4.12: Other Ligands for Biological Oxygen Carriers

As noted above, a variety of other α-donor or π-acceptor ligands will bind to the active sites of biological oxygen carriers.

Carbon Monoxide

As documented in Table 4.2, carbon monoxide (CO) generally binds more strongly to hemoglobin than does dioxygen, hence causing carbon-monoxide poisoning. In addition to being readily available from car exhausts and tobacco smoke to convert oxyhemoglobin to carbonmonoxyhemoglobin, CO is produced in the catabolism of heme molecules.[117] Thus under even the most favorable of conditions, about 3 percent of human hemoglobin is in the carbonmonoxy form. When CO binds to a single metal atom in nonbiological systems, *without exception* it does so through the carbon atom and in a linear manner:[56]

$$Fe—C=O \leftarrow Fe^{II} + {}^{-}C=O^{+} \tag{4.40}$$

Model systems for carbonmonoxy (also called carbonyl) hemoglobin show a geometry similar to that of the Fe—C≡O group, linear or nearly so and essentially perpendicular to the porphyrin plane.[110,118-121] The biochemical literature is littered with reports that this is *not* the geometry adopted by CO in binding to hemoglobins.[122-128] We will return to this topic later in this chapter, since the physiological consequences are potentially important.

Carbon monoxide binds weakly as a σ-donor ligand to four-coordinate cobalt(II) systems.[129] Despite a bout of artifactual excitement,[130] CO has never been observed to bind significantly to five-coordinate Co^{II} systems with a nitrogenous axial base to yield octahedral six-coordinate species.[131] The sulfur analogue thiocarbonyl (CS), although not stable as a free entity, binds very strongly to iron-porphyrin species in a linear manner.[132]

Nitric Oxide

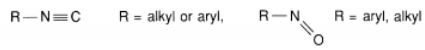
Nitric oxide (NO) binds to hemes even more strongly than CO (and hence O_2),[10] so strongly, in fact, that the Fe—N_{1m} bond is very weak and easily ruptured.[11,111,133] Attachment to the metal is via the nitrogen atom; however, the geometry of attachment is sensitive to the π basicity of the metalloporphyrin, and ranges from linear to strongly bent. In binding to Co^{II} the NO ligand is effectively reduced to NO^{-}, with concomitant oxidation of Co^{II} to Co^{III}.:[111]

(4.42)

In much the same way that cobalt-dioxygen systems are paramagnetic (S = $\frac{1}{2}$) and amenable to EPR studies, iron-nitric oxide (also called iron nitrosyl) species are also paramagnetic and isoelectronic with cobalt-dioxygen species. The unpaired spin is localized mostly on the NO group.

Isocyanide and Nitroso Species

In contrast to the dioxygen, carbon-monoxide, and nitric-oxide ligands, the isocyanide and nitroso functions bear an organic tail. Moreover, nitroso ligands are isoelectronic with dioxygen.



(4.42)

Thus, in principle, not only may the steric bulk of the ligand be varied, in order to probe the dimensions[35] of the dioxygen-binding pocket,* but also the σ-donor/π-acceptor properties of the ligands may be varied by appropriate substituents on the aryl ring.

Isocyanide groups may bind to metals in a variety of ways. For 1:1 adducts (Figure 4.19), the isocyanide group is approximately linear, although some flexibility seems to exist in a bis(t-butylisocyanide)iron(Il)tetraphenylporphyrinato complex.[135] For zerovalent metals with much electron density available for donation into ligand π^* orbitals, the isocyanide ligand has been observed to bend at the N atom.[136] One prediction exists that an isocyanide ligand binds in this manner to hemoglobin.[137]

For 1:1 adducts of nitroso ligands, side-on,[138] O-, and N-ligated modes are possible (Figure 4.19). No O-nitroso complexes have been definitively characterized by diffraction methods. For hemoglobin the N-nitroso mode is likely, since this is the mode found

for the nitrosoalkane in Fe(TPP)(amine)(RNO).[139]

To date isocyanide ligands have not achieved their potential as probes of the geometry of the ligand-binding pocket in hemoglobin, partly because we lack structural data on the preferred geometry of attachment of these ligands in a sterically uncongested environment.

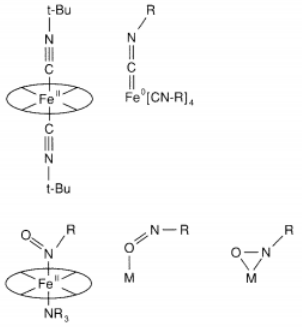


Figure 4.19 - Modes of coordination of isocyanide and nitroso species.

* In fact, this classic experiment of St. George and Pauling established, for the first time and before any crystallographic data were available, that the heme group and the ligand-binding site in hemoglobin reside at least partway inside the protein, rather than on the surface.[134]