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# Slow Interconversion of Aquo- and Hydroxo-Ligated Iron(III) Porphyrins

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Proton transfer to or from oxygen is usually assumed to be rapid, with limiting rates for protonation being diffusion controlled under conditions of large driving force.[1] However, recent reports have shown that proton transfer to bridging oxo ligands of $d^3$, $d^4$, or $d^5$ transition metal dimers can be slow.[2,3] The reasons for the slow protonation/deprotonation reactions in these complexes are not completely understood but may depend on the change in the electronic coupling between the metal centers and on a change in geometry in the molecules.[3] We recently observed that interconversion between the aquo and hydroxo forms of the iron(III) complex of tetrakis(2,3,5,6-tetrafluoro-*N,N,N*-trimethylanilinium-4-yl)porphyrin (Fe$^{III}$(TF$_4$TMAP)$^{5+}$)[4] (Figure 1) in acetonitrile−water solutions is slow on the NMR time scale at room temperature. This result implies that the rate of interconversion between aquo and hydroxo forms for this porphyrin is over 2 orders of magnitude slower than those reported for other aquo metal complexes,[5−8] and raises the possibility that slow proton transfer to oxygen is not restricted to $\mu$-oxo dimers. In this paper we report our evidence for the slow interconversion and report data which suggest that the rate of this reaction is controlled by changes in the coordination and geometry of the iron(III) center, rather than actual slow proton transfer.

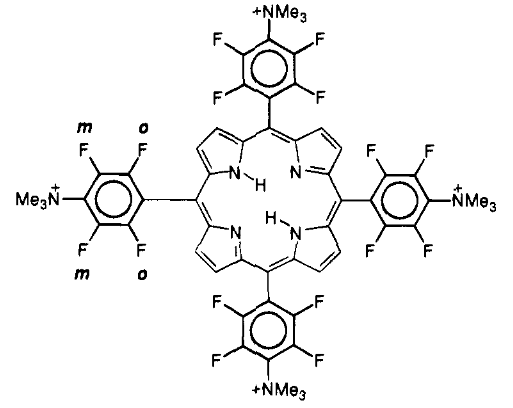

**Figure 1.** Diagram of $H_2TF_4TMAP^{4+}$, showing positions of ortho and meta fluorines.

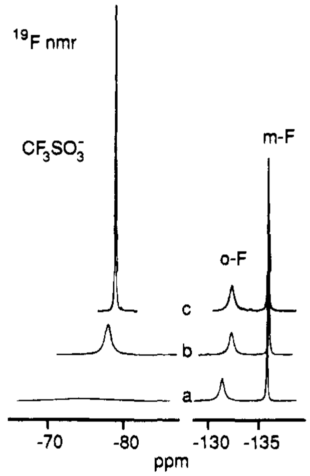

**Figure 2.** Effect of adding $D_2O$ to an acetonitrile-$d_3$ solution of Fe(TF$_4$TMAP)(CF$_3$SO$_3$)$_5$ (2.4 mM). $^{19}$F NMR measured at 338.8 MHz relative to CFCl$_3$. (a) No added $D_2O$; (b) 0.13 M $D_2O$; (c) 5.8 M $D_2O$.

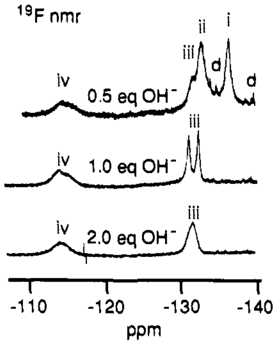

**Figure 3.** Effect of adding NaOH/$D_2O$ solution to a sample of Fe(TF$_4$TMAP)$^{5+}$ (2.2 mM) in acetonitrile-$d_3$−$D_2O$ (5.8 M $D_2O$). $^{19}$F NMR measured at 338.8 MHz relative to CFCl$_3$. (i) *m*-F of Fe(H$_2$O)$_{1-2}$(TF$_4$TMAP)$^{5+}$; (ii) *o*-F of Fe(H$_2$O)$_{1-2}$(TF$_4$TMAP)$^{5+}$; (iii) *m*-F of Fe(OH)(TF$_4$TMAP)$^{4+}$; (iv) *o*-F of Fe(OH)(TF$_4$TMAP)$^{4+}$. Peaks marked d are due to the $\mu$-oxo dimer.

The $^1$H NMR spectrum of Fe$^{III}$(TF$_4$TMAP)(CF$_3$SO$_3$)$_5$ in acetonitrile−$d_3$ shows a broad peak at 59 ppm, which we assign to the $\beta$-pyrrole resonance of the triflato complex.[9] As reported previously, $^{19}$F NMR shows that this complex exchanges CF$_3$SO$_3^-$ ligands rapidly at room temperature (the ortho and meta F appear as broad singlets, and the CF$_3$SO$_3^-$ resonance at −74 ppm is very broad)[9] (Figure 2a), but at −28 °C, the exchange is slowed and the two faces of the porphyrin appear inequivalent (the CF$_3$SO$_3^-$ resonance sharpens and the ortho and meta fluorine resonances[10] each split into two peaks).[4] Addition of $D_2O$ to the acetonitrile causes the CF$_3$SO$_3^-$ resonance to sharpen, and a broad HOD peak appears in the $^1$H NMR. Addition of more $D_2O$ causes the HOD peak to grow, sharpen, and move to lower $\delta$, the $\beta$-pyrrole $^1$H resonance moves to 72 ppm, and the CF$_3$SO$_3^-$ peak in the $^{19}$F NMR moves to −78 ppm and becomes very sharp, indicating that the iron(III) is now coordinated by water (Figure 2b,c).[11] Addition of OD$^-$ to this solution causes the peaks due to the aquo porphyrin to decrease, and new peaks grow in at 85 ppm in the $^1$H NMR spectrum and at −114 and −132 ppm in the $^{19}$F NMR spectrum (Figure 3). After the addition of 1 equiv of OD$^-$, the ortho and meta fluorine peaks are split into two, showing that the two faces of the porphyrin are inequivalent and are not

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(8) Wang, K.; Jordan, R. B. *Inorg. Chem.* **1993**, *32*, 895, assuming that the $k_3$([H$^+$]$^{-1}$) path corresponds to reaction of (H$_2$O)$_5$CrCH$_2$CN$^{2+}$ and (H$_2$O)$_4$(OH)CrCH$_2$CN$^+$ with p$K_a$ = 4.3.

(9) $^1$H NMR spectra were measured on a 360 MHz Bruker spectrometer and are referenced to TMS. $^{19}$F NMR spectra were measured at 338.8 MHz on the same machine and are referenced to CFCl$_3$. Results similar to those reported were obtained in 1:1 acetonitrile−water and in acetone−water mixtures. The CF$_3$SO$_3^-$ $^{19}$F NMR chemical shift given in ref 4 (−76.3 ppm) was measured in slightly wet acetonitrile.

(10) The ortho and meta descriptors are with respect to the porphyrin−anilinium bond.

(11) We have no absolute evidence for whether the acidic form has two coordinated waters or has one with rapid exchange. However, a preliminary solution for the crystal structure of [Fe(TF$_4$TMAP)](CF$_3$SO$_3$)$_5$ grown from acetonitrile−ether in ambient conditions shows two axial waters, suggesting that under the conditions of this paper the acid form will also have two axial waters.

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undergoing interconversion on the NMR time scale. Further addition of $OH^-$ causes the two faces of the porphyrin to become equivalent, with the phenyl fluorines appearing at the average chemical shift of the split peaks, as shown at the bottom of Figure 3. Addition of 1 or 2 equiv of the hindered base diisopropylethylamine to a solution of $Fe^{III}(TF_4TMAP)(CF_3SO_3)_5$ gives sharp doublets similar to those seen after addition of 1 equiv of $OH^-$.

The fact that the NMR peaks for the porphyrin with coordinated water and those for the porphyrin with coordinated hydroxide are separate at room temperature shows that exchange between these two forms is slow under these conditions (second-order rate constant $< 10^6$ $M^{-1}$ $s^{-1}$). This cannot be ascribed to steric interactions preventing the two porphyrins from interacting, since this porphyrin can dimerize to form a $\mu$-oxo dimer with a dimerization constant of about 300 $M^{-1}$.[12] In addition, the broad water signal in acidic solution shows that water can readily exchange with the aquo porphyrin.

The chemistry in acetonitrile−water is in marked contrast to the behavior in aqueous solution. In aqueous solution the aquated, hydroxo, and dihydroxo porphyrins are all in rapid equilibrium on the NMR time scale, as has been reported for other iron(III) porphyrins,[13,14] so the NMR signals observed are the weighted averages of the respective individual signals. The $\beta$-pyrrole $^1H$ and meta fluorine $^{19}F$ NMR resonances of both forms and the $^{19}F$ resonances for the ortho fluorines of the acidic form of the porphyrin are in approximately the same positions for both solvent systems. However, the $^{19}F$ NMR resonance for the ortho F of the hydroxo porphyrin moves from approximately −114 ppm in water-poor acetonitrile−water mixtures (<80% v/v $H_2O$) to −130 ppm in water, and both faces of the hydroxo iron porphyrin are equivalent on the NMR time scale in water. We propose that these changes reflect a change from a five-coordinate species in mixed solvent systems to a six-coordinate species in water.[15] The six-coordinate $Fe^{III}(OH)(OH_2)(TF_4TMAP)^{4+}$ can undergo rapid proton transfer and can also undergo rapid interconversion of $OH^-$ and $H_2O$ ligands, possibly via a Grotthus chain mechanism.[16]

Consideration of the above results in water and in acetonitrile−water leads to the following rationale for the slow interconversion in mixed solvent. The hydrophobic character of the distal face of $Fe^{III}(OH)(TF_4TMAP)^{4+}$ disfavors the addition of water to the porphyrin to form a six-coordinate species. Conversion to the aquo form then occurs via one of three routes: (i) the five-coordinate OH can be protonated, and the iron then relaxes into the plane and binds a second water molecule; (ii) the iron can move into the porphyrin plane prior to subsequent reaction with water or $H^+$; or (iii) the six-coordinate $(H_2O)(OH)$ is formed and is then protonated. Our current results do not differentiate between these possibilities, although the fact that we observe $Fe^{III}(OH)(TF_4TMAP)^{4+}$ and $Fe^{III}(OH)(H_2O)(TF_4TMAP)^{4+}$ in 4:1 water−acetonitrile[16] strongly suggests that path (ii) or (iii) operates in water-rich solution.

Two previous reports have suggested that slow protonation of iron porphyrins can occur in aqueous solution.[13,17] However, one of these observations was based on electrochemistry, which can give double peaks in poorly buffered solutions,[17] and the other is more likely to be an example of a slow $\mu$-oxo-$\mu$-hydroxo proton transfer between porphyrin dimers.[13] Our results suggest that proton equilibria in aqueous solution will be rapid unless significant steric blocking of one porphyrin face occurs.

The slow effective proton transfer reported in this paper is unusual because proton transfers in oxo−aquo and hydroxo−aquo systems are usually rapid.[3] The decrease in rate may be because the hydroxo porphyrin is five-coordinate—in typical high-spin five-coordinate complexes the Fe is considerably (ca. 0.4 Å) out of the plane of the porphyrin nitrogens[18]—while the aquo porphyrin is either a six-coordinate species or is a rapidly-exchanging five-coordinate complex with the iron close to or in the porphyrin plane. Interconversion of the two forms then requires considerable nuclear motion. The "normal" behavior of the porphyrin in aqueous solution suggests that the presence of an axial water in the trans position accelerates the rate of interconversion between coordinated hydroxide and water. The $pK_a$ of $Fe^{III}(H_2O)_{1-2}(TF_4TMAP)^{5+}$ is 6.0,[9] (measured in $H_2O$, $\mu = 0.1$ M; apparent $pK_a$ in 1:1 acetonitrile−$H_2O$ is also 6.0), so if interconversion of the acid and base forms was occurring via isolated transfer to solvent, the measured pseudo first-order rate constants should be ca. $10^3$ $s^{-1}$ if the reaction of the basic form with $H^+$ is diffusion controlled. In solutions containing approximately equal concentrations of the acid and basic forms of the porphyrin, it is therefore expected that the predominant pathway for proton self-exchange will be direct or solvent-mediated reaction between $Fe^{III}(H_2O)_{1-2}(TF_4TMAP)^{5+}$ and $Fe^{III}(OH)(TF_4TMAP)^{4+}$.[1]

We are investigating whether the behavior described above is unique to fluorine-substituted porphyrins, or whether it is more general. Previous studies of sterically-hindered hydroxo porphyrins have failed to mention this phenomenon,[19−22] but most of the nonaqueous studies used chloro complexes, so that acidification of the solution led to the chloro rather than the aquo complex. We intend to re-examine some of these other systems using less coordinating anions so that water can compete for the coordination sites.

The slow interconversion reported in this paper may be relevant to the mechanism for metalloenzymes in which an iron porphyrin center is preferentially five-coordinate, such as cytochromes with no axial ligand. A recent report of slow pH-related interconversions in modified metmyoglobins is suggested to occur via equilibrium between five-coordinate (acid form) and six-coordinate (base form) iron porphyrin.[23] While not directly comparable, this result also demonstrates the effect of exclusion of water from the iron center. Examination of aquo ligands in hydrophobic metal sites may lead to additional examples of these slow interconversions.

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(12) The dimer shows $^{19}F$ NMR resonances at −137 and −139 ppm (*m*-F) and −133.5 and −136 ppm (*o*-F) and a $\beta$-pyrrole $^1H$ NMR resonance at 14.2 ppm.

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(15) Our assignment of the species in water-rich solution as six-coordinate $Fe(OH)(OH_2)TF_4TMAP^{4+}$ and that in predominantly nonaqueous solution as five-coordinate $FeP(OH)TF_4TMAP^{4+}$ is strengthened by the observation of two peaks upon addition of base to 4:1 water−acetonitrile solution—one at −116 ppm (corresponding to the *o*-F of the low-water content form) and one at −122 ppm (corresponding to the water-rich form).

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