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Axial Ligation of Iron(III) Porphyrin with a Series of Aliphatic Bases: Piperazine, Piperidine and Pyrrolidine[1]

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Abstract—The binding of a series of nitrogen donor ligands (Piperazine (Pipz), Piperidine (Pip) and Pyrrolidine (Pyr)) to iron porphyrin, $OEPFeClO_4$, where OEP is octaethylporphyrin, has been characterized by electronic spectroscopy in CH_2Cl_2. In nonaqueous media, in the presence of a neutral ligand, the equilibria observed are: $OEPFeClO_4 + 2L \rightleftharpoons [OEPFeL_2]^+ ClO_4^-$ (β_2) where the product is an ion pair and in some cases: $OEPFeClO_4 + L \rightleftharpoons OEPFeLClO_4$ (K_1), where the product may either be the six-coordinate or the five-coordinate $[OEPFeL]^+ ClO_4^-$ ion pair, that L denotes neutral N-donor ligands. This behavior for the nitrogen donor ligands (L = Pipz, Pip, Pyr) is confirmed by spectrophotometric titrations data and the binding constants for the substitution reaction have been reported.

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Metalloporphyrins have been used to mimic biological systems. A great number of experimental results have been reported over the past decades concerning the axial ligation properties of metallo– porphyrins with S, O, P and N bases [1]. The interaction of metalloporphyrins with donor molecules either in their ground or excited states can strongly influence the absorption properties and the efficiency of energy or electron transfer processes of porphyrin derivatives. Thus, understanding the effects of axial ligands on the electronic spectra of metalloporphyrins is a basic but important subject because of its biological relevance [2]. Variations in the biological role of the naturally occurring hemoproteins are intimately associated with changes in the axial ligation of the heme moiety. Relevant to our understanding of the mechanism of the action of the hemoproteins is an understanding of the manner in which axial ligation affects the electronic structure and reactivity of a metalloporphyrin system [3].

In all of the heme proteins investigated to date, the heme moiety is bound to the protein by at least one coordinate covalent bond between iron and the "aromatic" nitrogen of a histidine residue of the protein. Iron porphyrin complexes of imidazole are a logical starting point in the search for appropriate spectroscopic models for heme centers in metalloproteins [4], since the histidyl imidazole side chain in the most common axial ligand bound to iron in such enzymes. Six-coordinate heme centers with two axial imidazole ligands in metalloproteins are known to act as electron transfer redox centers, e.g., in cytochrome b_5. In some cases there are additional covalent or coordinate covalent linkages as well, as in the cytochromes *b* and *c*, but the iron-imidazole linkage is common to all those where axial ligands have been identified [5, 6]. One is thus led to the question of why some ligands such imidazole should be the ligand of choice for hemes rather than some other Lewis base and why some Fe(III)–porphyrin-imidazole complexes are so much more stable [7]. Several studies of the axial ligation reactions of Fe(III) porphyrins have already been reported [6, 8–13]. Two steps of axial ligand addition to Fe(III) porphyrin are possible. The first step is the formation of the 1 : 1 complex:

$$OEPFeCl + L \rightleftharpoons OEPFeLCl \quad K_1 \qquad (1)$$

which may either be the six-coordinate model complex of ferrihemoglobin or ferrimyoglobin, or the five-coordinate $[OEPFeL]^+ ClO_4^-$ ion pair [6]. The distinction between these two possible coordination numbers and, indeed, the potential interconversion between these two forms of the 1 : 1 complex is made difficult due to the intervention of the second step of axial ligand addition to form the 2 :1 complex:

$$OEPFeLCl + L \rightleftharpoons [OEPFeL_2]^+Cl^- \quad K_2. \qquad (2)$$

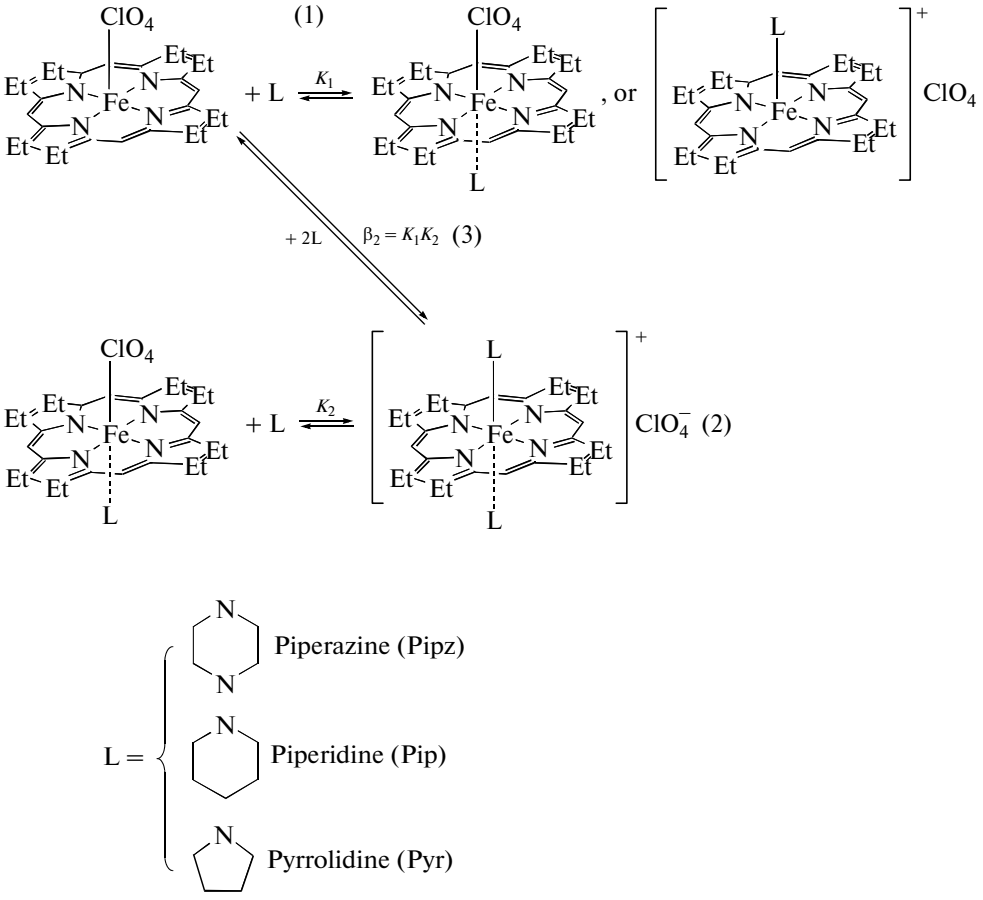
Since, as we shall see, the stepwise constant, K_2, is in general larger than K_1. In fact, as we shall also see, formation of the 1 : 1 complex is not always detectable, leading to the frequent experimental observation of addition of two ligands in an apparent single step:

[1] The article is published in the original.

$$OEPFeCl + 2L \rightleftharpoons [OEPFeL_2]^+Cl^- \ \beta_2. \quad (3)$$

Equation (3) is the sum of equations (1) and (2), and $\beta_2 = K_1K_2$. The product of reactions (2) and (3) is usually an ion pair [9, 12, 14] which, in the stoichiometry found for the equilibrium constants K_2 and β_2, behaves as one unit rather than as two ions.

We describe here the binding of $OEPFeClO_4$, to a group of aliphatic nitrogen donor ligands (L = Pipz, Pip, Pyr). These ligands bind to porphyrin, through 1 : 1 complex, to form a 1 : 2 complex even in the presence of an excess of the ligands. By using UV-visible absorption we have elucidated the equilibrium constants for the reactions of these ligands with porphyrin (Scheme 1).



Scheme 1.

EXPERIMENTAL

Material and Instrumentation

$[OEPFeClO_4]$ was prepared by the method of Ogoshi et al. [15]. All reagents and solvents used in this study were obtained from Merck and Aldrich Chem. Co. Dichloromethane was dried by refluxing under an inert gas over a drying agent, such as phosphorous pentoxide or calcium hydride, and distilled immediately before use. Piperidine was distilled from zinc dust and then barium oxide. UV-visible spectra were recorded on an analytikjena SPECORD S100 spectrometer with photodiode array detector with thermostat cell compartment, that control the temperature around the cell within cuvette at 25.0 ± 0.1°C in the cell compartment.

Ligand Substitution Measurement

Equilibrium constants were measured by a spectrophotometric titration method. During the titration, the temperature of the solution was maintained at 25.0 ± 0.1°C and a dichloromethane solution containing ligands were added to a dichloromethane solution of $OEPFe(ClO_4)$ (4.14×10^{-4} M) in separately steps. In general, the spectra were recorded in the 300 to 650 nm region during the titration. In each step 2 mL of the porphyrin solution was placed in a cuvette and the UV-visible absorption spectrum was recorded. 5–10 μL aliquots of ligand solution were sequentially added to the porphyrin solution, and the spectrum was recorded after each addition. The values of the absorbance at a fixed wavelength were used in our calculation to obtain the relevant binding constants. The

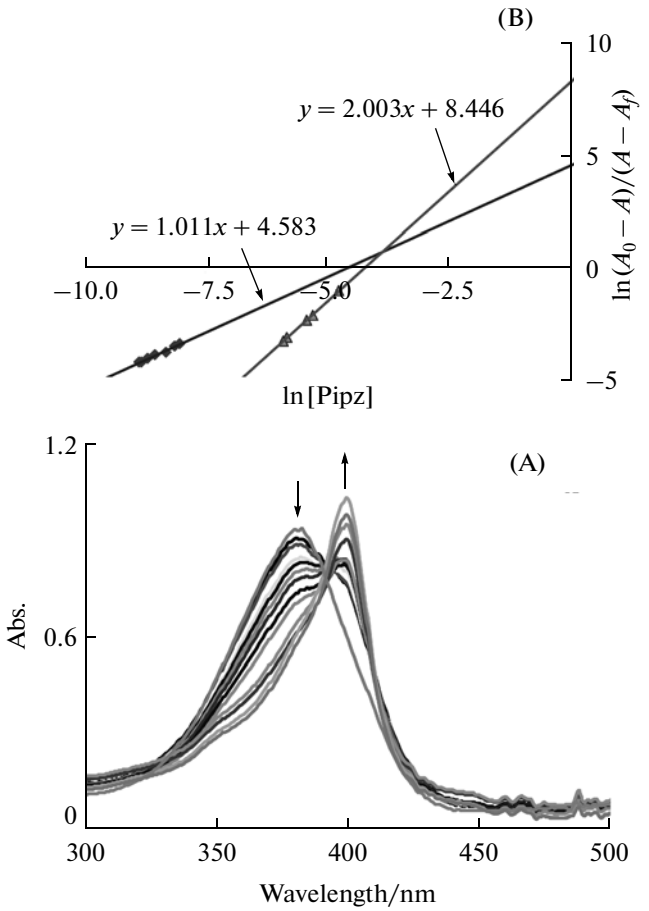


Fig. 1. A—Visible spectral changes observed upon addition of Pipz to $OEPFeClO_4$ in CH_2Cl_2. B—Plot of $\ln(A_0 - A)/(A - A_f)$ versus ln[Pipz] to calculate K_1 and β_2.

titration shows isosbestic points and the data can be fitted with equation (4) [16–20]:

$$\ln\frac{A_0 - A}{A - A_f} = n\ln[L] + \ln K \qquad (4)$$

where A_0, initial absorbance (uncomplexed porphyrin); A_f final absorbance (fully complex porphyrin; and A, absorbance at a specific [L]; and K is the binding constant. Values for ln$K$ were obtained from they intercept of the regression line for a plot of $\ln(A_0 - A)/(A - A_f)$ vs ln[L]. In all cases, isosbestic points were maintained throughout most of the titration. Deviations from isosbestic behavior during the latter stages of the titration could be quantitatively related to dilution effects.

Table 1. Absorption maxima and extinction coefficients (ε) for addition of ligands to $OEPFeClO_4$ in CH_2Cl_2

Ligand	Soret bond/nm	$\varepsilon/M^{-1}cm^{-1}$
None	382	2.37×10^3
Pip	399	2.66×10^3
Pipz	400	2.50×10^3
Pyr	402	2.93×10^3

RESULTS AND DISCUSSION

The origin of the marked differences in electronic spectra between metalloporphyrin ligand complex and the metalioporphyrin without axial ligand(s) has been subjected of several discussions. Corwin and coworkers (1963) have purposed the Soret shift upon ligand binding arises from the stereoelectronic effect of ligand upon the porphyrin n system; the shift to longer wavelength of the metalloporphyrin ligand complex compared with the metalloporphyrin without axial ligand(s) was ascribed to sreric interference between the ligand and the π-electron system of the porphyrin ring. Mauzerall (1965) has suggested the shift could be unrelated to ligand binding but rather could result from differences in solvent interactions with the porphyrin π system. Caughey et al. [21] has considered the factor most likely to make a dominant contribution to the spectral shift to be the change in interaction between porphyrin and metal ion which results upon binding the axial ligands. The binding of nitrogen bases as axial ligands can be expected to reduce markedly the electronegativity of iron ion; that is, the iron ion will serve as a less effective electron acceptor from the porphyrin nitrogens.

UV-Vis spectrophotometric titration method was used to determine the equilibrium constants between $OEPFeClO_4$ and three aliphatic nitrogen donor ligands (L = Pipz, Pip, Pyr). Addition of several drops of a nitrogenous ligand to a cuvette containing a dichloromethane solution of $OEPFeClO_4$ results in an immediate change in the visible spectrum to one identical spectrum of the dichloromethane solution of the no reacted iron porphyrin. In all cases, the red shift of the Soret band has been observed after addition of nitrogen donor ligands, due to axial ligand binding. Figure 1 shows the absorption spectral change of $OEPFeClO_4$ in the presence of various concentrations of Piperazine (2.50×10^{-4} to 8.3×10^{-3} M) in CH_2Cl_2. The Soret band at 382 nm decreased and a new band appeared at 400 nm with clear two isosbestic points: one at low ratios of amine to Fe(III) (392 nm) and a second at 408 nm for higher ratios. The spectral patterns at high ratios of amine to Fe(III) are similar to those of the six-coordinated iron porphyrins [6]; therefore, the reaction corresponds to the axial ligation of Piperazine (Pipz) to the Fe(III) center.

The absorption maxima and extinction coefficients of $OEPFeClO_4$ and its amine adduct in CH_2Cl_2 are listed in Table 1. The effects of the axial ligands on the absorption spectra of iron porphyrins include considerable red shifts of the absoiption bands. Visible spectral changes observed upon addition of ligands to $OEPFeClO_4$ in CH_2Cl_2 are shown in Figs. 1–3.

Typically in the case of Piperazine as ligand, calculations were done on absorbance data taken at 382 nm and the wavelength maximum of the product, which is 400 nm. For addition of one base molecule, $\ln K_1$ is estimated from the intercept of the portion of the graph which yields slope of 1.0, and $\ln\beta_2$ is obtained from the intercept of the portion of the graph which yields a slope of 2.0. The values of $\ln K_1$ and $\ln\beta_2$ have been obtained from the y intercept extrapolation in Fig. 1B. The assumption made in the determination of $\ln K_1$ in Fig. 1 is that A_f for the 1 : 1 complex is similar to A_f, for the 2 : 1 complex. This is probably not true, except, perhaps, at 382 nm, but in the absence of spectral data for the isolated 1 : 1 complexes, it is the only reasonable assumption which can be made. That the spectra of the 1 : 1 and 2 : 1 complexes are at least similar at 382 nm is suggested by the behavior of isosbestic points. Typically, only two or three data points, for different ln[L] values, were available for drawing the slope = 1.0 line. Thus, the values of $\ln K_1$ should be considered as only rough estimates. The method of calculation of β_2 is based on the stoichiometry of Eq. (3) that is three moles of reactants forming one mole of product. Thus the product behaves as one unit, an "associated" ion pair, and β_2 has units of M^{-2} [6]. Measurement of β_2 for addition of nitrogenous ligands as a function of total [$OEPFeClO_4$], with CH_2Cl_2 as solvent, indicates that at concentrations greater than 10^{-5} M, β_2 and K_1 are constants, while at lower concentrations of $OEPFeClO_4$, β_2 varies as the concentration of base varies. Thus the equilibrium constant for the second step of complex formation can be estimated from spectral changes which occur when more than 1 equiv. of ligands are added to $OEPFeClO_4$.

Also, titration of $OEPFeClO_4$ with Pip and Pyr were followed by UV-visible absorption spectroscopy by using the coordination shift of the Soret absorption (Figs. 2, 3). The Soret band of Pip titration decreased at 382 nm and a new band appeared at 399 nm and for Pyr titration the new band appeared at 402 nm (Table 1). Also, titration with Pip and Pyr results in well defined isosbestic points at 390 nm. The values of β_2 and K_1 were obtained from Eq. (4) (Figs. 2B, 3B) and the data was reported in Table 2. Values of K_1 can be estimated from samples containing less than 1 equiv. of ligand. The equilibrium constant for the second step of complex formation can be estimated from spectral changes which occur when more than 1 equiv. of ligands are added to $OEPFeClO_4$ (The concentration range is 1.22×10^{-4} to 1.01×10^{-2} M for Pip and 4.11×10^{-5} to 2.58×10^{-3} M for Pyr titrations).

The values of K_1 and β_2 were reported in Table 2. As seen in Table 2, the value of β_2 for Pyr is significantly higher than the binding constants for two other ligands that it can be refer to the effect of basicity of this ligand.

In addition of basicity of the ligand, π bonding interaction of ligand with metalloporphyrin effects to the equilibrium constant. It is clear that π bonding is of little or no importance in the coordination of aliphatic ligand to iron(III) porphyrin. In other hand, the basicity of these aliphatic ligands is more than ligands such as imidazole. The values of β_2 are in reasonable agreement with the result obtained by Walker et al. [22] for ligation of imidazole and its derivatives with OEPFeCl. In comparison, K_1 value for these aliphatic ligands is higher than K_1 value for aromatic ligands that it can be refer to the effect of basicity of these aliphatic ligands.

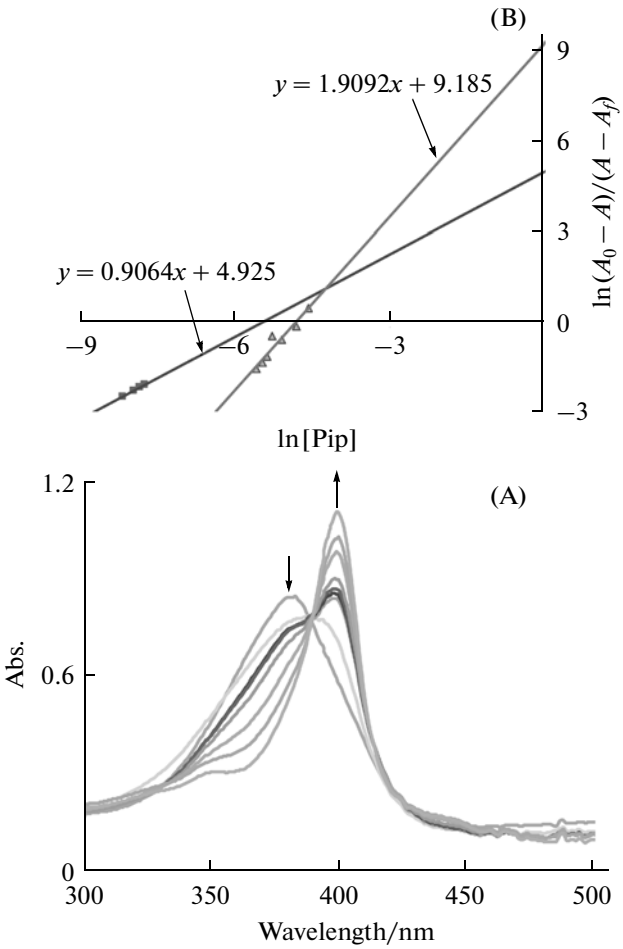


Fig. 2. A—Visible spectral changes observed upon addition of Pip to $OEPFeClO_4$ in CH_2Cl_2. B—Plot of $\ln(A_0 - A)/(A - A_f)$ versus ln[Pip] to calculate K_1 and β_2.

Table 2. Equilibrium constants for addition of ligands to $OEPFeClO_4$ in CH_2Cl_2 at 25°C

Ligand	K_1, M^{-1}	β_2, M^{-2}
Pipz	97.81	4.66×10^3
Pip	137.69	9.75×10^3
Pyr	349.46	9.11×10^5

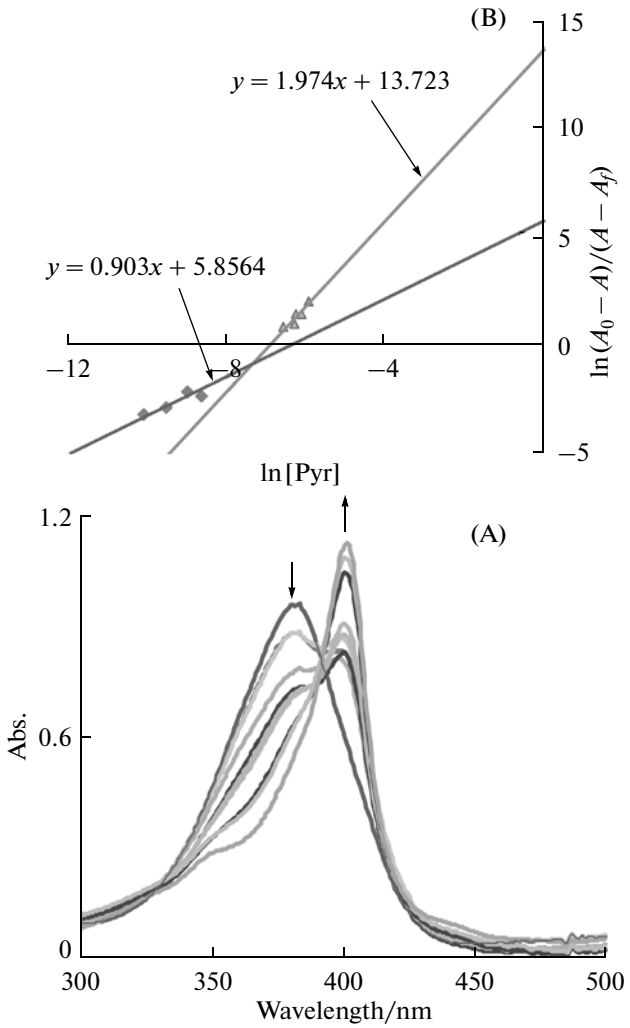


Fig. 3. A—Visible spectral changes observed upon addition of Pyr to $OEPFeClO_4$ in CH_2Cl_2. B—Plot of $\ln(A_0 - A)/(A - A_f)$ versus ln[Pyr] to calculate K_1 and β_2.

CONCLUSIONS

Our results show that the binding processes for aliphatic nitrogen donor ligands (L = Pipz, Pip, Pyr) to $OEPFeClO_4$ are similar. Also, the data available suggested that two steps of axial ligand (L) addition to Fe(III) porphyrin are possible and there are two equilibrium constants (K_1 and K_2) for addition of these ligands to iron(III) porphyrin, since, as we shall see, the stepwise constant, K_2, is in general larger than K_1.

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