Synthetic Iron Porphyrins as Models for Heme Proteins

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Iron porphyrins are a ubiquitous active site in biological systems [1]. This is due to the ability of the robust porphyrin macrocycle to stabilize iron in at least four oxidation states and six spin states [2]. Impetus for the study of iron porphyrins lies in the desire to understand how they work such chemical magic as shape selective oxidations [3] and oxygen transport and storage [4].

Initial efforts were aimed at understanding how axial ligation controls the oxidation chemistry of single-atom-bridged dimers. This led into a study of a complex which is capable of reversibly interacting with dioxygen in frozen glass media. Attempts to extend the pantheon of single-atom-bridged dimers to sulfur resulted in the synthesis and characterization of the first low-spin five-coordinate ferric porphyrin thiolate.

$(FeTPP)_2O$, where TPP is the dianion of tetraphenylporphyrin, contains two high-spin ferric atoms [5]. Oxidation of this complex to the dication occurs on the porphyrin rings yielding porphyrin pi-cation radicals [6]. This behavior can be contrasted with the isoelectronic complexes $(FeTPP)_2N^+$ and $(FeTPP)_2C$. These species are oxidized at iron yielding Fe(IV) complexes [7,8]. The results can be rationalized in terms of relative electronegativities and pi-bonding abilities.

$(FePor)_2N^+$ complexes (where Por can be a number of tetra-arylporphyrins) can be further oxidized to yield $(FePor)_2N^{2+}$, a stable iron(IV) porphyrin pi-cation radical. These nitride-bridged systems are the only such complexes which are stable at room temperature to date. The electronic structure of these species is dependent on the counterions and porphyrin substituents. For example, $[(FeTPP)_2N](SbCl_6)_2$ has the pi-cation-radical localized on one porphyrin ligand, while $[(FeTPP)_2N](CF_3SO_3)_2$ has the radical delocalized over both of the porphyrin ligands. These results indicate that nitride is able to stabilize highly oxidized iron porphyrins. This reinforces the theory that highly-charged axial ligands capable of forming strong pi-bonding interactions are necessary to stabilize highly oxidized biological intermediates [4].

$(FeTPP)_2N$ was reported to bind pyridine in a polar frozen glass medium [9]. Further investigation of this phenomenon revealed that the presence of dioxygen was responsible for the alteration of the EPR signals of the dimer [10]. The reaction with oxygen is totally reversible. The oxygen adduct has been studied by a battery of physical techniques. The optical spectrum of the oxygen adduct is equivalent to that of the lone dimer; this indicates that the interaction is quite weak. Mössbauer spectra demonstrate that the iron atoms are inequivalent in the adduct while EPR data indicate a less anisotropic g tensor and appreciably diminished ^{14}N and ^{57}Fe hyperfine coupling relative to the nonadducted species. O_2 titrations, as monitored by EPR,

show that the adduct's stoichiometry is one O_2 per dimer. All these data are consistent with a weak axial interaction of O_2 with one side of the μ-nitrido dimer. This is the first report of the reversible interaction of O_2 with a ferric porphyrin.

To date, synthetic five-coordinate ferric porphyrin thiolates are all high-spin [11,12,13]. Reaction of S_8 and $LiB(Et)_3H$ with Fe(TAP)Cl, where TAP is the dianion of p-methoxyphenylporphyrin, produces Fe(TAP)SH. The product is a low-spin ferric species as indicated by the following data: The magnetic moment corresponds to an $S=\frac{1}{2}$ system. A toluene glass of Fe(TAP)SH gives an EPR spectrum with g values of 3.9 and 1.7 at 4K. The Mössbauer spectrum consists of a single doublet with an isomer shift and quadrupole splitting similar to that of other low-spin ferric complexes [14]. The pyrrole proton resonance at -19 ppm is typical of low-spin iron porphyrins [15]. Splitting of the ortho and meta resonances is consistent with five-coordination. The stereochemistry of Fe(TAP)SH has been determined by a single-crystal x-ray structure. The average $Fe-N_{por}$ distance of 2.01 A is indicative of a low-spin iron center [2].

Fe(TAP)SH represents a new class of porphyrins relevant to heme enzymes containing sulfur ligation, such as chloroperoxidase (CPO) and cytochrome P-450. While thiolate ligation has been demonstrated for cytochrome P-450 [16], EPR studies suggest that CPO has an axial ligand with similar electron-donating properties that is not thiolate [17]. The EPR characteristics of CPO are reproduced most faithfully by the HS^- adduct of hemoglobin [17]. The isolation of Fe(TAP)SH indicates that exogenous sulfur may be a realistic alternative to thiolate axial ligation in CPO.

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