Magnetic Resonance Investigation of the Autoreduction of Tetraphenylporphinatoiron(III) Chloride in the Presence of Piperidine

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Abstract: ^{1}H NMR and ESR spectroscopy have been employed to probe the mechanism of the solution autoreduction reaction of tetraphenylporphinatoiron(III) chloride in the presence of piperidine and *N*-hydroxypiperidine. The reducing agent has been identified as the piperidine base by detecting the previously characterized piperidine-1-oxyl radical. The various paramagnetic and diamagnetic porphyrin complexes involved in the reaction are identified by their characteristic pyrrole-H shifts. Determination of the percent reduction as a function of time using NMR shifts or peak areas reveals that the reduction rate is critically dependent on free ligand concentration. The observation of a large isotope effect on the reduction rate indicates that the breaking of an N-H bond is involved in the rate-determining step. These results are interpreted in terms of a base-assisted intramolecular electron transfer where the electron transfer step is facilitated by the deprotonation of the coordinated piperidine by free piperidine. The role of the free piperidine as a base is supported by the observations that noncoordinating bases also accelerate the autoreduction reaction. The relevance of our proposed mechanism to amino acid side chain free radical intermediates in the reduction of ferricytochrome *c* is discussed.

Introduction

It has been known for some time now that ferric porphyrins can autoreduce in solution in the presence of certain potential ligands,[1-4] of which the best known example is the autoreduction of tetraphenylporphinatoiron(III) chloride (TPPFeCl) in piperidine (pip). This reaction,

$$TPPFe^{III}Cl \xrightarrow{pip} TPPFe^{II}(pip)_2 \qquad (1)$$

was the focus of attention several years ago since it afforded the product which yielded to the first successful x-ray crystallographic characterization of a low-spin bis-ligated ferrous porphyrin.[5] This crystallographic report, however, emphasized[5] a lack of understanding of the reaction mechanism which led to the desired product.

We have recently shown[6,7] that this autoreduction also occurs in the presence of cyanide, thiols, and phosphines, and, in the case of cyanide ion, demonstrated that the one-electron reducing agent is the cyanide ion. We demonstrated[6,7] that magnetic resonance techniques are particularly well suited for characterizing the reaction, with ^{1}H NMR serving as a convenient probe of the iron porphyrin oxidation/spin states, while ESR provided the identity of the ligand free radical.

The autoreduction of metal ions and the apparent oxidation of the ligands is not confined to iron porphyrin systems.[8-11] The metal ion promoted oxidation of amines in a variety of tetraazo macrocyclic complexes has been reported[9-11] but only in one case involving a $Ni^{III} \rightarrow Ni^{II}$ reaction was the organic radical detected.[10] In the area of hemoproteins, the reaction of peroxidase[12] compound I or II with amines leads to a one-electron reduction of the iron and the oxidation of the amines.[13]

In our belief that these autoreductions proceed by very similar pathways for a variety of ligands, and that the mechanism of these reactions may be relevant to understanding both the activation of coordinated ligands in certain hemoproteins[12,13] and modes of intramolecular electron transfer in cytochromes,[14-17] we have extended our magnetic resonance studies to the piperidine reaction,[1] i.e., eq 1.

Our present magnetic resonance study will provide evidence that the autoreduction of ferric porphyrins involves an unusual base-catalyzed intramolecular electron transfer which yields the ferrous complex and a deprotonated piperidine radical. The role of the base is crucial in permitting the electron-transfer step where otherwise there exists a large thermodynamic barrier. Overcoming this thermodynamic barrier[16,17] to intramolecular electron transfer may have some relevance to the participation of amino acid side chain radicals as intermediates[14,15] in the reduction of ferricytochrome *c*.

Experimental Section

Materials. TPPFeCl and TPPFeI were prepared and purified by literature methods,[18] and their purity was confirmed by their optical and ^{1}H NMR spectra.[18,19] Piperidine (pip), 2-methylpiperidine (Mepip), and 2,6-dimethylpiperidine (Me_2pip) were degassed by one freeze-pump-thaw cycle, and then distilled under N_2 from KOH through an 8-in Vigreux column; the first and last 20% were discarded. The bases were again degassed by three freeze-pump-thaw cycles, stored over molecular sieves in an inert atmosphere box, and protected from all light. *N*-Hydroxypiperidine (NOHpip) was stirred for several hours with KOH at 45 °C (under N_2) in a sublimation apparatus. The contents were then cooled to 20 °C and purified by sublimation. The pure product was similarly stored under N_2 and protected from light.

N-Deuterated piperidine ($C_5H_{10}N^2H$), pip-d_1, was prepared by stirring 5 mL of ^2H_2O with 15 mL of piperidine, and then swirling the contents over molecular sieves to remove the water; this process was repeated three times. The piperidine was then distilled from calcium hydride. Integration of the ^{1}H NMR spectrum indicated ≥85% deuteration. Perdeuterated piperidine, pip-d_{11}, obtained from Merck, was degassed, dried over molecular sieves, and stored in the dark under N_2. Deuterated *N*-hydroxypiperidine ($C_5H_{10}NO^2H$, NODpip) was prepared by stirring a solution of 1.0 g of NOHpip and 50 mL of ^2H_2O. The solution was then evaporated to a syrup and subsequently sublimed from calcium sulfate. Integration of the proton peak indicated ~85% deuteration. Both NOHpip and NODpip were resublimed from P_2O_5 prior to use.

Commercial deuterated solvents, methylene chloride-d_2 (99%) and toluene-d_8 (99.5%), were used for preparing NMR samples, while spectrograde solvents were used for optical spectra. All solvents were carefully degassed by multiple freeze-pump-thaw cycles and dried by stirring over molecular sieves.

Sample Preparation. All handling of materials and solutions was carried out under a N_2 atmosphere and in the absence of light, unless stated otherwise. Samples were prepared in NMR or ESR tubes immediately prior to use. The base was added either in the inert atmosphere box or by syringing into an N_2-flushed serum-capped NMR tube. Gas-tight syringes were used for all transfers and all NMR tubes and vials were maintained under a slight positive N_2 pressure to inhibit diffusion through the cap. In the case of NOHpip, which is hygroscopic, samples were weighed in vials under N_2 and kept sealed with

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Table I. Tetraphenylporphyrin Chemical Shifts for Iron Complexes in Various Oxidation and Spin States[a]

Oxidation state	Spin state	Complex	Pyrrole H	Phenyl		
				o-H	*m*-H	*p*-H
Fe(III)	5/2	TPPFeX[b]	−75 to −80	−5 to −12	−11 to −16	−4 to −8
Fe(III)	1/2	TPPFeLL'[c]	+8 to +22	←	−3 to −8	→
Fe(II)	2	TPPFeL[d]	−50 to −52	←	−7 to −8	→
Fe(II)	1	TPPFe[e]	−4	−20	−12	−12
Fe(II)	0	TPPFeLL'[f]	−7 to −9	←	−7 to −8	→

[a] Shifts in parts per million at 25 °C referenced to $(CH_3)_4Si$; shifts at other temperatures are approximately predictable by the Curie law ($\propto T^{-1}$). [b] X = Cl, Br, I, N_3, F, OCH_3; ref 19, 21, 22. [c] L,L' = CN^-, Im, Py; L = CN^-, L' = Im, Py; ref 21, 23-26. [d] L = 2-CH_3Im, 2-CH_3Py, THF, ^2H_2O; ref 27. [e] Reference 28. [f] L = L' = Py, Im; L = CO, L' = Im, Py; ref 29.

serum caps in the glove box. Immediately prior to use, the appropriate amount of solvent was syringed into the vial and the resulting solution syringed into an NMR tube. Precautions were taken to prevent the contact of the TPPFeCl solution with the serum cap.

The concentration of pip needed to completely form a ferric pip complex at 25 °C produced a reaction rate too rapid to detect anything but the product. Hence kinetic studies at low temperatures (−70 °C) were more practical. Samples were prepared from fresh stock solution of TPPFeCl in $C^2H_2Cl_2$ in a serum-capped NMR tube which was cooled to −78 °C under N_2 in an ethanol/dry ice bath. The appropriate amount of base was syringed into the cooled NMR tube, shaken rapidly to ensure mixing, and placed immediately into the NMR probe which was preequilibrated at −70 °C. The reaction was monitored in the NMR probe. The exact concentration of TPPFeCl and base used in each case is cited in the text. The single experiment using pip-d_{11} had $[TPPFeCl]_0$ = 1.58 mM, $[pip\text{-}d_{11}]_0$ = 27.1 mM, and T = −70 °C.

The progress of the reaction was followed in one of two ways. For the low-temperature pip reactions, averaged chemical shifts over the starting ferric and product ferrous complexes are observed,[6,7] i.e.

$$(\Delta H/H)_{obsd} = f_{III}(\Delta H/H)_{III} + f_{II}(\Delta H/H)_{II}$$

where f_{III} and f_{II} are the mole fractions and $(\Delta H/H)_{III}$ and $(\Delta H/H)_{II}$ the shifts (in parts per million from Me_4Si) of the ferric and ferrous species, respectively. Since the shifts in the pure ferric and ferrous forms are easily obtained, the percent reduction ($f_{II} \times 100$) is obtained directly from $(\Delta H/H)_{obsd}$. Since shifts are measured to an accuracy of ±0.02 ppm, the percent reduction is accurate to better than ±3%.

The NOHpip reaction was much slower and hence was carried out at 25 °C. Samples were prepared as for the pip reaction, except at 25 °C. For the NMR studies in C^2H_2Cl, $[TPPFeCl]_0$ = 3.57 M and $[NOHpip]_0 = [NODpip]_0$ = 27.0 mM; in toluene-d_8, $[TPPFeCl]_0$ = 7.13 mM and $[NOHpip]_0 = [NODpip]_0$ = 22.7 mM. For the NOHpip reduction, separate signals are obtained for the ferric reactant and ferrous product, so that the percent reduction could be determined by ratios of area of the pyrrole H in the ferrous form over the sum of the pyrrole H areas in both ferric and ferrous forms. Since the areas could not be determined to an accuracy better than ~5%, the resulting percent reduction is accurate only to ±10%. The accuracy in the case of the $C^2H_2Cl_2$ solution in comparing the rate for NOHpip and NODpip is even worse, since there is a tendency to form small amounts of $(TPPFe)_2O$, whose pyrrole H peak overlaps the averaged pyrrole H peak in the ferrous species. For this reason, the comparison of NOHpip and NODpip was extended to toluene-d_8.[20]

The photochemical effect on the autoreduction was determined by preparing identical samples, $[TPPFeCl]_0$ = 10.9 mM, $[pip]_0$ = 13 mM in $C^2H_2Cl_2$, at −78 °C. One sample was wrapped in black plastic sheeting, while the other one was exposed to the normal fluorescent laboratory light. The samples were transferred periodically to the precooled (−70 °C) NMR probe to monitor the reaction progress. The sample exposed to light reproducibly reacted faster.

Instrumentation. The visible spectra were recorded on a Cary 14 spectrophotometer on a sample which had completely autoreduced.

The ^1H NMR spectra were recorded on a JEOL PFT-100 FT NMR spectrometer operating at 99.55 MHz. Spectra were recorded over 2.5-15 kHz bandwidths using 4K-8K data points; 200-5000 transients were collected using a 20-μs 90° pulse. Data collected during a kinetic run were stored on a disk until the completion of the reaction. In these cases, data collection proceeded over a time period during which negligible reaction took place, as determined by checking the effect of length of the data collection period on the line width or relative areas of the ferric and ferrous pyrrole-H peaks.

The ESR spectra were recorded on a Varian E4 X-band spectrometer. The autoreduction was followed at 25 °C directly in the cavity for samples identical with those on which NMR studies were performed.

Results and Discussion

NMR Studies. The overall reaction, as characterized earlier by product analysis, is given by eq 1. As we will show below, ^1H NMR and ESR are very useful in detecting a variety of intermediate species during the course of this reaction.[6,7] These reactions involve both labile ligation equilibria for a given oxidation state as well as the irreversible reduction step. These possible reversible equilibria may be written:

$$PFe^{III}X(S = 5/2) + L \overset{K_1}{\rightleftharpoons} PFe^{III}L^+X^-(S = 5/2) \quad (2)$$

$$PFe^{III}L^+X^-(S = 5/2) + L \overset{K_2}{\rightleftharpoons} PFe^{III}L_2^+X^-(S = 1/2) \quad (3)$$

$$PFe^{II}(S = 1) + L \overset{K'_1}{\rightleftharpoons} PFe^{II}L\ (S = 2) \quad (4)$$

$$PFe^{II}L(S = 2) + L \overset{K'_2}{\rightleftharpoons} PFe^{II}L_2(S = 0) \quad (5)$$

Three of these equilibria are important in following the reactions by NMR and we therefore wish to consider the NMR characteristics for each of the possible species. Table I lists the typical NMR shift ranges for the pyrrole-H and phenyl-H resonances in previously characterized complexes in all relevant oxidation/spin states[19,21-29] These shifts are highly indicative of the species as shown by the essential invariance of shifts with different L for given type of species, as compared to the differences in shifts for different species.

Room Temperature Reaction of Piperidine. The reaction of TPPFeCl with pip at 25 °C is very rapid. If enough pip is added so that reaction 1 goes to completion (i.e., only $TPPFe^{II}(pip)_2$ remains in solution), the reaction proceeds too fast to obtain NMR spectra of any species but the final product. However, some insight into the possible species involved in the reaction can be gained by performing a *titration* of TPPFeCl with pip in $C^2H_2Cl_2$. This allows us to observe both the possible ferric and ferrous intermediates in the reaction.

The trace of TPPFeCl in $C^2H_2Cl_2$ is illustrated in A of Figure 1. Upon addition of a small amount of pip, a second HS species is formed with slightly altered positions as shown in B of Figure 1. The identical species is formed when TPPFeI is used, although with a larger equilibrium constant,[30] suggesting that the product in reaction 2 does not have the halogen coordinated. Complete conversion to $TPPFe^{III}(pip)^+X^-$ prior to any detectable reduction occurs only for X = I. However, the *rate* of converting TPPFeX to $TPPFeL^+X^-$ is much faster than the rate of autoreduction.[31]

Addition of more pip fails to produce any detectable low-spin (LS) species (i.e., eq 3) but does produce a new set of peaks

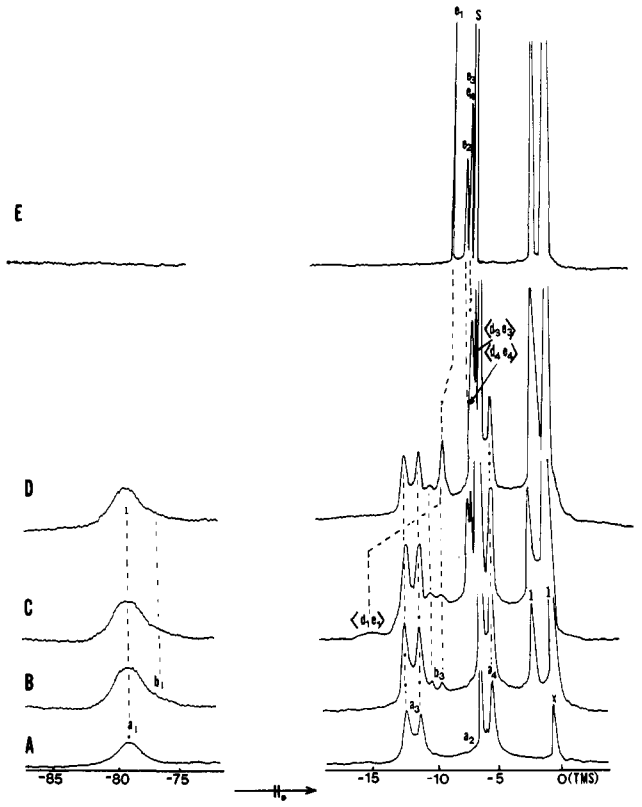

Figure 1. ^{1}H NMR *titration* of TPPFeCl in 0.4 mL of $C^2H_2Cl_2$ with piperidine at 25 °C, $[TPPFeCl]_0$ = 10 mM; with added pip: A, none; B, 0.5 μL; C, 0.75 μL; D, 1.0 μL; E, 4.0 μL. Chemical shifts are in parts per million, referenced to internal Me_4Si. Peaks are designated by letter depending on the species, TPPFeCl = a, $TPPFe^{III}L^+Cl^-$ = b, $TPPFe^{III}L_2^+Cl^-$ = c, $TPPFe^{II}L$ = d, and $TPPFe^{II}L_2$ = e, and by a numbered subscript to denote position, pyrrole H = 1, *o*-H = 2, *m*-H = 3, and *p*-H = 4; peaks averaged over two species are indicated by brackets, i.e., $\langle d_1, e_1 \rangle$ is the averaged pyrrole-H peak for the $TPPFe^{II}L$ and $TPPFe^{II}L_2$ species. The solvent resonance is designated S, and impurities X.

consistent with the reduction of the iron to the expected HS ferrous $TPPFe^{II}(pip)$ and the diamagnetic $TPPFe^{II}(pip)_2$ (C, D in Figure 1). Since there is an excess of pip present when the reaction is initiated, the unligated, S = 1, $TPPFe^{II}$ is not formed,[28] and equilibrium 3 is also unimportant at room temperature. The appearance of HS and LS Fe^{II} complexes in equilibrium 4 is evidenced by the downfield pyrrole-H peak, $\langle d_1, e_1 \rangle$ in C of Figure 1, which grows in intensity (D in Figure 1) and shifts upfield and narrows as the equilibrium 4 is shifted to the right. The position of peak $\langle d_1, e_1 \rangle$ between −10 and −50 ppm is a qualitative index of the fraction of S = 0 and S = 2 species in solution.[27] Separate titration of $TPPFe^{II}$ with pip yields the same spectral effects when more than 1 equiv of pip is added. Completion of the reaction yields the completely diamagnetic $TPPFe^{II}(pip)_2$, whose trace is shown in E of Figure 1. An identical trace is obtained by adding excess pip to $TPPFe^{II}$. The resolution of separate HS $TPPFe^{III}(pip)^+$ and $TPPFe^{II}(pip)$ (averaged via rapid ligand exchange with $TPPFe^{II}(pip)_2$) indicates that electron exchange between the ferrous and ferric HS five-coordinate species is slow on the NMR time scale (i.e., $\ll 10^4$ s^{-1}).

Although a LS bisferric complex (eq 2) is not detected, this could be due to the fact that this species autoreduced too fast. As more pip is added in the attempt to force reaction 2 to the right, the autoreduction rate becomes too rapid for NMR detection of any of the species except the final product. This reaction is followed much more conveniently at lower temperatures.

Low-Temperature Reaction of Piperidine. The autoreduction reaction at −70 °C is slowed considerably, and at the same time, the equilibrium constants K_1 and K_2 in reactions 2 and 3 are increased so that, in the presence of >2 equiv of pip, the equilibria are shifted completely in favor of the LS ferric $TPPFe^{III}(pip)_2^+$ prior to detecting any autoreduction. The spectrum of the typical LS ferric complex, $TPPFe^{III}(pip)_2^+$, is illustrated in A of Figure 2. Ligand exchange is slow on the NMR time scale and integration of the composite of the unassigned downfield coordinated pip peaks relative to the upfield pyrrole H peak (a) provides direct evidence for the bis formulation of the complex.[32] The origin of the downfield peaks in coordinated pip is confirmed by their disappearance upon using pip-d_{11}; the TPP peaks remained unchanged.

The spectrum of the iron porphyrin complex in A is time dependent, with all paramagnetic peaks shifting from those typical of LS ferric species to those typical for diamagnetic $TPPFe^{II}(pip)_2$, as shown in B and C of Figure 2. These changes are consistent only with reduction of the ferric to an isostructural ferrous species where the shifts for the two species are averaged by a rapid electronic exchange,[3,6,7] i.e.

$$TPPFe^{II}(pip)_2 + TPPFe^{*III}(pip)_2^+ \rightleftharpoons TPPFe^{III}(pip)_2^+ + TPPFe^{*II}(pip)_2 \quad (6)$$

at a rate $>10^4$ s^{-1}. Since the shifts for all positions at any time period are obtained from a linear combination of the shifts from the LS ferric and LS ferrous complex, no other porphyrin species have detectable concentrations during the reaction. The slower autoreduction rate and the averaged chemical shifts for reactant and product permit the convenient use of FT NMR for following the reaction.

Room Temperature Reaction of *N*-Hydroxypiperidine. In order to provide direct evidence for the identity of the reducing agent in this autoreduction reactions, it is convenient to introduce another piperidine derivative, *N*-hydroxypiperidine (NOHpip). Addition of this ligand to TPPFeCl in $C^2H_2Cl_2$ at 25 °C also leads to the reduction of the iron complex to diamagnetic $TPPFe^{II}(NOHpip)_2$. The optical spectrum of the product of this reaction is illustrated in Figure 3, where it is compared to that of the previously characterized[33] $TPPFe^{II}(pip)_2$; thus NOHpip undergoes the same overall reaction as pip (vide infra).

The reaction of TPPFeCl with NOHpip at 25 °C is considerably slower than with pip under identical conditions (by a factor of ≳250), so that the actual course of the reaction may be followed by NMR. The proton traces in Figure 4 illustrate the time evolution of this reaction. The traces have a very strong resemblance to those generated by the 25 °C *titration* of TPPFeCl with pip (i.e., compare to Figure 1), permitting ready identification of all species.

A in Figure 4 illustrates the trace for $TPPFe^{III}(NOHpip)^+Cl^-$ (the trace of unreacted TPPFeCl is not shown). The characteristic shifts again identify it as a HS species. Trace B provides the first evidence for Fe^{II} (pyrrole H averaged over S = 2 and S = 0 by ligand exchange, i.e., $\langle d_1, e_1 \rangle$) which shifts upfield (C) and narrows (D) as the autoreduction is completed. The trace of the same solution as in D at −70 °C is depicted in E of Figure 4. Lowering the temperature shifts equilibrium 5 completely to the right to yield only bis, S = 0 species, as identified by the characteristic shifts. The bis formulation is unambiguously established[34] by the relative integrals of the pyrrole H and the upfield, ring-current shifted peaks of the coordinated NOHpip at −70 °C.

The ^{1}H NMR traces of TPPFeCl and NOHpip at −78 °C give evidence only for the same HS $TPPFe(NOHpip)^+Cl^-$ species as depicted in A of Figure 4, with no detectable LS species formed. At this temperature, the autoreduction proceeds at much too slow a rate to make NMR measurements practical. Thus the one-electron autoreduction of the ferric

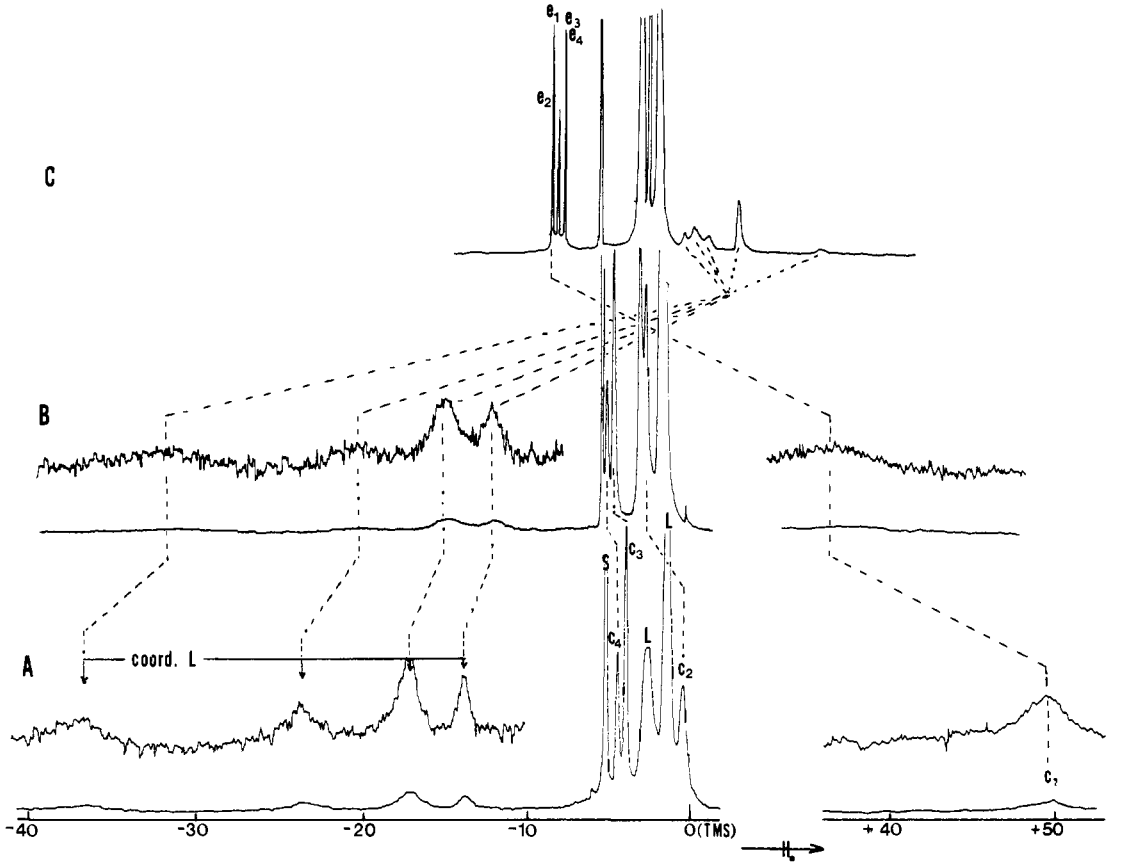

Figure 2. ^1H NMR traces depicting the autoreduction at −78 °C of a $C^2H_2Cl_2$ solution with $[TPPFe^{III}(pip)_2{}^+Cl^-]$ = 3.2 mM, free [pip] = 37.2 mM: A, right after preparation of solution (all ferric); B, after ~2 h; and C, after ~16 h (all ferrous). Shifts are in parts per million, referenced to Me_4Si. For symbols for peaks, see caption to Figure 1. The broadening of the pyrrole-H peak in B is due to electron exchange.

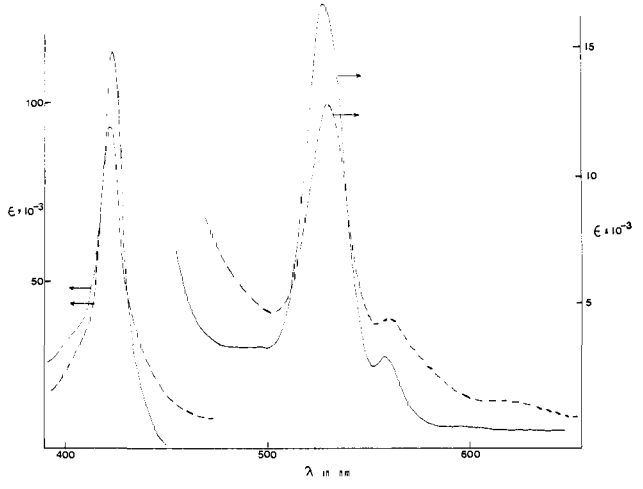

Figure 3. Visible spectra for the products of the reaction at 25 °C resulting from adding 100 μL of piperidine (- - - -) and 100 μL of N-hydroxypiperidine (—) to 0.20-mL volumes of 0.38 mM TPPFeCl in toluene-d_8.

porphyrin appears to proceed primarily from the five-coordinate, HS, species for pip at 25 °C and NOHpip at both 25 and −70 °C. At low temperatures, the pip reaction appears to occur exclusively from the bis, LS species. The retardation of the reaction with NOHpip relative to pip may be electronic (lower basicity of the nitrogen) as well as steric. Addition of a large excess of NOHpip does not yield the bis LS ferric complex either at room temperature or at −70 °C, suggesting a steric destabilization of the bis complex for the ferric state. The bis complex in the ferrous state, on the other hand, is readily formed, indicating that electronic factors are also important. A similar difference in the relative stabilities of the five- and six-coordinate ferric and ferrous porphyrins with 2-methylimidazole has been noted.[30,35]

ESR Studies. The one-electron reduction of the ferric porphyrin in the presence of pip and NOHpip suggests that there should occur a one-electron oxidation of the organic ligand. As in the case of the related autoreduction of the cyanide ion,[6,7] we turn to ESR to detect and identify the expected free radical. In spite of several attempts to locate an ESR signal from the pip radical, no signal unambiguously attributable to this species was observed,[36] probably because of the known very short lifetimes and high reactivity of alkylamine radicals.[37] Several attempts to use spin traps such as nitrosylamine and *tert*-butylnitrosyl were also unsuccessful.

The *N*-hydroxy group (NOH), however, is known to stabilize the one-electron oxidized product of NOHpip, and its ESR spectra at various temperatures have been reported.[38] When TPPFeCl is dissolved in $C^2H_2Cl_2$ containing NOHpip and is placed in the cavity of an ESR spectrometer at 25 °C, the autoreduction reaction gives rise to a species with the ESR spectrum depicted in Figure 5. This radical exhibits the same spectrum as reported earlier[39] and is therefore identified as **1**,

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and establishes that the reducing agent is NOHpip. The similarity of the reactions of NOHpip and pip provides strong support that pip is also the reducing agent (vide infra). The fates of the NOHpip and presumed pip radicals were not in-

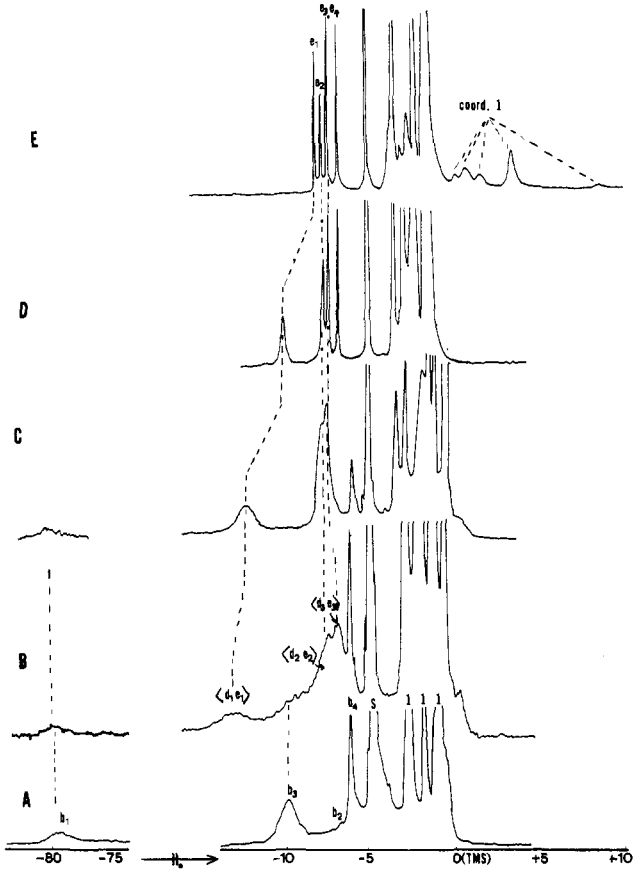

Figure 4. ^1H NMR traces depicting various states in the autoreduction at 25 °C of a $C^2H_2Cl_2$ solution with $[TPPFeCl]_0$ = 3.6 mM, $[NOHpip]_0$ = 33.6 mM: A, right after mixing (only ferric); B, after 26 min; C, after 74 min; D, after 124 min (only ferrous); and E, the trace for the same solution as in D after cooling to −25 °C. Shifts are in parts per million, referenced to Me_4Si. For symbols for peaks, see caption to Figure 1.

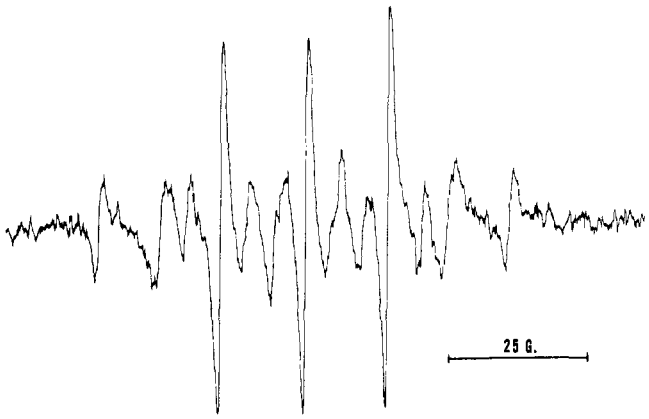

Figure 5. X-band ESR signal at 25 °C recorded during autoreduction of a $C^2H_2Cl_2$ solution with $[TPPFeCl]_0$ = 10 mM, $[NOHpip]_0$ = 50 mM.

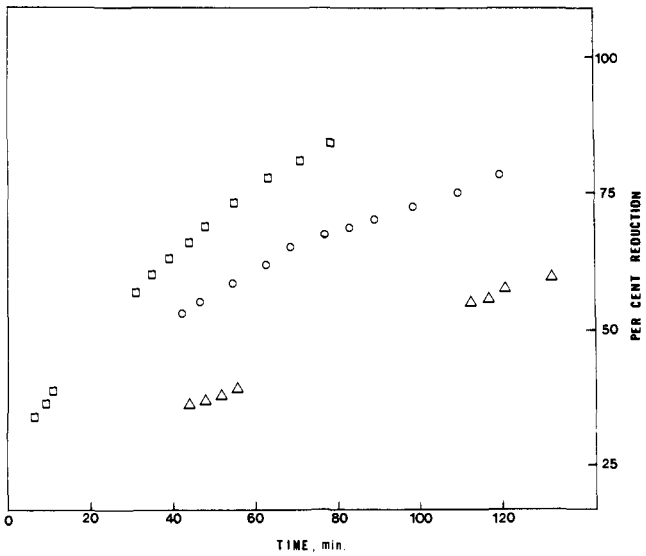

Figure 6. Plots of the percent reductions vs. time at −70 °C for a $C^2H_2Cl_2$ solution with $[TPPFe(pip)_2^+Cl^-]$ = 1.58 mM, and free [pip] = 17.0 mM, △; 22.1 mM, ○; and 27.1 mM, □.

vestigated,although it is likely that they react with free ligand and/or dimerize.[37]

Thus, the overall reaction involving the autoreduction can be written:

$$TPPFe^{III}L_n^+ \xrightarrow[\text{slow}]{L} TPPFe^{II}L_{n-1} + L\cdot \qquad (7)$$
$$\downarrow L \text{ (rapid)} \rightarrow TPPFe^{II}L_2$$

where n = 1 for L = pip and NOHpip at 25 °C and n = 2 for L = pip at −70 °C.

The Reaction Mechanism. As a prelude to elucidating a reasonable mechanism for this novel reaction, the effects of several parameters under experimental control upon the rate of the reaction were investigated. No attempt was made to perform a quantitative kinetic analysis for a number of experimental reasons.[40] Rather, we focus here on some semiquantitative comparisons of autoreduction rates under restricted conditions which allow us to draw some conclusions as to the most likely mechanism for the reaction. During the course of our magnetic resonance investigation of mechanistic aspects of this reaction, we became aware of such a detailed kinetic analysis in progress elsewhere.[41]

The autoreduction is photocatalyzed. At −78 °C, under conditions of excess pip, where the only detectable species in $TPPFe^{III}(pip)_2^+$, a sample exposed to normal fluorescent laboratory light was 50% reduced after 2 h, while an identical sample carefully shielded from light was only 35% reduced.[42] The photocatalytic acceleration is relatively small but indicates that there is both a thermal and a photocatalytic route. All further discussion in this report will be restricted to the thermal pathway with all experiments performed with the rigorous exclusion of light for both sample handling and measurements.

A strong dependence of the reaction rate on the concentration of pip or NOHpip was observed under all conditions. At 25 °C, this effect may involve a shift in equilibrium as well as a direct effect on the mechanism in a manner not involving coordination. However, the effect of [pip] is most clearly defined at −70 °C, when all of the porphyrin can be shown to be present as LS $TPPFe^{III}(pip)_2^+$. The effect of the excess or free [pip] on the rate of autoreduction is illustrated in Figure 6; the rate[43] clearly increases dramatically with [pip]. A similar effect of the concentration of excess cyanide ion on the autoreduction of $TPPFe^{III}(CN)_2^-$ has been observed[7] previously, although it was not clearly defined at that time. Thus the autoreduction reaction for the complex is assisted in some manner by free ligand. Such a general mechanism is qualitatively depicted in A of Figure 7. The exact role of free L will be shown to depend on the nature of L.

An outer-sphere oxidation of free pip is considered extremely unlikely, since the ferric bis complex is not a sufficiently strong oxidizing agent, i.e., −0.21 V vs. SCE in dimethyl sulfoxide[44] for $TPPFe(pip)_2^+$, while for alkylamines, the potential is in the region[45] 1.2 V vs. SCE. This represents a thermodynamic

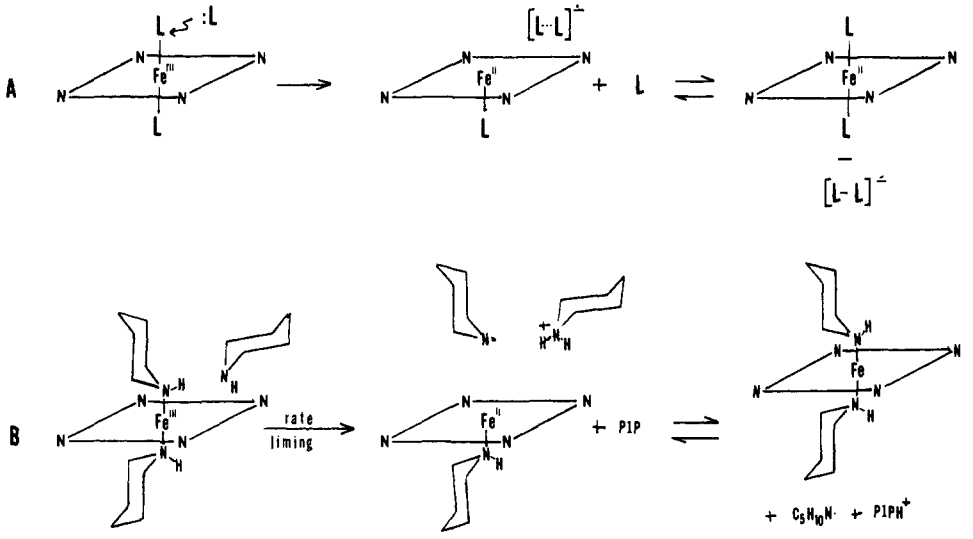

Figure 7. Schematic depicting: A, general attack by a base (free L) to induce intramolecular transfer and subsequent dissociation of [L- - -L]·, and B, the deprotonation of coordinated pip by a base (free pip) which permits intramolecular electron transfer and dissociation of the deprotonated pip radical.

barrier of over 1 V.[46] A mechanism involving simple homolytic bond cleavage may be relevant to the photocatalytic pathway, but is also deemed very unlikely for the thermal pathway in view of the effect of excess pip.

In the present reactions, one of the possible roles of the free ligand is to act as a base to deprotonate the coordinated ligand.[47] This deprotonated coordinated ligand is then more easily oxidized, such that intramolecular electron transfer and subsequent dissociation (homolytic bond cleavage) would yield the identified products, as shown in eq 7. The most acidic proton in pip is NH, so that if transfer of the proton from the coordinated pip to free pip is involved in the rate-limiting step, a significant isotope effect on the overall reaction rate may be anticipated.[48]

Several experimental approaches were adopted in order to clarify the role of the free ligand or base in the reaction mechanism. The effect of deuterium substitution on the reaction rate was investigated at −70 °C in $C^2H_2Cl_2$, under conditions where the only detectable species in solution are $TPPFe^{III}(pip)_2^+$ and free pip. Comparison of the rates under identical conditions using pip and pip-d_1 (i.e., $C_5H_{10}N^2H$) shows that the overall rate of reduction is retarded by a factor of ~2 for pip-d_1 compared to pip,[49] as illustrated in Figure 8. Thus the breaking of the N-H (N-^{2}H) bond appears to be important in the rate-determining step. Although the α-CH_2 protons of the coordinated pip may also be weakly acidic (but are less sterically blocked for interaction with the free base), they do not appear to be involved significantly in the proton transfer, inasmuch as the use of perdeuterated pip, pip-d_{11}, does not retard the autoreduction rate perceptibly over that observed for pip-d_1.

The autoreduction of $TPPFe^{III}(NOHpip)_2^+$ is also found to be dependent on free [NOHpip] in a manner similar to that illustrated for pip in Figure 6. Furthermore, the use of NOHpip-d_1 (i.e., NODpip) also leads to a decrease in the reduction rate at room temperature.[50] Although, in this case, primarily HS species are present in solution, the results support the same mechanism for the autoreduction reaction for pip and NOHpip. A detailed comparison between the two ligands requires consideration of the differences in the coordination geometry of the complex, the ligand basicity, and steric effects,and is beyond the scope of the present discussion. The similarities in the dependence on concentration and isotope are sufficient to indicate that the free radical identified in the case of NOHpip is relevant to the pip reaction.

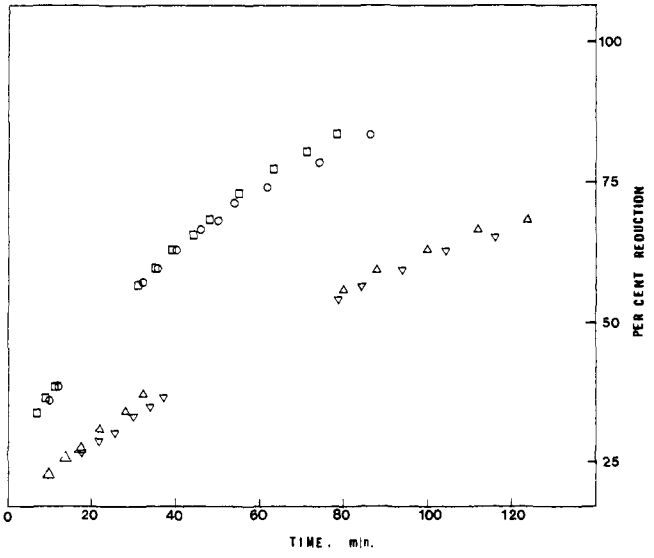

Figure 8. Plots of the percent reduction *vs.* time at −70 °C for a $C^2H_2Cl_2$ solution with $[TPPFe(pip)_2^+Cl^-]$ = 1.57 mM, and free [pip] = 27.1 mM, ○, □, and free [pip-d_1] = 27.1 mM, △, ▽. The two sets of symbols for each case represent independent duplicate experiments.

These results suggest that the autoreduction of $TPPFe^{III}(pip)_2^+$ may be induced by any base capable of deprotonating the coordinated pip. The difficulty in using other bases is that most that are capable of deprotonating the coordinated piperidine are also capable of competing effectively with piperidine as the axial ligand, yielding a mixture of reactants and products, and leading to an ambiguous interpretation of the results.[51] This problem appears to be overcome by the use of the substituted piperidines, 2-methylpiperidine (2-Mepip) and 2,6-dimethylpiperidine (2,6-Me_2pip). The 2,6 positions of a coordinated piperidine are known[5] to sterically interact with the porphyrin ring. Methyl substitution of these positions increases this steric interaction such that neither 2-Mepip nor 2,6-Me_2pip yields detectable LS species at −70 °C for the ferric complex, in contrast to pip. Furthermore, these two ligands, when used alone in the autoreduction reaction, exhibit reduction rates some 10^3-10^4 slower than pip at identical conditions at −70 °C. These much smaller binding constants for the two methyl-substituted ligands allow us to add them to a solution containing $TPPFe^{III}(pip)_2^+$ and only a very small

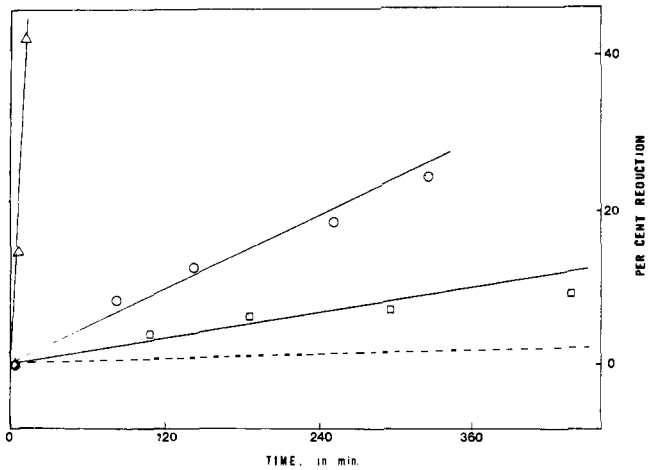

Figure 9. Plot of the percent reduction *vs.* time at −78 °C for a $C^2H_2Cl_2$ solution, with $[TPPFe(pip)_2^+Cl^-]$ = 4.3 mM, and free [pip] = 2.1 mM, -□-; free [pip] = 2.1 mM and free [2,6-Me_2pip] = 26.3 mM, -O-; free [pip] = 2.1 mM and free [2-Mepip] = 26.3 mM, -Δ-. The dashed line is the interpolated percent reduction for a $C^2H_2Cl_2$ solution at −78 °C with $[TPPFeCl]_0$ = 4.3 mM and $[2\text{-Mepip}]_0$ = 37 mM (only HS TPPFe(2-Mepip)$^+Cl^-$ detected by NMR).

amount of free pip, without forming any detectable (by NMR) mixed complexes (i.e., $TPPFe^{III}(pip)(2\text{-}CH_3pip)^+$).

The influence on the reduction rate of $TPPFe^{III}(pip)_2^+$ upon addition of the two sterically hindered piperidines is illustrated in Figure 9. The slow rate of reduction in the absence of the sterically hindered ligands is due to the small amount of the free pip in solution (2.1 mM). The effect of adding 25 mM 2,6-Me_2pip increases the initial rate approximately fivefold, while adding an identical amount of 2-Mepip speeds up the reaction by a factor of >50. The effect of a comparable amount of free pip yields too rapid a reaction rate to follow by NMR. When *only* 2-Mepip is present at the same concentration as the sum of pip and 2-Mepip in the above experiment, the rate of autoreduction is negligible (i.e., dotted line in Figure 9). Thus both noncoordinating bases, 2-Mepip and 2,6-Me_2pip, will accelerate the autoreduction rate, which is consistent with the role of the free ligand as a base for abstracting the proton from the coordinated pip. The larger effect of 2-CH_3pip relative to 2,6-$(CH_3)_2$pip is probably due to a steric effect on the stereochemistry of the interaction involving the proton transfer, since the latter ligand should be a better base.

Thus both the isotope effect and the influence of sterically hindered piperidines on the reduction rate support the role of the free ligand in the reaction as a base to deprotonate the coordinated piperidine, which facilitates the transfer of an electron from the piperidine to the iron. The role of the free ligand in the case of piperidine can be visualized as depicted in B of Figure 7.

The present mechanism may also account for the base-catalyzed oxidative dehydrogenation of macrocyclic ligands reported[9-11] for a number of systems where, though less mechanistic information was available, the oxidized products were characterized. We suggest that base-catalyzed intramolecular electron transfer is the general mechanism for the autoreduction of ferric porphyrins in the presence of organic ligands. In the case of cyanide ion, the increase reaction rate[6,7] with excess $[CN^-]$ may now be reinterpreted in terms of a similar mechanism, where the initial leaving group in A of Figure 7 would be $(CN)_2\cdot$, which, like CN·, is also a precursor of the ESR-detected[52] free radical, $(CN)_4^-\cdot$.

Thus the >1 V thermodynamic barrier to the oxidation of pip by the ferric porphyrins is readily overcome by the deprotonation by the base, suggesting that other electron transfer reactions may occur where similar arguments about thermodynamic barriers have been raised. Thus in the case of cytochrome *c*, similar arguments[16,17] based on thermodynamic barriers have been forwarded to discount amino acid side chain free radicals as intermediates[14] in the reduction of ferricytochrome *c*. Our results on the present piperidine system suggest that nearby basic side chains could play a role similar to that of free pip to lower the oxidation potential of the amino acid side chain sufficiently to permit the electron transfer step.

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lack of knowledge of the subsequent reaction of pip radicals with excess pip (i.e., total consumption of pip), and the relatively low $[pip]_0/[TPPFeC]]_0$ ratios used to keep the autoreduction rate slow enough to follow by FT NMR. The relatively low sensitivity of NMR also did not permit a significant variation in $[TPPFeCl]_0$.

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Synthetic and Mechanistic Studies of the Reduction of α,β-Unsaturated Carbonyl Compounds by the Binuclear Cluster, $NaHFe_2(CO)_8$

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Abstract: A detailed synthetic and mechanistic study of the reactions of $NaHFe_2(CO)_8$ is presented including efficient preparations of $Na_2Fe_2(CO)_8$ and $NaHFe_2(CO)_8$. The use of $NaHFe_2(CO)_8$ for the mild, high-yield reductions of only the olefinic bond in α,β-unsaturated esters, ketones, aldehydes, amides, lactones, and nitriles is documented and these reductions are compared with other available methods. A mechanism for these reductions is presented. The key pieces of evidence for the mechanism, (a) a first order each in metal hydride and activated olefin, (b) isotopic labeling experiments demonstrating a reversible, regiospecific hydride addition step, and (c) a reasonably large, inverse isotope effect ($k_D/k_H = 3.5$), serve as diagnostics of the mechanism for reduction of activated olefins. We have considered plausible $NaHFe_2(CO)_8$ dissociation, fragmentation, or fragmentation-recombination mechanisms. The simplest interpretation of these results is that the active reagent in these reductions is binuclear $NaHFe_2(CO)_8$, although other possibilities are suggested and discussed. The above evidence and a complete reaction stoichiometry suggest that this mechanism involves concerted reversible and regiospecific $NaHFe_2(CO)_8$ addition to activated olefins such as $RCH{=}CHCOR'$, to yield $Na^+(RCH_2CH(Fe_2(CO)_8)COR')^-$, followed by competing rate-determining steps of iron-iron bond cleavage or protonolysis affording $Na^+[RCH_2CH(Fe(CO)_4)COR']^-$ and RCH_2CH_2COR', respectively. This reduction mechanism using binuclear $NaHFe_2(CO)_8$ is compared with that of mononuclear $NaHFe(CO)_4$. The effect of ion pairing in these reductions, the PPh_3 and CO ligand substitution mechanism of $NaHFe_2(CO)_8$, as well as the acid-independent and acid-dependent mechanisms of $NaHFe_2(CO)_8$ decomposition are also presented.

Introduction

Transition metal carbonyl clusters[1] and their hydrides[2] have been known for many years, the first review on clusters appearing in 1965.[1g] Since that time, many studies probing the chemical composition and structural types,[1,4] the simple methods of synthesis,[1b] the relationship between the number of skeletal electrons and the structure,[3] and the fluxional behavior[5] of clusters have appeared. However, general, systematic, efficient synthetic routes for the preparation of clusters still do not exist.[6] Unfortunately, even less is known about the chemical reactivity[7,8,9] (especially the catalytic organometallic chemistry) and detailed reaction mechanisms[10] of clusters.

Our interest in binuclear and higher transition metal cluster compounds arises from the possibility that they will exhibit chemistry unknown to mononuclear homogeneous metal carbonyl compounds and may eventually serve as homogeneous models for reactions occurring on metal surfaces.[1b,11] Homogeneous mononuclear catalysts are unknown for many of the reactions catalyzed by heterogeneous catalysts, such as the Fischer-Tropsch reaction[12] or reactions involving carbon-hydrogen[13] or carbon-carbon[14] bond activation. These and similar structure-sensitive[15] reactions may require two or more adjacent metals, a feature present in heterogeneous and homogeneous cluster catalysts but absent in mononuclear homogeneous catalysts. However, certain inherent properties and side reactions of clusters will severely thwart the development of their chemistry. In particular, metal-metal bonds are often weak,[16] imparting limited thermal stability to first- and second-row clusters. Photolysis usually results in metal-metal bond cleavage.[17] Homolysis[18] and disproportion[16] of clusters can occur giving rise to mononuclear and other fragments. Although not well studied, oxidation or reduction of clusters[1b,16] generally gives metal-metal bond cleavage. Clusters are often unstable under high CO pressure,[1b,1e] cleaving to mononuclear compounds. Added ligands, such as phosphines, may result in ligand substitution or metal-metal bond cleavage.[1b,1e,10] Indeed, the present study has demonstrated most of these side reactions in this simple binuclear cluster, NaH-

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