4.8: General Aspects of the Chemistry of Iron

Irreversible Oxidation

In the presence of dioxygen, iron(II) species are readily oxidized to iron(III) species. In the presence of water, iron(III) species frequently associate into μ-oxodiiron(III) dimers. For iron(II)-porphyrin complexes this process may take only milliseconds at room temperature. The following mechanism was proposed in 1968 for the irreversible oxidation of iron(II)-porphyrinato species;[67,68] subsequent work has largely confirmed it.[69-71]

$$Fe^{II} + O_2 \rightleftharpoons Fe^{III}—O_2^{I-} \tag{4.29a}$$

$$Fe^{III}—O_2^{I-} + Fe^{II} \rightleftharpoons Fe^{III}—O_2^{II-}—Fe^{III} \tag{4.29b}$$

$$Fe^{III}—O_2^{II-}—Fe^{III} \rightarrow 2Fe^{IV} = O \tag{4.29c}$$

$$Fe^{IV} = O + Fe^{II} \rightarrow Fe^{III}—O—Fe^{III} \tag{4.29d}$$

In particular, the dimerization reaction (4.29b) may be rendered less favorable by low temperatures (< -40 °C) or by sterically preventing the bimolecular contact of an Fe^{III}-O_2^{I-} moiety with an Fe^{II} moiety. In the latter case, sterically bulky substituents on the equatorial ligand surround the coordinated O_2 ligand and the other axial position, trans to the coordinated dioxygen ligand, is protected with a nitrogenous base, such as imidazole, or with additional bulky substituents on the equatorial ligand (Figure 4.14).[72] The protein effectively provides such protection and thus plays a key role in preventing the bimolecular contact of two hemes. The first observation of reversible binding of dioxygen to an iron(II)-porphyrin in the absence of protein was made in 1958.[73] In that pioneering study, a heme group was immobilized on a polymer support specially modified to contain imidazole functions. The structurally characterizable hemoglobin or myoglobin species was replaced by a noncrystalline structurally uncharacterized polymer.

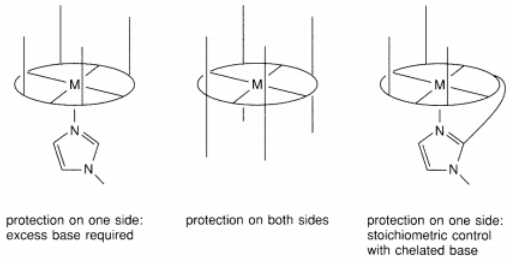


Figure 4.14 - Stylized representation of steric hindrances preventing irreversible oxidation.

Why does this irreversible oxidation not occur analogously for cobalt systems? Step (4.29c) involves cleavage of the O—O bond, which in H_2O_2 has a bond energy of 34.3 kcal/mol or in Na_2O_2 of 48.4 kcal/mol. By way of comparison, for O_2 the bond energy is 117.2 and for HO_2• it is 55.5 kcal/mol.[64] A simple molecular orbital picture gives insight into why an Fe^{IV}=O species is stabilized relative to the analogous Co^{IV}=O species.[74] From Figure 4.15 we see that for metals with electronic configuration d^n, where $n \leq 5$, no electrons occupy the antibonding orbital π^* for Fe^{III}-$O^{I-•}$ or Fe^{IV}=O moieties. For Co^{III} (d^6) the extra electron goes into the antibonding orbital π^*. As predicted by the model, Mn^{III} is observed indeed to behave like Fe^{III}.

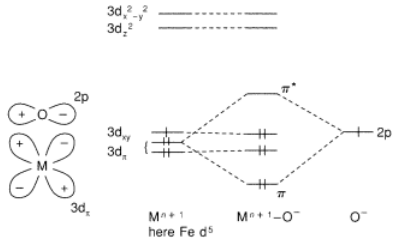


Figure 4.15 - Orbital scheme showing the differing stabilities of M—O species, M = Co(d^6), Fe(d^5); σ-bonding of $2p_z$ with $3d_{z^2}$ not shown.[74]

A second oxidation pathway does not require the bimolecular contact of two iron(II)-porphyrins. Coordinated dioxygen may be released not as O_2, as in normal dioxygen transport, but, as noted in Section I.C, as a superoxide radical anion $O_2^{-•}$ in a process

called *autoxidation*:

$$Fe^{III}—O_2^{I-} \rightleftharpoons Fe^{III} + O_2 \tag{4.30}$$

This process is assisted by the presence of other nucleophiles that are stronger than the superoxide anion, such as chloride, and by protons that stabilize the $O_2^{-\bullet}$ anion as $HO_2^{\bullet}$:

$$Fe_{III} + Cl^- \rightleftharpoons Fe^{III}—Cl^- \tag{4.31}$$

The formation of methemoglobin occurs *in vivo*, probably by the above mechanism, at the rate of ~ 3 percent of total hemoglobin per day.

If exogenous reductants are present, then further reduction of dioxygen can occur:

$$2H^+ + Fe^{III}—O_2^{I-} + e^- \rightarrow Fe^V = O + H_2O \tag{4.32}$$

Such processes are important, for example, in the cytochrome P-450 system. With suitably small reductants, oxygenase activity also has been observed for hemoglobin A. This has led to the characterization of hemoglobin as a "frustrated oxidase."[75] Note the formal similarity between this process (Equation 4.32) and the bimolecular irreversible oxidation of iron(II) porphyrins: the second Fe(II) complex in Reaction (4.29b) functions like the electron in Reaction (4.32).

Spectroscopy of the Fe^{III}—O—Fe^{III} moiety

The end products of the irreversible bimolecular oxidation of Fe^{II} species contain the Fe^{III}—O—Fe^{III} fragment. Given the facile formation of μ-oxodiiron(III) species, it is not surprising that the Fe—O—Fe motif is incorporated into a variety of metalloproteins, including the oxygen-carrier hemerythrin (Figure 4.10),[16-18] the hydrolase purple acid phosphatase,[76] the oxidoreductases ribonucleotide reductase[77] and methane monoxygenase,[78] an iron-sulfur protein rubrerythrin,[79a] and the iron-transport protein ferritin.[79b] In ferritin higher-order oligomers are formed.

This μ-oxodiiron(III) moiety has a distinctive fingerprint that has made it easy to identify this motif in proteins.[80] Regardless of the number (4, 5, 6, or 7), geometry (tetrahedral, square pyramidal, tetragonally distorted octahedral, or pentagonal bipyramidal), and type of ligands (halide, RO^-, $RCOO^-$, aliphatic N, or aromatic N) around the iron center, and of the Fe—O—Fe angle, the magnetic susceptibility at room temperature lies in the range 1.5 to 2.0 Bohr magnetons per Fe^{III}—O—Fe^{III} group, equivalent to about one unpaired electron. [81,82] In other words, the high-spin ($S = \frac{5}{2}$) iron centers are strongly antiferromagnetically coupled. Other bridging groups, such as OH^-, Cl^-, carboxylate, alkoxide, or phenoxide, give very weak coupling.[83-86]

The asymmetric Fe—O stretch, ν_{as}(Fe—O), lies in the range 730 to 880 cm^{-1}; in multiply bridged complexes this mode is weak in the infrared region. The symmetric vibration, ν_s(Fe—O), forbidden in the infrared region for linear, symmetric Fe—O—Fe groups, occurs in the range 360 to 545 cm^{-1}. The symmetric mode is usually,[87a] but not always,[87b] observed by resonance Raman techniques upon irradiating on the low-energy side of the Fe—O chargetransfer band that occurs at about 350 nm.

Few dinuclear iron(II) complexes are known where the ligands approximately resemble those believed or known to occur in the family of μ-oxodiiron(III) proteins.[88] The dioxygen-binding process in hemerythrin has no close nonbiological analogue. Although spectroscopically similar to oxyhemerythrin, the unstable monomeric purple peroxo complex formed by the addition of hydrogen peroxide to basic aqueous Fe^{III}(EDTA) solutions remains structurally uncharacterized.[89,90]

Oxidation and Spin State of Iron Porphyrins

Iron porphyrins, the active sites of the hemoglobin family, have a rich magnetochemistry.[91] Iron porphyrins may be octahedral (two axial ligands), square pyramidal (one axial ligand), or square planar (no axial ligand). The metal d orbitals, now having partial porphyrin π^* character, are split, as shown in Figure 4.16. The radius of the metal atom is much greater when it is high spin (S = 2 for Fe^{II}, S = $\frac{5}{2}$ for Fe^{III}) than when it is low spin (S = 0 for Fe^{II}, S = $\frac{1}{2}$ for Fe^{III}). This difference influences Fe—N_{porph} separations, porphyrin conformation, and the displacement of the iron center with respect to the porphyrin plane. For iron(II)-porphyrins, two strong-field axial ligands, such as a pair of imidazoles or an imidazole and carbon monoxide, lead to diamagnetic complexes (S = 0) with the six 3d electrons occupying those orbitals of approximate t_{2g} symmetry. In a classic experiment in 1936, Pauling and Coryell proved that oxyhemoglobin and carbonmonoxyhemoglobin are diamagnetic.[92]*

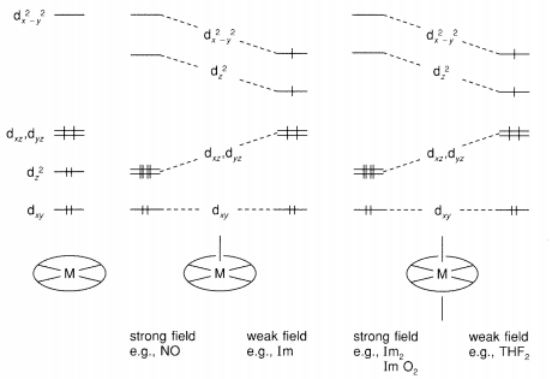


Figure 4.16 - d-Orbital splitting in metalloporphyrins as a function of number and ligand-field strength of ligands.[91] Orbital occupancy is illustrated for a d^6 species (Fe^{II} or CO^{III}).

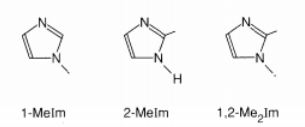
---

* There was a considerable flurry of interest when an Italian group, using a SQUID (Superconducting Quantum Mechanical Interference Device), reported that at room temperature oxyhemoglobin was significantly paramagnetic.[93] Not surprisingly, several theoretical papers followed that "proved" the existence of low-lying triplet and quintet excited states[94-96] Subsequently, the residual paramagnetism was doubted[97] and shown to arise from incomplete saturation of hemoglobin by O_2; in other words, small amounts of deoxy hemoglobin remained[98] Since oxygen affinity increases with decreased temperature, the concentration of paramagnetic impurity decreased with decreasing temperature.

No axial ligands at all may lead to a spin state of S = 1, with unpaired electrons in the d_{xy} and d_{z2} orbitals. Five-coordinate iron(II)-porphyrinato complexes are commonly high spin, S = 2, although strong σ-donor π-acceptor ligands, such as phosphines, carbon monoxide, nitric oxide, and benzyl isocyanide,[99] enforce a low-spin state. Five-coordinate iron(II)-porphyrinato complexes with aromatic nitrogenous axial ligands, such as pyridine or 1-methylimidazole, bind a second such axial ligand 10 to 30 times more avidly than the first to give the thermodynamically and kinetically (d^6, S = 0) stable hemochrome species, a process that is avoided by hemoglobins. That is, the equilibrium constant for the following disproportionation reaction is greater than unity,

$$Fe\text{—}N + Fe\text{—}N \rightleftharpoons N\text{—}Fe\text{—}N + Fe \tag{4.33}$$

except for bulky ligand N, such as 2-methylimidazole and 1,2-dimethylimidazole, for which the five-coordinate species predominates at room temperature even with a mild excess of ligand:[100]



(4.34)

For iron(III)-porphyrinato complexes, strong-field ligands lead to low-spin ($S = \frac{1}{2}$) complexes. A pair of identical weak-field ligands, such as tetrahydrofuran, leads to intermediate-spin ($S = \frac{3}{2}$) species. Five-coordinate species are, with few exceptions, high-spin ($S = \frac{5}{2}$), with all five 3d electrons in separate orbitals. Spin equilibria $S = \frac{1}{2} \rightleftharpoons S = \frac{5}{2}$ and $S = \frac{3}{2} \rightleftharpoons S = \frac{5}{2}$ are not unusual. Specific examples of these spin systems are given in Table 4.4.[65,91] Higher oxidation states are found in some other hemoproteins. Fe(V)-porphyrin systems actually occur as Fe(IV)-porphyrin cation radical species, and Fe(I)-porphyrin systems exist as Fe(II)-porphyrin anion radical species.

Substantial structural changes occur upon the addition of ligands and upon changes in spin state. In one mechanism of cooperativity these changes are the "trigger" (metrical details are deferred until the next section). Spectral changes in the UV-visible region are observed also (Figure 4.17)[10] and may be monitored conveniently to evaluate the kinetic and thermodynamic parameters of ligand binding to hemoglobin.

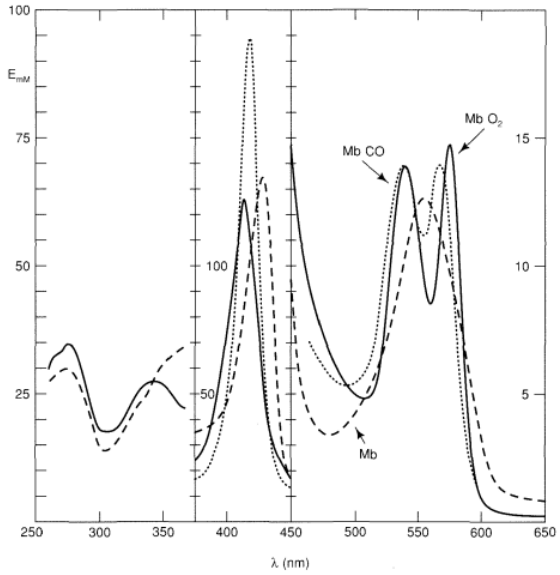


Figure 4.17 - Spectral changes accompanying the oxygenation and carbonylation of myoglobin.[10] Reproduced with permission from E. Antonini and M. Brunori, Hemoglobin and Myoglobin in Their Reactions with Ligands, North Holland, 1971.

Table 4.4 - Oxidation and spin states of iron porphyrins and their biological occurrences

a) Could be placed in Fe^{III} column

b) Could be placed in Fe^{III} column with spin = 0.

c) Non-linear Fe—NCS moiety.

State	Fe^{II}		Fe^{III}	
High spin	Fe(PF)(2-MeIm) Hb	5-coord	Fe(TPP)Cl Cytochrome P-450(ox)	5-coord
Fe^{II} $S = 2(d^6)$ Fe^{III} $S = \frac{5}{2}(d^5)$	Fe (TPP)$(THF)_2$ Hb(H_2O)?	6-coord	$[Fe(TPP)(H_2O)_2]^+$ $[Fe(OEP)(3\text{-}ClPy)_2]^+$ (293 K) Fe(OEP)(Py)(NCS) Met Hb(H_2O)	6-coord
Intermediate spin Fe^{II} $S = 1$ (d^6) Fe^{III} $S = \frac{3}{2}(d^5)$	Fe(TPP) no biol. occurrence	4-coord	$[Fe(TPP)(C(CN)_3)]_n$ Fe(TPP)$(OClO_3)$ ($S = \frac{3}{2}, \frac{5}{2}$) cytochrome c'	
Low spin Fe^{II} $S = 0(d^6)$ Fe^{III} $S = \frac{1}{2}(d^5)$ ($S = \frac{1}{2}$, Fe—NO adducts)	Fe(TPP)(NO)[a] Hb(NO)·DPG(T)	5-coord	[Fe(TPP)(Ph)]	5-coord
	Fe(PF)(2-MeIm)(O_2)[b] Fe(TPP)(1-MeIm)(NO) Fe(TPP)(Py)(CO) Fe(TPP)(1-MeIm)$_2$ Hb(CO), Hb(NO),[a] Hb(O_2)[b] cytochrome b_5, c, c_3	6-coord	$[Fe(TPP)(Im)_2]^+$ $[Fe(OEP)(3\text{-}Cl\text{-}Py)_2]^+$ (98 K) Fe(TPP)(Py)(CN) Fe(TPP)(Py)(NCS)[c] cytochrome b_5, c, c_3 metHb (CN)	6-coord

4.8: General Aspects of the Chemistry of Iron is shared under a CC BY-NC-SA 4.0 license and was authored, remixed, and/or curated by LibreTexts.