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Effect of Axial Base on Dioxygen and Carbon Monoxide Affinities of Iron(II) Porphyrins. Imidazole vs. Pyridine

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The synthesis of "picket fence" porphyrin derivatives bearing covalently attached imidazole and pyridine nuclei is described. The oxygen and carbon monoxide affinities of the iron(II) complexes of these porphyrins are reported. Electronic effects due to replacement of imidazole by pyridine have been isolated from steric constraints. These electronic effects, deriving from a decreased basicity of the axial base, give rise to 40-fold and 13-fold reduction, respectively, in oxygen and carbon monoxide affinities upon replacing imidazole by pyridine. Kinetic measurements of oxygen and carbon monoxide association rates suggest that these changes are manifested primarily in ligand dissociation rates.

The effect of axial base on the oxygen-binding capability of iron(II) porphyrin complexes is of long-standing interest.[1,2] Model complexes mimicking the O_2 affinities of the oxygen transport and storage proteins, hemoglobin and myoglobin, have been developed,[3,4] with use of imidazole or substituted imidazoles as the axial base. An early report[5] on O_2 binding to a pyridine-ligated iron(II) porphyrin, mesoheme *N*-[3-(3-pyridyl)propyl] ester, at low temperatures suggested that this complex bound O_2 about 2000 times more poorly (i.e., with lower affinity) than did an analogous complex, pyrroheme *N*-[3-(1-imidazolyl)propyl] amide, with imidazole as the axial ligand. These initial results suggested that the pyridine ligand was unsuited for supporting oxygenation in iron(II) porphyrins. Basolo and co-workers,[9,10a] however, found that an iron(II) dioxygen complex could be formed by the addition of O_2 to Fe(TPP(py)$_2$) at −78 °C. At this temperature the rate of O_2 dissociation was found to be ca. 25 times greater for the pyridine adduct, Fe(TPP(py))(O_2), than for the analogous 1-methylimidazole complex, Fe(TPP(1-MeIm))(O_2).[10b] In a later kinetic study with "chelated" pyrrohemes, Chang and Traylor[2] reported that in aqueous suspension at 22 °C an imidazole-ligated heme bound O_2 with ca. 20-fold higher affinity than did a pyridine-ligated analogue. As we had obtained preliminary evidence that pyridine was indeed capable of supporting oxygenation of a "picket fence" iron(II) porphyrin complex at room temperature, we chose this system to investigate in more detail the effect that changes in axial base have on the O_2 affinities of iron(II) porphyrin complexes. Our quantitative equilibrium results show that, in the picket fence porphyrin series, replacement of imidazole by pyridine lowers the O_2 affinity by a factor of about 40, an effect consistent with the later results of Chang and Traylor[2] (but not with the earlier reports[1,5]). Kinetic studies indicate that this change is predominantly manifested in the rates of dioxygen dissociation from the O_2 adducts. During the course of this work, Basolo and co-workers[11] reported the results of a thorough study of the binding of dioxygen to various five-coordinate iron(II) complexes derived from the "capped" porphyrin by the addition of external nitrogenous bases. With this system, substitution of pyridine for 1-methylimidazole effected, respectively, an 8- and 3.6-fold lowering of O_2 affinity in toluene solution at +25 and −45 °C. As yet, no kinetic data have been reported for this interesting system.

Carbon monoxide is also a ligand for hemoglobin and myoglobin and, as such, its binding to simple iron(II) porphyrins is a subject of current interest.[13,14] Several studies have addressed the effect of axial base on the kinetics and equilibria of CO binding to iron(II) porphyrins.[15-19] In an early study, Chang and Traylor[15] reported that the CO affinity of imidazole chelated pyrroheme was similar to that of pyridine chelated mesoheme. The CO affinity for a very similar

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(9) Abbreviations: TPP, dianion of *meso*-tetraphenylporphine; TpivPP, dianion of picket fence porphyrin, *meso*-5α,10α,15α,20α-tetrakis(*o*-pivalamidophenyl)porphyrin; (Piv)$_3$5CIm, dianion of tailed picket fence *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-(5-(*N*-imidazolyl)-valeramido)phenyl)porphyrin; (Piv)$_3$4CIm, dianion of tailed picket fence, *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-(4-(*N*-imidazolyl)butyramido)phenyl)porphyrin; PF3CUIm, dianion of tailed picket fence, *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(*N*-imidazolyl)propyl)ureido)phenyl)porphyrin; PF3CUPy, dianion of tailed picket fence, *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(3-pyridyl)propyl)ureido)phenyl)porphyrin; PF4CUPy, dianion of tailed picket fence, *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(3-pyridyl)butyl)ureido)phenyl)porphyrin; DHD, dianion of deuteroporphyrin, dimethyl ester; Cap, dianion of capped porphyrin 5,10,15,20-[pyromellitoyl(tetrakis(*o*-oxyethoxyphenyl))]porphyrin; Im-mesoheme, chelated mesoheme *N*-[3-(1-imidazolyl)propyl] amide; Py-mesoheme, chelated mesoheme *N*-[3-(3-pyridyl)propyl] ester; Im-pyrroheme, chelated pyrroheme *N*-[3-(1-imidazolyl)propyl] amide; py, pyridine; 4-CNpy, 4-cyanopyridine; 1-HIm, imidazole; 1-MeIm, 1-methylimidazole; 1,2-Me$_2$Im, 1,2-dimethylimidazole; $P_{1/2}{}^{L}$, pressure of gaseous ligand (O_2, CO) necessary to ligate half of the available sites.
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pyridine chelated mesoheme in aqueous suspension was, however, subsequently reported[16] to be several orders of magnitude higher ($P_{1/2}^{CO} = 0.002$) than originally reported.[15] This latter value is similar to that obtained with an analogous imidazole chelated mesoheme ($P_{1/2}^{CO} = 0.001$) in aqueous suspension[4a,16a] and has led to the conclusion that substitution of pyridine for imidazole has little effect on CO affinities of iron(II) porphyrins.[4b] In a competitive equilibrium study, Rougee and Brault[18] have shown that, with deuteroheme dimethyl ester, substitution of 4-cyanopyridine for imidazole causes about a 9-fold decrease in the affinity for the binding of CO to the five-coordinate heme. With this simple iron(II) porphyrin, six-coordinate bisligated species predominate in the absence of carbon monoxide. These affinities were, therefore, not measured directly; they were obtained by mathematical analysis. In a recent kinetic study with $Fe^{II}TPP$, Hoffman and co-workers[19] found that substitution of pyridine for imidazole caused but slight changes in the effective rate of carbon monoxide association to the five-coordinate Fe(TPP(B)) species. However, no dissociation rates or ligand affinities were reported. Our results with the picket fence porphyrin complexes, reported here, indicate that pyridine for imidazole substitution lowers CO affinities but that this effect is ca. 3 times smaller than that observed for the binding of O_2. Kinetic analysis indicates that this reduction in CO affinity is reflected primarily in increased ligand dissociation rates.

The equilibria of interest in this study are shown by eq 1–4,

$$FeP + B \underset{k_{-B}}{\overset{k_B}{\rightleftharpoons}} Fe(P(B)) \qquad K_B = k_B/k_{-B} \tag{1}$$

$$Fe(P(B)) + B \underset{k^{-B}{}_B}{\overset{k^B{}_B}{\rightleftharpoons}} Fe(P(B)_2) \qquad K^B{}_B = k^B{}_B/k^{-B}{}_B \tag{2}$$

$$Fe(P(B)) + L \underset{k^{-L}{}_B}{\overset{k^L{}_B}{\rightleftharpoons}} Fe(P(B))(L) \qquad K^L{}_B = k^L{}_B/k^{-L}{}_B \tag{3}$$

$$Fe(P(B))(O_2) + CO \overset{M}{\rightleftharpoons} Fe(P(B))(CO) + O_2 \qquad M = K^{CO}{}_B/K^{O_2}{}_B \tag{4}$$

where P represents the porphyrin ligand, B an axial base, and L a gaseous ligand, either CO or O_2. For a sterically unhindered nitrogen base such as pyridine or 1-methylimidazole, $K^B{}_B$ is greater than K_B, thus precluding the direct measurement of $K^{O_2}{}_B$ with use of a simple iron(II) porphyrin and an external axial base.[18] Similar considerations complicate kinetic studies.[19,20] Furthermore, simple iron(II) porphyrins irreversibly oxidize when exposed to oxygen at room temperature in solution.[21-24] These considerations led to the development of "tailed" picket fence porphyrins,[3,25,26] which both enforce five-coordination about iron (i.e., effectively reducing $K^B{}_B$ to zero) and sterically inhibit irreversible oxidation. For the picket fence complexes, however, the high CO affinities[13a] preclude the direct measurement of $K^{CO}{}_B$; it can only be obtained reliably by competitive binding in the presence of O_2 (eq 4).

In that stable dioxygen complexes are formed with complexes of the picket fence porphyrins, the binding properties of gaseous ligands can be studied by direct equilibrium (as well as kinetic) methods. Furthermore, a comparison of axial base effects on both O_2 and CO affinities can be made with the same iron(II) porphyrin system. We have, therefore, prepared a new series of tailed picket fence porphyrins bearing appended imidazole or pyridine nuclei and now wish to report a comparative study of the binding of both O_2 and CO to the iron(II) complexes of these porphyrins, as well as the actual synthesis of the complexes.

Experimental Section

All solvents and reagents were obtained commercially and purified as follows: Tetrahydrofuran (THF) was distilled from CaH_2 under N_2. Toluene and benzene were distilled from sodium under N_2. Heptane was stirred with 6 N H_2SO_4 and then 0.5 M $KMnO_4$ in 6 N H_2SO_4, washed with dilute $NaHCO_3$ and H_2O, dried over $MgSO_4$, and distilled from CaH_2 under N_2. Methanol was distilled from $Mg(OMe)_2$ under N_2. 2,6-Lutidine was passed through Al_2O_3 and then distilled from $BF_3{\cdot}Et_2O$ under N_2. Iron powder was converted to $FeBr_2$ by a literature procedure.[27] 3-(*N*-Imidazolyl)propylamine,[28] 3-(3-pyridyl)propylamine,[29] and 4-(3-pyridyl)butylamine[29] were prepared by literature procedures.

Syntheses and purifications of the free-base tailed porphyrins were carried out in a darkroom illuminated by a 25-W red light bulb, as similar compounds were found to be sensitive to the combination of light and oxygen.[25,26] Further manipulations were carried out under N_2 in a Vacuum Atmospheres drybox equipped with an MO-40 Dri-Train. NMR spectra were recorded on a Varian XL-100 FT spectrometer. Chemical shifts are reported downfield relative to Me_4Si. UV/visible spectra were recorded on a Cary 219 spectrophotometer. Oxygen-binding equilibria were determined with an apparatus consisting of a cuvette equipped with gas inlet and outlet tubes, attached to a pair of calibrated Matheson 600 rotometers, which mixed pure N_2 with pure O_2 or with premixed O_2 in N_2 (Liquid Carbonics certified mixture, 0.140% O_2 in N_2). *M* values were determined with the same flow cell apparatus by mixing pure O_2 with premixed 0.0478% CO in N_2 (Airco certified mixture). These methods have been described previously.[13a,30] For O_2 affinity measurements, concentrations of metalloporphyrin were ca. 6×10^{-5} M, and changes in the optical absorption spectra in the 480–700-nm region were monitored. For the *M*-value determinations, concentrations of ca. 5×10^{-6} M were used and changes in optical absorbance in the 350–500-nm region were monitored. The temperature during these measurements was maintained at 25.0 ± 0.2 °C.

For kinetic studies, samples of the five-coordinate iron(II) complexes were transported to Ithaca under N_2. In a homemade N_2 box equipped with an O_2 scrubbing tower (Ridox catalyst, BASF), deoxygenated solutions of ca. 2×10^{-6} M in metalloporphyrin were loaded into glass tonometers of known volume which were directly fused to 0.2-mm path length cuvettes. These tonometers were closed with Teflon stopcocks and serum stoppers. Following removal from the N_2 box, aliquots of O_2 or CO were added by means of gastight syringes. Laser flash photolysis experiments were performed at 25.0 ± 0.1 °C with a Phase R Model 2100B flashlamp pumped dye laser capable of generating up to 2 J of 540-nm light within 500 ns. Light attenuation was performed with use of a variety of differing transmittance neutral-density filters. Observations of the change in absorption following photolysis were made at several wavelengths (λ = 440, 436, 432, 427 nm) with use of a Spex Minimate monochromator and Oriel xenon arc lamp. Changes in current were converted to changes in voltage,

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digitalized with a Biomation Model 805 waveform recorder, and transferred to a PDP 8f computer for signal averaging and further analysis. Further details are presented elsewhere.[13c]

***meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(*N*-imidazolyl)propyl)ureido)phenyl)porphyrin, H_2PF3CUIm (4a).** A 200-mg (0.22-mmol) sample of *meso*-5α,10α,15α-(*o*-pivalamidophenyl)-20β-(*o*-aminophenyl)porphyrin[26] (**3**) was dissolved in 75 mL of THF in a three-necked round-bottom flask equipped with a three-way stopcock, stopper, and rubber septum. Phosgene (*Caution!*) was blown over the stirred solution for 20 min, with the excess bubbled through aqueous base. The solvent was removed in vacuo; 15 mL of THF was added with an N_2 purge and removed in vacuo. The green residue was dissolved in 50 mL of THF and 0.5 mL of pyridine. 3-(*N*-Imidazolyl)propylamine (162 mg, 1.29 mmol) was dissolved in 3 mL of THF and a trace of pyridine, and the solution was dripped into the red-brown porphyrin solution in the dark. The solution was stirred for 2 h, and then solvent was removed in vacuo. The residue was taken up in toluene (in a dark room with a weak red light), washed three times with H_2O, and run into a 1 in. × 6 in. column of dry 60–200 mesh silica gel (W. R. Grace). Elution with EtOAc removed unreacted amino porphyrin, and then THF was used to elute a broad reddish purple band of product. The solvent was removed on a rotary evaporator, and the product was recrystallized in the drybox by vapor diffusion of heptane into a concentrated toluene solution, yielding 170 mg (73%) of purple-red powder. IR (KBr): ν_{CO} = 1660–1700 cm^{-1} (broad). NMR (CD_2Cl_2): δ 2.87 (s, 2 H, internal NH), 0.01 (s, 9 H, $C(CH_3)_3$), 0.07 (s, 18 H, $C(CH_3)_3$), 0.75 (m, 2 H, CH_2), 1.50 (t, 2 H, CH_2), 2.09 (t, 2 H, CH_2), 2.80 (m, 1 H), 4.54 (m, 1 H), 5.07 (s, 2 H), 6.26 (s, 1 H), 7.09 (s, 2 H), 7.3–9.0 (m, 24 H). *m/e*: calcd for $C_{66}H_{67}N_{11}O_4$, 1078.543; found, 1078.566 ± 0.05.

***meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(3-pyridyl)propyl)ureido)phenyl)porphyrin, H_2PF3CUPy (4b).** The β-amino compound **3** (50 mg, 0.054 mmol) in 35 mL of THF was treated with phosgene as above. The resulting green residue was dissolved in 25 mL of THF and 0.5 mL of pyridine. In the dark, a solution of 3-(3-pyridyl)propylamine (46 mg, 0.34 mmol) in 1 mL THF and a trace of pyridine was dripped into the red-brown porphyrin solution. After 2 h of stirring, the solvent was removed in vacuo. The residue was taken up in toluene, washed well with H_2O, and dried over Na_2SO_4. The solution was then filtered and run into a 1 in. × 6 in. column of dry 60–200 mesh silica. Elution with 5:1 CH_2Cl_2/EtOAc removed a trace of unreacted amino porphyrin, and then EtOAc was used to elute a broad red band of product. The solvent was removed on a rotary evaporator, and the product precipitated from toluene/heptane in the drybox, yielding 50 mg (85%) of purple-red powder. IR (KBr): ν_{CO} = 1660–1700 cm^{-1} (broad). NMR (CD_2Cl_2): δ 2.93 (s, 2 H, internal NH), 0.01 (s, 9 H, $C(CH_3)_3$), 0.07 (s, 18 H, $C(CH_3)_3$), 0.67 (t, 2 H, CH_2), 1.02 (t, 2 H, CH_2), 2.42 (m, 2 H, CH_2), 4.18 (m, 1 H), 5.5–6.2 (m, 3 H), 6.64 (s, 1 H), 6.92 (s, 1 H), 7.05 (s, 3 H), 7.3–9.0 (m, 24 H). *m/e*: calcd for $C_{66}H_{68}N_{11}O_4$, 1089.549; found, 1089.556 ± 0.05.

***meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((4-(3-pyridyl)butyl)ureido)phenyl)porphyrin, H_2PF4CUPy (4c).** This compound was prepared from 50 mg (0.054 mmol) of the β-amino porphyrin **3** and 48 mg (0.32 mmol) of 4-(3-pyridyl)butylamine in the same manner as described above for H_2PF3CUPy, yielding 45 mg (71%) of purple-red powder. IR (KBr): ν_{CO} = 1660–1700 cm^{-1} (broad). NMR (CD_2Cl_2): δ 2.90 (s, 2 H, internal NH), 0.01 (s, 9 H, $C(CH_3)_3$), 0.07 (s, 18 H, $C(CH_3)_3$), 0.49 (t, 2 H, CH_2), 1.33 (m, 2 H, CH_2), 2.50 (m, 2 H, CH_2), 3.36 (m, 1 H), 4.13 (m, 1 H), 5.99 (s, 2 H), 6.11 (s, 1 H), 6.77 (s, 1 H), 7.08 (s, 3 H), 7.2–9.0 (m, 24 H). *m/e*: calcd for $C_{69}H_{70}N_{10}O_4$, 1103.564; found, 1103.598 ± 0.05.

[*meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(*N*-imidazolyl)propyl)ureido)phenyl)porphyrinato]iron(II), Fe(PF3CUIm). In the inert-atmosphere box, H_2PF3CUIm (**4a**; 100 mg, 0.093 mmol) was dissolved in 10 mL of benzene, 10 mL of THF, and 0.1 mL of 2,6-lutidine (~0.85 mmol). Anhydrous $FeBr_2$ (100 mg, 0.46 mmol) was added, and then the solution was heated at reflux for 25 min. After the solvents were removed in vacuo, the residue was chromatographed on a 1 in. × 2 in. column of neutral activity I Al_2O_3 (Woelm), with 5% MeOH in toluene as the eluent. The leading band was collected and brought to dryness in vacuo. The residue was dissolved in a minimum of THF and then precipitated by the addition of heptane, yielding 100 mg (95%) of red powder. UV/visible (toluene solution): five-coordinate, 373, 428, 533, 556, 606 (sh) nm; $+O_2$, 425, 544, 584 (sh) nm; +CO, 424, 540, 580 (sh) nm. NMR (CD_2Cl_2): five-coordinate, δ 0–10 (m), 49 (s), 49.5 (s), 54 (s), 55.5 (s), 62 (s); $+O_2$, δ 0.09 (s, 18 H, $C(CH_3)_3$), 0.12 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand; +CO, δ 0.09 (s, 18 H, $C(CH_3)_3$), 0.23 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand.

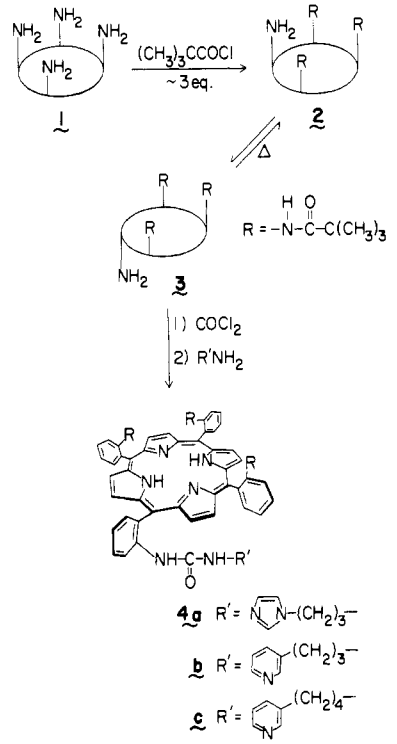

Figure 1. Synthesis of urea-linked "tailed picket fence" porphyrins.

[*meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(3-pyridyl)propyl)ureido)phenyl)porphyrinato]iron(II), Fe(PF3CUPy). This compound was prepared as described above for Fe(PF3CUIm). UV/visible (toluene solution): five-coordinate, 365, 425, 530, 560 (sh), 608 (sh) nm; $+O_2$, 423, 544, 582 (sh), 618 (sh) nm; +CO, 423, 540, 580 (sh), 606 (sh) nm. NMR (CD_2Cl_2): five-coordinate, δ0–10 (m), 47 (broad s); $+O_2$, δ 0.10 (s, 18 H, $C(CH_3)_3$), 0.23 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand; +CO, 0.09 (s, 18 H, $C(CH_3)_3$), 0.23 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand.

[*meso*-5α,10α,15α-Tris(*o*-pivalamidophenyl)-20β-(*o*-((4-(3-pyridyl)butyl)ureido)phenyl)porphyrinato]iron(II), Fe(PF4CUPy). This compound was prepared as described above for Fe(PF3CUIm). UV/visible (toluene solution): five-coordinate, 368, 424, 530, 560 (sh), 610 (sh) nm; $+O_2$, 422, 543, 578 (sh) nm; +CO, 423, 539, 580 (sh) nm. NMR (CD_2Cl_2): five-coordinate, δ 0–10 (m), downfield features broadened beyond recognition; $+O_2$, δ 0.09 (s, 18 H, $C(CH_3)_3$), 0.23 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand; +CO: δ 0.09 (s, 18 H, $C(CH_3)_3$), 0.23 (s, 9 H, $C(CH_3)_3$), other features much as for the free ligand.

Results

meso-5α,10α,15α,20α-Tetrakis(*o*-aminophenyl)porphyrin (**1**) (Figure 1), a readily available intermediate from the original "picket fence" porphyrin synthesis,[31] was treated with 3.2 equiv of pivaloyl chloride, yielding the "three-picket" β-amino porphyrin **2** in roughly 35% yield after chromatography. Heating in solution equilibrated this α-amino porphyrin to a 1:1 mixture of the α-amino and β-amino isomers, from which the β-amino isomer, **3**, was separated by chromatography.[25,26]

We have previously[25,26] appended axial bases to this β-amino porphyrin via an amide linkage. The "tail" precursors for such porphyrins, however, are neither stable nor well-behaved. Suitable "tails" for appending axial bases via a urea linkage, on the other hand, are stable, distillable compounds. Thus, the β-amino porphyrin **3** was treated with phosgene, yielding

(31) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975**, *97*, 1427–1439.

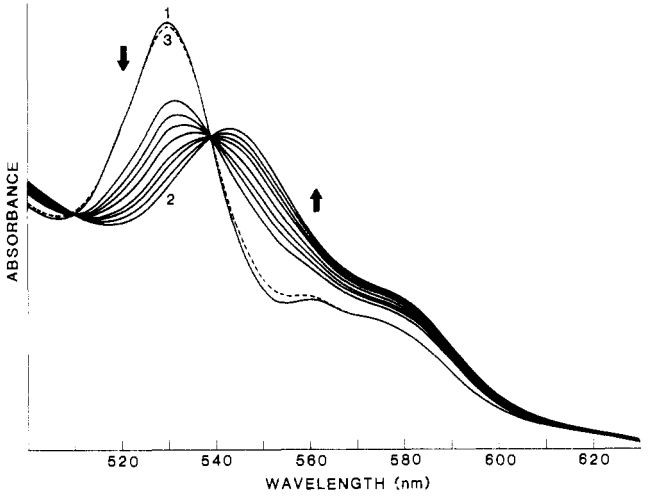

Figure 2. Spectral changes observed upon treatment of a deoxygenated toluene solution of Fe(PF4CUPy) with O_2: (1) under 1 atm of N_2; (2) under 1 atm of oxygen; (3) under 1 atm of N_2 after treatment with O_2. Intermediate curves were obtained by diluting N_2 with increased quantities of 0.14% O_2/N_2. The following intermediate partial pressures of O_2 were used: 24.2, 37.0, 69.7, 105, 195, 269, 420 torr.

either the carbamoyl chloride or the isocyanate. Addition of 3-(*N*-imidazolyl)propylamine[28] gave, in quite good yield, the desired tailed picket fence porphyrin, *meso*-5α,10α,15α-tris-(*o*-pivalamidophenyl)-20β-(*o*-((3-(*N*-imidazolyl)propyl)ureido)phenyl)porphyrin (**4a**). Analogous reactions led to *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-((3-(3-pyridyl)-propyl)ureido)phenyl)porphyrin (**4b**) and *meso*-5α,10α,15α-tris(*o*-pivalamidophenyl)-20β-(*o*-((4-(3-pyridyl)butyl)ureido)phenyl)porphyrin (**4c**).

Iron was introduced[25,26] as iron(II), with use of anhydrous $FeBr_2$ and a noncoordinating base (2,6-lutidine). After removal of 2,6-lutidine hydrobromide and excess $FeBr_2$ by filtration through activity I neutral alumina, essentially quantitative yields of the five-coordinate iron(II) tailed picket fence porphyrins Fe(PF3CUIm), Fe(PF3CUPy), and Fe(PF4CUPy) were obtained.

The O_2 affinities of these iron(II) tailed picket fence porphyrins in dilute toluene solution were determined spectrophotometrically, with an apparatus described elsewhere[30] and standard data treatment.[3,30] M values were determined spectrophotometrically with use of the method described earlier.[13a] Typical spectral changes are shown in Figures 2 and 3. Only data from sets of spectra displaying good isosbestic points were used for calculations. The results of these equilibrium studies are summarized in Table I and compared with those for the amide-linked imidazole tailed picket fence porphyrins.[3,13a] We continue to favor reporting affinities as $P_{1/2}{}^{L}$ rather than as $K^{L}{}_{B}$.[13a] Interconversion between these two is, however, straightforward.[32]

The O_2 and CO complexes of Fe(PF3CUIm) and Fe(PF3CUPy) are photolabile. The kinetics of ligand binding can, therefore, be studied with use of laser flash techniques. In the absence of gaseous ligand, for large values of K_B, five-coordination about iron pertains on the kinetic time scale following flash photolysis when either

$$k_{-B} << k^{L}{}_{B}[L] \quad \text{or} \quad k_{B}[B] >> k_{L}$$

(32) The interconversion of $P_{1/2}{}^{L}$ to $K^{L}{}_{B}$ requires knowing the solubility of the gaseous ligand L. We have used $[O_2] = 9.1 \times 10^{-3}$ M/atm at STP and $[CO] = 7.5 \times 10^{-3}$ M/atm at STP as given in ref 33. For instance, with a $P_{1/2}{}^{O_2} = 52.2$ torr for Fe(PF3CUPy), $K^{O_2}{}_{B} = 52.2^{-1} \times 760 \times (9.1 \times 10^{-3})^{-1} = 1.6 \times 10^{3}$ M^{-1}.

(33) Linke, W. F.; Seidell, A. "Solubilities of Inorganic and Metal-Organic Compounds", 4th ed; Van Nostrand: Princeton, NJ, 1958.

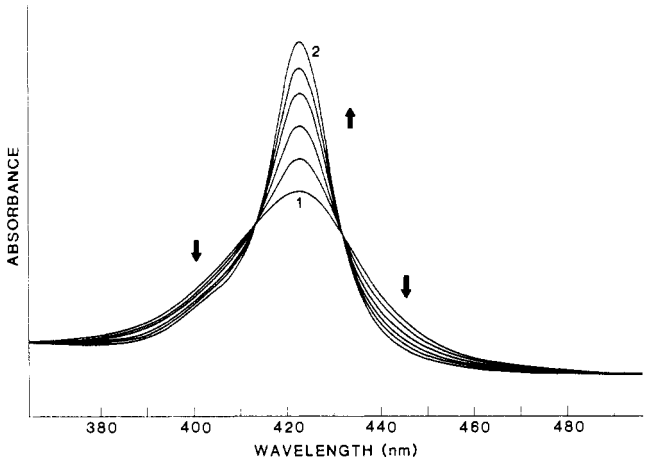

Figure 3. Spectral changes observed upon treatment of Fe(PF4CUPy)(O_2) with CO: (1) under 1 atm of O_2; (2) under 1 atm of CO. Intermediate curves were obtained by diluting O_2 with increased quantities of 0.0478% CO/N_2. The following intermediate ratios of CO to O_2 were used: 3.42×10^{-6}, 1.21×10^{-5}, 2.90×10^{-5}, 7.04×10^{-5}.

Table I. O_2 Affinities of Various Five-Coordinate Iron(II) Porphyrin Complexes

complex	$P_{1/2}{}^{O_2}$, torr	$k^{O_2}{}_{B}$, M^{-1} s^{-1}	$k^{-O_2}{}_{B}$	ref
Fe((Piv)$_3$4CImP)[a]	0.60			3a
Fe((Piv)$_3$5CImP)[a]	0.58	4.3×10^{8}	2.9×10^{3}	3a, 13c
Fe(PF3CUIm)[a]	1.26[e]	2.6×10^{8} [e]	3.9×10^{3} [f]	this work
Fe(PF3CUPy)[a]	52.2[e]	3.0×10^{8} [e]	1.9×10^{5} [f]	this work
Fe(PF4CUPy)[a]	41.6[e]			this work
Fe(Cap(1-MeIm))[a]	23[g]			11
Fe[Cap(3-Cl(py))][a]	180[g]			11
Im-mesoheme dimethyl ester[b]	0.57[h]	2.2×10^{7}	23	4a
Py-mesoheme dimethyl ester[b]	12.2[h]	1.7×10^{7}	380	16b
Py-mesoheme[c]	>760			1
Py-pyrroheme[d]	≈400			5
Im-pyrroheme[c]	0.2			1

[a] Toluene, 25 °C. [b] Aqueous suspension, 2% cetyltrimethylammonium bromide, pH 7.3, 22 °C. [c] CH_2Cl_2, −45 °C. [d] Toluene, −45 °C. [e] Measured directly, estimated errors ≲15%. [f] Calculated from $P_{1/2}{}^{O_2}$ and $k^{O_2}{}_{B}$. [g] Extrapolated to 25 °C from thermodynamic data. [h] Calculated from $k^{O_2}{}_{B}$ and k^{-O_2}.

where k_L represents the rate of ligand binding to the four-coordinate iron(II) porphyrin and k_B, k_{-B} and $k^{L}{}_{B}$ are defined as in eq 1–3. The following reaction then occurs

$$\text{Fe(P(B))(L)} \xrightarrow{h\nu} \text{Fe(P(B))} \underset{k^{-L}{}_{B}}{\overset{k^{L}{}_{B}}{\rightleftharpoons}} \text{Fe(P(B))(L)} \quad (5)$$

with the rate of return to equilibrium, k_{obsd}, being

$$k_{obsd} = k^{L}{}_{B}[L] + k^{-L}{}_{B} \quad \text{or} \quad k_{obsd} = k^{L}{}_{B}([L] + 1/K^{L}{}_{B}) \quad (6)$$

At high concentrations of L where $k^{L}{}_{B}[L] >> k^{-L}{}_{B}$, the following approximation is valid

$$k^{L}{}_{B} \approx k_{obsd}/[L] \quad (7)$$

and the association rate $k^{L}{}_{B}$ is simply obtained. We have recently found that reliable values for O_2 dissociation rates may be calculated from $k^{L}{}_{B}$ and $K^{L}{}_{B}$ for iron(II) complexes of the picket fence and tailed picket fence porphyrins.[13c] Similar observations had previously been made for CO binding to iron(II) deuteroporphyrin.[20]

For complexes of Fe(PF3CUIm) and Fe(PF3CUPy), at low ligand concentrations, plots of the log of the change in ab-

Table II. CO Affinities of Various Five-Coordinate Iron(II) Porphyrin Complexes

complex	$P_{1/2}^{CO}$, torr	$10^{-7}k^{CO}_B$, M^{-1} s^{-1}	k^{-CO}_B, s^{-1}	M	ref
Fe((Piv)$_3$5CImP)	2.2×10^{-5}	3.6	7.8×10^{-3}	26 600	13a, 13b
Fe(PF3CUIm)	4.9×10^{-5} [f]	2.9[e]	1.4×10^{-2} [g]	26 000[e]	this work
Fe(PF3CUPy)[a]	6.4×10^{-4} [f]	4.8[e]	3.3×10^{-1} [g]	76 000[e]	this work
Fe(PF4CUPy)[a]	6.5×10^{-4} [f]			64 000[e]	this work
Fe(DHD(1-HIm))[b]	2.4×10^{-4} [c]				18
Fe(DHD(4-CNpy))[b]	2.0×10^{-3} [c]				18
Im-mesoheme dimethyl ester[d]	1.3×10^{-3}	1.1	1.9×10^{-2}	450	4a, 16a
Py-mesoheme dimethyl ester[d]	2.1×10^{-3}	1.2	3.5×10^{-2}	5 700	16

[a] Toluene, 25 °C. [b] Benzene, 25 °C. [c] CO affinity derived by mathematical analysis; six-coordination pertains for this complex in the absence of carbon monoxide. [d] Aqueous suspension, 2% cetyltrimethylammonium bromide, pH 7.3, 20 °C. [e] Measured directly, estimated errors $\lesssim$15%. [f] Calculated from $P_{1/2}^{O_2}$ and M value. [g] Calculated from $P_{1/2}^{O_2}$, M, and k^{CO}_B values.

sorbance vs. time following laser flash were biphasic, indicating that appreciable rebinding to the four-coordinate iron(II) porphyrin was occurring via the so-called "base-off" mechanism.[20] At high gaseous ligand concentrations ($3 \times 10^{-4} \leq [O_2] \geq 1.1 \times 10^{-3}$ M, [CO] = 7.5×10^{-3} M), plots of ln Δ(Abs) vs. time were linear, suggesting that clean first-order decays were occurring (Figure 4).[34] Furthermore, k_{obsd} was found to be fairly independent (±10%) of the wavelength used to observe the spectral changes. At these ligand concentrations, the assumption that $k^{L}_B[L] >> k^{-L}_B$ holds for O_2 rebinding to Fe(PF3CUIm), as well as for CO rebinding to Fe(PF3CUIm) and Fe(PF3CUPy). Values for k^{L}_B are obtained directly from eq 7. With the Fe(PF3CUPy) system, in this range of O_2 concentrations, laser flash photolysis generates the five-coordinate Fe(PF3CUPy) complex, which returns to an equilibrium mixture of *both* five- and six-coordinate species according to eq 6. With $K^{O_2}_B = 1.6 \times 10^3$ M^{-1}, as measured by direct titration, $k_{obsd} = k^{O_2}_B[O_2] + k^{O_2}_B/1.6 \times 10^3$. At $[O_2] = 7.45 \times 10^{-4}$ M, $k_{obsd} = 4.08 \times 10^5$ s^{-1}, indicating that $k^{O_2}_B = 2.98 \times 10^5$ M^{-1} s^{-1} for Fe(PF3CUPy). $k^{O_2}_B$ calculated in this manner remained invariant ($\lesssim$15%) to a $\gtrsim$250% change in $[O_2]$. Unfortunately the range of oxygen concentrations we could examine was limited; at $[O_2] \gtrsim 1.1 \times 10^{-3}$ M, k_{obsd} was too large to measure accurately with our apparatus. The results of our kinetic studies with the tailed picket fence complexes are also included in Tables I and II.[35]

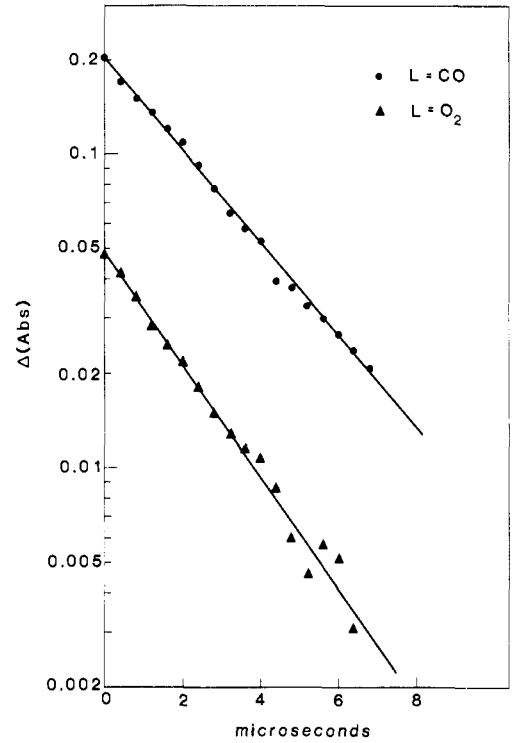

Figure 4. Plots of the fraction of five-coordinate complex, Fe(PF3CUPy), vs. time after laser flash photolysis of Fe(PF3CUPy)(L): (●) [CO] = 7.50×10^{-3} M, λ_{obsd} = 440 nm; (▲) $[O_2] = 7.45 \times 10^{-4}$ M, λ_{obsd} = 436 nm. The solid lines are least-squares fits through the experimental values (points).

Discussion

Both electronic effects[1] and steric effects[3,4] in axial base coordination may influence the affinities of iron(II) porphyrins for gaseous ligands. Steric effects are appreciable.[3,4] For instance, in the picket fence series Fe(TpivPP(1,2-Me$_2$Im)) shows O_2 and CO affinities 75 and 400 times lower than the unconstrained complex Fe((Piv)$_3$5CIm).[3] These reductions were ascribed to the severe steric interaction between the 2-methyl group of the imidazole and the porphyrin plane.[3,36] In the case of appended-base ("tailed") porphyrins, Traylor and co-workers[4] have found that geometrical or orientational constraints imposed by shortening the length, or increasing the rigidity, of the covalent linkage leads to reduced O_2 binding affinities. Furthermore, with the carbonyl complexes of these strained systems, it was found that direct recombination of CO to the four-coordinate (rather than to the five-coordinate) iron(II) porphyrin occurred, via what was labeled the "base-off" mechanism.[4] Therefore, in order to discuss effectively any basicity-induced effects on O_2 and CO binding that pyridine for imidazole substitution may engender in tailed iron(II) porphyrins, it is necessary to ensure that any steric influences imposed by the linkage are minor.

As the tailed porphyrins described here bear a urea linkage between tail and porphyrin, while our previous work[3,13a] was with compounds bearing amide linkages, we have also examined the binding properties of a urea-linked imidazole tail compound as well as the pyridine tail compounds of interest in this study. Our "control" experiment indicates that the change in linkage has only a very small effect on the O_2 and CO affinities of the imidazole tail compounds, as shown by the data in Tables I and II. The slight reduction in fact observed probably indicates that some slight steric strain may exist in the urea complexes. The effect of changing the linkage is, however, small compared to that seen upon replacing the imidazole with a pyridine nucleus. The data in Tables I and II show that, upon doing so, a reduction of about 40-fold in O_2 and 13-fold in CO affinities are achieved. Similar O_2 and CO affinities are observed for two different pyridine tail complexes, one (**4b**) having a shorter linkage than the other (**4c**), further suggesting that the decreased affinities of the pyridine tailed complexes are not simply due to an unfavorable ligand geometry enforced by the linkage.

(34) All recombination rates measured in this study were made under pseudo-first-order conditions.
(35) No kinetic experiments were made with the Fe(PF4CUPy) complexes.
(36) Jameson, G. B.; Molinaro, F. S.; Ibers, J. A.; Collman, J. P.; Brauman, J. I.; Rose, E.; Suslick, K. S. *J. Am. Chem. Soc.* **1980**, *102*, 3224–3237.

Our observation with the picket fence system that an approximately 40-fold reduction in O_2 affinity is obtained upon pyridine for imidazole substitution is in accord with results obtained with the "chelated" mesohemes[4,16b] at room temperature (ca. 20-fold reduction) and with the "capped" system,[11] where an 8-fold reduction was found. Although some scatter is observed between these systems,[37] it now appears established that approximately an order of magnitude reduction in O_2 affinity can reasonably be expected when pyridine is substituted for imidazole in five-coordinate iron(II) porphyrins. The extent of these decreases is thus similar to those previously observed in cobalt(II)[38,39] and manganese(II)[40] porphyrins.

Traylor has argued[1] that the >2000-fold difference in O_2 affinity between the pyridine- and imidazole-ligated iron(II) porphyrins his group has studied at low temperatures is due to the decreased π-basicity of pyridine vs. imidazole, resulting in lessened iron-to-oxygen back-bonding and thus decreased O_2 affinity. In essence, an increased π-basicity could serve to stabilize an oxygen adduct by supporting the separation of charge in the $Fe^{\delta+}$–O–$O^{\delta-}$ unit.[41] The more recent data (Table I) support this analysis but suggest that the extent of this π-basicity effect on O_2 binding to iron(II)porphyrins is less than the three orders of magnitude reduction originally proposed.[42] It is worth noting here the observation by Basolo and co-workers[11] that the O_2 affinities of various iron(II) capped porphyrin complexes were insensitive to the pK_b of various substituted pyridines is consistent with the original proposal[1] that it is the good π-electron-donating properties of imidazole, as opposed to the Brønsted basicity, that is responsible for the 10–50-fold higher O_2 affinity of iron(II) imidazole ligated complexes when compared to that for analogous pyridine adducts.

The kinetic data presented in Table I indicate that the increased ability of imidazole to support oxygenation in iron(II) porphyrins leads to decreased O_2 dissociation rates. By contrast, these observed changes in relative stability of the six-coordinate ligated complexes do not appear to affect greatly the rates of O_2 association to these five-coordinate iron(II) picket fence porphyrin complexes (**4a**, **4b**). This suggests that other factors such as diffusion to the iron(II) center, motion of the iron into the porphyrin plane, or other changes independent of the axial base may serve to determine the magnitude of these ligand "on" rates. Moreover, this suggests that the transition states for O_2 binding (association) to the iron(II) picket fence porphyrin complexes resemble the reactants.[44] This is in accord with similar proposals made with regard to O_2 binding to hemoglobin.[45,46] The kinetic data further support the proposal (vide supra) that the increased affinities of the imidazole-ligated iron(II) porphyrins arise from a stabilization of the six-coordinate ligated form rather than from changes in the nature of the five-coordinate species. This is consistent with the hypothesis[1] that the increased π-basicity of imidazole is supporting a separation of charge in the Fe–O–O unit. These kinetic results are also in agreement with previous studies[2,4,47] with iron(II) porphyrins that have demonstrated that other factors that presumably, mediate the separation of charge in the $Fe–O_2$ unit are manifested predominantly as changes in O_2 dissociation rates.

Chang and Traylor[1] have suggested that the greater σ-basicity (protic basicity) of the carbonyl ligand as compared to that of dioxygen should make the CO bonding affinities of iron(II) porphyrins less susceptible to changes in iron to CO back-bonding arising from changes in the π-basicity of the axial base. Table II shows that the CO affinities of the chelated mesoheme system in aqueous suspension are rather insensitive to changes in axial base: only a factor of 2 reduction is observed when pyridine is substituted for imidazole.[4,16] In contrast, a similar exchange in the picket fence series effects a 13-fold reduction, which is similar in extent to the 9-fold difference seen between Fe(DHD(1-HIm)) and Fe(DHD(4-CNpy)).[18] Although the effect on CO binding for the picket fence compounds is appreciably smaller than that observed with O_2, our results nonetheless suggest that the increased π-basicity of an imidazole affords some stabilization of the bound carbonyl. As with O_2, these affinity changes in the picket fence complexes are predominantly observed in CO dissociation rates. These results apparently suggest that greater separation of charge exists in the Fe–CO unit of the picket fence carbonyl complexes (in toluene) than in the carbonyl adducts of the chelated mesohemes (in aqueous micellar suspension).

In comparing results from these two different pyridine for imidazole substitution studies, it should clearly be noted that both different iron(II) porphyrin systems (chelated mesoheme and Fe(II) picket fence porphyrin) and different solvent systems (toluene and aqueous suspension) were used. Understanding which factors might be responsible for the slight, but significant, differences in the relative binding behavior of these two systems remains as a matter of some interest.

Acknowledgment. This work was supported by the National Institutes of Health (NIH Grant Nos. GM17880 and GM14276) and by the National Science Foundation (NSF Grant Nos. CHE78-09443 and CHE79-10446). NMR spectra were recorded on an instrument supported by the National Science Foundation (Grant No. GP-28142). Mass spectral data were obtained at the Middle Atlantic Mass Spectrometry Laboratory, The Johns Hopkins University, Baltimore, MD. This facility is supported under the National Science Foundation Regional Instrumentation Facilities Program.

Registry No. **3**, 75557-90-3; **4a**, 75526-89-5; **4b**, 84849-04-7; **4c**, 84849-05-8; Fe(PF3CUIm), 84849-06-9; Fe(PF3CUPy), 84849-07-0; Fe(PF4CUPy), 84849-08-1; CO, 630-08-0; O_2, 7782-44-7; 3-(*N*-imidazolyl)propylamine, 5036-48-6; 3-(3-pyridyl)propylamine, 41038-69-1; 4-(3-pyridyl)butylamine, 6021-23-4.

(37) A number of factors such as solvation effects, the electronic nature of the heme, polarity of the binding site, and the degree of structural rearrangement upon ligand binding may influence the binding affinity of gaseous ligands for iron(II) porphyrins. Insomuch as the extent of these factors may differ from system to system, direct comparisons between dissimilar iron(II) porphyrins are complicated. A discussion of these influences is not appropriate here. Nonetheless, in *relative* comparisons of axial base effects within a given system, the extent of these differences may effectively cancel out.

(38) Stynes, H. C.; Ibers, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 1559–1562.

(39) Walker, F. A. *J. Am. Chem. Soc.* **1973**, *95*, 1154–1159.

(40) Jones, R. D.; Summerville, D. A.; Basolo, F. *J. Am. Chem. Soc.* **1978**, *100*, 4416–4424.

(41) This argument has been adequately presented[1] and need not be discussed further here.

(42) We originally suspected that the large difference in O_2 affinities these workers observed might be due to steric effects, inasmuch as slightly different covalent linkages were used in the covalent attachment of the two bases. The control experiments we have carried out suggest that this is not the case. The relative insensitivity of the ratio of O_2 affinities of Fe(Cap(Py)) and Fe(Cap(1-MeIm)) to temperature[11] indicates that no unusual effects are associated with comparisons at low temperatures. It is known,[26,43] however, that tailed iron(II) porphyrins dimerize at low temperatures. It is therefore conceivable that at low temperatures equilibria other than that of eq 3 interfere with ligand binding (e.g. those of eq 1 and 2). This particular result of Chang and Traylor[1] might warrant reinvestigation.

(43) Momenteau, M.; Rougee, M.; Loock, B. *Eur. J. Biochem.* **1976**, *71*, 63–76.

(44) This point is discussed further in ref 13c.

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(46) Moffat, K.; Deatherage, J. F.; Seybert, D. W. *Science (Washington, D.C.)* **1979**, *206*, 1035–1042.

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