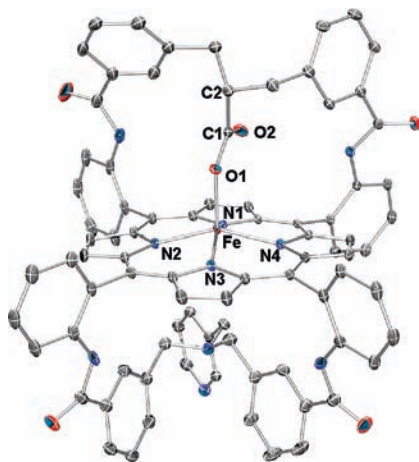

Figure 2. X-ray structure of five-coordinate complex **3Fe^{III}**.

The coordination motif encountered in **2Fe^{II}** could also be consistent with a carboxylate-bound iron(III) cation. However, this scenario was ruled out by the following observations. First, as previously reported,[8,9] a consequence of the extremely rare in-plane iron(II) atom is the large radial expansion of the porphyrinic core as illustrated by both the long Fe−N bond lengths (Figure 3) and the distances between the iron atom and the meso carbons (3.463, 3.443, 3.472, and 3.441 Å). Second, **2Fe^{II}** does bind dioxygen and carbon monoxide (Figure 6, SI).[5] However, its effective paramagnetic moment of 4.7 μ_B measured by Evans' method[10] is consistent with $S = 2$ high spin iron(II) (Figure 8, SI). Solid state magnetic measurements (Figure 9, SI) performed under anaerobic conditions are also consistent with high-spin iron(II) (4.1 μ_B). As further proof, in the crystal structure of the iron(III) decarboxylated counterpart **3Fe^{III}** (Figure 2), the iron(III) is five-coordinate. The carboxylate ligand O2−C1−O1 is located in an apical position, and the metal lies 0.532 Å above the mean porphyrin plane. In this complex, the average Fe−N bond length of 2.069 Å compares well with those of similar compounds in which the fifth ligand is an acetato group.[11]

The high-spin quintet state of **2Fe^{II}** was confirmed by DFT calculations[12] performed on the experimental X-ray structure with equatorial ($d_{x^2-y^2}$) and apical (d_{z^2}) singly occupied metal−ligand antibonding molecular orbitals, in agreement with the long equatorial and apical Fe−N distances. Despite the rather short apical

Fe−O1 distance, this oxygen atom is loosely bound. Indeed, in the DFT-optimized structure of **2Fe^{II}** O1 is not coordinated to iron, resulting in an arrangement close to that of **1Fe^{II}**,[5] with a similar splitting of the d orbitals. This indicates that the hydrogen bond involving O2 and O3 might be the driving force that brings O1 close to Fe.
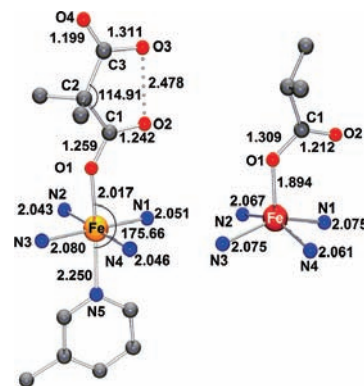

Figure 3. Comparison of the X-ray structures **2Fe^{II}** (left) and **3Fe^{III}** (right). The dashed line represents a hydrogen bond.

In conclusion, although initially synthesized in order to structurally characterize a superoxo complex stabilized by hydrogen bonding, porphyrin **2Fe^{II}** leads to an unprecedented six-coordinate high spin complex with a hanging carboxylic acid bound to iron. This coordination motif is made possible by the flexibility of the strap. However, because this strap can either bend over the coordination site, as in **2Fe^{II}**, or remain in a vertical position as described previously,[13] the ferrous complex still reacts with small molecules such as dioxygen or carbon monoxide. This remarkable compound illustrates a novel dynamic process in the coordination chemistry of ferroporphyrins.

Supporting Information Available: Experimental details, NMR spectra and crystallographic data of **2Fe^{II}** and **3Fe^{III}**, and complete ref 12 (CIF, PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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