# Extraction and Metalation of Porphyrins in Fluorous Liquids with Carboxylic Acids and Metal Salts

**Kristi L. O'Neal and Stephen G. Weber***

*Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260-3900*

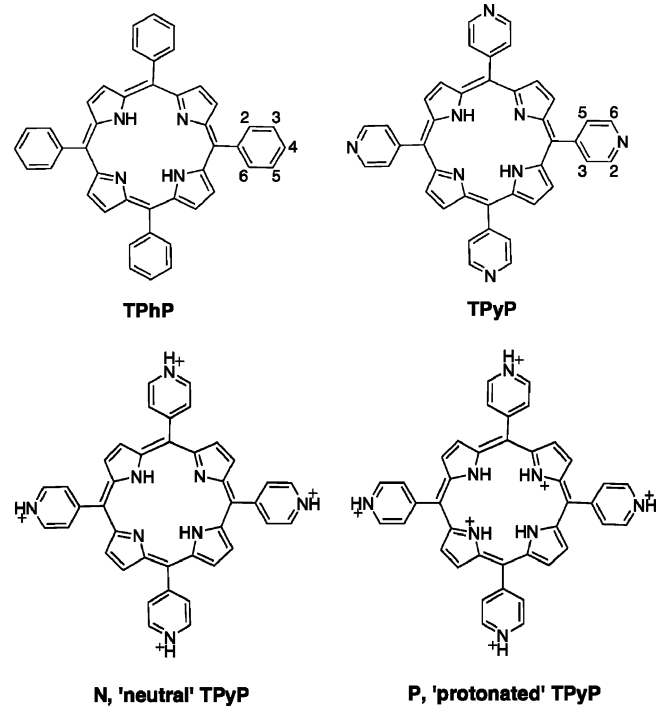
*Received: March 4, 2009; Revised Manuscript Received: April 10, 2009*

Porphyrins have found application in a remarkable variety of areas such as sensors, ion selective electrodes, photodynamic therapy, and energy-transfer systems. Here, we demonstrate the extraction of 5,10,15,20-tetraphenylporphyrin (TPhP) and 5,10,15,20-tetra(4-pyridyl)porphyrin (TPyP) into a mixture of perfluorohexanes (FC-72) through noncovalent interactions with Krytox (**1**), a carboxylic acid terminated perfluoropolyether. We found that **1** transfers two protons to the TPhP tetrapyrrole ring to create the porphyrin dication ($H_2TPhP^{2+}$) in FC-72 while up to six protons are transferred to the TPyP pyridyl and tetrapyrrole nitrogens to create a hexavalent cation macrocycle in the fluorous phase. The total charge on TPyP is controlled by adjusting the concentration of **1** in the fluorous phase. In addition, we observed extraction of ZnTPyP from $CDCl_3$ with **1**/FC-72, while ZnTPhP is not extracted by **1**/FC-72. We prepared the Zn salt of **1** and found that it extracts (from $CDCl_3$) and metalates TPyP but not TPhP. Competitive binding between the porphyrins and an ethanol cosolvent hinders the extraction of both TPhP and TPyP and inhibits the formation of the TPyP hexacation in FC-72. By controlling the concentration of porphyrin, **1**, and ethanol, it is possible to reversibly solubilize TPyP in the fluorous phase through noncovalent interactions between the pyridyl moieties and **1** while leaving the tetrapyrrole ring available to interact with metals or other substrates. In addition, both porphyrins and ZnTPyP are easily recovered from the fluorous phase using commercially available fluorous solid-phase extraction cartridges. Understanding noncovalent interactions in fluorous matrices should lead to development of more robust devices for sensing and energy transfer.

## 1. Introduction

Porphyrins have interesting optical and electrical properties resulting from their highly conjugated $\pi$-electron system that is sensitive to changes to the conjugation pathway. This makes porphyrins and their derivatives particularly useful in optical sensor development.[1−18] In addition, there has been great interest in synthetic functionalized metalloporphyrins as photosensitizers in photodynamic therapy, molecular[19−21] and ion-pair[22] receptors, electrodes in molecular photovoltaic devices,[23,24] and building blocks in supramolecular chemistry.[25,26] Porphyrins and metalloporphyrins have been exploited as ionophores in the development of ion selective electrodes[27−32] and as chemically modified electrodes[27] in amperometric and voltammetric sensors.

In general, chemical sensors involve some sensing material embedded in a matrix. It is well-known that sensor performance, although highly dependent on the properties of the sensing material, is often limited by this supporting matrix.[28] A poorly solvating matrix provides a more selective environment for chemical sensing by reducing the concentration of interfering species in the matrix. Fluorous liquids are the ultimate noncompetitive solvent.[29] However, solubilization of large organic molecules, such as porphyrins, in extremely nonpolar fluorous liquids at room temperature is challenging. There are only a handful of reports on covalently modified fluorous-tagged porphyrins that are soluble in fluorous liquids[30−34] and even fewer reports on nonfluorous-tagged porphyrins in a fluorous matrix.[35,36] In fact, there are only a few reports exploiting noncovalent interactions in perfluorocarbons,[35,43−48] and the fundamental science is not fully understood. El Bakkari et al.[35] have demonstrated near-complete reversible extraction of 5,10,15,20-tetra(4-pyridyl)porphyrin (TPyP) from chloroform into a perfluorodecalin solution using an excess of a "heavy fluorous" (i.e., containing eight perfluorooctyl fragments) $Cu(II)_2$−tetracarboxylate complex (**2**).



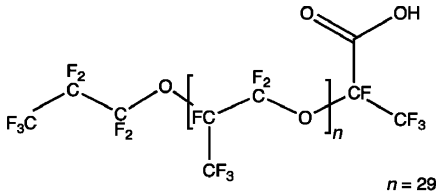

The resulting perfluorosoluble **2**-TPyP supramolecular assembly showed no evidence of TPyP metalation by copper(II) ions under the conditions used.[37] With an equimolar ratio of **2** to TPyP, a red precipitate formed and was postulated to be a

* To whom correspondence should be addressed. E-mail: sweber@pitt.edu.

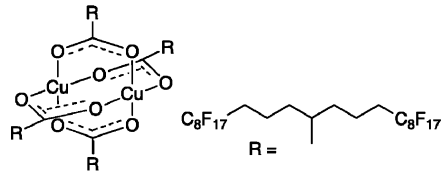
10.1021/jp902000v CCC: $40.75 
Published on Web 05/05/2009

polymeric supramolecular assembly with limited solubility in perfluorocarbons.[35] Because **2** was not able to extract 5,10,15,20-tetraphenylporphyrin (TPhP), it was concluded that the interaction between **2** and TPyP occurred only through the pyridyl nitrogens.

We have observed[38] that Krytox (**1**), a carboxylic acid terminated poly-hexafluoropropylene oxide, significantly enhances the extraction of pyridine (100-fold with excess **1** as compared to **1**-free) and substituted pyridines from chloroform into a mixture of perfluorohexanes (FC-72) while having little effect on the nonheterocyclic counterparts (i.e., phenol or aniline).




**1**




**2**

Knowing this, we wondered if the much simpler **1** (compared to **2**[35,37,39]) would effectively extract TPyP. Here, we demonstrate reversible extraction of both TPhP and TPyP from $CHCl_3$ with **1** in FC-72. Two protons are transferred from **1** to the macrocyclic tetrapyrrole (tetrapyrrole hereafter) of TPhP. In addition to the two protons transferred to the tetrapyrrole, four protons can be transferred from **1** to the TPyP pyridyl nitrogens for a total of six protons. The overall charge on TPyP is controlled through adjusting the relative concentrations of **1** and TPyP. Interestingly, we observed that $Zn\mathbf{1}_2$ salts effectively extract and rapidly metalate TPyP in the fluorous phase under ambient conditions while we saw no interaction with TPhP. The copper complex (**2**) previously employed to extract TPyP into the fluorous phase did not metalate TPyP under similar conditions.[37,39] However, $Zn\mathbf{1}_2$ is able to metalate TPyP. Easy recovery of both the porphyrin (metalated and free base) and **1** is achieved using commercially available fluorous solid-phase extraction (F-SPE) cartridges. The purpose of this work is to gain a fundamental understanding of the nature of the interactions of porphyrins with **1** in a highly fluorinated matrix, which leads to the development of more robust and selective porphyrin-based sensors and devices for energy transfer, optical communication, and data storage in fluorous media.

## 2. Experimental Section

**2.1. Chemicals and Solutions.** Chloroform (Fisher Scientific, Fair Lawn, NJ) and deuterated chloroform (Cambridge Isotope Laboratories, Inc., Andover, MA) were dried over activated molecular sieves and treated with potassium carbonate (EM Science, Cherry Hill, NJ) to neutralize any HCl that had formed as a result of exposure to light.[40,41] Commercially available $CHCl_3$ contains ~1% (v/v) ethanol as a stabilizer to prevent the formation of HCl and phosgene[40,41] while deuterated chloroform does not. Methanol, ethanol, and dimethylformamide (DMF) were purchased from J. T. Baker (Phillipsburg, NJ) and dried over molecular sieves. *meso*-Tetraphenylporphyrin (TPhP), 5,10,15,20-tetra(4-pyridyl)porphyrin (TPyP), and 2,2,2-trifluoroethanol were purchased from Sigma-Aldrich and used as received. FC-72 Fluorinert Electronic Liquid (a mixture of perfluorohexanes) was purchased from 3M (St. Paul, MN), and Krytox 157FSH (**1**), from Miller-Stephenson Chemical Co., Inc. (Danbury, CT). $^{19}F$ NMR analysis of **1** resulted in a number-averaged molecular weight of 5150 g $mol^{-1}$ with an average of 29 polymer repeat units. We have previously reported a molecular weight of 5840 g $mol^{-1}$ with 33 repeat units[38] from a different lot.

As mentioned above, all $CHCl_3$ solutions within this work contain ethanol. Solutions made from $CDCl_3$ contain 0.00, 1.00, or 2.00% (v/v) added ethanol as specified. Separate stock solutions of 1.0 mM TPhP and TPyP were made in $CHCl_3$ and $CDCl_3$ with 0.00, 1.00, and 2.00% (v/v) ethanol as the solvent. All containers of stock solutions were placed in a Cole-Parmer (Chicago, IL) ultrasonicator bath for 10−30 min to ensure dissolution of the materials in their respective solvents.

**2.2. Preparation of Zinc Salt and Metalloporphyrins.** The following procedure was adapted from Doan et al.[42] for the preparation of the zinc salt of **1** ($Zn\mathbf{1}_2$). Equal weights (2.0 g each) of **1** and a 1.0 M $ZnCO_3$ aqueous slurry were mixed in a separatory funnel and shaken vigorously until an emulsion formed. To break the emulsion, 2.0 mL each of methanol and trifluoroethanol were added to the separatory funnel. The resulting mixture was extracted with 2.0 mL of FC-72 several times. The FC-72 solution was then stirred over activated molecular sieves overnight and passed through a 0.22 $\mu$m pore-size nylon syringe filter (Acrodisc) before the solvent was allowed to evaporate. The resulting $Zn\mathbf{1}_2$ oil was then dried overnight at 180 °C. FTIR spectra confirmed the formation of the salt with the disappearance of the **1**−carboxylic acid dimer band and the appearance of a carboxylate band (Figure S1 in Supporting Information). $^1H$ NMR spectra taken before and after formation of $Zn\mathbf{1}_2$ (Figure S2 in Supporting Information) show that the **1** proton signal disappears upon salt formation. The zinc metalloporphyrins, ZnTPhP and ZnTPyP, were synthesized according to Adler,[43] and formation of the metalloporphyrin was verified using UV/vis and $^1H$ NMR.

**2.3. Fluorous Biphasic Extractions.** A series of liquid−liquid fluorous biphasic extractions was carried out by placing aliquots of each porphyrin solution and 0.0−20.0 mM **1**/FC-72 (phase ratio, $\Phi = 1.0$ for all extractions) in GC autosampler vials and shaking for 10 min on a mechanical shaker (in-house construction) to ensure homogeneity (see Supporting Information for photographs). The samples were allowed to rest for 10 min before measurements were taken. Samples of each porphyrin solution were extracted with **1**-free FC-72 as controls. The layers were physically separated using a syringe and all baseline-corrected absorbance values were measured under ambient conditions (22.0 ± 1 °C). $^1H$ NMR measurements of the stock solutions and FC-72 receiving phase were carried out.

Extractions of TPhP and TPyP were carried out similar to those discussed above but with $Zn\mathbf{1}_2$ in place of **1** in the FC-72 receiving phase. Extractions of ZnTPhP and ZnTPyP from $CHCl_3$ were also carried out as discussed above.

Extractions were carried out to determine the distribution of ethanol between $CDCl_3$ and FC-72 with and without **1** in FC-72. One milliliter of $CDCl_3$ with 1.00% (v/v) ethanol was shaken separately with 1.0 mL of FC-72 and a 10.0 mM solution of **1**/FC-72. A 0.3 mL aliquot of each resulting FC-72 solution was transferred to an NMR tube, and 10.0 $\mu$L trifluoroethanol

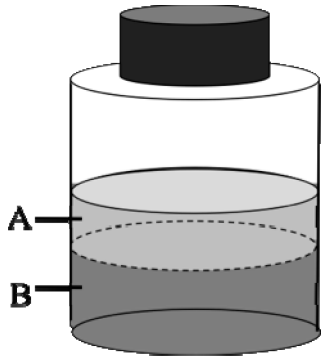



**Figure 1.** Diagram of biphasic extraction experiments. Phase A (source phase) contains TPhP or TPyP dissolved in $CHCl_3$ with ~1% (v/v) ethanol, $CDCl_3$, $CDCl_3$ with 1.00% (v/v) ethanol, or $CDCl_3$ with 2.00% (v/v) ethanol while phase B contains **1** (concentration varies by sample) in FC-72 (phase ratio, $\Phi = 1.0$).

was added as an internal standard. $^1$H NMR measurements were taken at 25 °C using a melting-point capillary filled with deuterated acetone as the locking solvent. Using the same procedure, extractions with $CHCl_3$ containing ~1% (v/v) ethanol in place of $CDCl_3$ were carried out to determine the concentration of $CHCl_3$ in FC-72.

**2.4. Recovery of Porphyrins Using Fluorous Solid-Phase Extraction.** Both TPhP and TPyP were recovered using fluorous solid-phase extraction (F-SPE). A commercially available 5 g Fluoro*Flash* F-SPE cartridge (Fluorous Technologies Incorporated, Pittsburgh, PA) was emptied, and 0.25 g of the fluorous silica sorbent material was placed into a 1 g capacity tube (Sigma Aldrich, St. Louis, MO) and topped with a frit. The cartridge was then conditioned by first loading 0.5 mL of DMF onto the cartridge using a vacuum and then by passing 2.0 mL of a hydrophilic eluant (80:20 methanol/$H_2O$) through the cartridge. After each fluorous biphasic extraction (described above), the resulting fluorous receiving phase contains the **1**−porphyrin complex. The fluorous phase was separated with a syringe, and 0.3 mL was loaded onto the cartridge under a vacuum. The porphyrin was then desorbed by passing two 0.5 mL aliquots of a fluorophobic eluent (50:50 $CHCl_3$/ethanol) through the cartridge. **1** was then recovered separately with two separate washes of 0.3 mL of FC-72 eluent under vacuum.

**2.5. Instrumentation.** A Hewlett-Packard 8452A UV−visible diode array spectrophotometer was used for all UV absorbance measurements. All samples were measured in a 0.1 cm path length sample cell (Fisher Scientific, Pittsburgh, PA). A Varian Excalibur Fourier transform infrared (FT-IR) spectrophotometer was used for IR measurements, and all samples were measured in a 0.1 mm path length cell against a blank background at a resolution of 2 $cm^{-1}$ with 50 scans averaged. All IR spectra were smoothed using a 5 point boxcar and baseline corrected. $^1$H and $^{19}$F NMR spectra were collected with a Bruker 300 MHz spectrometer. For FC-72 samples, a melting point capillary was filled with $CDCl_3$ and inserted into the NMR tube so that the fluorous solvent remained unaffected by the locking solvent.

## 3. Results and Discussion

**3.1. Receptor-Based Extractions of TPhP and TPyP into FC-72.** A series of liquid−liquid fluorous biphasic extractions was carried out with 0.1 mM TPhP/$CHCl_3$ in the source phase and from 0.0 to 10.0 mM **1**/FC-72 in the receiving phase. Absorbance spectra of the FC-72 receiving phase resulting from these extractions along with a plot of the absorbance as a function of [**1**] are shown in Figure 2.

A solution of TPhP/$CHCl_3$ is deep red in color, and the Q-band region of the spectrum is the typical four-banded spectrum of the free base. Upon extraction into FC-72, the solution turns bright green (see Figure S6 in Supporting Information) and the spectrum changes to the two-banded form indicative of the dication[44] (Figure 2a). This two-banded spectrum is the only type observed in the FC-72 phase. The absorbance intensity, but not the shape of the spectrum, changes with increasing [**1**]. The two hydrogen bond accepting tetrapyrrole nitrogens of TPhP are the only available binding sites for **1**. Thus, the macrocycle is "pulled" into the fluorous phase through interactions between **1** carboxylic acid groups and the TPhP tetrapyrrole nitrogens. Figure 2b shows that >90% of 0.1 mM TPhP is extracted with an equal volume of 2.0 mM **1**.

A series of liquid−liquid fluorous biphasic extractions was also carried out with 1.0 mM TPyP/$CHCl_3$ in the source phase and from 0.0 to 20.0 mM **1**/FC-72 in the receiving phase. Absorbance spectra of the FC-72 receiving phase resulting from these fluorous biphasic extractions along with a plot of the absorbance as a function of [**1**] are shown in Figure 3.

The extraction of TPyP (Figure 3) is not as straightforward as that of TPhP (Figure 2). A solution of TPyP/$CHCl_3$ is deep red in color, and the Q-band region of the spectrum is the four-banded spectrum of the free base. Upon extraction into FC-72, the solution does not turn bright green typical of the fully protonated tetrapyrrole[44] (P) as we observe for TPhP (see Figures S6 and S9 in Supporting Information). Instead, the spectrum of a solution of **1**−TPyP/FC-72 remains the four-banded type as seen with the free base, although the relative intensities of the *Q* bands have changed. Figure 3b shows that with increasing [**1**], the absorbance of the highest energy *Q* band (516 nm) reaches a maximum around 12 mM **1**. On the other hand, the absorbance of the lowest energy *Q* band continues to increase even though the concentration of TPyP in the receiving phase remains relatively constant beyond solutions of 12.0 mM **1**. As El Bakkari[39] observed in the extraction of TPyP with receptor **2**, it is expected that the receptor−TPyP interaction occurs through the pyridyl nitrogens. However, we have shown in Figure 2 that receptor **1** extracts TPhP by protonating the tetrapyrrole nitrogens whereas **2** showed no interaction with TPhP.[45] Consequently, it is possible that **1** has some interaction with TPyP tetrapyrrole nitrogens. Fleisher[46] reported that the TPyP tetrapyrrole nitrogen atoms are considerably less basic than the pyridyl nitrogens. Thus, we expect the interaction with **1** to be more favorable with the pyridyl over the tetrapyrrole nitrogens on TPyP.

Both TPhP and TPyP can be easily recovered from the fluorous phase using commercially available F-SPE cartridges. Figure 4 shows the absorbance spectra of the **1**-porphyrin complex before it is loaded onto the F-SPE cartridge (black lines) and of an organic eluent containing the porphyrin (gray lines). F-SPE cartridges contain a silica-based perfluoroalkyl bonded phase that retains compounds on the basis of fluorine content. The spectra of the samples following extraction (black lines, Figure 4) match that of the respective **1**−TPhP and **1**−TPyP complexes (compare to Figures 2a and 3a). When this solution was loaded onto the column under vacuum, the **1**−porphyrin complex was retained on the F-SPE column through interactions with **1**. The porphyrin was then eluted with an organic eluent (50:50 $CHCl_3$/ethanol). The Q-band spectra of the eluted porphyrin in the organic eluent correspond to the four-banded spectra of the free base. In other words, the porphyrin is eluted by the organic eluent while **1** is retained

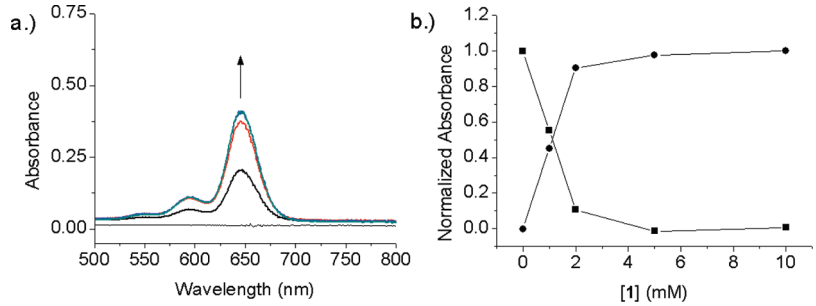



**Figure 2.** Series of fluorous biphasic extractions of 0.1 mM TPhP/$CHCl_3$ with increasing **1**/FC-72 (0.0−10.0 mM) in FC-72 (see Figure 1). (a) Q-band region of the absorbance spectra from the FC-72 receiving phase following extraction. The arrow indicates direction of change with samples containing higher [**1**]. (b) Normalized absorbance of the $CHCl_3$ source phase at 516 nm (squares) and of the FC-72 receiving phase at 645 nm (circles) as a function of [**1**]. **1** is nonabsorbing above 205 nm.

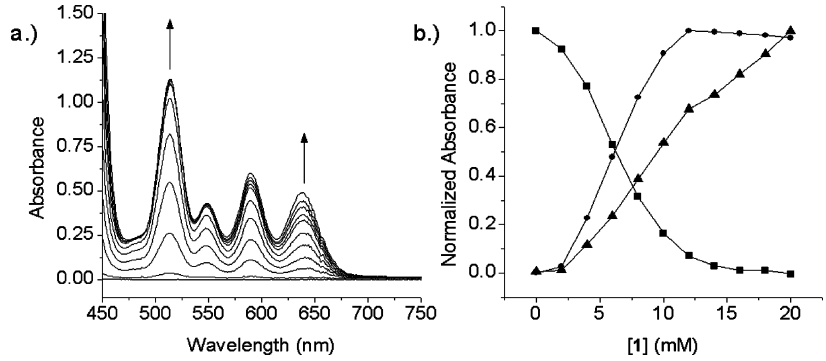



**Figure 3.** Series of fluorous biphasic extractions of 1.0 mM TPyP/$CHCl_3$ with increasing **1**/FC-72 (0.0−20.0 mM). (a) Q-band region of the absorbance spectra from the FC-72 receiving phase following extraction. The arrows indicate direction of change for samples with increasing [**1**]. (b) Normalized absorbance of the $CHCl_3$ source phase at 514 nm (squares) and of the FC-72 receiving phase at 516 nm (circles) and 638 nm (triangles). **1** is nonabsorbing above 205 nm.

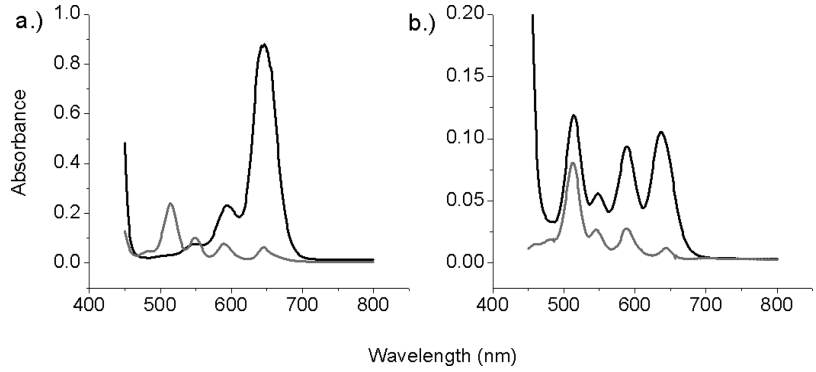



**Figure 4.** Q-band region of the absorbance spectrum of a fluorous phase (black) resulting from the extraction of (a) 1.0 mM TPhP and (b) 1.0 mM TPyP in $CDCl_3$ before loading onto a F-SPE cartridge and of a 50:50 $CHCl_3$/ethanol eluant of the loaded cartridge (gray).

through fluorophilic interactions with the fluorous silica. **1** was then eluted from the cartridge with FC-72.

To investigate further the nature of **1**−TPyP interactions, TPyP was first extracted from $CHCl_3$ with a solution of **1** in FC-72, then separated from the source phase and titrated with additional **1** in FC-72. The resulting spectra are shown in Figure 5. Addition of **1** causes the absorbance of the high energy *Q* band in the TPyP spectrum to decrease while the low energy band increases. This is consistent with protonation of the tetrapyrrole ring.

Absorbance spectroscopy is impractical for studying the nature of the **1**−TPyP pyridyl interactions because protons on the pyridine nitrogens do not interact significantly with the porphyrin tetrapyrrole conjugation pathway.[46,47] Therefore, $^1H$ NMR was employed to verify that **1** transfers a proton to the pyridyl moieties on TPyP in FC-72. The effects of increasing [**1**] on the $^1H$ NMR spectra of a series of **1**−TPyP and **1**−TPhP solutions in FC-72 are shown in Figure 6. Here, an extraction of TPyP was carried out with $CDCl_3$ as the source phase in place of $CHCl_3$, so that the small amount of source phase dissolved in the receiving phase did not interfere with the resulting spectrum.

The signals of the $H_{2,6}$ and $H_{3,5}$ protons (see structures) of the peripheral aromatic rings of TPyP shift downfield with increasing [**1**] while the difference in chemical shifts ($\Delta\delta$) between these two types of protons, as well as the chemical shift of the tetrapyrrole protons, all remain fairly constant. Meanwhile, **1** protons are becoming more shielded as the peaks shift upfield (Figure S3 in Supporting Information). A similar experiment was performed with TPhP as a control because the TPhP phenyl moieties are not proton acceptors. The chemical shifts of the protons associated with the TPhP phenyl groups (Figure 6b) remain constant with the addition of **1**. Therefore, the downfield shift of the pyridyl protons and concurrent upfield

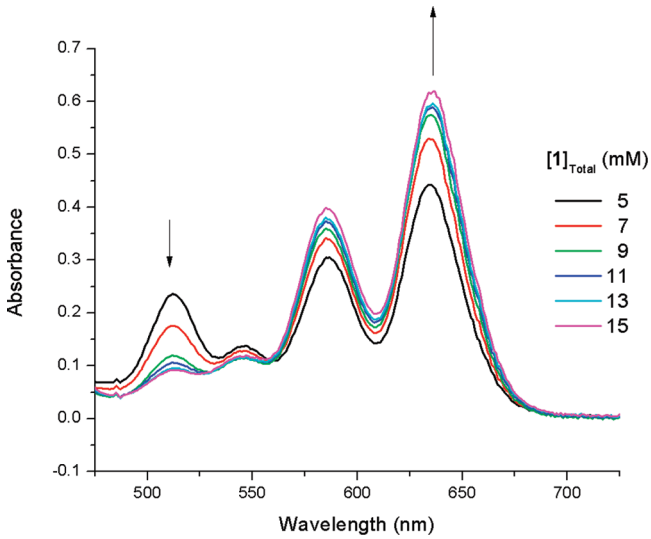



**Figure 5.** Q-band region of the spectra resulting from a constant-volume titration of a **1**−TPyP solution in FC-72 with additional **1**. Each sample contains 0.36 mM TPyP. Spectra are labeled according to total [**1**], and arrows indicate direction of change with increasing [**1**] (nonabsorbing in visible range).

shift of **1** protons can be attributed to the formation of pyridinium ions, as we have previously seen between **1** and pyridine-like bases in fluorous solvents.[38,48]

We draw the conclusion that the interaction between **1** and TPhP is through protonation of the porphyrin ring while the interaction between **1** and TPyP depends on the ratio of **1** to TPyP. At low **1**/TPyP ratios, the interaction is primarily through protonation of the more basic pyridyl moieties while protonation of the porphyrin tetrapyrrole ring occurs only under a greater excess of **1**.

The Q-band spectrum of TPyP is sensitive to whether the tetrapyrrole is neutral (N) or fully protonated (P) (refer to structures) and it is independent of the state of protonation of the pyridine moieties.[46] Despite the presence of charge on the pyridinium moieties, we will use N and P to refer to the molecule as a whole. The molar absorptivity ($\varepsilon$) of P at the wavelength of the high energy *Q* band (513 nm) is equal to zero (eq 1).

$$\varepsilon^{P}_{513} = 0 \tag{1}$$

This allows us to determine the concentrations of N, P, and total TPyP in the fluorous phase ($C_N$, $C_P$, and $C_T$, respectively, where $C_T$ is the sum of $C_N$ and $C_P$) from a spectrum containing both species using only the absorbance ($A$) at 513 and 638 nm (see Supporting Information for derivation).

$$C_N = 1.28A_{513} \tag{2}$$

$$C_P = 0.97A_{638} - 0.097A_{513} \tag{3}$$

$$C_T = 1.28A_{513} + 0.97A_{638} - 0.097A_{513} \tag{4}$$

In addition, $C_T$ can be determined independently from the fluorous-phase spectra through mass balance from the source phase ($C_T = C^i_N - C^f_N$), where $C^i_N$ and $C^f_N$ represent the initial and final concentration of neutral porphyrin in the source phase, respectively. $C_T$ from mass balance agrees quite well with the sum of $C_N$ and $C_P$ in the fluorous phase (see Figure 7).

Protonation of the tetrapyrrole nitrogens follows protonation of the TPyP pyridyl nitrogens with greater excess **1** (Figure 7). Thus, it is no surprise that the $C_P$ increases with increasing [**1**]. It is interesting that not only does **1** extract the nonfluorous macrocycle into the fluorous phase through noncovalent interactions but also the nonpolar fluorous environment can support such a highly charged species (i.e., a total charge of 6+ for the four pyridyl moieties and two tetrapyrrole nitrogens).

We have previously performed a detailed study on the interaction between **1** and pyridine, showing that proton transfer can occur even in extremely nonpolar fluorous environments.[38] A further study on complexation between N-heterocyclic bases and carboxylic acids in a range of solvents showed that proton transfer occurs in fluorous environments when both the acid/base ratio and the difference in p$K_a$ between the acid and conjugate acid of the base ($\Delta$p$K_a$) are sufficiently high.[48] Specifically, we have observed proton transfer with 3:1 **1**/base ratios and $\Delta$p$K_a$ in the range from 4.0 to 6.0, where the p$K_a$ of **1** is approximately 0.26.[48] On the basis of previous observations, protonation of the TPhP tetrapyrrole (p$K_a$ = 4.0[49]) with excess **1** ($\Delta$p$K_a$ = 3.7) is not unexpected. On the other hand, TPyP has a significantly less basic tetrapyrrole (p$K_a$ = 1.8[49]) as a result of the four charged pyridine moieties. It seems surprising that such a highly charged hexacationic macrocycle (P) would exist in the fluorous phase because $\Delta$p$K_a$ = 1.5 deviates significantly from the range in which we have previously observed proton transfer in FC-72. However, TPyP differs from the small bases studied in that the less basic tetrapyrrole ring is surrounded by four contact ion pairs. Although the macromolecule is electronically neutral, the local dipolarity is increased. Thus, the solvation environment perceived by the tetrapyrrole is substantially more polar than a solution of **1**/FC-72, and we observe proton transfer as a result.

**3.2. Metalloporphyrins.** It is well-known that $Cu^{2+}$ can be incorporated into porphyrins with an excess of copper(II) acetate in organic solvents, where the basic acetate anions act to deprotonate the pyrrole rings.[37,50] El Bakkari et al.[37] have demonstrated complete metalation of 5,10,15-tripyridyl-20-phenylporphyrin after 5 h and of 5,15-dipyridyl-10,20-diphenylporphyrin in less than 10 min in perfluorodecalin with **2**. However, **2** did not metalate TPyP even after several hours of stirring. On the basis of kinetics experiments and space-filling models, the authors postulate that steric rather than electronic effects explain the differences in metalation behavior by the bulky **2**.

The absorbance spectra of the fluorous phase resulting from an extraction of TPyP from $CHCl_3$ with the zinc salt of **1** ($Zn\mathbf{1}_2$) in FC-72 are shown in Figure 8. The absorbance spectrum of separately synthesized ZnTPyP in $CHCl_3$ is shown for comparison in the inset of Figure 8. It is clear that TPyP is metalated in the fluorous phase. The absorbance increases with increasing concentration of **1**, but the shape of the spectrum does not change, demonstrating that there is only one form of TPyP in the fluorous phase. The products of the reaction between TPyP and $Zn\mathbf{1}_2$ are ZnTPyP and **1**. The interactions between **1** and the pyridyl groups of ZnTPyP stabilize the complex in the fluorous phase. An extraction of 0.2 mM ZnTPyP in $CHCl_3$ with **1** in FC-72 resulted in similar spectra, owing to the formation of the same product in the fluorous phase, a **1**-ZnTPyP supramolecular complex. In both cases, $^1$H NMR shows disappearance of the pyrrolic N−H proton signal, indicative of metalation. We conclude that the $Zn\mathbf{1}_2$ salt reacts with TPyP, which yields the metalated porphyrin and **1** in the time it takes to shake the solutions. In addition, the metalloporphyrin is recovered when the resulting **1**-ZnTPyP complex is subjected to F-SPE. As discussed above with TPhP and TPyP, the porphyrin is eluted in the organic fluorophobic eluant while **1** elutes with the fluorous solvent.

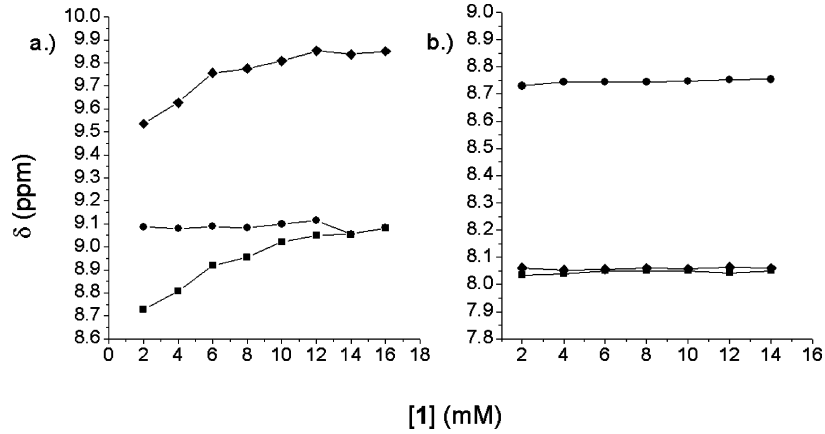



**Figure 6.** $^1$H NMR chemical shifts of peaks due to (a) TPyP pyridyl $H_3$, $H_5$ (square), tetrapyrrole (circle), and pyridyl $H_2$, $H_6$ (diamond) protons and (b) TPhP phenyl $H_3$, $H_5$ (square), tetrapyrrole (circle), and phenyl $H_2$, $H_4$, $H_6$ (diamond) protons as a function of [**1**] in FC-72 resulting from extraction of 1.0 mM porphyrin in $CDCl_3$ with FC-72 containing **1**.

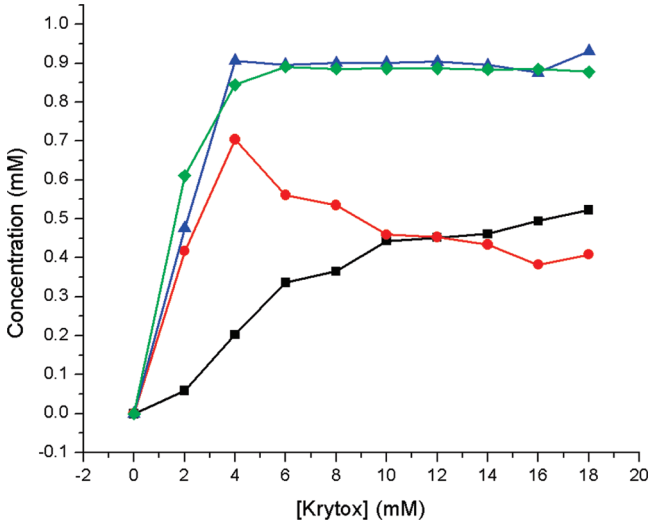



**Figure 7.** Concentrations of P (■) and N (●) forms of TPyP in the receiving phase resulting from an extraction of TPyP from a 1.0 mM TPyP solution in a $CDCl_3$ source phase with a **1**-containing FC-72 receiving phase, shown as a function of [**1**]. $C_T$ in the fluorous phase determined by the sum of $C_N$ and $C_P$ (▲) as well as mass balance from $CDCl_3$ phase measurements (◆) is also shown.

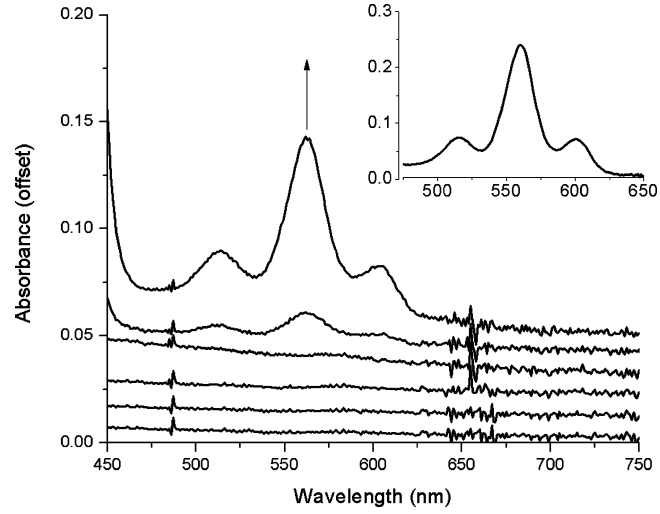



**Figure 8.** UV/vis absorbance *Q* bands from the fluorous phase resulting from an extraction of 0.1 mM TPyP in $CHCl_3$ with $Zn\mathbf{1}_2$ in FC-72. The arrow indicates increasing [$Zn\mathbf{1}_2$] from 0.0−10.0 mM. Inset: absorbance spectrum of ZnTPyP in $CHCl_3$.

Similar extractions with TPhP were carried out to confirm the significance of the **1**−pyridyl interaction in solubilizing the complex. There was no partitioning of 0.1 mM TPhP into the fluorous phase observed with up to 10.0 mM $Zn\mathbf{1}_2$. Correspondingly, there was no detectable partitioning of ZnTPhP from $CHCl_3$ to an FC-72 phase containing up to 20.0 mM **1**. Thus, ZnTPhP showed no interaction with **1.** With $Zn^{2+}$ occupying the TPhP tetrapyrrole ring, the only possible binding site for **1** would be through axial metal−ligand coordination. The lack of interaction confirms that axial coordination of a Lewis acid (ZnTPhP) and carboxylic acid (**1**) is unfavorable. Thus, we conclude that it must be the interaction between **1** and the pyridyl moieties that immobilizes ZnTPyP in FC-72.

**3.3. Competitive Equilibria.** Chloroform was chosen as the source phase for this study because it is relatively unreactive, is miscible with most organic solvents, and is minimally soluble in fluorous solvents at room temperature.[51,52] We found that the solubility of $CHCl_3$ in FC-72 is 0.28 M by $^1$H NMR measurements. Although common knowledge, it is often overlooked that commercial chloroform contains approximately 1% (v/v) ethanol stabilizer to prevent the formation of HCl and phosgene during storage.[40,41] Quantitative $^1$H NMR measurements of the FC-72 phase after being shaken with with $CDCl_3$ containing 1.00% (v/v) ethanol show that the ethanol fluorous/organic distribution coefficient ($D_{c,F/O}$) is 0.09. This doubles to $D_{c,F/O} = 0.18$ with 10.0 mM **1** dissolved in FC-72.

The fractions of TPhP and TPyP extracted from $CHCl_3$ containing ~1% (v/v) ethanol and $CDCl_3$ containing 0.00, 1.00, and 2.00% (v/v) ethanol with **1** in FC-72 are shown in panels a and b of Figure 9, respectively. It is evident that the addition of ethanol significantly hinders the extraction of both TPhP and TPyP into **1**-containing FC-72. For a given [**1**], the fraction extracted from $CHCl_3$ with ~1% (v/v) ethanol and $CDCl_3$ with 1.00% (v/v) ethanol differ. This is because the addition of ethanol to $CHCl_3$ is from the factory and not quantitatively accurate, especially after a particular bottle is opened, whereas the $CDCl_3$ with 1.00% (v/v) ethanol solution was made fresh before the experiment. In addition to reducing the effectiveness of the receptor in the receiving phase, ethanol acts as a hydrogen bond donor in the source phase, therefore reducing the porphyrin chemical potential and the thermodynamic driving force for extraction. Thus, to clarify the role of ethanol in the fluorous phase more completely, we attempted to determine the state of protonation of TPyP in **1**/FC-72 with ethanol.

We have described above a method for determining the absolute concentrations of TPyP in both the protonated (P) and

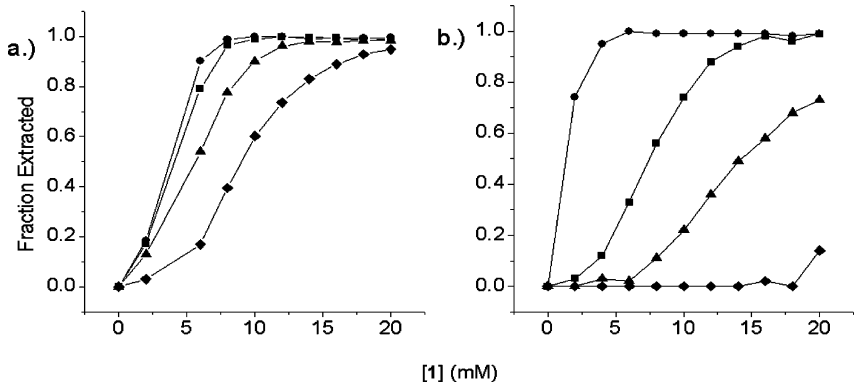



**Figure 9.** Fraction of (a) TPhP and (b) TPyP extracted from a 1.0 mM solution in $CHCl_3$ with ~1% (v/v) ethanol (squares), $CDCl_3$ (circles), $CDCl_3$ with 1.00% (v/v) ethanol (triangles), and $CDCl_3$ with 2.00% (v/v) ethanol (diamonds). Source phase with a **1**-containing FC-72. Receiving phase shown as a function of [**1**].

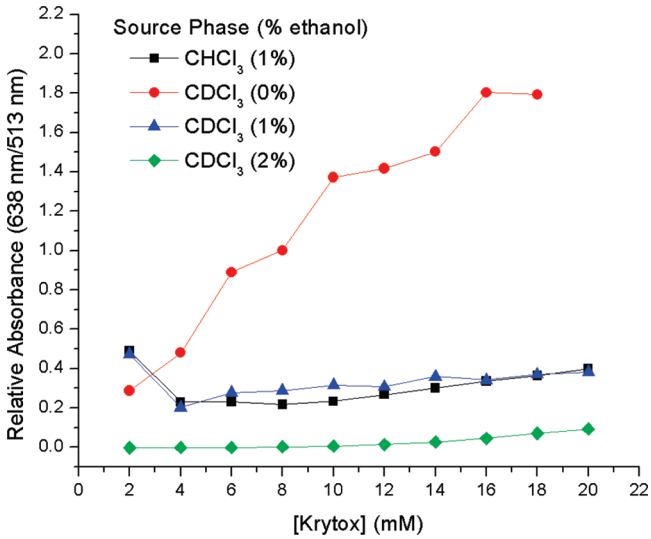



**Figure 10.** Relative total absorbance (638 nm/513 nm) of the receiving phase resulting from an extraction of TPyP from a 1.0 mM TPyP solution in $CHCl_3$ with ~1% (v/v) ethanol (■), $CDCl_3$ (●), $CDCl_3$ with 1.00% (v/v) ethanol (▲), and $CDCl_3$ with 2.00% (v/v) ethanol (◆). Source phase with a **1**-containing FC-72. Receiving phase shown as a function of [**1**].

unprotonated (N) form in the fluorous phase. Recall that all four pyridyl groups are protonated in both species (see Supporting Information). Unfortunately, the presence of ethanol in FC-72 significantly changes the solvent environment and thus the molar absorptivities at both 513 and 638 nm. As a result of the multiple equilibria between ethanol, **1**, and TPyP, the previously described method is no longer applicable. Nonetheless, because the molar absorptivity of N at 638 nm is much smaller than that of P at 638 nm ($\varepsilon^{N}_{638} << \varepsilon^{P}_{638}$), the ratio of the absorbances at 638 and 513 nm ($A_{638}/A_{513}$) is approximately related to the ratio of P to N in the fluorous phase. Figure 10 shows $A_{638}/A_{513}$ in the fluorous phase plotted against [**1**] from extractions of TPyP from $CHCl_3$ containing ~1% ethanol (v/v) and $CDCl_3$ containing 0.00, 1.00, and 2.00% (v/v) ethanol with **1** in FC-72. Although necessarily approximate, Figure 10 demonstrates that ethanol decreases the acidity in the fluorous phase, which inhibits the formation of the hexacation (P). Ethanol, then, modulates the solution environment in **1**/FC-72.

Interestingly, the inhibitory effect of ethanol on the formation of the hexacation is reversible. As ethanol evaporates from FC-72, the absorbance at 597 nm of an FC-72 solution containing 10.0 mM **1** and TPyP that has been extracted from a 1.0 mM solution of $CHCl_3$ with ~1% ethanol (v/v) increases to match that of the same solution extracted from $CDCl_3$ (ethanol free) (see Figure S13 in Supporting Information).

## 4. Conclusion

We have shown that **1** is an effective fluorous receptor for extracting both TPhP and TPyP from $CHCl_3$ into FC-72. While **1** transfers two protons to the tetrapyrrole ring of TPhP to create the porphyrin dication ($H_2TPhP^{2+}$), the interaction between **1** and TPyP occurs through protonation of both the pyridyl and tetrapyrrole nitrogens. It is interesting that a hexacation is formed in the fluorous environment. Protonation of the TPyP tetrapyrrole can be attributed to the surrounding contact ion pairs increasing the polarity of the immediate solvation environment. In other words, the "solvent" perceived by the tetrapyrrole is substantially more polar than a solution of **1**/FC-72. Thus, the overall charge on TPyP can be "tuned" by adjusting the relative concentrations of **1** and TPyP. In addition, the charge on the macromolecular complex can be manipulated by a competitive cosolvent. Less of the fully protonated TPyP (P) is formed in the presence of ethanol in the fluorous phase because ethanol lowers the acidity in **1**/FC-72. Adjusting the relative concentration of ethanol then makes it possible to reversibly solubilize TPyP in the fluorous phase through noncovalent interactions while leaving the tetrapyrrole ring available to interact with metals or other substrates.

We have also observed near-complete extraction of ZnTPyP from $CDCl_3$ with **1** in FC-72 and extraction and metalation of TPyP with Zn**1**$_2$. However, there was no interaction between ZnTPhP and **1** or between Zn**1**$_2$ and TPhP. This is because Zn**1**$_2$ metalates TPyP yielding ZnTPyP and **1**, and the liberated **1** maintains the solubility of the complex in FC-72 through interactions with the TPyP pyridyl groups. Once metalated, ZnTPhP has no binding sites for **1**. This is the first report demonstrating metalation of TPyP in a fluorous environment. This fundamental understanding of the interactions of porphyrins and metalloporphyrins with **1** in the fluorous phase should lead to the development of more robust and selective porphyrin-based sensors and application to other devices.

**Acknowledgment.** This research was funded by the National Science Foundation (NSF) through Grant CHE0615952.

**Supporting Information Available:** Figures S1and S2 show FTIR and $^1$H NMR spectra of **1** and the Zn(II)-**1**$_2$ metal-salt, respectively; Figure S3 shows the $^1$H NMR position of **1**-protons as a function of concentration in FC-72 resulting from an extraction of 1.0 mM TPyP in $CDCl_3$ and **1**/ FC-72 control; the

derivation of a method for determining absolute concentrations of neutral and protonated TPyP in **1**-containing FC-72; Figure S4 plots absorbance at 638 nm vs absorbance at 513 nm ($b$ = 0.1 cm) from the receiving phase of an extraction of TPyP from $CDCl_3$ with **1** in FC-72; Figures S5−S8 show photographs of the extraction of 1.0 mM TPhP in $CHCl_3$ and $CDCl_3$ with 0, 1, and 2% ethanol, respectively, with 0−20 mM Krytox in FC-72; Figures S9−S12 show photographs of the extraction of 1.0 mM TPyP in $CHCl_3$ and $CDCl_3$ with 0, 1, and 2% ethanol, respectively, with 0−20 mM Krytox in FC-72; and Figure S13 shows the absorbance at 597 nm of an FC-72 solution containing 10.0 mM **1** and TPyP that has been extracted from a 1.0 mM solution of $CHCl_3$ containing 1% ethanol. This material is available free of charge via the Internet at http://pubs.acs.org.

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JP902000V