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O_2 and CO Binding to Iron(II) Porphyrins: A Comparison of the "Picket Fence" and "Pocket" Porphyrins[1a]

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Abstract: Kinetic and equilibrium O_2 and CO binding behavior for various iron(II) porphyrin systems are reported. Compared to the "picket fence" complexes, unprotected iron(II) porphyrins have both lowered ligand affinities and lowered ligand association rates. This is explained in terms of a solvation effect which stabilizes the five-coordinate form in the unprotected iron(II) porphyrins. Five-coordinate iron(II) complexes of the sterically encumbered "medium" and "small" "pocket" porphyrins show substantially reduced CO affinities as compared to the analogous open-cavity "picket fence" complexes. Kinetic data indicate that the lowered CO affinities in the "pocket" complexes are primarily reflected in decreased association rates. By contrast, the "pocket" models show both decreased O_2 dissociation and association rates as compared to the "picket fence" analogues. As such, the O_2 affinities are virtually identical throughout the series of "pocket" and "picket fence" complexes. These results are discussed in terms of distal-side steric interactions.

Understanding the role the protein plays in regulating the binding of small ligands to hemoproteins continues to be a topic of active interest.[2-6] In particular, recent attention has focused on whether the heme cavity sterically discriminates between small ligands such as CO and O_2, thereby affecting their relative binding affinities.[4-6] Structural analyses in carbonylated hemoproteins reveal that the CO unit is bent and/or tilted from the perpendicular to the porphyrin plane, owing to interactions with the distal residues.[7] In structures of oxygenated hemoproteins the O_2 unit is found to be bent.[8] In Fe(II) porphyrin systems, free from protein effects, the FeCO unit is linear and normal to the porphyrin plane,[9] whereas O_2 binds in a bent fashion.[10] We[11,12] and others[13,14] have proposed that in hemoproteins distortion of the FeCO unit reduces CO affinities without affecting the O_2 affinity of the intrinsically bent FeO_2 group.[2b-d,8,10] This so-called "distal-side steric effect"[15] could serve as an important detoxification mechanism for CO.[11]

Studies with iron(II) porphyrins offer the possibility of modeling various aspects of hemoprotein reactivity[16-18] as well as exploring specific structure-function relationships in well-characterized systems.[19,20] In order to explore the role of distal steric effects

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in model porphyrins, we[21] and others[22-26] have been studying the CO and O_2 binding behavior of sterically encumbered iron(II) complexes. As yet, no clear picture has emerged from these studies, since evidence both for[21,23] and against[22,24] the discriminatory binding of CO relative to O_2 has been presented. In order to carry out valid comparisons, however, it is necessary to identify all extraneous effects and assess their relative importance. The factors influencing CO and O_2 affinities in simple iron(II) porphyrins continue to be investigated.[27-31] In order to explore these factors more fully, we have carried out extensive equilibrium studies of ligand binding to various iron(II) porphyrins. In conjunction with those in the literature, these results establish that (1) simple hemes bind CO and O_2 with a ca. "order of magnitude" *lower* affinity than the "picket fence"[32] porphyrins (Figure 1) and that (2) valid comparisons *can* be made between the open-cavity "picket fence" and sterically encumbered "pocket" porphyrin (Figure 1) complexes. On the basis of these comparisons we conclude that steric encumbrance *can* reduce CO binding affinity relative to that of O_2 in model iron(II) porphyrin compounds and

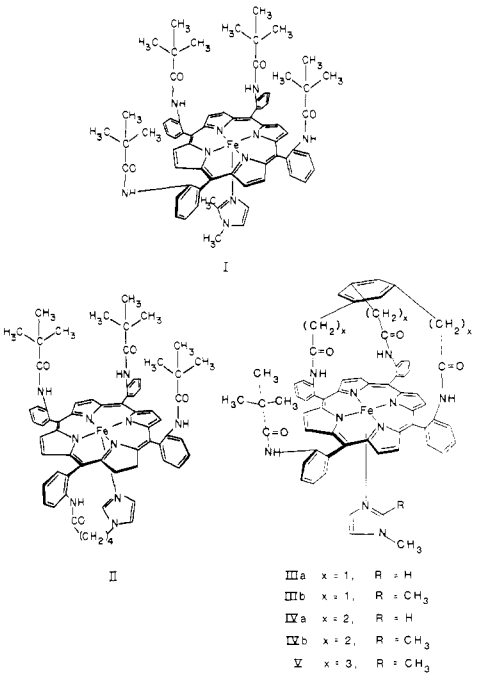

Figure 1. Five-coordinate iron(II) porphyrins: FeTPivP(1,2-Me_2Im), I; $FePiv_35CIm$, II; FePocPiv(1-MeIm), IIIa; FePocPiv(1,2-Me_2Im), IIIb; FeMedPoc(1-MeIm), IVa; FeMedPoc(1,2-Me_2Im), IVb; FeTalPoc(1,2-Me_2Im), V.

therefore *may* play a role in regulating ligand binding in natural hemoprotein systems. Kinetic studies with the "picket fence" and "pocket" complexes[32] indicate that increased steric encumbrance leads to reduced O_2 association *and* dissociation rates. By contrast steric encumbrance serves to reduce only CO association rates.

The equilibria of interest in this study are as follows:

$$P + B \underset{k_{-B}}{\overset{k_B}{\rightleftharpoons}} P(B) \quad (1)$$

$$K_B = k_B/k_{-B}$$

$$P(B) + B \underset{k_B^{-B}}{\overset{k_B^{B}}{\rightleftharpoons}} P(B)_2 \quad (2)$$

$$K_B^{B} = k_B^{B}/k_B^{-B}$$

$$P(B) + L \underset{k_B^{-L}}{\overset{k_B^{L}}{\rightleftharpoons}} P(B)(L) \quad (3)$$

$$K_B^{L} = k_B^{L}/k_B^{-L}$$

$$P(B)(O_2) + CO \rightleftharpoons P(B)(CO) \quad (4)$$

$$M = K_B^{CO}/K_B^{O_2}$$

where P represents the porphyrinato ligand, B an axial base, and L a gaseous ligand, either CO or O_2. For a sterically unhindered nitrogenous base (such as 1-methylimidazole), K_B^B is greater than K_B for simple unprotected iron(II) porphyrins.[33] This precludes the *direct* measurement of K_B^L according to eq 3.[34] When sterically hindered bases (such as 1,2-dimethylimidazole) are used, the value of K_B^B is reduced[35,36] and K_B^L can often be measured directly.[34] The value of K_B^L so obtained[34,36] is, however, found to be lower than that derived for complexes formed from unhindered bases.

Furthermore, simple iron(II) porphyrin complexes irreversibly oxidize when exposed to O_2 in solution at room temperature,[37-40]

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whereas sterically protected ones, such as the "picket fence" porphyrin, do not.[16,19] To date, therefore, solution equilibrium studies with models have focused on systems which overcome these problems in one of two ways: (1) sterically inhibiting irreversible oxidation, while covalently attaching an axial base so as to enforce five-coordination about iron (i.e., effectively reducing K_B^B to zero), or by (2) encumbering one face of the porphyrin in a manner sufficient to preclude the coordination of a second axial ligand while preventing oxidation (of course gaseous ligand binding must still be allowed). The first of these approaches was demonstrated with the iron(II) "tailed" "picket fence"[32] porphyrins;[41] the second by the elegant "capped" porphyrins[32] of Baldwin and Basolo et al.[19] Analogous control of coordination was observed in our own "pocket" porphyrins.[21,42] These "pocket" porphyrin systems form stable oxygen complexes, and therefore both O_2 affinities (eq 3) and CO vs. O_2 competition equilibria (eq 4) may be directly measured. CO affinities were obtained from these values, and in several cases directly measured (eq 3) as well.

When five-coordination about iron(II) is maintained following flash photolysis, ligand binding to a photolabile complex FeP(B)(L) occurs according to eq 5.[43] For simple iron(II) porphyrins,

$$\mathrm{FeP(B)(L)} \xrightarrow{h\nu} \mathrm{FeP(B)} \underset{k_B^{-L}}{\overset{k_B^{L}}{\rightleftharpoons}} \mathrm{FeP(B)(L)} \qquad (5)$$

complications arising from the formation of either the four-coordinate unligated or six-coordinate bis-ligated species (eq 1 and 2) occur.[43,44] To overcome this, Traylor and co-workers have synthesized simple iron(II) porphyrins bearing covalently attached axial ligands.[18] The CO binding to these systems has been extensively investigated.[18] These complexes do not form stable dioxygen adducts. The competitive rebinding technique[45] has been used to determine O_2 binding parameters (eq 6) and affinities.[18]

$$\mathrm{FeP(B)(CO)} \underset{k_B^{CO}}{\overset{h\nu}{\rightleftharpoons}} \mathrm{FeP(B)} \underset{k_B^{-O_2}}{\overset{k_B^{O_2}}{\rightleftharpoons}} \mathrm{FeP(B)(O_2)} \qquad (6)$$

$$k_R$$

When stable O_2 complexes of iron(II) porphyrins are formed, O_2 binding affinities may be directly determined with *both* kinetic and equilibrium methods. Thus, the congruency of these two methods can be checked; indeed, this was an ancilliary objective in undertaking the present study.[46] Interestingly, of the six air-stable complexes (I, II, IIIa,b, IVa,b) so investigated, the kinetically and thermodynamically determined O_2 affinities agree for only three (I, II, IVb). This discrepancy originates in the difficulty associated with accurately determining O_2 dissociation rates for the more sterically encumbered members of the "pocket" porphyrin series. In general, reliable ligand association rates (for O_2 and CO) could be obtained for the "picket fence" and "pocket" porphyrin complexes.

Experimental Section

Materials. All solvents and reagents were purchased commercially and further purified as detailed in ref 42 or as follows. Methanol was distilled from $Mg(OMe)_2$ under N_2. Acetonitrile and benzonitrile were distilled from CaH_2 under an N_2 atmosphere at reduced pressure and stored over 3-Å molecular sieves. Iron powder was converted to $FeBr_2$ by literature procedure.[47] Prepurified N_2, CO, and O_2 gases were obtained from either Liquid Carbonic or Matheson. Premixed gases, 0.140% and 2.05% O_2 in N_2 and 2.65% and 4.95% CO in N_2 were Liquid Carbonic certified mixtures. Premixed 0.047% CO in N_2 was obtained from Airco Specialty Gases, as an analyzed (nondispersive IR) mixture.

Synthesis. The following compounds[32] were prepared as described in the literature: H_2TPP,[48,49] H_2OEP,[48] H_2TMesP,[50] H_2TPivP,[51] $H_2T(pCl)PP$,[50] H_2TTP,[48] $H_2PocPiv$,[21] $H_2MedPoc$,[21] $H_2TalPoc$,[21] H_2AmPoc.[42] Iron(II) was inserted in the usual manner[41] to yield the four-coordinate, iron(II) porphyrins, FeP. H_2Piv_35CIm and $H_24CImPP$ were prepared by literature methods and iron inserted to yield the five-coordinate ferrous complexes.[41] Iron insertions and all subsequent manipulations requiring the exclusion of oxygen were carried out under N_2 in a Vacuum Atmospheres drybox equipped with an MO-40 Dri-Train. In general, solutions of FeP(B) were made up from FeP directly prior to use. For long-term storage, however, solid samples of five-coordinate iron(II) complexes of I, IIIa,b, IVa,b, and B could be precipitated from toluene solutions by the slow addition of heptane. For kinetic studies, solid five-coordinate samples were transported to Ithaca under N_2, where further manipulations requiring the exclusion of oxygen were carried out in a homemade N_2 box equipped with an O_2 scrubbing tower (Ridox catalyst, BASF).

Equilibrium Measurements. The O_2, CO affinity and M values were measured spectrophotometrically under equilibrium conditions with a Cary 219 spectrophotometer. Unless otherwise noted, measurements were made with toluene solutions thermostated in the spectrophotometer to 25.0 ± 0.3 °C with a FormaScientific Model 2095 constant-temperature bath and circulator. Appropriate concentrations of axial base were used to ensure samples of initially five-coordinate iron(II) porphyrins. In practice, a range of base concentrations were used to check the base concentration independence of the values obtained for equilibria 3 and 4 (cf. Results).

CO and O_2 affinities for oxygen stable complexes were measured by the flow method.[30] Solutions of the five-coordinate iron(II) porphyrin complexes were prepared in the drybox and transferred to a 1.0-cm path length flow cuvette. This cuvette was equipped with gas inlet and outlet tubes attached to a gas-mixing apparatus, similar to the one described earlier.[30] This assembly allowed sets of optical spectra for the iron(II) porphyrin solution to be recorded in the absence of and at various increasing partial pressures of gaseous ligand. In general, concentrations of metalloporphyrin of 50 μM were used and spectral changes in the 700–480-nm range were monitored. Our original gas-mixing apparatus has been slightly modified by the addition of a third Matheson calibrated rotometer. This allows either (1) various quantities of pure O_2 (or prediluted O_2 in N_2) to be mixed with N_2, (2) various quantities of pure CO (or prediluted CO in N_2) to be mixed with N_2, or (3) various quantities of pure CO (or prediluted CO in N_2) to be mixed with pure O_2. Reliable O_2 (or CO) partial pressures of between 3×10^{-2} (and 1×10^{-2}) and 730 torr, and P_{CO} to P_{O_2} ratios of between 2×10^{-5} and 1 could be obtained with this assembly. With this modified apparatus, both an O_2 affinity and M value determination could be made with the same sample. In practice, the oxygen affinities were obtained by directly equilibrating the five-coordinate complex with increasing partial pressures of O_2 until oxygenation was complete. The sample could then be equilibrated with mixtures of increased CO in O_2 until carbonylation was complete, thus determining the M value. The solution of the resulting carbonyl complex could then be bubbled with either N_2 or O_2 so as to check the reversibility of reactions 3 or 4. (Similarly, the reversibility of oxygenation could be checked by directly rebubbling a solution of the O_2 complex with N_2.) When CO affinities were low enough to allow direct measurement, they were determined directly by bubbling solutions of the five-coordinate porphyrin complex with CO/N_2 mixtures in a manner analogous to that used in measuring O_2 affinities.

For compounds which do not form kinetically stable O_2 complexes, the CO affinities were measured by using a 100-mL tonometer fused onto

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(46) Prior to this present investigation, only one other study[23] has appeared in which the O_2 affinity of an iron(II) porphyrin was independently measured by both equilibrium and kinetic methods. A complete discussion of CO binding to simple iron(II) porphyrins as measured by both equilibria and kinetic methods is given in ref 43.

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a 0.1-cm cuvette. The tonometer was sealed with a Teflon stopcock and rubber serum stopper. Known amounts of CO or prediluted CO in N_2 were anaerobically injected into the tonometer, and the sample was allowed to equilibrate. Metalloporphyrin concentrations of (2–5) × 10^{-5} M were used and spectral changes were monitored in the 500–350-nm region. This technique proved to be slightly less reliable than the flow system in assuring true equilibration of the samples at intermediate partial pressures of CO, since equilibria could not be approached from both high and low partial pressures of CO. Nonetheless, this technique was extremely valuable in completely avoiding spurious oxidation of particularly air-sensitive samples. This method was also convenient for measuring CO affinities of FeTPP(1,2-Me_2Im) in mixed solvent systems.

Sets of spectra were recorded for a range of gaseous ligand partial pressures, and those which showed isosbestic points were used to calculate equilibrium constants for ligand binding (eq 3). We continue to prefer reporting ligand affinities as $P_{1/2}{}^{L}$ rather than as $K_B{}^{L}$.[11] Interconversion of the two is, however, straightforward;[52] it requires the solubility of the gaseous ligand L in the solvent of interest. We have taken the solubilities of O_2 in toluene and in methanol as 9.10 × 10^{-3} and 9.61 × 10^{-3} M/atm at STP. For CO we have used 7.50 × 10^{-3} and 8.37 × 10^{-3} M/atm at STP for these solvents.[53] Solubilities for mixed solvents were assumed to be a linear function of composition. Data were treated in one of two standard ways.[36,55]

Kinetic Measurements. All kinetic studies were performed at Ithaca, using laser flash photolysis techniques.[54] Laser flash photolysis experiments were carried out with a Phase R Model 2100B flashlamp-pumped dye laser (Phase R Corp., New Durham, NH) capable of generating up to 2 J of 540-nm light within 500 ns when using Pilot 495 laser dye (New England Nuclear, Westwood, MA) in absolute ethanol. Laser light attenuation was performed by using a variety of differing transmittance neutral density filters.

The detection system consisted of a 75-W xenon arc lamp (Oriel Corp., Stamford, CT) focused onto a 2-mm path length cell located in a temperature-controlled housing at 25 °C. The transmitted light was collected and refocused onto the slits of a Spex Minimate monochromator of 3-nm bandwidth. An RCA IP28 photomultiplier (RCA, Harrison, NH) detected the light and produced a proportional output current which was subsequently converted to voltage, amplified, and finally fed into the vertical amplifier of a Biomation Model 805 waveform recorder (Biomation, Cupertino, CA). The digitized signal was transferred to a PDP8f computer for signal averaging and further analysis. Data were collected at several wavelengths (λ = 440, 436, 432, 427 nm, with λ = 436 nm being usually used), using appropriate interference filters to minimize photolysis by the interrogation beam. Computer simulations of experimentally observed absorbance changes were also made with the PDP8f computer according to standard methods.[55]

In general, deoxygenated toluene (or 1:1 v/v toluene/MeOH) solutions of ca. 2 × 10^{-6} M concentrations in iron(II) porphyrin were made up directly from the solid five-coordinate complexes in a homemade N_2 atmosphere drybox. These solutions were loaded into tonometers of known volume, which were fused to optical cells of 0.1- or 0.2-mm path length. The tonometers were closed with Teflon stopcocks and serum stoppers. Known volumes of O_2 or CO were then added out of the drybox by means of gas-tight syringes. The concentrations of axial base (1-MeIm or 1,2-Me_2Im) could be systematically increased by anaerobically injecting aliquots of deaerated stock solutions containing known concentrations of base into the tonometer. In general, fresh solutions of the five-coordinate iron(II) porphyrin complex were made up for each set of experiments. When convenient, extensive flushing of the tonometer with toluene-saturated argon could be used to regenerate the unligated five-coordinate complex from the oxygenated or carbonylated species. Experiments were carried out in the range of 0–40 °C with most experiments being made at a temperature of 25.0 ± 0.1 °C.

Since simple iron(II) porphyrins can bind one or two axial ligands, 12 rate constants are needed to fully describe the interrelation of the six possible species ($FeP(B)_2$, FeP(B), FeP, FeP(CO), FeP(B)(CO), $FeP(CO)_2$) obtained following laser flash photolysis of the carbonyl complexes of simple hemes carried out in the presence of excess carbon monoxide and nitrogenous base.[43,44] With the "pocket porphyrins", III–V, one face of the porphyrin is sterically protected, thus reducing $K_B{}^{B}$ and, at equilibrium, the propensity for formation of the bis-ligated species, $FeP(B)_2$.[21] Using a sterically hindered base achieves the same effect with the "picket fence"[36] complex I. As such, raising the base concentration ensures predominance of the five-coordinate species FeP(B) at equilibrium. We therefore approached the kinetic problem by seeking conditions where direct gaseous ligand recombination to the five-coordinate species occurred exclusively. In practice, this was accomplished by carrying out separate flash photolysis experiments while varying the axial base concentration systematically over ca. four orders of magnitude. This process was then repeated at different (constant) concentrations of gaseous ligand. Regimes were sought where k_{obsd}, the rate of return to equilibrium following photolysis, was independent of axial base concentration (cf. Results). When no species other than the five-coordinate complex FeP(B) are formed following flash photolysis, recombination occurs according to eq 5 with k_{obsd} given by eq 7. Values of k_{obsd} were

$$k_{obsd} = k_B{}^{L}[L] + k_B{}^{-L} \quad (7)$$

obtained directly from log plots of the change in absorbance vs. time following laser flash photolysis. In this study, all experiments were carried out under pseudo-first-order conditions. Values of k_{obsd} were found reproducible to within 1% between successive laser "shots" on the same sample and to within better than 10% on independently prepared identical samples. In the context of the kinetic studies we have found it more convenient to work in units of concentration rather than pressure; this is in accord with the practice of other workers in this field.[22,23]

For direct recombination experiments two approaches were taken:

(1) When $k_B{}^{L}[L] \gg k_B{}^{-L}$, eq 7 reduces to eq 8. Conditions could be

$$k_{obsd} \approx k_B{}^{L}[L] \quad (8)$$

found where $k_{obsd}/[L]$ was independent of [L] for CO rebinding to the complexes I, II, IIIa,b, IVa,b, allowing eq 8 to be used. For O_2 rebinding, the assumption that $k_B{}^{O_2}[O_2] \gg k_B{}^{-O_2}$ is only valid at high bulk concentrations of O_2 (cf. Results). From the known ligand affinities, $K_B{}^{L}$, values for the dissociation rates $k_B{}^{-L}$ were calculated (eq 3).[56]

(2) When $k_B{}^{O_2}[O_2] \approx k_B{}^{-O_2}$ values of k_{obsd} were determined over a range of O_2 concentrations, and computer fit to eq 7 to yield values for $k_B{}^{O_2}$ and $k_B{}^{-O_2}$. The value of $k_B{}^{O_2}$ so derived was compared to that obtained by eq 8.

O_2 dissociation rates were also determined in select cases, using the competitive rebinding technique.[18,45] Solutions of the six-coordinate carbonyl complex were photolyzed in the presence of both O_2 and CO. Equation 6 describes the kinetics which occur following flash photolysis (assuming, of course, that no interference occurs from species such as FeP or FeP(L), which might arise from the loss of axial base in the course of the experiment). For five-coordinate iron(II) porphyrins $K_B{}^{CO} \gg K_B{}^{O_2}$ and $k_B{}^{CO}[CO] < k_B{}^{O_2}[O_2]$ for a wide range of $[O_2]$ and [CO]. As such, photolysis of FeP(B)(CO) in the presence of an appropriate CO and O_2 mixture shows first a rapid recombination to mostly $FeP(B)(O_2)$ followed by a slow return to FeP(B)(CO). Assuming that the CO dissociation rate $k_B{}^{-CO}$ is small in the absence of light, the following equations pertain:

$$k_{obsd}(\text{fast}) = k_B{}^{O_2}[O_2] + k_B{}^{-O_2} + k_B{}^{CO}[CO] \quad (9)$$

$$k_{obsd}(\text{slow}) = k_B{}^{CO}k_B{}^{-O_2}[CO]\left(\frac{1}{k_B{}^{CO}[CO] + k_B{}^{O_2}[O_2]}\right) \quad (10)$$

After measurement of both the fast and slow rates of recombination over a range of CO and O_2 concentrations, the above equations were computer fit to yield values for $k_B{}^{CO}$, $k_B{}^{O_2}$, and $k_B{}^{-O_2}$. Alternatively, rearrangement of eq 10 gives the Gibson equation (eq 11):

$$1/k_{obsd}(\text{slow}) = \frac{1}{k_B{}^{-O_2}} + \frac{k_B{}^{O_2}[O_2]}{k_B{}^{-O_2}k_B{}^{CO}[CO]} \quad (11)$$

A plot of $1/k_{obsd}$(slow) vs. $[O_2]/[CO]$ should yield a straight line with slope $k_B{}^{O_2}/k_B{}^{-O_2}k_B{}^{CO}$ and intercept $1/k_B{}^{-O_2}$. The values for $k_B{}^{O_2}$ and $k_B{}^{CO}$ could be compared to those obtained by the direct recombination method (eq 7), and the value for $K_B{}^{O_2}$ obtained kinetically with that determined under equilibrium conditions.

The enthalpy and entropy of activation for ligand association were determined by measuring ligand rebinding rates (≥four) over at least a 35 °C range in temperature. A plot of ln $[hk_B{}^{L}/kT]$ vs. $1/T$ should be

(52) $P_{1/2}{}^{L}$ (torr) = $760/K_B{}^{L}(M^{-1})[L]_0$, where $[L]_0$ is the solubility of the gaseous ligand L in the solvent of interest in M/atm. Similarly, $k_B{}^{L}$ (M^{-1} s^{-1})$[L]_0$ = $k_B{}^{L}(atm^{-1}\ s^{-1})$.

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(56) No CO dissociation rates were measured in this study; they are best measured by stopped-flow methods.[57] Toluene was found incompatible with our stopped-flow apparatus.

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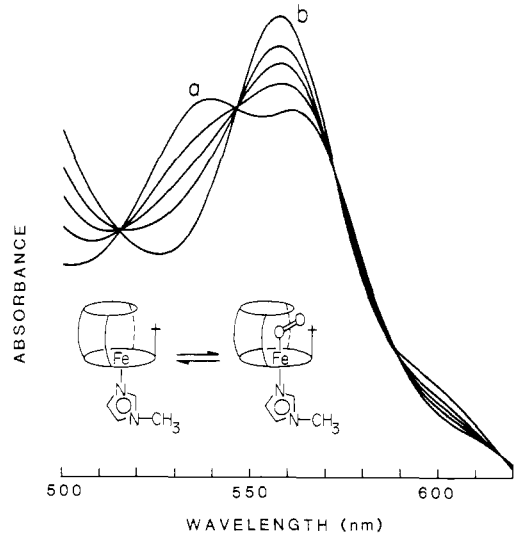

Figure 2. Determination of $P_{1/2}^{O_2}$ for FePocPiv(1-MeIm) (IIIa). IIIa, ca. 5×10^{-5} M in toluene, 1.0 M in 1-methylimidazole, 25.0 °C: (curve a) under 1 atm of N_2; (curve b) under 1 atm of O_2. Intermediate curves produced by diluting N_2 with increased partial pressures of O_2. The following intermediate partial pressures of O_2 were used: 0.076, 0.358, and 1.03 torr.

linear, with slope of $-\Delta H^{\ddagger}_{assoc}/R$ and intercept of $\Delta S^{\ddagger}_{assoc}/R$.

Results

Equilibrium Results, O_2 Binding. Exposing dilute toluene solutions of FePocPiv(1-MeIm), IIIa, FePocPiv(1,2-Me_2Im), IIIb, FeMedPoc(1-MeIm), IVa, FeMedPoc(1,2-Me_2Im), IVb, or FeTalPoc(1,2-Me_2Im), V, to air in the absence of a large excess of the appropriate coordinating base leads to rapid, irreversible oxidation to the μ-oxo dimers.[21,42] When sufficiently high concentrations of axial base are used, however, kinetically stable oxygen adducts are reversibly formed.[21,42] The equilibrium constant for oxygenation could therefore be directly determined. In order to ensure that the equilibrium constants measured are indeed those referring to O_2 binding according to eq 3, it is necessary to establish that at these high concentrations of base, five-coordination pertains about iron in the absence of O_2 or other gaseous ligands.[42] If ligand binding is occurring according to eq 3, then the following two criteria will be met: (1) adequate isosbestic behavior will be maintained during the course of a spectrophotometric "titration", and (2) values of $P_{1/2}^{L}$ obtained at various concentrations of axial base will be identical. The specific results of our equilibrium gas binding experiments to five-coordinate iron(II) porphyrins are now discussed in terms of the two criteria mentioned above.

Provided base concentrations of 0.3 M are used, clean isosbestic points are observed in the series of optical spectra obtained when toluene solutions of initially five-coordinate FePocPiv(1-MeIm) (IIIa) (or FePocPiv(1,2-Me_2Im) (IIIb)) are equilibrated with increasing partial pressures of oxygen (Figure 2). Moreover, when the axial base concentration is varied between 0.1 and 1.0 M, virtually identical sets of spectra are obtained for IIIa (or IIIb) if the same increases in O_2 partial pressures are used. We conclude that O_2 binding is occurring according to eq 3 without interference from formation of a six-coordinate, bis-ligated species, FePocPiv(1-MeIm)$_2$ (or FePocPiv(1,2-Me_2Im)$_2$). The $P_{1/2}^{O_2}$ values so obtained (Tables I and II) show no dependence on axial base concentration and all agree within ±15%.

Toluene solutions of FeMedPoc(1,2-Me_2Im) (IVb) produce isosbestic spectra throughout O_2 binding experiments when the 1,2-Me_2Im concentration is no higher than 0.3 M. Repeated experiments yielded $P_{1/2}^{O_2}$ values consistent to within ±15%. When the 1,2-Me_2Im concentration is raised to 0.5 M, the O_2 binding spectra remain isosbestic only through ca. 95% conversion to FeMedPoc(1,2-Me_2Im)(O_2), with deviation occurring at the higher P_{O_2} values. This suggests that at these higher 1,2-Me_2Im concentrations (in the absence of O_2) a small quantity of the

Table I. O_2 and CO Binding to R-State Models of Hemoglobin[a]

	k_B^{CO}, M^{-1} s^{-1}	k_B^{-CO}, s^{-1}	$P_{1/2}^{CO}$, torr	$k_B^{O_2}$, M^{-1} s^{-1}	$k_B^{-O_2}$, s^{-1}	$P_{1/2}^{O_2}$, torr	M	ref
Mb[b] [0.1 M KP_i]	$3–5 \times 10^5$	0.0015–0.04	0.014–0.025	$1–2 \times 10^7$	10–30	0.37–1	20–40	29, 58
HbA, R state[b] [0.05–0.1 M KP_i] α	4.6×10^6	0.009	0.0014[g]	3.3×10^7	13.1	0.22	150	73–76
β					12.1	0.36	190	
Hb chains[b] [0.2 M KP_i] α_A^{SH}	4×10^6	1.3×10^{-2}	0.0025	5×10^7	28	0.46	180	2a, 71
β_A^{SH}	4.5×10^6	8×10^{-3}	0.0016	6×10^7	16	0.45	250	
Hb^{Zn} isolated mutant chain[b] [0.2 M KP_i] β_{SH}^{Zn}	2.2×10^7			6.5×10^7	34	0.31[g]		72
Hb^{Zn} tetramer[b] [0.1 M KP_i]			1.0×10^{-3} [f]				>500[h]	2d
FeTPP4ClIm[c]			2.4×10^{-4} [h]					this work
DHD(Im)[d] [0.001–0.008 M]	1.2×10^7	0.28	2.3×10^{-4} [g]	6.2×10^7	4200	5.6[g]	24 000[g]	34, 43
chelated protoheme[d]	1.1×10^7	0.25[i]	4.9×10^{-4} [g]	5.3×10^7 [j]	1700[j]	2.8[g]	5700[g]	22, 29, 58
chelated mesoheme[d]	1.04×10^7	~0.05	2.2×10^{-5} [k]	4.3×10^8	2900	0.58[e]	26 600[e]	18, 22, 69
$FePiv_3$5ClIm[c] (II)	3.6×10^7	7.8×10^{-3} [m]	4.3×10^{-3} [k]					this work, 11, 12
FePocPiv(1-MeIm)[c] (IIIa) [0.1–1 M]	5.8×10^5	8.6×10^{-3} [m]	1.5×10^{-3} [k]	2.2×10^6	9[g]	0.36[e]	270[e]	this work, 21
FeMedPoc(1-MeIm)[c] (IVa) [0.1–0.5 M]	1.5×10^6	9.4×10^{-3} [m]	6.5×10^{-4} [k]	1.7×10^7	71[g]	0.36[e,p]	550[e]	this work
6,6-cyclophane(1,5DCl)[d] [1.2 M]	3×10^4	0.05	0.169[g]	1×10^5	800[g]	696[g]	41004[g]	22
7,7-cyclophane(1,5DCl)[d] [0.03–0.08 M]	6×10^6	0.05	9.2×10^{-4} [g]	6.5×10^7	1000	1.4[g]	15004[g]	22
FeCu5(THPIm)[d] [0.2 M]	9×10^4	0.02	0.02[g]	1.8×10^6	91	5[e]	2504[g]	22
FeCu4(1-MeIm)[d] [0.2 M]	2×10^4	0.02	0.1[g]	5.2×10^5	160	31[e]	3104[g]	23
Fe(C_2-cap)(1-MeIm)[c] [1.0 M]	9.5×10^5	0.05	5.4×10^{-3}			23[l]	4300[o]	19d, 24
Fe(C_3-cap)(1,5DCl)[c] [1.0 M]	4.1×10^6	0.17	4.1×10^{-3}					24

[a] Errors ≤±15%, unless otherwise noted. [b] Aqueous, pH 7–7.4, 20 °C. [c] 25 °C, toluene. [d] 20 °C, benzene. [e] Measured by the flow technique. [f] Measured with the tonometer. [g] Derived from kinetic measurements. [h] Measured by competition. [i] 1:20 MeOH:toluene. [j] 9:1 Toluene:CH_2Cl_2, 22 °C. [k] Calculated from $P_{1/2}^{O_2}$ and M value. [l] Calculated from thermodynamic values. [m] Calculated from $P_{1/2}^{CO}$ and k_B^{CO}. [n] Calculated from $P_{1/2}^{O_2}$ and $k_B^{O_2}$. [o] Calculated from $P_{1/2}^{O_2}$ and $P_{1/2}^{CO}$. [p] ±20% Error.

Table II. O_2 and CO Binding to T-State Models of Hemoglobin[a]

	k_B^{CO}, M^{-1} s^{-1}	k_B-CO, s^{-1}	$P_{1/2}^{CO}$, torr	$k_B^{O_2}$, M^{-1} s^{-1}	k_B-O_2, s^{-1}	$P_{1/2}O_2$, torr	M	ref
Hb(T)[b] [0.1 M KP_i] α	2.2×10^5	0.09	0.30	2.9×10^6	180	40	135	75, 76
β				1.18×10^7	2500	140	460	77
FeTPP(2-MeIm)[c] [1×10^{-3} M]			0.74[f]					this work
FeTPP(1,2-Me_2Im) [3×10^{-3} M]	1.6×10^5	0.24[m]	0.15[f]					this work, 24
FeTTP(1,2-Me_2Im)[c] [3×10^{-3} M]			0.15[f]					this work
FeOEP(1,2-Me_2Im)[c] [3×10^{-3} M]			0.10[f]					this work
Fe(T(pOMe)PP)(1,2-Me_2Im)[c] [3.1×10^{-3} M]			0.08					24
Fe(T(*p*Cl)PP)(1,2-Me_2Im)[c] [3×10^{-3} M]			0.18[f]					this work
FeTMesP(1,2-Me_2Im) [3×10^{-3} M]			8.0×10^{-3} [f]					this work
FeTPivP(1,2-Me_2Im)[c] (I) [~0.01 M]	1.4×10^6	0.14[m]	8.9×10^{-3} [k]	1.06×10^8	46 000	38[c]	4280[c]	this work, 11
FePocPiv(1,2-Me_2Im)[c] (IIIb) [0.3–1 M]	9.8×10^4	0.055[m]	0.067[e,f]	1.9×10^6	280[n]	12.6[e]	216[e]	this work, 21
FeMedPoc(1,2-Me_2Im)[c] (IVb) [0.3–0.5 M]	2.1×10^5	0.053[m]	0.026[e]	5.2×10^6	800	12.4[e]	480[e]	this work
FeTalPoc(1,2-Me_2Im)[c] (V) [0.006–0.1 M]			1.1×10^{-3}	7.4×10^8	34 500[n]	4[e]	3500	this work
FeDHD(2-MeIm) [3×10^{-4} to 1×10^{-3} M]	9×10^5 [d,g]	0.45[d,g]	0.046[d]					34, 43
Fe(C_2-cap)(1,2-Me_2Im)[c] [1 M]			0.20			4000[l]	2×10^4 [o]	19d, 24
Fe(C_3-cap)(1,2-Me_2Im)[c] [1 M]			0.14					24

[a] Errors ≤±15%, unless otherwise noted. [b] Aqueous, pH 7–7.4, 20 °C. [c] 25 °C, toluene. [d] 20 °C, benzene. [e] Measured by the flow technique. [f] Measured with the tonometer. [g] Derived from kinetic measurements. [h] Measured by competition. [i] 1:20 MeOH:toluene. [j] 9:1 Toluene:CH_2Cl_2, 22 °C. [k] Calculated from $P_{1/2}O_2$ and M value. [l] Calculated from thermodynamic values. [m] Calculated from $P_{1/2}^{CO}$ and k_B^{CO}. [n] Calculated from $P_{1/2}O_2$ and $k_B O_2$. [o] Calculated from $P_{1/2}O_2$ and $P_{1/2}^{CO}$. [p] ±20% Error.

bis-ligated FeMedPoc(1,2-Me_2Im)$_2$ exists in equilibrium with the dominant species IVb. (K_B^B proved too small to measure directly.) $P_{1/2}^{O_2}$ could still be calculated.[36] $P_{1/2}^{O_2}$ values obtained in this way agreed to within 5% of the average value of $P_{1/2}^{O_2}$ obtained when a 0.3 M concentration of 1,2-Me_2Im was used.

Toluene solutions of FeMedPoc(1-MeIm) (IVa) oxidized too rapidly to allow $P_{1/2}^{O_2}$ determinations unless the concentration of 1-MeIm was ≳0.2 M. At this axial base concentration, the O_2 binding spectra were only isosbestic until ca. 85% conversion to FeMedPoc(1-MeIm)(O_2) (K_B^B was estimated as 0.2 M^{-1}). Repeated experiments over a range of 1-MeIm concentrations (0.1 ≤ [1-MeIm] ≤ 0.5 M) produced $P_{1/2}^{O_2}$ values consistent to within ±20%.

Toluene solutions of FeTalPoc(1,2-Me_2Im) (V) also contained some detectable amounts of bis-ligated FeTalPoc(1,2-MeIm)$_2$ when the 1,2-Me_2Im concentrations were as low as 0.006 M. At this concentration of 1,2-Me_2Im, stable O_2 complexes were formed, so $P_{1/2}^{O_2}$ values for V could be calculated. Experiments were repeated with 1,2-Me_2Im concentrations between 0.006 and 0.1 M, yielding $P_{1/2}^{O_2}$ values consistent to within ±15%.

Compounds IIIa,b, IVa,b, and V all exhibit $P_{1/2}^{O_2}$ values constant over the given range of axial base concentrations. This result indicates five-coordination predominates in the absence of gaseous ligand and that O_2 binding occurs regioselectively within the pocket.

Equilibrium Results, CO Binding. The CO binding affinities for IIIb and IVb were measured directly by the flow technique. The same range of 1,2-Me_2Im concentrations were used to determine repeatedly $P_{1/2}^{CO}$ as were used for the $P_{1/2}^{O_2}$ measurements. The $P_{1/2}^{CO}$ values so determined proved independent of base concentration. The $P_{1/2}^{CO}$ of IIIb was also measured by the tonometer method (Figure 3). The value of $P_{1/2}^{CO}$ obtained in this way agreed within error with that determined by the flow method, thus confirming the validity of the tonometer technique. These results are included in Table II.

Basolo[24] recently determined the $P_{1/2}^{CO}$ for FeTPP(1,2-Me_2Im) by using a flow technique. We have confirmed his value by our tonometer method. The $P_{1/2}^{CO}$ values for a number of other 1,2-Me_2Im-ligated, five-coordinate iron(II) porphyrins were also measured with our tonometer. The detailed base binding properties of these systems are not known so we used a 1,2-Me_2Im concentration of both 3×10^{-3} and 1.5×10^{-3} M. The $P_{1/2}^{CO}$ values obtained with the two different 1,2-Me_2Im concentrations always agreed within error (15%) (Table II). The $P_{1/2}^{CO}$ for FeTPP4ClIm[32] (an imidazole-tailed derivative of TPP)[32] was also measured by the tonometer method and this result is included in Table I. The $P_{1/2}^{CO}$ values for FeTPP(1,2-Me_2Im) and IIIb measured by tonometer in several solvent systems are listed in Table III.

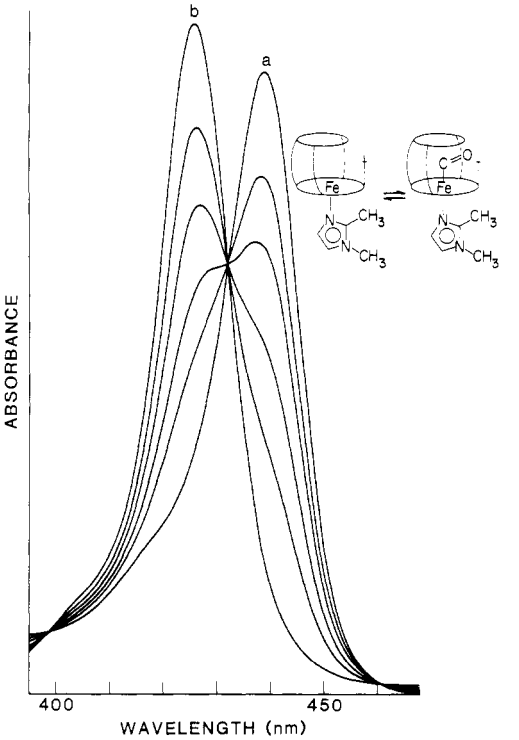

Figure 3. Determination of $P_{1/2}^{CO}$ for FePocPiv(1,2-Me_2Im) (IIIb). IIIb, ca. 3×10^{-5} M in toluene, 1.0 M in 1,2-dimethylimidazole, 25.0 °C: (curve a) under 1 atm of N_2; (curve b) CO partial pressure of 200 torr. Intermediate curves obtained by adding increasing quantities of 2.65% CO/N_2 to a 106-mL volume tonometer. The following intermediate partial pressures of CO pertained: 0.019, 0.038, 0.076, 0.152 torr.

M values for competitive binding of CO in the presence of O_2 (eq 4) were determined for the five "pocket" complexes IIIa,b, IVa,b, and V. For IIIb and IVb, the experimentally determined M value matched (to within 15%) those calculated by taking the ratio of directly measured $P_{1/2}^{O_2}$ and $P_{1/2}^{CO}$ values. For IIIa, IVa, and V, the M value was used exclusively to derive the $P_{1/2}^{CO}$ values given in Tables I and II.

The thermodynamic values were determined by using the tonometer to measure $P_{1/2}^{CO}$ values at five different temperatures over a 30 °C range. Values of $\Delta H°$ and $\Delta S°$ were then determined from van't Hoff plots. These values are included in Table IV.

Kinetic Results. Both the CO and O_2 adducts of the iron(II) "picket fence" and "pocket" porphyrin complexes (Ia, II, IIIa,b,

Table III. Solvent and Polarity Effects on Ligand Binding to Five-Coordinate Iron(II) Porphyrin Complexes

compd	conditions	k_B^{CO}, M^{-1} s^{-1}	k_B^{-CO} s^{-1}	$P_{1/2}^{CO}$, torr	$k_B^{O_2}$, M^{-1} s^{-1}	$k_B^{-O_2}$, s^{-1}	$P_{1/2}O_2$, torr	M	ref
"chelated protoheme"	aqueous suspension (2% MTAB), 20 °C, pH 7.3	3.6×10^6	5×10^{-3}	1×10^{-3}	2.6×10^7	47	1	980	29, 58
"chelated protoheme"	benzene, 20 °C	1.1×10^7	2.5×10^{-2} [b]	2.3×10^{-4}	6.2×10^7	4200	5.6	24 000	22, 58
$FePiv_3$5CIm (II)	1:1 toluene/MeOH, 25 °C	8.38×10^6 [a]	2.6×10^{-4}	3.0×10^{-6}	1.7×10^8 [a]	130	5.9×10^{-2}	19 900	11, this work
$FePiv_3$5CIm (II)	toluene, 25 °C	3.6×10^7 [a]	7.8×10^{-3}	2.2×10^{-5}	4.3×10^8 [a]	2900	5.8×10^{-1}	26 600	11, this work
Fe "amide" "hanging base"[c]	toluene, 20 °C	3.5×10^7			3.6×10^8	5000	2		31
Fe "ether" "hanging base"[c]	toluene, 20 °C	6.8×10^7			3.0×10^8	40 000	18.6		31
FeTPP(1,2-Me_2Im)	toluene, 25 °C			0.15[a]					24, this work
	1:1 toluene/benzonitrile, 25 °C			0.27[a]					this work
	1:1 toluene/acetonitrile, 25 °C			0.11[a]					this work
	1:1 toluene/DMF, 25 °C			0.13[a]					this work
FeTPivP(1,2-Me_2Im) (I)	toluene, 25 °C	1.4×10^6 [a]	1.4×10^{-1}	8.9×10^{-3}	1.06×10^8 [a]	46 000	38	4280	11, this work
FeTMesP(1,2-Me_2Im)	toluene, 25 °C			8.0×10^{-3} [a]					this work
FePocPiv(1,2-Me_2Im) (IIIb)	toluene, 25 °C	9.8×10^4 [a]	5.5×10^{-2}	6.7×10^{-2}	1.9×10^6 [a]	280	12.6	216	21, this work
FeAmPoc(1,2-Me_2Im)	toluene, 25 °C			5.0×10^{-2}			[d]		this work

[a] Estimated errors <15%. [b] 9:1 Toluene:CH_2Cl_2, 22 °C. [c] Covalently attached pyridine is axial base. [d] O_2 binding behavior is complex.

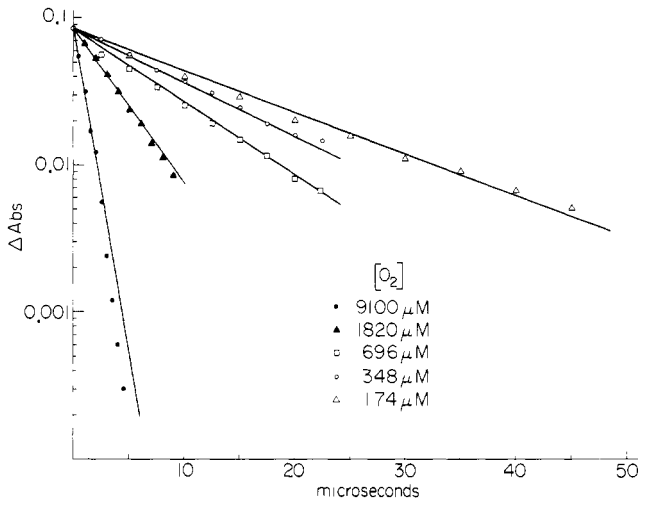

Figure 4. Determination of $k_B^{O_2}$ and $k_B^{-O_2}$ values for the binding of O_2 to FeTPivP(1,2-Me_2Im), I, obtained by flash photolysis of FeTPivP-(1,2-Me_2Im)(O_2) in the presence of various concentrations of O_2. Points are experimental; solid lines are calculated values obtained by fitting the data to eq 7. I, ca. 2×10^{-6} M in toluene, 0.01 M in 1,2-Me_2Im, 25.0 °C, λ = 436 nm.

IVa,b, and V) were found to be photolabile.[58] As such, the dynamics of ligand binding could be explored by laser flash photolysis, both by the direct recombination (eq 5) and competitive rebinding (eq 6) methods. Specifically, for the photolysis experiments carried out under conditions where direct rebinding according to eq 8 is believed to be occurring, adherence to the following criteria is considered as sufficient evidence that rebinding is indeed to the five-coordinate species, FeP(B): (1) Log plots of the change in absorbance vs. time following the laser flash are linear over at least 3 half-lives. (2) The derived second-order association rate constants, k_B^L (eq 8) are independent of [B] (and [L]) over a wide range of [B] (and [L]). (3) $k_B^L[L] \gg k_B^{-L}$, where k_B^{-L} is calculated from K_B^L and k_B^L by eq 3.

By contrast, when ligand rebinding is believed to be occurring according to eq 7 or 9 and 10, simple criteria such as those given above cannot easily be checked. Kinetic complications arising from the presence of extraneous species (e.g., FeP(L), FeP, etc.) could be ruled out if (1) a good agreement is observed between the experimentally observed decay rates and those calculated from eq 7 or 9 and 10, as appropriate, and (2) the kinetically derived O_2 affinities matched those directly obtained under equilibrium conditions.

Our actual kinetic results are now presented in the context of the above considerations, with the numerical values obtained being summarized in Tables I and II.

When dilute toluene solutions of FeTPivP(1,2-Me_2Im)(CO) are photolyzed, linear decay plots of ln ΔA vs. t are obtained provided concentrations of 1,2-Me_2Im greater than 0.01 M are used. The value of k_B^{CO} for I, calculated by eq 8, proved invariant (±10%), as the bulk concentration of CO in solution was increased from 7.5×10^{-5} to 7.5×10^{-3} M. We appear fortunate that, in contrast to the behavior of hindered imidazole complexes of simple iron(II) porphyrins,[43] rebinding of CO to I is occurring exclusively to the five-coordinate complex, FeTPivP(1,2-Me_2Im), I. At 0.01 M 1,2-Me_2Im concentrations, flash photolyses of the air-stable complex, FeTPivP(1,2-Me_2Im)(O_2) were carried out over a range of O_2 concentrations. Figure 4 shows both the experimentally observed spectral changes following flash photolysis and those calculated using eq 7. The root mean square of the residuals was found to be less than 1.5% of the total absorbance excursion, suggesting a good fit. The $K_B^{O_2}$ derived from the $k_B^{O_2}$ and $k_B^{-O_2}$ match (±5%) that obtained directly under equilibrium conditions. Furthermore, the $k_B^{O_2}$ calculated from eq 7 agrees (±5%) with that obtained directly when FeTPivP(1,2-Me_2Im)(O_2) is photo-

(58) Morris, R. M.; Gibson, Q. H.; Collman, J. P.; Sessler, J. L., manuscript in preparation.

Table IV. Thermodynamic Values for Ligand Binding to Fe(II) Porphyrin Complexes

complex	ligand	$\Delta H_{assoc}^{\ddagger}$, kcal/mol	$\Delta S_{assoc}^{\ddagger}$,[a] eu	ΔH°, kcal/mol	ΔS°, eu	ref
hemoglobin, pH 7.4	O_2			−13.6 to 15.5	−27.7 to −31.7	78
	CO			−17.7		79
hemoglobin isolated chains, pH 7.4 α_{SH}	O_2			−14.2		80
	CO			−21.8		80
β_{SH}	O_2			−16.9		80
	CO			−24.4		80
myoglobin	O_2			−15.3 to −21.0	−38.1 to −56.1	81
chelated protoheme[b]	O_2	7.2	−13	−14.0	−35	15
	CO	7.2	−17	−17.5	−34	15
$FePiv_3$5CIm[c] (II)	O_2	0.18 ± 0.08	−27.9 ± 0.6	−16.3 ± 0.8	−40 ± 3	this work, 12
	CO	1.0 ± 0.08	−30.2 ± 0.6			this work
FeTPivP(1,2-Me_2Im)[c] (I)	O_2	2.5 ± 0.4	−22.8 ± 1.0	−14.3 ± 0.5	−42 ± 2	this work, 12
FeMedPoc(1-MeIm)[c] (IVa)	O_2	1.7 ± 0.6	−29 ± 2			this work
	CO	1.6 ± 0.6	−35 ± 2			this work
FePocPiv(1-MeIm)[c] (IIIa)	O_2	8.3 ± 0.6	−10.8 ± 2.5			this work
FePocPiv(1,2-Me_2Im)[c] (IIIa)	CO			−13.9 ± 1	−28 ± 3	this work
FeTPP(1,2-Me_2Im)[c]	CO			−12.8 ± 1	−26.1 ± 2	this work
Fe(C_2-cap)(1-MeIm)[c]	O_2			−10.5	−27.9	24
Fe(C_2-cap)(1,2-Me_2Im)[c]	O_2			−9.7	−35.9	24

[a] Standard state, 1 atm. [b] 2% Aqueous MTAB suspension, pH 7.3. [c] Toluene.

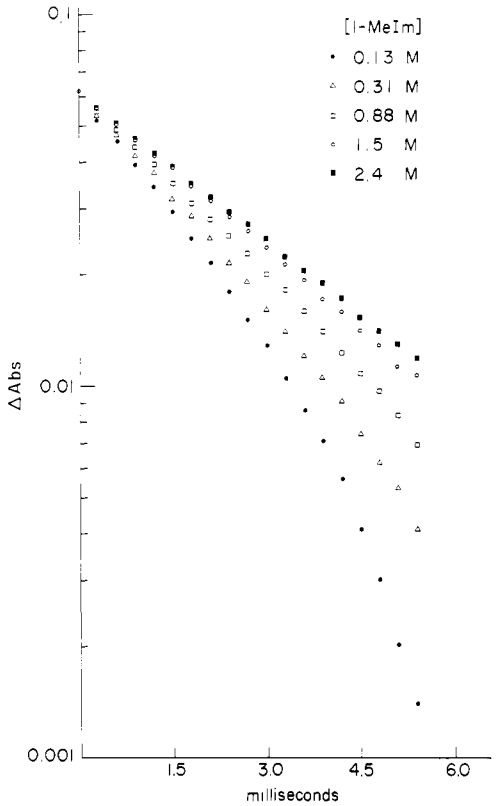

Figure 5. CO rebinding to FePocPiv(1-MeIm), IIIa. Points are experimental values obtained when FePocPiv(1-MeIm)(CO) is photolyzed in the presence of increasing concentrations of (1-MeIm). IIIa, ca. 2×10^{-6} M in toluene, [CO] = 5.66×10^{-4} M, 25.0 °C, λ = 436 nm.

lyzed in O_2-saturated toluene containing 0.01 M base.

The "tailed" "picket fence" porphyrin complex, $FePiv_3$5CIm, II, incorporates a covalently appended imidazole. Five-coordination pertains at equilibrium;[41] in analogy to the findings of Traylor,[18] we therefore expected well-behaved kinetics. Indeed, k_B^{CO} and $k_B^{O_2}$ for II were obtained directly (eq 8) under the same conditions as used for FeTPivP + 0.01 M 1,2-Me_2Im. In addition, association rates were measured in 1:1 toluene/MeOH (v/v); again, no evidence of kinetic complications was observed. The carbonyl complex, $FePiv_3$5CIm(CO), was also photolyzed in the presence of various CO and O_2 concentrations. Both the slow and fast rates of decay were computer-fit to eq 9 and 10 to yield $k_B^{O_2}$, $k_B^{-O_2}$, and k_B^{CO}. The rms residuals were ≤1.5% of the total change in absorbance. (Similar values for these rates were calculated from a Gibson plot constructed by using just the k_{obsd}(slow) values obtained from these experiments.) The association rates obtained from eq 9 and 10 matched (±10%) those obtained directly under conditions where eq 8 is valid. Good agreement (±10%) was obtained between the kinetic and equilibrium oxygen affinities.

When the carbonyl complexes of the iron(II) "small" "pocket" porphyrins, IIIa and IIIb, are subject to flash photolysis at various low (bulk) concentrations of CO and axial base, biphasic decay plots are observed. The same fast rebinding component is observed for both complexes and probably corresponds to CO rebinding to the four-coordinate unligated iron(II) porphyrin ($k_{CO} = 1.3 \times 10^8$), generated via loss of base from the intermediate five-coordinate species obtained upon photolysis.[43] At moderate to high CO concentrations ($3 \times 10^{-4} \leq [CO] \leq 1 \times 10^{-3}$ M) concentrations as high as 1–2 M in base (1-MeIm, 1,2-Me_2Im) were required before monophasic decay plots were observed and the value of $k_{obsd}/[CO]$ became independent of base concentration. Figure 5 shows a series of logarithmic plots of the change in absorbance vs. time following laser flash photolysis of FePocPiv(1-MeIm)(CO), as the concentration of 1-MeIm is systematically increased. At the higher concentrations of base, five-coordination is presumably being enforced around iron after photolysis. The limiting values of k_B^{CO} obtained for IIIa and IIIb under these conditions are invariant to changes in CO concentration.

Figure 6 shows the effect of varying the 1-MeIm concentration upon the rate of carbon monoxide rebinding to FeMedPoc(1-MeIm), IVa. A systematic decrease in $k_{obsd}/[CO]$ occurs until a 1-MeIm concentration of ca. 1×10^{-3} M is reached. In the range of $1 \times 10^{-3} \leq$ [1-MeIm] $\leq 5 \times 10^{-2}$ M, and $3 \times 10^{-4} \leq [CO] \leq 3 \times 10^{-3}$ M, the value of $k_{obsd}/[CO]$ is invariant within ca. 15%, and a value of k_B^{CO} can be calculated from eq 8. At base concentrations about ca. 5×10^{-2} M, an appreciable quantity of six-coordinate bis-ligated species, FeMedPoc(1-MeIm)$_2$, is apparently being rapidly formed following flash photolysis. The value of $k_{obsd}/[CO]$ is thus less than k_B^{CO}, as loss of the second base must occur prior to complete CO rebinding. For MeMedPoc(1,2-Me_2Im), IVb, similar base concentrations of $\geq 1 \times 10^{-3}$ M are required to preclude appreciable binding to the four-coordinate species, FeMedPoc. At very high 1,2-Me_2Im concentrations (≥1 M) some slight reduction in $k_{obsd}/[CO]$ is again observed. For the photolysis of FeTalPoc(1,2-Me_2Im)(CO), no regime could be found where $k_{obsd}/[CO]$ was independent of CO and base concentrations; no value of k_B^{CO} was obtained for this complex. The values of k_B^{CO} for the various "pocket" complexes are summarized in Tables I and II.

When the oxygen complexes of the various "pocket" porphyrins (IIIa,b, IVa,b) were photolyzed at the same base concentration as were used for the analogous CO adducts, clean first-order

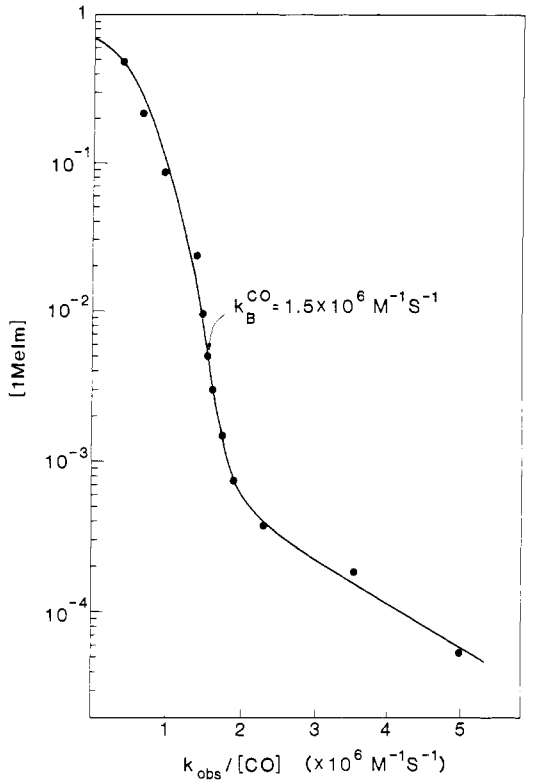

Figure 6. CO rebinding to FeMedPoc(1-MeIm), IVa. Points are experimental values of $k_{obsd}/[CO]$ obtained when FeMedPoc(1-MeIm)(CO) is photolyzed at increasing concentrations of 1-MeIm; line is hand-drawn to aid in visualization. IVa, ca. 2×10^{-6} M in toluene, [CO] = 2.83×10^{-4} M, 25.0 °C, λ = 436 nm.

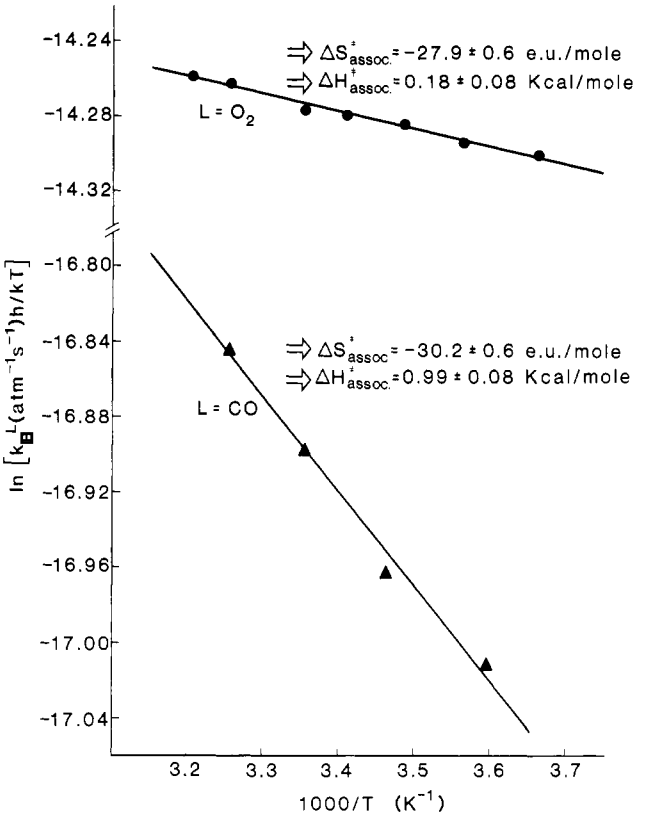

Figure 7. Plots of the association rate constants $\ln [k_B^L(atm^{-1}\ s^{-1})h/kT]$ for O_2 (upper points) and CO (lower points) binding to $FePiv_35CIm$, II, vs. the reciprocal of temperature.

rebinding to the corresponding five-coordinate deoxy complexes was observed. Under these conditions, there was no evidence of oxidation occurring between successive laser flashes. At high concentrations of O_2, plots of $\ln \Delta A$ vs. t are linear and $k_B^{O_2}[O_2] \gg k_B^{-O_2}$. Values for the association rate constants were thus obtained for "pocket" complexes IIIa,b, IVa,b, using eq 8. In contrast to the CO adduct, photolysis of FeTalPoc + ($1,2\text{-}Me_2Im$)(O_2) leads to clean monophasic rebinding (plots of $\ln \Delta A$ vs. t are linear) with $k_{obsd}/[O_2]$ independent of [B] and $[O_2]$, if $0.005 \leq [1,2\text{-}Me_2Im] \leq 0.2$ M and $[O_2] \geq 5 \times 10^{-4}$ M. Apparently, the higher value of $k_B^{O_2}$ as compared to k_B^{CO} allows O_2 rebinding to compete successfully with the binding of a second base to the intermediate five-coordinate complex, FeTalPoc-($1,2\text{-}Me_2Im$).

Dilute toluene solutions of FeMedPoc($1,2\text{-}Me_2Im$)(O_2), IVb, containing ca. 0.1 M concentrations of $1,2\text{-}Me_2Im$ were photolyzed at various O_2 concentrations (ca. 20-fold change in O_2 was used). The values for k_{obsd} were computer fit to eq 7. A good match between experimental and calculated values for the change in absorbance vs. time was obtained (the rms residual was less than 3% of the total absorbance excursion). The value for $k_B^{-O_2}$ so obtained is considered reliable in that the kinetically derived affinity matches (±10%) that obtained by equilibrium methods. Attempts to determine the O_2 dissociation rate constants, $k_B^{-O_2}$, for FePocPiv(1-MeIm)(O_2), FePocPiv($1,2\text{-}Me_2Im$)(O_2), and FeMedPoc(1-MeIm)(O_2) proved unsuccessful. Again, solutions of the oxygen complexes were photolyzed over a range of oxygen concentrations, using axial base concentrations at which eq 8 was previously found to be valid. From a computer fit to eq 7, values of $k_B^{-O_2}$ were obtained which were between ca. 2 and 10 times higher than those calculated from the independently measured $k_B^{O_2}$ and $K_B^{O_2}$ values; values for $k_B^{O_2}$ obtained from the fit to eq 7 were similar to those obtained directly (eq 8). Furthermore, when large deviations between kinetic and equilibrium oxygen affinities were found, poor fits were obtained when the experimental data were fit to eq 7. Since the $P_{1/2}^{O_2}$ values for FeMedPoc($1,2\text{-}Me_2Im$), IVb, and FePocPiv($1,2\text{-}Me_2Im$), IIIb, are essentially identical and were obtained with the same apparatus under the same conditions, the discrepancy between the kinetic and equilibrium oxygen affinities for FePocPiv($1,2\text{-}Me_2Im$), IIIb, is probably significant. It is not at present clear whether this discrepancy simply reflects the fact that the dissociation rates for the more encumbered "pocket" complexes are too low to be measured accurately by the laser flash methods or indicates that the kinetically observed "off" rate reflects, in whole or in part, the rate of base dissociation from the six-coordinated oxygen complex:

$$\begin{aligned} FeP(B)(O_2) &\rightleftarrows FeP(O_2) + B \\ FeP(O_2) &\rightleftarrows FeP + O_2 \\ FeP + B &\rightleftarrows FeP(B) \end{aligned} \qquad (12)$$

Attempts to use eq 11 to obtain reliable $k_B^{-O_2}$ values for FePocPiv(1-MeIm), IIIa, and FeMedPoc(1-MeIm), IVa, proved similarly unsuccessful. In analogy to the experiments with $FePiv_35CIm$, II, solutions of FeMedPoc(1-MeIm)(CO) were subjected to laser photolysis in the presence of various concentrations of both O_2 and CO. Plots of $1/k_{obsd}$(slow) vs. $[O_2]/[CO]$ gave a value of 45 s^{-1} for the reciprocal of the intercept and a value of 2.8 s for the slope. If the conditions of eq 6 and 11 hold, values of ca. 70 s^{-1} and 10 s would be expected for these quantities (which should correspond to $k_B^{-O_2}$ and $k_B^{O_2}/k_B^{-O_2}k_B^{CO}$, respectively). Similar numerical discrepancies were obtained when analogous experiments and analyses were carried out with complex IIIa. Although further investigations are certainly needed to establish the exact ligand dissociation kinetics of these more encumbered systems, we feel that the oxygen association rates and affinities reported in Tables I and II are accurate within the stated errors. *Our findings also indicate the desirability of measuring ligand (especially O_2) affinities by both equilibrium and kinetic methods whenever possible.*

The enthalpy and entropy of activation for ligand association were determined by measuring ligand rebinding rates (at least four) over at least a 35-deg range in temperature. Since the same sample was measured at all temperatures and k_{obsd} was obtained

by fitting the change in absorbance data directly to a single exponential by a least-squares program, changes as slight as 1% in k_B^L were reliably detected. Figure 7 shows a typical set of these plots. Values for $H_{assoc}^{\ddagger}$ and $S_{assoc}^{\ddagger}$ obtained from these plots are summarized in Table IV.

Discussion

Table I contains equilibrium and kinetic parameters for the oxygenation and carbonylation of unhindered imidazole complexes of various five-coordinate iron(II) porphyrins (eq 3). Table II contains similar binding data for hindered imidazole complexes. These data allow for a number of interesting comparisons.

It has been known for some time[34,36] that the gaseous ligand affinities of five-coordinate iron(II) porphyrin complexes utilizing as axial base imidazoles substituted in the 2-position are ca. 2 orders of magnitude lower than those of the analogous complexes derived from unhindered imidazoles. For instance, in the "picket fence" series, FeTPivP(1,2-Me_2Im), I, shows O_2 and CO affinities 75 and 400 times lower, respectively, than the unconstrained $FePiv_3$5CIm complex.[36] These reductions were ascribed to the severe proximal steric interaction between the 2-methyl group of the imidazole and the porphyrin plane.[10] Since the degree of affinity reduction parallels that seen between the high affinity, or relaxed (R), form of HbA and the low affinity, or tense (T) form of HbA,[2a] the "picket fence" systems I and II, as well as other unhindered and hindered imidazole complexes of iron(II) porphyrins, have been considered as models for the R and T states of hemoglobin.[36,43,59] The kinetic data obtained in this study suggest that the lowered affinities of the T-state models are reflected in lowered ligand association and increased dissociation rates for the binding of carbon monoxide, and primarily in increased dissociation rates for O_2 binding. This is qualitatively similar to the behavior seen in Hb(R) and Hb(T);[2a,60] however, the absolute magnitude of the rate constants are appreciably larger in the model systems. Although these observations are of interest, the main objective of the present work has not been to intercompare further the binding behavior of R- and T-state models nor to compare quantitatively the behavior of the models with the hemoproteins.

We find it preferable to make direct quantitative comparisons solely among similar iron(II) porphyrin compounds, even though comparisons between natural hemoproteins and model compounds may be useful in suggesting what factors serve to regulate the binding of gaseous ligands in the hemoproteins. Direct quantitative comparisons between a model compound and a hemoprotein are complicated by several factors. In particular, models such as the "picket fence" are derived from a different porphyrin than the hemoproteins, have no protein interactions and are examined in a different solvent system. The conclusions drawn from comparisons based on similar model compounds are likely to be less ambiguous. Intelligently designed model systems can focus attention on one pertinent variable at a time by holding the magnitude of extraneous effects relatively constant.

In this study, we shall make a number of limited comparisons between ostensibly similar iron(II) porphyrins. We will explore the following two questions: (1) What factors other than distal-side steric encumbrance influence O_2 and CO binding to iron(II) porphyrins? (2) Does steric encumbrance introduced into otherwise similar porphyrin models selectively lower the $P_{1/2}^{CO}$ as compared to $P_{1/2}^{O_2}$ values? It is clear that to address question 2 an answer to question 1 is required.

Toluene was used in our original iron(II) porphyrin studies[36] because of both solubility considerations and the fact that the sterically protected "picket fence" complexes I and II form long-lived oxygen adducts in nonpolar solvents.[51] (The rate of autoxidation of iron(II)[27a,39,51] and cobalt(II)[61] porphyrins are considerably accelerated in protic media.) A significant advantage of using toluene for our present kinetic and equilibrium binding investigations is that toluene is also used as solvent in our spectroscopic characterization studies.[21,41,42] Other workers have also favored toluene as solvent for equilibrium studies.[19,31] Traylor and co-workers[18] have carried out extensive kinetic analyses of, and derived O_2 and CO affinities for, a number of simple five-coordinate iron(II) porphyrins in several solvent systems. His[18] and other[11] similar data have demonstrated clear solvent dependence of ligand affinity values (vida infra). Therefore, there is no advantage in comparing values for two sets of models unless these values are obtained in similar solvent systems.

I. Unencumbered Models. The data in Tables I and II suggest that, in general, unprotected iron(II) porphyrin complexes show lower gaseous ligand affinities than do the "picket fence" complexes I and II. For instance, under similar experimental conditions, $FePiv_3$5CIm, II, binds both O_2 and CO with approximately an order of magnitude higher affinity than does the "chelated protoheme" model of Traylor and co-workers.[18,22] The kinetic data suggest that, particularly for O_2, the greater affinities of the "tailed" "picket fence" complex are predominantly reflected in increased ligand *association* rates. Both models incorporate the same covalently attached imidazole ligand but the "tailed" "picket fence" complex, II, is derived from a tris(o-pivalamido)-substituted tetraphenylporphyrin, and the "chelated protoheme" from protoporphyrin IX. The gaseous ligand affinities for the "picket fence" complexes I and II are substantially higher than other unprotected hemes as well. The CO affinity for the similar yet unprotected FeTPP4CIm complex is 50 times lower than that for the corresponding picket fence complex II. Similarly for the T-state models, FeTPP(1,2-Me_2Im) has a 17-fold lower affinity than does FeTPivP(1,2-Me_2Im).

We[11,12,30,36] and others[14,24] continue to speculate as to why the binding behavior (for both O_2 and CO) of the "picket fence" complexes, I and II, differs from that of the other unprotected model compounds. The four factors discussed in the ensuing paragraphs should be considered as possibly accounting for the differences. It should be stressed that these factors may affect O_2 and CO binding to different extents. Moreover, their contribution to changes in affinity may be reflected in differing rates of ligand association *or* dissociation.

Electronic Nature of the Porphyrin. Electronic effects have been extensively studied.[24,29,62,63] For instance, in a recent paper[29] Traylor and co-workers used a series of similar "chelated hemes" to investigate changes in O_2 and CO affinities arising from changes in the electronic nature of the porphyrin. These workers found that changes in the electronic nature of the heme effected little change in CO affinity but that by contrast O_2 affinities and *dissociation* rates were markedly affected. We and others[24] have measured the CO binding affinities for several para-substituted iron(II) tetraphenylporphyrins. These data (Table II) further suggest that electronic substitution effects may have but a small effect on CO affinity. We conclude that other factors must be primarily responsible for the high ligand (both O_2 *and* CO) affinities of the "picket fence" complexes.

Structural Nature of Porphyrin. Structural studies have shown that the binding of a ligand to a five-coordinate iron(II) porphyrin is accompanied by movement of the iron into the porphyrin plane.[9b,10b] Slight structural changes in the porphyrin macrocycle accompany this transition. The extent to which these changes occur may vary from one porphyrin system to another. There is not at present sufficient structural data available to assess whether the higher affinity of the "picket fence" complexes can be rationalized in structural terms.

Polarity of the Ligand Binding Site. Structural studies[10] have shown that, in the solid state, there is no interaction between the amide proton and the bound dioxygen in the "picket fence"

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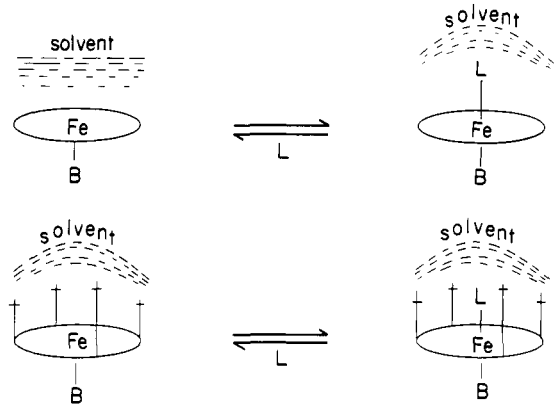

Figure 8. Schematic representation of the effects of solvent interactions on iron(II) porphyrins. Upper scheme, simple "flat" porphyrins; lower scheme, protected porphyrins.

porphyrins. Nonetheless, the possibility that these amide groups increase the polarity at the ligand binding site must be considered. Polarity effects may be investigated in one of two ways. The first of these involves simply changing the solvent in which the ligand equilibria (eq 3) are measured.[64] The combined results (Table III) from our own work and from other laboratories suggest that changing from a polar to a nonpolar solvent serves to lower O_2 affinities by a factor of 10–40 for iron(II)[11,15,22] and cobalt(II)[65] porphyrins. For the most part, however, such changes affect CO affinities to a lesser extent.

A second and potentially more accurate approach to exploring polarity effects is to construct protected porphyrins which differ only by virtue of the polarity in the binding cavity. In contrast to FeTPP(1,2-Me_2Im), the CO affinity of FeTMesP(1,2-Me_2Im) is very similar to that of FeTPivP(1,2-Me_2Im) (Table III), yet it incorporates only nonpolar methyl groups in the orthophenyl positions instead of amido-linked "pickets". Moreover, an analogue of IIIb, FeAmPoc(1,2-Me_2Im), which incorporates a primary aryl amine at the binding site, has been synthesized and studied.[32,42] This apparently drastic change in polarity has little effect on CO affinity, as $P_{1/2}^{CO}$ for FeAmPoc(1,2-Me_2Im) is 0.050 torr (compared to 0.067 torr for FePocPiv(1,2-Me_2Im)). This insensitivity of CO affinities to local polarity effects is in contrast to that observed by Momenteau and Lavalette[31] for O_2 binding to two similar "hanging base" porphyrins. Changing the mode of attachment from amide to ether linkages effected an approximately 10-fold reduction in O_2 affinities (Table III). This reduction was predominantly manifested in increased *dissociation* rates. (As yet, no CO affinity data are available for these systems.) On the basis of the available evidence, we conclude that factors other than polarity must be considered if both the high O_2 *and* CO affinities (and high association rates) of the "picket fence" porphyrins are to be explained.

Solvation Effects. We have previously discussed[11,30] solvation factors with regard to the equilibrium of eq 3. We suggested that in "flat" iron(II) porphyrins (e.g., FeTPP or "chelated mesoheme") the unligated five-coordinate form might be subject to a stronger solvation stabilization than the protected "picket fence" complexes. In the six-coordinate ligated forms, differences in solvation between the "flat" and protected porphyrins might be smaller (see Figure 8). This relative stabilization of the five-coordinate complex in the "flat" porphyrins could account for the lower affinities of these species relative to "picket fence" porphyrins. Recall that as compared to FeTPP(1,2-Me_2Im) or FeTTP(1,2-Me_2Im), the CO affinity for the more "protected" FeTMesP(1,2-Me_2Im) is nearly as high as that of the "picket fence" complex I. The strong solvation stabilization of the simple "flat" unligated species must be reduced or eliminated in the transition state for ligand association. Reduced rates of ligand association relative to the protected "picket fence" complexes are thus expected for "flat" or simple iron(II) porphyrins. The data in Tables I and II indicate that this is in fact the case. Therefore, we feel the equilibrium and kinetic data presented demonstrate that preferential solvation of the five-coordinate form of "unprotected" iron(II) porphyrins is an important phenomenon. Moreover, this solvation effect *is the dominant factor* responsible for the lower gaseous ligand affinities of these "flat" hemes as compared to the "protected" "picket fence" porphyrins.

II. Encumbered Models. We have synthesized the "pocket" complexes IIIa,b, IVa,b, and V (Figure 1),[21,42] which, in conjunction with the "picket fence complexes I and II, comprise a system for studying the effects of nonbonded steric interactions on the gaseous binding affinities of iron(II) porphyrins. In using a series of related complexes to explore a particular structure–function relationship, it is necessary to ensure that all other "variables" be held constant. Both the "pocket" and "picket fence" porphyrins are derived from ortho-substituted tetraphenylporphyrins and contain analogous amide linkages at the gaseous ligand binding site. Electronic and polarity effects are therefore expected to be similar within the series of compounds I–V. Furthermore, the protected nature of the "pocket" suggests to us that contributions from solvation effects are likely to be nearly identical in both the "picket fence" and "pocket" complexes. Although at present we cannot rule out possible contributions from porphyrin-related structural changes (i.e., the extent to which "doming", "ruffling", or porphyrin core expansion occurs[32]), we consider the "picket fence" and "pocket" porphyrin derivatives I–V to be a set of congruent complexes with which useful comparisons can be made.

No structural data are yet available from single-crystal X-ray analysis for the "pocket" porphyrins. Nonetheless, analysis of CPK molecular models suggests that in both the "small" and "medium" "pocket" porphyrins the covalently attached benzene ring is rigidly constrained above the porphyrin macrocycle. In the iron(II) "pocket" porphyrins IIIa,b and IVa,b, O_2 should be bound in its intrinsically bent fashion without sustaining appreciable distortion. CO, on the other hand, should only be accommodated by binding in a bent or tilted fashion as a result of steric interactions with the benzene cap.[66] The extent of this distortion is expected (by the CPK models) to be larger in the derivatives of FePocPiv, IIIa,b, than in those of FeMedPoc, i.e., IVa,b. In contrast to the "medium" and "small" "pockets", CPK models show that the appended benzene ring in the "tall pocket" porphyrin is "floppy" since it is free to move both from positions directly above, to positions well away from, the center of the porphyrin macrocycle. It is not clear what effect these possible motions might have on either porphyrin related structural changes or on nonbonded steric interactions with gaseous ligands. Because of the above considerations, direct comparisons between the ligand affinities of I–IVb should be most valid.

The data in Tables I and II indicate that the increasing distal-side encumbrance in the iron(II) "pocket" porphyrin series reduces CO affinities without substantially affecting O_2 affinities. Specifically, in the R-state models, a comparison between the "tailed" "picket fence" complex FePiv$_3$5CIm (II) and FeMedPoc(1-MeIm) (IVa) shows a 30-fold reduction in CO affinity. Furthermore, the CO affinity for the more encumbered FePocPiv(1-MeIm) (IIIa) is another 2-fold lower than that of IVa. Significantly, O_2 affinities of these two R-state "pocket" porphyrin models are identical and similar to that of the "picket fence" complex, II.

Similar but smaller effects are observed in the series of T-state models I, IIIb, IVb, and V. The CO affinity of FeMedPoc(1,2-Me_2Im) (IVb) is about 3 times lower than that of either FeT-

(64) In drawing conclusions about polarity effects based on finding studies carried out in different solvents, it should be noted that (1) the numerical value for the apparent change in ligand affinity depends on the choice of units for K_B^L, and (2) such studies do not necessarily differentiate between changes in local polarity and changes in solvation.

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(66) An analysis of EXAFS data indicates that the CO unit in FePocPiv(Im)(CO) is very similar to that in MbCO. (Powers, L., Bell Laboratories, to be published.)

alPoc(1,2-Me_2Im) (V) or FeTPivP(1,2-Me_2Im) (I). Again, the CO affinity is ca. 2-fold lower for the smaller "pocket" complex IIIb than for IVb (the O_2 affinities of these two systems are identical).

In contrast to the trend seen in CO binding, the O_2 affinities of the "pocket" porphyrins IIIb and IVb are somewhat higher than than of the "picket fence" complex I, and in fact the O_2 affinity of FeTalPoc(1,2-Me_2Im), V, is nearly an order of magnitude higher than that of I. This suggests that apart from steric effects there are some small differences between the behavior of the "picket fence" and "pocket" complexes. The degree of porphyrin-related structural changes which accompany ligand binding may in fact be slightly different for the two sets of models. These suggested differences in structural changes appear to raise slightly ligand affinities in the T-state models (as evidenced by the raised O_2 affinities), but probably not in a ligand-selective manner. Therefore, we feel that the systematically lower CO affinities of the "pocket" porphyrins IIIa,b and IVa,b can only be ascribed to steric interactions between the bound CO ligand and the protecting pocket.

The equilibrium results obtained with our model compounds may be relevant to the study of natural hemoproteins. Structural studies have shown there is steric encumbrance in hemoproteins sufficient to distort the bound CO ligand.[7] Our model compound studies have shown that increased steric encumbrance does reduce CO affinities. Therefore, as we have previously suggested,[11,12] distal-side steric interactions may play a role in differentiating CO relative to O_2. This differentiation may serve as an important mechanism for the detoxification of carbon monoxide.[11-14]

The kinetic results obtained with our encumbered "pocket" complexes suggest that the lowered CO affinities are almost entirely reflected in decreased association rates (Tables I and II). Of interest is the observation that as the size of the binding "pocket" is reduced, the association rate for O_2 binding is also severely decreased in magnitude. The degree of this reduction is similar in extent to, and in fact slightly larger than that observed in CO association. In the case of O_2 binding, a commensurate reduction in dissociation rates is observed and the overall O_2 affinity remains relatively unchanged throughout either the R- or T-state series of "pocket" and "picket fence" models. In the case of CO binding, constant values for ligand dissociation are seen in both the R- and T-state series; the CO affinity is therefore lowered as the size of the "pocket" is decreased.

Assuming that ligand binding can be treated as a single-step process, these kinetic results suggest that the transition state for CO association to our iron(II) porphyrin models resembles the products in both the hindered and unhindered complexes. Increased steric hindrance in the "pocket" models is expected to cause the CO moiety to be bent and/or tilted relative to the geometry seen in the "picket fence" models. This distortion should serve to destabilize the CO adducts of the "pocket" series. The decreased CO association rates seen with the encumbered models indicate that the CO binding transition state is disrupted by steric hindrance and is therefore product-like. Since the magnitude of this transition state distortion should be similar to that seen in the ground state CO adduct, the CO dissociation rates should remain relatively constant throughout the series of encumbered and unencumbered porphyrins. The experimental data are consistent with the above suggestions. By contrast, the bound O_2 geometry is expected to be similar in both the encumbered and unencumbered models. The high $k_B^{O_2}$ values indicate that the transition state for O_2 association in the unhindered complexes (e.g., the "picket fence" complex II) may well resemble the reactants rather than the products. Since increasing steric encumbrance apparently causes drastic yet similar reduction in both O_2 association and O_2 dissociation rates, the O_2 binding transition state in the encumbered models resembles neither products nor reactants. One might speculate that the preferred transition state geometry for O_2 binding requires an O_2 access trajectory normal to the porphyrin plane. The sterically encumbered "pocket" models (i.e., III and IV) apparently preclude this direct access. Rather, the dioxygen ligand is forced to "squeeze" into and out of the "pocket" in an arrangement not favored relative to the optimal transition-state geometry. Therefore, steric encumbrance would disrupt O_2 association and dissociation *to a similar extent* and produce the experimentally observed lowered O_2 association and dissociation rates.

Preliminary studies were carried out to ascertain the effect of temperature on ligand binding, and the results obtained for several complexes are given in Table IV. The current data do not permit a detailed analysis, but several observations are of interest. The lower association rates of the "pocket" complexes (as compared to the "picket fence" system (II)) seen at 25 °C are reflected in higher activation energies. Furthermore, the rates of ligand association are much more sensitive to temperature in the encumbered systems IIIa and IVa than in the unencumbered system II. We find it of interest that the rates of ligand association (in aqueous suspension) for the "chelated protoheme" model (which is expected to be strongly solvated) of Traylor[15] are also much more sensitive to temperature than those of II (in toluene). It appears possible that both solvation effects and distal-side steric interactions may lead to similar kinetic behavior since both factors seem to reduce association rates and lead to greater temperature dependence in these rates. Furthermore, within the given errors, we are unable to detect any appreciable differences in the thermodynamic values of $\Delta H°$ and $\Delta S°$ for the CO binding to FeTPP(1,2-Me_2Im) and FePocPiv(1,2-Me_2Im), IIIb. The low affinity (relative to FeTPivPP(1,2-Me_2Im), I) of the former is ascribed to solvation effects, whereas that of the latter is ascribed to steric interactions.

Several other groups have explored the effects of distal-side steric encumbrance on the binding of CO and O_2.[22-24] The CO affinities of the "capped" porphyrin complexes have recently been measured.[24] Basolo and co-workers[24] have suggested that in these "capped" systems O_2 affinities are selectively reduced compared to those of CO. This was rationalized as a "peripheral steric effect", wherein the interactions with the bridging groups of the "cap"[67] are thought to distort preferentially the intrinsically bent O_2 ligand. This conclusion appears based in part on the fact that the CO affinities of these "capped" porphyrins are similar to those obtained with simple "flat" iron(II) porphyrins. We suggest that in light of solvation effects, unencumbered ortho-substituted iron(II) porphyrins (e.g., FeTMesP(1,2-Me_2Im)) might be better control systems with which to compare the ligand affinities of the protected "capped" complexes. Traylor et al.,[22] using "cyclophane" porphyrin models, have suggested that increased steric encumbrance serves to lower both the O_2 and CO affinities to a similar extent in iron(II) porphyrins. In contrast to findings on our "pocket" models, the lower ligand affinities found with their encumbered "6,6-cyclophane" model were ascribed solely to reductions in ligand association rates, while no effect was reported on either O_2 or CO dissociation rates. As yet, for the "6,6-cyclophane" system, no O_2 affinities have been directly measured under equilibrium conditions.[68] It has been suggested[24] that

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"peripheral steric interaction" might interfere with O_2 binding in these models. Chang[23] has made a comparison between two iron(II)-copper(II) cofacial dimeric porphyrins and "chelated mesoheme" and found that increased steric encumbrance led to both reduced O_2 and CO affinities. A degree of steric differentiation was noted in the dimeric system; the CO affinities were reduced to a ca. 4-fold greater extent than the O_2 affinities.

It remains of interest that these other workers, using other model systems, fail to observe the same degree of discrimination that we do. At present there is no simple explanation, structural or otherwise, for why this should be so. Certainly, our own experience indicates that extreme caution must be used in making comparisons—even among ostensibly similar heme systems—since many factors can serve to influence O_2 and CO binding behavior.

Summary

Derivatives of the iron(II) "pocket" and "picket fence" porphyrins constitute a series of congruent complexes with which the effects of distal-side steric interactions on gaseous ligand binding can be explored. The "pocket" porphyrins have been designed to possess the same electronic nature and polarity in their binding cavity as that found in the "picket fence" complexes. Further, because both sets of models have one protected face, solvation is thought to be similar. Whereas the O_2 affinities for the iron(II) "pocket" porphyrins are similar to those of the iron(II) "picket fence" porphyrins, the CO affinities of the "pocket" complexes are substantially lower than those of the "picket fence" analogues. We attribute this behavior to the design of the "pocket", which should not substantially effect the intrinsically bent FeO_2 unit, yet still present steric hindrance sufficient to distort the FeCO moiety from its favored linear binding geometry. Our results therefore indicate that it *is* possible to discriminate between CO and O_2 binding in model iron(II) porphyrins. We suggest on this basis that distal-side interactions *may* play a role in regulating ligand binding to natural hemoproteins.

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Registry No. I, 75597-81-8; I(O_2), 74171-97-4; II, 75557-97-0; IIIa, 77338-87-5; IIIa(CO), 78694-32-3; IIIb, 77338-86-4; IVa, 85293-87-4; IVa(CO), 85293-92-1; IVb, 85293-88-5; V, 85293-89-6; FeTPP4CIm, 75529-05-4; FeTPP(2-MeIm), 48243-44-3; FeTPP(1,2-Me_2Im), 72186-60-8; FeOEP(1,2-Me_2Im), 75811-16-4; Fe(T(*p*-Cl)PP)(1,2-Me_2Im), 85293-90-9; FeTMesP(1,2-Me_2Im), 85293-91-0; FeAmPoc(1,2-Me_2Im), 85304-55-8; O_2, 7782-44-7; CO, 630-08-0; Fe "ether" "hanging base", 85293-93-2.

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Photochemistry of [W(CO)$_5${C(OMe)Ph}]. Formation of Alkyne-Carbene Complexes and Studies of Their Decomposition Reactions

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Abstract: The photochemistry of [W(CO)$_5${C(OMe)Ph}] has been examined and been shown to involve CO loss as the only detectable photoreaction. Irradiation in acetonitrile solution leads smoothly to the formation of [W(CO)$_4$(CH$_3$CN){C(OMe)Ph}] in quantitative yield. The 366- and 313-nm quantum yields for disappearance of [W(CO)$_5${C(OMe)Ph}] in CH$_3$CN solution are 0.009 and 0.011, respectively, but the quantum yield drops to $\leq 10^{-4}$ at 436 nm, even though the complex absorbs strongly at the latter wavelength. The lowest intense absorption band (λ_{max} 402 nm) (ϵ_{max} 10 560 L mol^{-1} cm^{-1}) has been assigned as a W $\rightarrow$ carbene(π^*) charge-transfer transition with ligand field bands lying at higher energy. The low-lying W $\rightarrow$ carbene charge-transfer state is inactive with respect to CO loss, with the latter occurring from ligand field excited states. Low-temperature photolysis in the presence of PhC≡CPh, MeC≡CPh, MeC≡CMe, PhC≡CH, and *n*-BuC≡CH leads to spectroscopically observable alkyne-carbene adducts, with the diphenylacetylene complex [W(CO)$_4$(PhC≡CPh){C(OMe)Ph}] isolated as a crystalline solid. None of the alkyne adducts are stable at 25 °C in solution, and they decompose to give products that depend markedly upon the nature of the alkyne. With terminal alkynes, only polyacetylenes form, whereas the PhC≡CPh and PhC≡CMe adducts decay exclusively to form 1-methoxy-2,3-diphenylindene and 1-methoxy-2-methyl-3-phenylindene, respectively. The MeC≡CMe adduct leads to both poly-2-butyne and 1-methoxy-2,3-dimethylindene.

Much attention has been given to studies of the thermal reactivity of transition-metal carbene complexes, because of their important role in a number of catalytic and stoichiometric transformations.[1] In contrast, relatively little attention has been devoted to the photochemical properties of this class of compounds,[2-10] even though photolysis might be expected to substantially alter the reactivity of the carbene ligand through population of charge-transfer excited states which involve that ligand. The compounds that have had their photochemistry most extensively studied are the pentacarbonyl carbene complexes of Cr and W, but even here a somewhat confusing pictue emerges concerning

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