Kinetics and Mechanism of Axial Ligand Substitution in Iron(III) Tetraphenylporphyrin Complexes

Gus Levey,[a] **Dwight A. Sweigart,**[*,a] **John G. Jones**[*,b] **and Andrea L. Prignano**[a]
[a] *Department of Chemistry, Brown University, Providence, RI 02912, USA*
[b] *Department of Applied Physical Sciences, University of Ulster, Coleraine BT52 1SA, UK*

Axial imidazole ligands in $[Fe(tpp)(R\text{-}im)_2]^+$ [tpp = 5,10,15,20-tetraphenylporphyrin dianion, R-im = imidazole or *N*-methylimidazole) are rapidly replaced by PBu_3 to form $[Fe(tpp)(R\text{-}im)(PBu_3)]^+$ and $[Fe(tpp)(PBu_3)_2]^+$. Substitution of the first R-im is rate-limiting and follows a strictly dissociative pathway. The five-co-ordinate intermediate $[Fe(tpp)(R\text{-}im)]^+$ reacts at similar rates with R-im and PBu_3. The kinetic *trans* effect of PBu_3 is much greater than that of R-im in these complexes, which may be of relevance to certain haemoprotein systems.

The use of tertiary phosphines as ligands in haemoprotein systems and in model metalloporphyrin complexes has recently attracted attention. Optical, ^1H and ^{31}P NMR spectra of phosphine-ligated haemoproteins have been demonstrated to be quite useful probes of electronic interactions, particularly those involving the *trans* proximal histidine ligand in haemoglobin and myoglobin.[1,2] It is also noteworthy that phosphines are the only bases other than thiolates that produce a hyperporphyrin spectrum with oxidized cytochrome P450 when functioning as a sixth ligand.[3] In the case of free iron porphyrins, both iron(II)[4–6] and iron(III)[2] complexes of the form $[Fe(por)(mim)(PR_3)]^{0,+}$ and $[Fe(por)(PR_3)_2]^{0,+}$ have been characterized (por = porphyrinate, mim = *N*-methylimidazole; R = alkyl or alkoxy). In the presence of excess of phosphine, the iron(III) complexes are susceptible to autoreduction to the iron(II) state, much as occurs with piperidine, cyanide and hydroxide ligands.[7]

For some time we have been interested in the thermodynamics and kinetics of axial ligand substitution in metalloporphyrin and phthalocyanine (H_2pc) complexes. Studies of reactions (1) and (2), in which M is Fe or Ru and R-im is imidazole (Him) or

$$[M(pc)(R\text{-}im)_2] + PBu_3 \longrightarrow [M(pc)(R\text{-}im)(PBu_3)] + R\text{-}im \quad (1)$$

$$[M(pc)(R\text{-}im)(PBu_3)] + PBu_3 \longrightarrow [M(pc)(PBu_3)_2] + R\text{-}im \quad (2)$$

$$[Fe(tpp)(R\text{-}im)_2]^+ + PBu_3 \longrightarrow [Fe(tpp)(R\text{-}im)(PBu_3)]^+ + R\text{-}im \quad (3)$$

$$[Fe(tpp)(R\text{-}im)(PBu_3)]^+ + PBu_3 \longrightarrow [Fe(tpp)(PBu_3)_2]^+ + R\text{-}im \quad (4)$$

N-methylimidazole (mim), showed that the mechanism is strictly dissociative (D), that the five-co-ordinate intermediate posseses little or no ability to discriminate between nucleophiles, and that PBu_3 is orders of magnitude better than R-im in activating the *trans* group to dissociation (*trans* effect).[8]

Herein we report a study of reactions (3) and (4), in which tpp is the dianion of 5,10,15,20-tetraphenylporphyrin. The primary interest was in determining the mechanism, the discriminating ability of the five-co-ordinate intermediate (see below), and the *trans*-effect of R-im compared to PBu_3. The *trans* effect should be of relevance to haemoprotein systems in which histidine and cysteine or methionine serve as ligands *trans* to a histidine or substrate.

Experimental

Reagent grade acetone was dried over Drierite for 2 h and then distilled. Just prior to use, the acetone was dried for 2 h over molecular sieves. Reagent grade chloroform was washed four times with half its volume of distilled water, dried over calcium chloride for 2 h, and passed through an activated basic alumina column. The chloroform was used within a few hours of purification. Tri-*n*-butylphosphine was distilled at reduced pressure and stored under nitrogen. All solutions of PBu_3 were prepared under nitrogen. Imidazole (Him) was recrystalled from absolute ethanol and then from benzene. *N*-Methylimidazole was distilled from KOH. The complex [Fe(tpp)Cl] was a commercial sample that was determined to be pure by examination of its optical spectrum. Proton NMR spectra were recorded at 250 MHz. Stopped-flow studies were performed at 25 °C. Most kinetic runs were done at 600 nm, a wavelength that minimizes interference from autoreduction of the products of reaction (3) and (4). For all reactions, R-im and PBu_3 were in pseudo-first-order excess over the iron porphyrin (*ca.* 1×10^{-4} mol dm^{-3}). The solutions combined for kinetic experiments consisted of (1) PBu_3 and (2) $[Fe(tpp)(R\text{-}im)_2]Cl$, which was generated *in situ* from [Fe(tpp)Cl] and excess of R-im.

Results and Discussion

Optical spectra of solutions of $[Fe(tpp)(R\text{-}im)_2]^+$ containing excess of R-im and PBu_3 showed that all the $[Fe(tpp)(R\text{-}im)_2]^+$ had reacted when the ratio of R-im to PBu_3 was 10:1. By comparison to published[2,4,5] spectra of iron porphyrins with R-im and PR_3 axial ligands, it was judged that in chloroform the products were those of reactions (3) and (4). In acetone the spectra were suggestive of the iron(II) complexes $[Fe(tpp)(PBu_3)_2]$ and $[Fe(tpp)(R\text{-}im)(PBu_3)]$, which likely were formed *via* autoreduction after the completion of reactions (3) and (4). The ratio of mono- to bis-phosphine complex in both iron-(II) and -(III) products depended on the R-im to PBu_3 ratio in the solution. When obtained on the same time-scale (tens of minutes) as the optical spectra, ^1H NMR spectra with PBu_3 as the only base present confirmed that reduction of $[Fe(tpp)(PBu_3)_2]^+$ occurs fairly rapidly in acetone but is much slower in chloroform. Thus, after adding excess of PBu_3 to [Fe(tpp)Cl] in $CDCl_3$, a typical[7] ^1H NMR spectrum for a six-co-ordinate

Table 1 Kinetic and thermodynamic parameters at 25 °C for equations (3) and (4)

Solvent	R-im	[R-im]/mol dm^{-3}	[PBu$_3$]/mol dm^{-3}	k_1/s^{-1}	k_3/k_2	K_4
CHCl$_3$	mim	0.10	0.0013–0.20	70 ± 10	1.0 ± 0.3	40 ± 10
CHCl$_3$	Him	0.050–0.010	0.0010–0.015	50 ± 10	1.0 ± 0.3	5 ± 3
Me$_2$CO	mim	0.090	0.010–0.15	12 ± 1.5	3.5 ± 1.5	
Me$_2$CO	Him	0.005–0.18	0.0025–0.050	9.5 ± 1	5.0 ± 1.5	8 ± 3

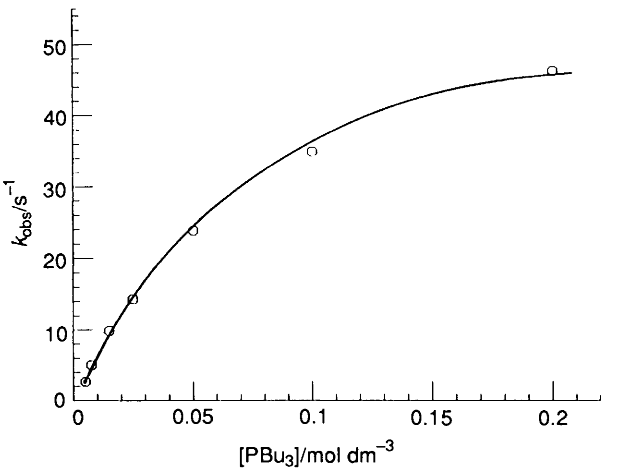

Fig. 1 Observed rate constants for reaction (3) in chloroform at 25 °C with [mim] at 0.10 mol dm^{-3}

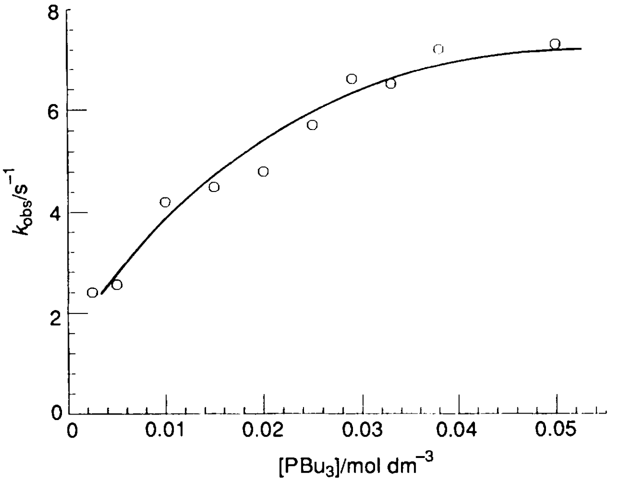

Fig. 2 Observed rate constants for reaction (3) in acetone at 25 °C with [Him] at 0.050 mol dm^{-3}

low-spin iron(III) complex was obtained. The pyrrole resonance at δ −19.4 is very close to the value of δ −20.0 reported[2] for [Fe(tpp)(PMe$_3$)$_2$]$^+$. In CD$_3$COCD$_3$ the same reaction mixture gave a spectrum having the pyrrole resonance at δ +8.4, a value that clearly signals[7] a six-co-ordinate low-spin iron(II) complex, [Fe(tpp)(PBu$_3$)$_2$].

Stopped-flow kinetic runs in acetone for a solution of [Fe(tpp)(R-im)$_2$]$^+$ and excess of R-im and a solution of PBu$_3$ showed a rapid absorbance change (second time-scale) followed by a very much slower (minutes) 'drifting' of the A_∞. In chloroform, there was also a very rapid absorbance change, but the A_∞ was much more stable. In conjunction with the optical and NMR spectral data mentioned above, it is reasonable to ascribe the slow drift of the A_∞ in acetone to reduction of the products of reactions (3) and (4). The A_∞ value in chloroform, as well as that in acetone obtained prior to significant reduction, was dependent on the [PBu$_3$]/[R-im] concentration ratio. The observed absorbance change (ΔA_{obs}) was also dependent on this ratio, but the initial absorbance (A_0) at the beginning of the rapid reaction was not. The invariance of A_0 with the [PBu$_3$]/[R-im] ratio is consistent with two possibilities: (*i*) reaction (3) is rate limiting and A_0 is identified with [Fe(tpp)(R-im)$_2$]$^+$ or (*ii*) reaction (4) is rate limiting and A_0 is identified with [Fe(tpp)(R-im)(PBu$_3$)]$^+$, which is formed completely before any absorbance change is observed. It is known[8] that the kinetic *trans* effect of PBu$_3$ exceeds that of R-im by orders of magnitude in phthalocyanine systems and for this reason it was anticipated that reaction (4) would be faster than (3). Confirmation of this was provided by a comparison of the rate data with the published[9] rate of mim exchange in [Fe(tpp)(mim)$_2$]$^+$ (see below). Close examination of spectra at the end of the reactions showed a mixture of mono- and bis-phosphine products, with no [Fe(tpp)(mim)$_2$]$^+$ remaining. From this we infer that the equilibrium constant for reaction (3), K_3, is large and exceeds that for reaction (4), K_4. The conclusion is that reaction (3) is the one responsible for the observed rate of change of absorbance. Reaction (4) is rapid by comparison, and therefore constitutes a post equilibrium that influences the values of A_∞ and ΔA_{obs}, but not the overall reaction rate.

With the assumption that reaction (3) lies essentially completely to the right at equilibrium, it follows that the ΔA_{obs} and A_∞ data obtained from the kinetic studies may be used to evaluate the equilibrium constant K_4. At the wavelengths chosen the magnitude of ΔA_{obs} was largely determined by the post-equilibrium step (4); the absorbance change associated with the rate-limiting step (3) was at most 20% of the total observed change. By ignoring the small contribution of reaction (3) to the magnitude of ΔA_{obs}, equation (5) can be derived,

$$1/\Delta A_{obs} = ([\text{R-im}]/[\text{PBu}_3])[1/(A^* - A_0)](1/K_4) + 1/(A^* - A_0) \quad (5)$$

$$[\text{R-im}]/[\text{PBu}_3] = ([\text{R-im}]/[\text{PBu}_3])[1/(A^* - A_\infty)](c_{Fe}\Delta\varepsilon) - K_4 \quad (6)$$

where A^* is the absorbance when the conversion into [Fe(tpp)(PBu$_3$)$_2$]$^+$ is 100%. Alternatively, equation (6) may be derived without any approximations, where c_{Fe} is the total porphyrin concentration and $\Delta\varepsilon$ is the difference in absorption coefficients of the bis- and mono-phosphine complexes. Equation (5) gives K_4 from a plot of $1/\Delta A_{obs}$ *versus* [R-im]/[PBu$_3$]. Equation (6) yields K_4 from a plot of [R-im]/[PBu$_3$] *versus* ([R-im]/[PBu$_3$])[1/($A^* - A_\infty$)] and requires an estimate of A^* to be available. Both equations gave similar values of K_4, which are listed in Table 1. The results suggest that K_3 is much larger than K_4; this accords with the reaction of PBu$_3$ with the analogous iron(II) complexes [FeL^1(mim)$_2$], for which K_3 exceeds K_4 by a factor of sixty (L^1 is the dianion of protoporphyrin IX dimethyl ester, *i.e.* dimethyl 3,7,12,17-tetramethyl-8,13-divinylporphyrin-2,18-dipropanoate).[6]

Some of the results of the kinetics experiments are presented in Figs. 1–3. As discussed above, we believe that equation (3) is the reaction observed. Reaction (4) follows as a post equilibrium. A mechanism consistent with all of the kinetic data is given in equations (7)–(9). The pseudo-first-order rate constant,

$$[\text{Fe(tpp)(R-im)}_2]^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} [\text{Fe(tpp)(R-im)}]^+ + \text{R-im} \quad (7)$$

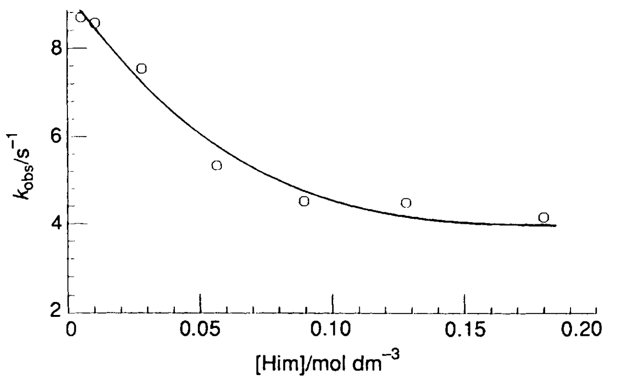

Fig. 3 Observed rate constants for reaction (3) in acetone at 25 °C with [PBu$_3$] at 0.020 mol dm^{-3}

$$[\mathrm{Fe(tpp)(R\text{-}im)}]^+ + \mathrm{PBu_3} \xrightarrow{k_3} [\mathrm{Fe(tpp)(R\text{-}im)(PBu_3)}]^+ \quad (8)$$

$$[\mathrm{Fe(tpp)(R\text{-}im)(PBu_3)}]^+ + \mathrm{PBu_3} \overset{K_4}{\rightleftharpoons} [\mathrm{Fe(tpp)(PBu_3)_2}]^+ + \mathrm{R\text{-}im} \quad (9)$$

$$k_{obs} = (k_1k_3[\mathrm{PBu_3}])/(k_2[\mathrm{R\text{-}im}] + k_3[\mathrm{PBu_3}]) \quad (10)$$

assuming the five-co-ordinate intermediate is in a steady state, is given in equation (10). Figs. 1 and 2 show the curvature predicted by equation (10), with k_{obs} tending towards a limit of k_1 at high concentrations of PBu$_3$. The predicted non-linear inhibition of k_{obs} with increasing R-im concentration is illustrated in Fig. 3.

The rate parameters k_1 and k_3/k_2 were extracted from the data *via* reciprocal plots of equation (10) and are summarized in Table 1. The reaction mechanism is postulated to be strictly dissociative, as is believed[8] to be the case with related reactions of phthalocyanine complexes, equations (1) and (2). Strong support for the mechanism in equations (7) and (8) is provided by the observation that the k_1 in Table 1 for dissociation of mim in CHCl$_3$ solvent (70 s^{-1}) is essentially identical to the rate constant reported for mim exchange in [Fe(tpp)(mim)$_2$]$^+$ in CDCl$_3$ (66 s^{-1}).[9]

The dissociation rate constant k_1 is significantly larger in chloroform compared to acetone (Table 1); it is likely that this is due to hydrogen-bonding interactions between the solvent chloroform and the N(1) nitrogen of the axial imidazole ligands.[10,11] The ratio k_3/k_2 is not far from unity for the four reactions studied. This probably means that the five-co-ordinate intermediate, [Fe(tpp)(R-im)]$^+$, is highly reactive and has little ability to discriminate; an alternative but most unlikely[12] interpretation is that R-im and PBu$_3$ just happen to react with the intermediate at similar rates. It is also concluded that the reactions of [Fe(tpp)(R-im)$_2$]$^+$ reported herein resemble their iron(II) phthalocyanine analogues, reactions (1) and (2), in that dissociation of R-im occurs much more rapidly when the *trans* ligand is PBu$_3$ rather than R-im.

Within the context of the proposed mechanism, K_3 can be written as k_1k_3/k_2k_4, where k_4 is the rate constant for the reverse of reaction (8). Since K_3 is large and k_2/k_3 is near unity, it follows that $k_1/k_4 \gg 1$. This means that the Fe–N bond *trans* to R-im needs less activation to break than the Fe–P bond *trans* to R-im. Incorporating the *trans* effect noted above leads to the following reactivity series for dissociation of L *trans* to T in T–Fe–L: Bu$_3$P–Fe–R-im > R-im–Fe–R-im > R-im–Fe–PBu$_3$. Combining this order with a similar analysis of the second step (K_4) and assuming that the intermediate [Fe(tpp)(PBu$_3$)]$^+$ is non-discriminating, leads to the overall ordering Bu$_3$P–Fe–R-im > Bu$_3$P–Fe–PBu$_3$, R-im–Fe–R-im > R-im–Fe–PBu$_3$.

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