Reduction of Fe(III) Porphyrin Hydroxides by Heterocyclic Aromatic Amines

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Abstract

The reduction of iron(III) porphyrin hydroxides by the heterocyclic aromatic amines, pyridine, 1-methylimidazole and derivatives, occurs in toluene to give the bisamine iron(II) porphyrin complexes. The reaction has not been fully characterized but is found to proceed through a different mechanism from that reported for the similar reductions by 1° and 2° amines in the absence of hydroxide ion. Preliminary data indicate that the first step in the reduction is formation of the bisamine Fe(III) porphyrin complex from the hydroxide. Nucleophilic attack by hydroxide ion on the aromatic ring of an axially ligated pyridine or methylimidazole of the Fe(III) complex followed by homolytic cleavage of the Fe–N bond is proposed.

Introduction

The autoreduction of Fe(III) porphyrin complexes caused by amines, thiols, cyanide ion and hydroxide ion has been a subject of recent interest due to mechanistic implications for the oxidation or reduction of substrates by peroxidases, oxygenases and cytochrome P-450 [1–5]. Recent work by Castro *et al.* demonstrated the ability of some 1° and 2° amines to reduce Fe(III) porphyrin chlorides to bisamine Fe(II) porphyrins and imine products [1]. A free radical mechanism is proposed for this reaction as well as for the base promoted autoreduction of Fe(III) porphyrin chlorides in dimethylsulfoxide, which occurs with the formation of a hydroxo iron(II) porphyrin complex [2]. Hydroxide has also been found to reduce Fe(III) porphyrin chlorides in pyridine [5]. This report describes the reactions of the hydroxides of iron(III) tetraphenylporphyrin ($FeTPP^+$) and iron(III)C_2cap porphyrin (C_2cap = dianion of 5,10,15,20-[pyromellitoyl tetrakis(*o*-(oxyethoxy)phenyl)]porphyrin) with various amines and important features of the reduction of FePorOH to iron(II) bisamine adducts in the presence of ligating heterocyclic aromatic amines. Of the possible counter ions for iron(III) porphyrins, the hydroxide ion is particularly relevant to biological systems, and the determination of the role of hydroxide in the reduction of these iron(III) porphyrins may provide insight into the mechanism of electron transfer in complex enzyme systems. Besides providing a system for the study of electron transfer in iron porphyrin complexes, the reactions described here should also provide a simple, 'bench top' route to bisamine adducts of iron(II) porphyrins that are at present only available using inert atmosphere or vacuum line techniques.

Experimental

FeTPPCl was obtained from Aldrich Chemicals. The Baldwin '$c_2$cap' porphyrin was prepared and iron was inserted by the literature method [6].

Fe(III)TPP(OH) was prepared as a secondary product from FeTPPCl by the literature method for preparation of the μ oxo dimer [7], shaking a chloroform solution of FeTPPCl with aqueous sodium hydroxide, washing the chloroform layer with water to remove excess hydroxide, and purification of the concentrated chloroform solution on a dry alumina column. The μ oxo dimer is obtained as the fast-moving, diffuse green band which comes off near the solvent front. A second, slow-moving, tight green band exhibits a visible spectrum which is very similar to that of the μ oxo dimer but shows a significant shift in the Soret absorption, 407.5 nm for the dimer and 416.9 nm for the hydroxide in toluene. Chromatography of FeTPPCl on dry alumina also affords FeTPPOH and with less conversion to the μ oxo dimer during workup. Exposure of a chloroform solution of Fe(II)TPP to air followed by chromatography of the green product formed on dry alumina gives similar results, a fast moving green band which is identified spectrally as the μ oxo dimer followed by a second green band which is identified as the hydroxide.

Fe(III)C_2capOH was prepared by chromatography on dry alumina in chloroform. A slow-moving green band is obtained with λ_{max} ($CHCl_3$) at 422 and 580 nm.

The amines were obtained from Aldrich Chemicals and distilled or recrystallized before use. Reactions

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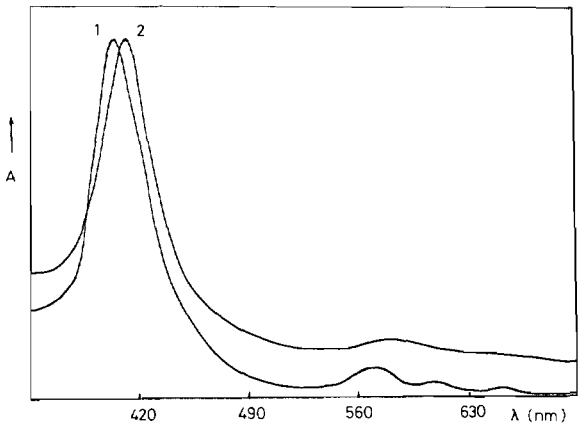

Fig. 1. UV–Vis spectra of TPPFe–O–FeTPP (1) and FeTPPOH (2) in toluene.

between amines and FePorOH were carried out in the neat amine and in toluene solution.

UV–Vis spectra were recorded on a Perkin-Elmer Lamda 4A UV–Vis spectrophotometer. Infrared data were obtained on a Perkin-Elmer 1750 Infrared Fourier Transform spectrometer.

Results and Discussion

Contamination of samples of FeTPPOH with the μ oxo dimer is a problem in studying reactions of the hydroxide. The visible spectra of FeTPPOH and TPPFe–O–FeTPP are similar, with the bands of the hydroxide broadened and slightly red shifted compared to those of the dimer. The two species can be easily distinguished in the Soret region, however. For comparison, the optical spectra of the hydroxide and the μ oxo dimer of Fe(III)TPP$^+$ are shown in Fig. 1. The hydroxide can also be distinguished from the μ oxo dimer by the absence of bands at 870 and 885 cm^{-1} in the infrared spectrum. These bands appear in the IR spectrum of the dimer and are assigned to the antisymmetric Fe–O–Fe stretch [8]. Unfortunately, facile conversion of the hydroxide species to the dimer prevents isolation of the hydroxide of FeTPP$^+$ without some μ oxo dimer impurity, and freshly prepared material must be used immediately. The hydroxide of Fec_2cap^+ has Soret and visible absorptions which are similar to that of a species previously identified as the μ oxo dimer of the iron(III) capped porphyrin [9]. However, the appearance of a strong broad band at 3475 cm^{-1} in the infrared spectrum which can be attributed to an O–H stretch coupled with the lack of a band between 1000 and 600 cm^{-1} which is also absent in the chloride, as well as the reactivity of this species as described below, permits its identification as Fe(III)-C_2capOH. Unlike FeTPPOH, no conversion to the μ oxo dimer was observed for FeC_2capOH, presumably

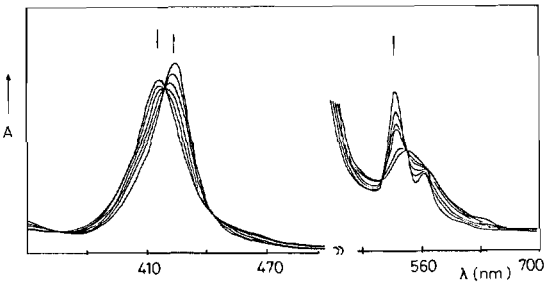

Fig. 2. Spectral changes observed on mixing FeTPPOH and 1-methylimidazole in toluene.

due to steric effects induced by the 'cap'. Conversion of hydroxo Fe(III) porphyrin species to the dimer has been postulated to occur via the formation of a doubly hydroxo bridged bis iron complex [10]. Attack of FeC_2capOH by a second molecule would occur at the side of the porphyrin opposite the 'cap'. Since the cap is attached via *ortho* linkages to the *meso* phenyl rings of the porphyrin, the effect of the cap should be to 'tilt' the phenyl rings and constrain them to be roughly perpendicular to the porphyrin plane. Close approach of the two porphyrin molecules on their 'unhindered' sides would thus be prevented by steric interaction between phenyl groups on the two porphyrin rings.

The increased stability toward reduction of the μ oxo dimer of FeTPP$^+$ over FeTPPCl has been demonstrated by Kadish *et al.* [11] in an electrochemical study of the reduction of Fe(III) porphyrins. The reluctance of the iron(III) centers in TPPFe–O–FeTPP to ligate nitrogenous bases despite empty sixth coordination sites has also been demonstrated [7]. It is not surprising then that no reaction is observed upon dissolution of the μ oxo dimer complex in neat amine. Fe(III)TPPOH, however, is reduced quantitatively to the bisamine adduct of Fe(II)TPP upon dissolution in pyridine, methylimidazole and a variety of other ligating amines as described below. The product is identified as the iron(II) species by its electronic spectrum. Figure 2 shows changes in the UV–Vis spectrum generated by adding 1-methylimidazole to a toluene solution of FeTPPOH.

Amine reduction of FeTPPOH demonstrates a selectivity toward amines based on size and structure. Table I lists the amines tested and the results of their reaction with FePorOH. The most obvious requirement for reaction with FeTPPOH is the ability of the amine to bind to FeTPP$^+$. Thus pyridine, 1-methylimidazole, piperidine and n-propylamine, all of which are known to form the bisadduct of FeTPPCl, reduce iron(III) to iron(II) in the porphyrin complex while diethylamine and triethylamine, which are too bulky to bind FeTPP$^+$, do not react. The same reactions were tried using the iron(III) complex of the Baldwin $c_2$cap porphyrin, which is sterically

TABLE I. Amine Reduction of FeTPPOH

Amine	Imidazole N–H?	Bisadduct with FeTPPCl?	Reduce FeTPPOH?	Bisadduct with Fec_2capCl?	Reduce Fec_2capOH?
Heterocyclic aromatic amines					
1-Methylimidazole	N	Y[a]	Y	N	N
1,2-Dimethylimidazole	N	Y[a]	Y	N	N
Imidazole	Y	Y[a]	N	N	N
2-Methylimidazole	Y	Y[a]	N	N	N
Pyridine	–	Y[a]	Y	N	N
Others					
n-Propylamine	(1°)	Y[b]	Y	Y	Y
tert-Butylamine	(1°)	Y[b]	N		
Diethylamine	(2°)	N	N		
Piperidine	(2°)	Y[b]	Y		
Triethylamine	(3°)	N	N		

[a]Ref. 12. [b]Ref. 1.

hindered on one side and does not form the bisadduct of bases as bulky as pyridine and imidazole. Bisligation is apparently required for reaction since Fec_2capOH is not reduced by 1-methylimidazole, pyridine or piperidine, but is reduced to the bisamine Fe(II) complex by sterically unhindered n-propylamine. Imidazole and tert-butylamine both bind FeTPPCl to give the bisamine adduct but do not cause reduction of FeTPPOH. The failure of these two amines to reduce this complex indicates that, while bisligation of $FePor^+$ is necessary for reaction, it is not sufficient. The present data suggest bisligation of the iron(III) species as an early step in the reduction. This is demonstrated in Fig. 2, where the earliest species detected after mixing FeTPPOH and 1-methylimidazole is FeTPP(1-methylimidazole)$_2^+$. Another distinction between amines which are reducing in this system and those that are not is found in the imidazole series. The presence of hydrogen bound to nitrogen inhibits the reaction so that imidazole and 2-methylimidazole do not cause reduction of iron(III) to iron(II). When methyl is substituted for hydrogen as in the 1-methyl- and 1,2-dimethyl-derivatives, reduction of the iron porphyrin occurs.

The chlorides of iron(III) porphyrins are known to undergo reduction in the presence of unhindered 1° and 2° amines but not pyridine or 1-methylimidazole. The difference in reactivity of FeTPPCl and FeTPPOH toward these amines suggests a difference between the mechanisms for reduction of the chloride by 1° and 2° amines and the hydroxide by heterocyclic aromatic amines, which may be due to hydroxide ion participation in the latter case. It has been suggested [5] that bound pyridine may undergo nucleophilic attack by hydroxide ion resulting in homolytic cleavage of the N–Fe coordinate bond, reducing iron(III) to iron(II) and forming a radical adduct of hydroxide and pyridine, which presumably undergoes polymerization. It is as yet unclear in this mechanism how homolytic bond cleavage would result from attack of the two electron donor, OH^-. However, initial attack of hydroxide on a bisamine iron(III) complex could account for the observed reduction of FeTPPOH by 1-methylimidazole and 1,2-dimethylimidazole. It would explain the formation of the bisamine adduct of $FeTPP^+$ prior to reduction as demonstrated in Fig. 2 and would also be consistent with the inability of imidazole and 2-methylimidazole to reduce Fe(III) to Fe(II) in this system. The addition of one equivalent of hydroxide ion to the bisimidazole adduct of FeTPPCl in benzene, toluene, methylene chloride and dimethylsulfoxide [13, 14] results in the deprotonation of bound imidazole and the formation of the unsymmetric imidazole/imidazolate $FeTPP^+$ adduct. Addition of two equivalents produces the bisimidazolate adduct. Deprotonation of bound imidazole or 2-methylimidazole in this system would consume hydroxide and result in the formation of a negatively charged ring which would not be susceptible to nucleophilic attack. In the present study, formation of an imidazolate adduct was not confirmed. The UV–Vis spectrum of the product of the reaction of FeTPPOH with imidazole resembles that of the bisimidazole adduct of $FeTPP^+$. However, the spectrum of the unsymmetrical and bisimidazolate adducts differ little from that of the bisimidazole adduct except for slightly red shifted bands. Since the reaction was performed in excess imidazole, the observed spectrum may arise from a mixture of the possible products or by displacement of an imidazolate ligand by imidazole.

The reductions observed in this investigation fall into one of two categories, reduction of iron(III) porphyrin hydroxides by 1° and 2° amines, which may proceed through a mechanism similar or iden-

tical to that observed by Castro for reduction of iron(III) porphyrin chlorides, and reduction by heterocyclic aromatic amines. In either case, bisligation of the iron(III) porphyrin by the reducing amine is implicated as an important mechanistic step, but in neither is bisligation by the amine sufficient in itself to bring about reduction. Reduction by the heterocyclic aromatic amines proceeds by a mechanism involving hydroxide ion participation and may be described by eqns. (1) and (2).

$$Fe(III)TPPOH + 2L \rightleftharpoons FeTPP(III)L_2^+OH^- \quad (1)$$

$$FeTPP(III)L_2^+ + OH^- \xrightarrow{L} FeTPP(II)L_2 + \text{'oxidized product'} \quad (2)$$

The oxidized product is currently unidentified but may arise from the adduct formed by OH^- attack on L. The reaction is presently under investigation using sterically hindered Fe(III) porphyrin hydroxides which are unable to form the μ oxo dimer complex but are not too sterically encumbered to form the bisamine adducts. Whatever the mechanism, reduction of hemin type molecules by hydroxide ion may prove a viable electron transfer route for consideration in biological systems.

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