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Mechanistic Study of the Reaction between Imidazoles and Iron(III) Protoporphyrin IX Dimethyl Ester Chloride

WILLIAM W. FISKE and D. A. SWEIGART*

Department of Chemistry, Swarthmore College, Swarthmore, Pa. 19081, U.S.A.

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The reaction of five-coordinate high-spin iron(III) porphyrin chlorides, Fe(Por)Cl, with imidazoles, RIm, to produce six-coordinate low-spin complexes according to equation (1) have received considerable

$$\mathrm{Fe(Por)Cl + 2RIm \rightarrow Fe(Por)(RIm)_2^+, Cl^-} \qquad (1)$$

attention [1–7]. The intermediate monoimidazole complex, Fe(Por)(RIm)Cl, is generally not seen in thermodynamic studies. However, we recently reported [8] the rapid reversible formation of a short-lived intermediate during the reaction of tetraphenylporphinatoiron(III) chloride and N-propylimidazole, and concluded that the intermediate was the six-coordinate complex Fe(TPP)(N-PrIm)Cl.

Herein we report a kinetic study of reaction (1) with iron(III) protoporphyrin IX dimethyl ester chloride, Fe(PPIXDME)Cl, and nucleophiles imidazole, Im, and N-methylimidazole, MeIm. The reactions were followed by the stopped-flow method in acetone at 25 °C with pseudo first-order conditions of excess nucleophile. The results (Table I) show that Im and MeIm follow very different rate laws.

Imidazole is known to form hydrogen bonds and we suggest that Im reacts more rapidly and follows a different rate law than MeIm because of assisted removal of the coordinated chloride *via* hydrogen bonding. The proposed mechanism for imidazole is,

$$\mathrm{Fe(PPIXDME)Cl + Im \overset{K}{\rightleftharpoons} Fe(PPIXDME)(Im)Cl} \qquad (2)$$

TABLE I. Kinetic Results for Reaction (1).

RIm	[RIm]/*M*	k_{obs}/s^{-1}
Im	0.0050–0.10	$7800[\mathrm{Im}]^2$
MeIm	0.025–0.50	$21[\mathrm{MeIm}]/(1 + 2.6[\mathrm{MeIm}])$

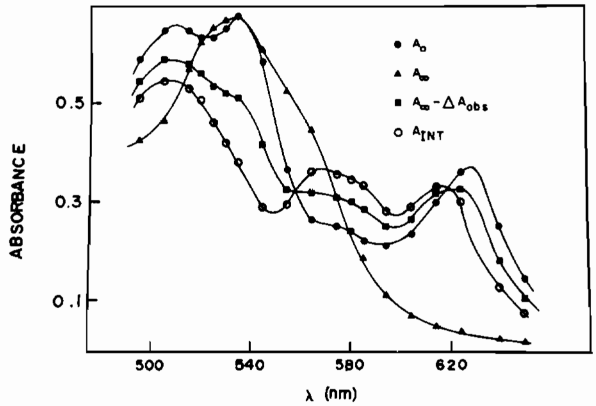

Fig. 1. Absorbance data obtained on the stopped-flow apparatus for reaction (1) with MeIm (0.46 *M*) at 25 °C. A_0 is Fe(PPIXDME)Cl; A_∞ is $\mathrm{Fe(PPIXDME)(MeIm)_2^+, Cl^-}$; A_{INT} is Fe(PPIXDME)(MeIm)Cl; $A_\infty - \Delta A_{obs}$ is the spectrum of the solution immediately after mixing and corresponds to an equilibrium mixture of Fe(PPIXDME)Cl and Fe(PPIXDME)(MeIm)Cl.

$$\mathrm{Fe(PPIXDME)(Im)Cl + Im \xrightarrow{k_1} Fe(PPIXDME)(Im)_2^+, Cl^-} \qquad (3)$$

and for N-methylimidazole is,

$$\mathrm{Fe(PPIXDME)Cl + MeIm \overset{K}{\rightleftharpoons} Fe(PPIXDME)(MeIm)Cl} \qquad (4)$$

$$\mathrm{Fe(PPIXDME)(MeIm)Cl \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Fe(PPIXDME)(MeIm)^+, Cl^-} \qquad (5)$$

$$\mathrm{Fe(PPIXDME)(MeIm)^+, Cl^- + MeIm \xrightarrow{k_3} Fe(PPIXDME)(MeIm)_2^+, Cl^-} \qquad (6)$$

Rapid pre-equilibrium formation of the six-coordinate intermediate, equations [2] and [4], is followed by assisted dissociation of chloride with Im and unassisted dissociation with MeIm. The observed rate constants, invoking the steady state approximation for $\mathrm{Fe(PPIXDME)(MeIm)^+, Cl^-}$ and assuming that $k_3[\mathrm{MeIm}] \gg k_2$ are given by equations (7) and (8):

$$k_{obs} = k_1K[\mathrm{Im}]^2/(1 + K[\mathrm{Im}]) \qquad (7)$$

$$k_{obs} = k_1K[\mathrm{MeIm}]/(1 + K[\mathrm{MeIm}]) \qquad (8)$$

For MeIm a plot of $1/k_{obs}$ *vs.* 1/[MeIm] is linear as required by equation (8) and yields $k_1 = 8.1 \pm 0.7\ s^{-1}$ and $K = 2.6 \pm 0.3\ M^{-1}$.

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*Author to whom correspondence should be addressed.

Strong evidence for the above mechanism is given in Fig. 1 which shows that with MeIm as the nucleophile the calculated absorbance change ($A_\infty - A_o$) and the observed change (ΔA_{obs}) differed, and moreover the discrepancy was itself a function of [MeIm]. This is clear evidence for the rapid reversible formation of an intermediate. For [MeIm] = 0.46 *M* the Figure shows that upon mixing the reactants the absorbance changed from A_o to $A_\infty - \Delta A_{obs}$ at a rate too rapid to measure. Decay to products, A_∞, then took place in the rate determining step. By fixing the porphyrin concentration and wavelength and varying [MeIm], a plot of equation (9) was used to determine

$$A_\infty - \Delta A_{obs} = -\frac{1}{K}\,\frac{(A_\infty - A_o - \Delta A_{obs})}{[MeIm]} + A_{INT} \quad (9)$$

K as 2.9 ± 0.2 M^{-1}. This value of K and the one determined from the curvature of the k_{obs} *vs.* [MeIm] plot are in good agreement. The optical spectrum of the intermediate species, Fe(PPIXDME)(MeIm)Cl, is shown as A_{INT} in Fig. 1, and suggests strongly [9] that the complex is high-spin. This means that the spin change in reaction (1) occurs upon addition of the second imidazole.

With Im as the nucleophile no intermediate was detected, probably because the large rate of reaction (1) precluded the use of nucleophile concentrations high enough to form a significant amount of the intermediate.

The role of hydrogen bonding in the reaction with imidazole may be related to the function of the E7 histidine in hemoglobin. Pauling [10] first suggested that the distal imidazole stabilizes bound oxygen *via* hydrogen bonding, and therefore must also affect the dynamics and thermodynamics of oxygenation. Although the exact role of the distal histidine is still unclear [11], the possibility of hydrogen bonding, especially if the bound dioxygen is viewed as $Fe(III)\text{–}O_2^-$, is supported by our work which shows that such an interaction is important in the $Fe(III)\text{–}Cl^-$ system.

James *et al.* [12] reported in 1973 that the reaction of Co(PPIXDME) complexes to produce peroxo dimers is accelerated in the presence of imidazole and suggested that hydrogen bonding to coordinated oxygen was responsible for this.

We are currently investigating reaction (1) with the chloride replaced by better hydrogen bonding bases, *e.g.*, fluoride and azide.

Conclusion

The reaction between imidazoles and Fe(PPIXDME)Cl to produce the low-spin *bis*-adduct proceeds through a six-coordinate high-spin intermediate and follows different mechanisms with imidazole and N-methylimidazole because of the ability of the former to hydrogen-bond to the chloride.

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