A Kinetic Study of the Demetalation Reaction of (5,10,15,20-tetraphenylporphinato)mercury(II) in the Presence of Imidazole

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Received February 25, 1983

The demetalation reaction of (5,10,15,20 tetraphenylporphinato)mercury(II) in $CHCl_3$, containing imidazole, 0.1 M *TBAP was studied by means of stopped-flow rapid-scanning spectroscopy. Addition of imidazole to TPPHg yielded first the formation of a mono ligand adduct, TPPHg(Im). This rapid step was followed by a slower demetalation reaction to produce $TPPH_2$. The demetalation reaction was first-order in both imidazole and metalloporphyrin and gave a rate constant of 0.63 M^{-1} s^{-1} at 25 °C. A mechanism for the overall reaction is discussed which involves a proposed transient six coordinate $TPPHg(Im)_2$ species.*

Introduction

In a recent paper [1], the axial ligation of (5,10,15,20-tetraphenylporphinato)mercury(II), TPPHg, was investigated in $CHCl_3$ containing twenty different substituted pyridines and imidazoles. For nineteen ligands, the reaction could be represented as shown in eqn. 1:

$$TPPHg + L \rightleftarrows TPPHg(L) \quad (1)$$

where TPPHg(L) was a relatively stable species. However, for the case of L = imidazole a rapid demetalation following reaction 1 was observed. In this present paper we present a kinetic study of this demetalation reaction. This study was performed using a stopped flow apparatus/rapid scanning spectrometer combination in order to obtain both kinetic and mechanistic information on the overall reactions associated with conversion of TPPHg to $TPPH_2$.

Experimental

5,10,15,20-tetraphenylporphyrin, $TPPH_2$, and its mercury complex, TPPHg, were prepared and purified by literature methods [2, 3]. Imidazole (Im) and 2-methylimidazole (2-MeIm) (Aldrich) were recrystallized three times from benzene. N-methylimidazole (N-MeIm) was purified by distillation over KOH and molecular sieves at 195–196 °C. Chloroform (Aldrich Gold Label) was used as solvent either as obtained for after purification to remove ethanol stabilizer and any traces of water. Similar kinetic results were obtained in both cases. In addition, all acidic impurities were removed from the chloroform, since TPPHg is known to undergo a slow demetalation reaction in $CHCl_3$ containing traces of dry hydrogen chloride [3, 4]. Each solution was prepared freshly before use, and was brought to an ionic strength of 0.1 with added 0.1 *M* TBAP.

The reactions were monitored by simultaneous kinetic and spectral analysis using a rapid scanning spectrometer (Tracor Northern TN 1710 multichannel analyzer). A stopped-flow drive system (Durrum D103) was combined with this instrument to provide a stopped-flow kinetic spectrometer capable of acquiring a 512 point electronic spectrum over a range of 620 nm in a time as fast as 5 ms and to store at least 16 complete spectra acquired as a function of time. The system was equipped with a thermostated bath to control the temperature to 25 °C and with a function generator to automatically acquire the spectra with accurate and constant time delays.

Reactions were run under pseudo-first-order conditions with imidazole in at least a 100 fold excess over TPPHg and the observed rate constants, k_{obsd}, calculated from plots of $\ln |A - A_\infty|$ as a function of time. In general, the above plots were linear over three half-lives indicating well behaved kinetics. However, because the data were acquired in a discrete mode, the final spectrum might not be as accurate as we would wish and therefore, additional data analysis was performed to confirm the values of k_{obsd}. Guggenheim [5] and Swinbourne [6] methods were used and the fit of the pseudo-first-order plot to the experimental data was optimized by varying A_∞ values within a 5% range around the observed value.

Results

The spectrum of TPPHg in $CHCl_3$ (shown as a dashed line in Fig. 1), agrees with spectra presented

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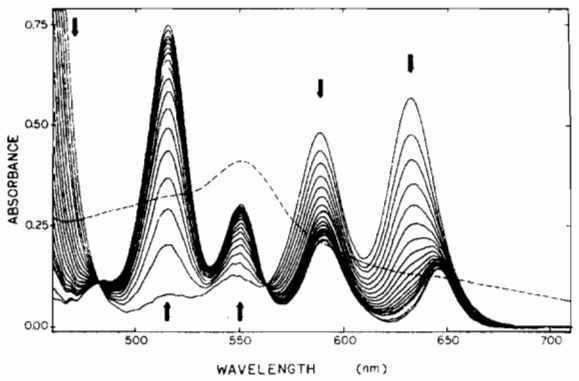


Fig. 1. Optical absorption spectra obtained between 450 and 710 nm during the reaction of 2.2×10^{-4} *M* TPPHg with 0.15 *M* Im (0.1 *M* TBAP in $CHCl_3$, 25 °C, 2 mm optical path) (——). The arrows show the optical changes during the demetalation process. The first spectrum is acquired after about 20 ms. Repetitive scans are then recorded at 2.0 s intervals and the two last spectra are acquired at 40 and 200 s. Superimposed on this plot is the spectrum of the initial reactant, TPPHg (– – –).

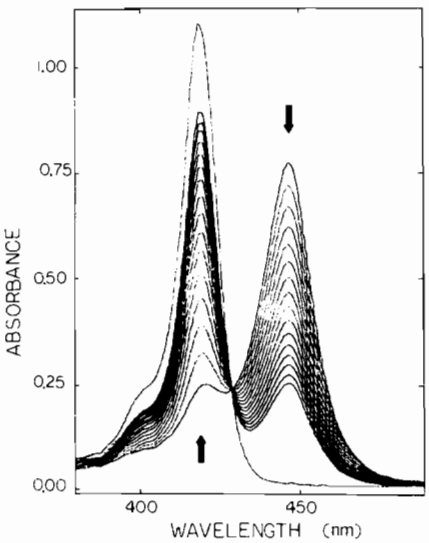


Fig. 2. Optical absorption spectra obtained in the Soret region during the reaction of 1.8×10^{-5} *M* TPPHg with 0.25 *M* Im. Repetitive scans were taken each 0.50 s with the first one after about 20 ms. The last spectrum is acquired at an infinite time = 60 s.

in the literature [1, 3, 7]. Upon mixing with imidazole this spectrum instantaneously changes indicating that a new species is formed during the first 5 ms of the experiment. This is also shown in Fig. 1 (solid lines) and in Fig. 2. This new species is a short-lived intermediate, but thanks to the use of rapid-scanning stopped-flow techniques, its electronic absorption spectrum is easily characterized (λ = 444 nm, (ϵ = 240,000), 632 nm (ϵ = 13,000) and 588 nm (ϵ = 11,200)). This spectrum may be identified as belonging to the five coordinate TPPHg(Im) complex on the basis of comparisons with other TPPHg(L) species in $CHCl_3$ and also on the basis of a spectrophotometric titration which confirms eqn. 1 as the initial reaction after mixing TPPHg and Im [8].

Attempts were made to determine the kinetics for imidazole addition to TPPHg according to reaction 1. Under all experimental conditions in which there was an excess of imidazole the equilibration reaction between TPPHg and its mono imidazole complex was too fast to be monitored. Even at low imidazole concentrations ([Im] = 10^{-3} *M*), the first spectrum of the reaction mixture (after 5–10 ms) always showed TPPHg(Im) in solution. Thus no kinetic information about this reaction could be obtained by our technique.

The first reaction observed upon mixing TPPHg and Im is the formation of TPPHg(Im). A subsequent reaction, which is the one actually monitored in Figs. 1 and 2, is characterized by the disappearance of TPPHg(Im) and the appearance of $TPPH_2$ (λ = 418, 515, 550, 589, 645 nm). A set of isosbestic points is maintained in both figures (λ = 427, 482, 563 nm), substantiating that only these two porphyrin species are present in notable quantities during the course of the reaction. In addition to the presence of these well defined isosbestic points, it should be noted that the absorption values for the final spectrum of $TPPH_2$ correspond to a concentration equal to that of the initial TPPHg which proves that total demetalation has occurred.

Kinetic treatment of the data was carried out at different wavelengths and similar results obtained in each case (Table I). The good fit of the data to first order plots as well as the invariance of k_{obsd} over a 10 fold range of initial TPPHg concentration lead to the conclusion that the reaction follows pseudo-first-order kinetics in metalloporphyrin. The dependence of k_{obsd} on the imidazole concentration was studied over the range $0.01\ M \leqslant [Im] \leqslant 0.3\ M$. It was observed that k_{obsd} varied linearly with [Im] at high imidazole concentrations but that this dependence was no longer obeyed at [Im] = 0.01 *M* or lower. These kinetic observations, along with the spectral evidence, are consistent with a simple mechanism where the demetalation reaction is first order in imidazole (eqn. 3) and occurs through a species which is generated by a rapid pre-equilibrium (eqn. 2).

$$\text{TPPHg} + \text{Im} \underset{\text{fast}}{\overset{K_{Im}}{\rightleftharpoons}} \text{TPPHg(Im)} \qquad (2)$$

$$\text{TPPHg(Im)} + \text{Im} \xrightarrow[\text{slow}]{k} TPPH_2 + \text{products} \qquad (3)$$

The rate law consistent with this mechanism gives the following formulation for the observed rate constant:

TABLE I. Observed Rate Constants (k_{obsd}) and Correlation Coefficients Obtained at Different Wavelengths and With Different Methods. The Data are Extracted from the Spectra Displayed in Fig. 1.

Wavelength (nm)	Observed Rate Constant, k_{obsd} (sec^{-1})[a]		
	Infinite time method[b]	Guggenheim method	Swinbourne method
460	0.099 (0.9998)	0.098 (0.9996)	0.098 (0.9999)
465	0.100 (0.9999)	0.098 (0.9996)	0.099 (0.9999)
515	0.098 (0.9999)	0.101 (0.9994)	0.097 (0.9998)
589	0.104 (0.9995)	0.109 (0.996)	0.098 (0.9996)
632	0.100 (0.9999)	0.100 (0.9998)	0.099 (0.9999)

[a]Correlation coefficients given in parentheses. [b]Calculated from plots of ln $|A_t - A_\infty|$ *vs.* t.

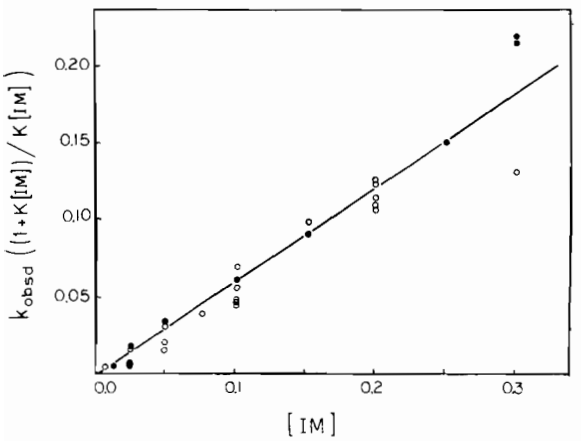


Fig. 3. The first order dependence of k_{obsd} on [Im] for the demetalation of TPPHg with imidazole in $CHCl_3$, 0.1 *M* TBAP at 25 °C. The initial TPPHg concentration is either 2×10^{-5} *M* (•) or 2.5×10^{-4} *M* (○).

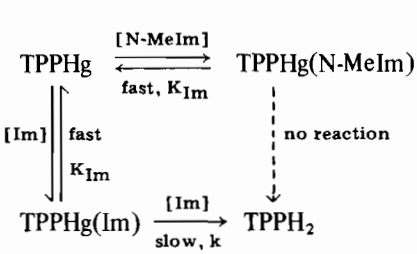
$$k_{obsd} = k[Im]\ \frac{K_{Im}[Im]}{1 + K_{Im}[Im]} \qquad (4)$$

As seen in this equation, the dependence of k_{obsd} on [Im] is first order for the highest values of [Im] and second order for the lowest ones. In the concentration range of our study, the term $K_{Im}[Im]/(1 + K_{Im}[Im])$ is approximately equal to unity (0.964 for 0.05 *M*, 0.994 for 0.3 *M*) which explains that k_{obsd} is found to be approximately proportional to [Im]. The plot of $k_{obsd}(1 + K_{Im}[Im])/K_{Im}[Im]$ *vs.* [Im] (from which the value of the rate constant k can be extracted) is shown in Fig. 3.

As seen in this figure, there was poor reproducibility of the data and large random variations were observed for k_{obsd}. In order to determine the source of these variations, certain variables were tested which included the purity of the reagents, the ethanol content of the chloroform and the trace oxygen content of the solutions, but none of these variables were found to cause significant rate variations. However, in spite of the scattering in the data, one can conclude that the plot in Fig. 3 yields a straight line with a zero intercept from which a demetalation rate constant, $k = 0.63\ M^{-1}\ s^{-1}$ is calculated. Additional proof for our postulated mechanism was obtained from spectral observations of the overall reaction at low imidazole concentrations (10^{-4}–10^{-3} *M*). Indeed, under these conditions, the sets of spectra obtained do not have the same characteristics as the one reported in Figs. 1 and 2. The first spectrum shows a mixture of TPPHg and TPPHg(Im) whose concentrations are correlated by the corresponding equilibration constant (log K = 2.73) [1] and a set of isosbestic points is obtained at different wavelengths from that reported at high imidazole concentrations. The presence of these new isosbestic points substantiates that the ratio between [TPPHg] and [TPPHg(Im)] remains constant throughout the reaction which definitely confirms a mechanism where a rapid pre-equilibrium is involved.

Qualitative studies were also carried out for the reaction of TPPHg with N-MeIm and with 2-MeIm. It was found that TPPHg(10^{-4} *M*) in neat N-MeIm (12.5 *M*) undergoes a very slow decomposition with about 10% demetalation after 24 hours, and that TPPHg (5×10^{-5} *M*) with 2-MeIm (0.8 *M*) in $CHCl_3$, 0.1 *M* TBAP demetalates more rapidly, with a half-life of about 3 hours. However, since TPPHg is quite unstable in solution [3, 4], any demetalation reactions which occur over a long period of time may be partly (or wholely) due to minute amounts of acidic impurities present in the solvent or traces of imidazole in the added nitrogenous base. Accordingly, care must be taken when interpreting these data. We can say, however, that any demetalation which might occur as a result of 2-MeIm or N-MeIm addition is at least 10^4 to 10^6 times slower than for the reaction with Im.

A competitive kinetic study was carried out to examine the behavior of TPPHg in the presence of a mixture of Im and N-MeIm. It was observed that the presence of N-MeIm in the medium definitely slows down the demetalation reaction. This point substantiates that the demetalation process cannot occur through the TPPHg(N-MeIm) species as represented in the scheme below:



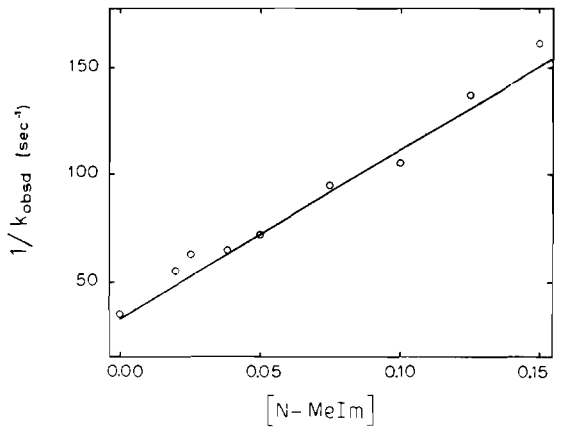


Fig. 4. Plot showing the linear dependence of $1/k_{obsd}$ on N-MeIm with [Im] = 0.05 *M*; 0.1 *M* TBAP in $CHCl_3$. The solid line is the theoretical line derived from eqn. 5 using the reported values [1] of K_{Im}, K_{NIm} and k = 0.63 sec^{-1} M^{-1} and with [Im] = 0.05 *M*.

Under the assumptions that Im and N-MeIm are in large excess relative to TPPHg and that the slow reaction is first-order both in imidazole and in metalloporphyrin, the observed rate constant can be expressed as

$$k_{obsd} = k[Im] \frac{K_{Im}[Im]}{1 + K_{Im}[Im] + K_{NIm}[N\text{-MeIm}]} \quad (5)$$

The results of the competitive study, shown in Fig. 4, are in accordance with this law and with the reported values of K_{Im} and K_{NIm} (log K_{Im} = 2.73, log K_{NIm} = 2.82) [1].

Discussion

Suggestions for the mechanism occurring in reaction 3 can be made on the basis of both spectral and kinetic observations. The spectral change in the Soret region (Fig. 2) is surprisingly similar to that obtained during the decomposition of bis-mercury(II) porphyrins [3, 4, 9]. However, the possibility of having such an adduct as an intermediate under our experimental conditions may be ruled out by the fact that the observed reaction is first order in both imidazole and metalloporphyrin as well as the fact that the starting species can be unequivocally identified as TPPHg(Im) with no trace of $TPPH_2$. For the same reasons, more sophisticated mechanisms can be rejected in favor of a simpler mechanism involving a bimolecular reaction between TPPHg(Im) and imidazole.

In order to assign a self-consistent mechanism to the demetalation, it is necessary to determine the actual role played by the imidazole molecule which is both a potential binding ligand and a prospective proton source. In terms of imidazole as a proton source, it is known that the hydrogen atom linked to the pyrrole nitrogen exhibits an acidic character and that its pK_a in water is 14.2–14.6 [10]. This acidity is further enhanced by about 4 log units upon complexation with a metalloporphyrin at the pyridinium nitrogen [10]. Thus, since there is no other acidic species in the medium it is likely that imidazole molecules (free or coordinated) act as the proton source during the course of the demetalation reaction. However, the possibility that proton transfer is the rate determining step in the demetalation process cannot be accepted in light of our results with 2-MeIm. Indeed, 2-MeIm has about the same pK_a as Im [11] so that if protonation were the rate determining step, the demetalation rate should be similar with these two ligands, which was not observed. The results of the competitive kinetic study can also rule out the possibility of a demetalation catalyzed by acidic impurities present in imidazole (imidazolium, for example).

Another possibility to consider for an imidazole rate-controlling demetalation is the ligation of a second imidazole as the slow step of the reaction. In this case, reaction 3 can be broken down as follows:

$$TPPHg(Im) + Im \rightleftharpoons TPPHg(Im)_2 \quad (6)$$

$$TPPHg(Im)_2 \rightarrow TPPH_2 + \text{products} \quad (7)$$

In this proposed series of reactions the interesting feature which merits discussion is the formation of a six coordinate $TPPHg(Im)_2$ complex in the course of the reaction. Such a species has never been reported in the literature and its occurrence may be thought to be quite unlikely. Nevertheless, under our experimental conditions, its formation can be envisioned with some credibility as long as it is considered only as a transient species.

Although mercury(II) shows a greater tendency to coordinate two or four N donor ligands [12], some examples have been reported which demonstrate that Hg(II) can also form five or six coordinate complexes [13]. In the case of porphyrin complexation, electronic and stereochemical considerations lead to the conclusion that two forms of $TPPHg(Im)_2$ are structurally possible. These are structures where the two axial ligands are found on opposite sides of the porphinato plane yielding complexes with tetragonal geometries or where the two axial donor atoms are placed on the same side of the plane. These are labelled structure A and structure B respectively in Fig. 5.

In most cases where the six coordinate species can be isolated, the determined geometry corresponds to structure A. However, this structure in which the metal has to be squeezed into the porphinato plane cannot be confidently envisioned for the case of $TPPHg(Im)_2$. Indeed, because of the large size of the metal, its location in the porphinato core would result in large steric constraints. In addition, the filled $d_{x^2-y^2}$ orbital of the metal would no longer

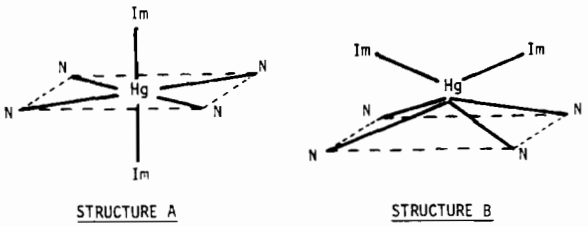


Fig. 5. Possible structures for $TPPHg(Im)_2$.

overlap with the porphyrin π^* system yielding zero bond order between Hg(II) and the porphinato ligand.

Structure B represents a rather unusual configuration for stable six-coordinate metalloporphyrins and is found only for some stable complexes such as $(TPP)Ti(O_2)$ [14] or $(TPP)Mo(O_2)$ [15]. In the mercury porphyrin case, because of the large displacement of the metal ion out of the porphinato plane in the TPPHg(Im) complex [16], the attack from a second imidazole is much more likely to occur from the top side of the molecule and accordingly structure B may be envisioned as the actual intermediate postulated in our mechanism. This intermediate turns out to be only a transient species in the overall reaction because its formation is rapidly followed by a proton transfer reaction (eqn. 7) to give the final products. The driving force for this reaction would be the elimination of huge ring deformations, the preference of Hg(II) for linear configurations (in this case $Hg(Im)_2^{2+}$ or $Hg(imidazolate)_2^0$) and the high stability of the bis imidazole (or imidazolate) Hg(II) species [18].

Intermolecular hydrogen bonding to coordinated imidazole and its effects on metalloporphyrin reactivity have been observed for other systems [19, 20]. The large metal displacement in $TPPHg(Im)_2$ and the bending of the axial ligands in structure B may allow the possibility of intramolecular hydrogen bonding between the nitrogen protons of the bound imidazoles and the phenyl groups or the pyrrole nitrogens of the porphyrin. We cannot be more specific about the exact mechanism of the proton transfer reaction which may occur either in several steps with formation of a 'sitting atop' complex, or by a concerted rearrangement with simultaneous transfer of two protons.

The last point which remains to be clarified is why the demetalation process is observed only with imidazole and not with other ligands, especially with imidazole derivatives. This most likely is related to the ease of formation of the bis-ligated intermediate. With imidazole as a ligand, this bis-ligation is already quite unfavorable as indicated by the slowness of the second step relative to the first one. For ligands less basic than imidazole, it would be expected that six coordination would be even less favored. For example, it was observed that pyridine which is a weaker base and a bulkier ligand than imidazole, does not form $TPPHg(Py)_2$ while, on the other hand, the smaller and stronger base NH_3 does induce TPPHg demetalation probably through a $TPPHg(NH_3)_2$ intermediate. The nitrogenous base 2-MeIm does not very easily give the bis-ligand adduct with TPPHg most likely for steric reasons. Such a dramatic effect of the 2-methyl group has already been observed with tetraphenylporphinatoiron(II) [21]. This species yields the bis-ligated complex with Im and only the mono-adduct with 2-MeIm.

The absence of TPPHg demetalation upon complexation with N-MeIm suggests that the imidazole proton plays an important part in the overall reaction. We postulate that this proton intervenes in the reaction through intramolecular hydrogen bonding interactions. These interactions can favor the formation of $TPPHg(L)_2$ by thermodynamically stabilizing this species as well as facilitate the proton transfer reaction by increasing the electronegativity of the TPP pyrrole nitrogens. This stabilizing effect can be quite important and would explain why no demetalation is possible with N-substituted imidazoles.

In conclusion, we have investigated, for the first time, the demetalation reaction of TPPHg in the presence of imidazole. This study also presents the first use of rapid-scanning stopped-flow techniques for investigating the axial ligand interactions of imidazole with a metalloporphyrin. Future studies with other synthetic metalloporphyrins of more biological interest are now in progress.

Acknowledgement

The support of the National Science Foundation (Grant CHE-821557) and the National Institutes of Health (GM 25172) is gratefully acknowledged. The authors also wish to thank Mr. Lih-Ren Shiue for the synthesis of TPPHg.

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