Observation of a Stable Water-Soluble Lithium Porphyrin

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The deprotonated form of the water-soluble porphyrin 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)porphyrin, $H_2OBT(4\text{-}N\text{-}MePy)P^{4+}$, has a strong affinity for lithium and forms a stable lithium complex in basic aqueous solution. The fully deprotonated form, $OBT(4\text{-}N\text{-}MePy)P^{2+}$, is present above pH 10 ($pK_{a3} = 6.5 \pm 0.1$ and $pK_{a4} = 10.2 \pm 0.1$). Lithium ions bind to this porphyrin in aqueous solution in a 1:1 stoichiometry with a binding constant of $(9.6 \pm 0.5) \times 10^2$ M^{-1} (0.1 M KOH, 298 K). The apparent binding constant for Li^+ is reduced in the presence of a large excess of Na^+, and a binding constant for Na^+ of 1.0 ± 0.3 M^{-1} was obtained. The Li^+ porphyrin in D_2O shows a ^7Li NMR signal at −10.25 ppm vs 1.1 M LiCl, and the line widths show exchange occurs at 299 K, in contrast to earlier lithium porphyrins, which exchange more slowly. The lithium-binding behavior and ^7Li NMR spectra for 5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)-porphyrin, $H_xT(4\text{-}N\text{-}MePy)P^{(2+x)+}$ ($x = 0-2$) are also reported.

Introduction

Development of methods for the bromination of the pyrrole β positions of tetraarylporphyrins[2−5] has led to a significant number of papers investigating the behavior of octabrominated porphyrins in nonaqueous media. Some of the most significant discoveries in this area have been the observations that these porphyrins are significantly buckled due to the steric interaction between the porphyrin substituents,[5−8] that the characteristic Soret bands are red-shifted by up to 60 nm,[2−5,9] that the redox potentials are significantly positive with respect to those of the parent porphyrins,[5,9−14] and that the iron derivatives of these porphyrins can act as catalysts for the oxidation of alkenes,[4,15,16] arenes,[17] or alkanes.[15,18] Since electron-withdrawing effects should also affect the Bronsted basicity of the porphyrin and since many redox processes involve transfer of protons, we decided to investigate the effects of octabromination upon the water-soluble, cationic porphyrin tetrakis(*N*-methylpyridinium-4-yl)porphyrin $H_2T(4\text{-}N\text{-}MePy)P^{4+}$. This paper reports our investigations of the porphyrin, 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)porphyrin, $H_2OBT(4\text{-}N\text{-}MePy)P^{4+}$, Figure 1, together with our observations of the first water-stable lithium porphyrin.

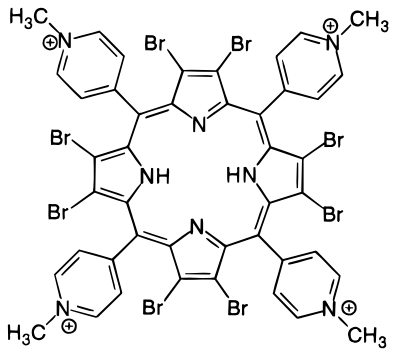

Figure 1. Diagram of $H_2OBT(4\text{-}N\text{-}MePy)P^{4+}$.

The earliest reports of alkali metal complexes of porphyrins were spectrophotometric observations in strongly basic solution.[19−21] Lithium porphyrins have since been used as synthetic intermediates in the synthesis of more stable metalloporphyrins.[22] Recent studies by Arnold[23−25] and Tsuchiya[26] showed that lithium,[23−26] sodium,[24] and potassium[24] porphyrins can be isolated under nonaqueous conditions. Arnold reported that one Li^+ can be bound to all four nitrogens in the porphyrin

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core (polar solvents) or two Li^+ ions can interact with the porphyrin nitrogens (nonpolar solvents) and that the coordinated Li^+ exchanges slowly with free Li^+ at room temperature.[23−25] However, the lithium porphyrins in these studies were demetalated upon the addition of water.

This observation of Li^+ binding to porphyrins in aqueous solution has additional implications. The development of lithium therapies for the treatment of mania and depression[27,28] has led to a need for monitoring lithium ion levels in aqueous solutions in the presence of a large excess of sodium ions.[28−31] This requires that a prospective analytical technique be both sensitive and selective. Plasma lithium levels are typically at the millimolar level,[27] so it is necessary for any potential analytical technique to operate in this concentration range. Most current analyses for Li^+ use ion-selective electrodes,[31] but colorimetric methods have also been reported.[29−31] These colorimetric reagents are all based on crown ethers[32] which have been derivatized with chromophores.[29,33,34] The observation of a water-stable lithium porphyrin is significant because it provides a new class of compounds which can act as colorimetric reagents for the determination of lithium in aqueous solutions.

Experimental Section

Synthesis of 2,3,7,8,12,13,17,18-Octabromo-5,10,15,20-tetrakis-(*N*-methylpyridinium-4-yl)porphyrin, H_2OBT(4-*N*-MePy)P^{4+}. The porphyrin [H_2OBT(4-*N*-MePy)P](PF_6)$_4$ was synthesized via bromination of the copper derivative of 5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)porphyrin tetratoluenesulfonate, [H_2T(4-*N*-MePy)P](4-toluenesulfonate)$_4$ (Hach), using a variant of the procedure reported by Bhyrappa and Krishnan.[5] The copper derivative of H_2T(4-*N*-MePy)P^{4+} was prepared by dissolving [H_2T(4-*N*-MePy)P](4-toluenesulfonate)$_4$ (0.51 g) and $CuCl_2$·$2H_2O$ (0.50 g) in methanol−water (50 mL:5 mL) and warming to 40−50 °C for 1 h. The copper porphyrin was isolated upon reduction of the solution volume to 15 mL and addition of an equal volume of 2-propanol. The precipitate obtained was washed with 2-propanol until the filtrate was colorless; then it was air-dried. This solid, [CuT(4-*N*-MePy)P]X_4 (X = 4-toluenesulfonate and/or chloride), was used without further purification for the synthesis of the brominated derivative.

CuOBT(4-*N*-MePy)P(Br_3)$_x$$Br_{4-x}$ was synthesized by dropwise addition over 30 min of 1 mL (20 mmol) of bromine in 10 mL of dimethylformamide (DMF) to a mixture containing 0.41 g (ca. 0.5 mmol) of [CuT(4-*N*-MePy)P]X_4 (X = 4-toluenesulfonate and/or chloride) in 25 mL of DMF at room temperature.[35] The initial red suspension forms a green solution during the addition of the bromine, but the solution was stirred for an additional 12 h at room temperature to ensure complete reaction. The reaction course was monitored by TLC (silica gel), eluting with a 2:3:5 saturated aqueous KNO_3:water:acetonitrile mixture,[36] with the brominated products moving successively more rapidly on the TLC plate. The reaction was quenched by addition of 25 mL of water to give a green precipitate, which was collected by vacuum filtration. On prolonged standing of the solution prior to filtration, the green solid redissolves, but it can be reprecipitated upon addition of a small volume of bromine. The solid was washed with 3 × 5 mL portions of water followed by a 1:1 ethanol:2-propanol solution. Any unreacted bromine in the filtrate was destroyed by addition of saturated sodium metabisulfate. The green powder (presumably the tribromide salt) was air-dried (0.54 g). Metathesis of this material with NH_4PF_6 led to the PF_6^- salt, and metathesis of the PF_6^- salt with tetrabutylammonium chloride in acetone led to the chloride salt. UV−visible data in H_2O (chloride salt) [λ/nm (log ϵ)]: 457 (4.87), 475 (sh), 596 (4.02), 639 (3.60). This material was used immediately to prepare the metal-free porphyrin.

[H_3OBT(4-*N*-MePy)P](PF_6)$_5$ was prepared by slowly adding 0.35 g of the copper derivative to 15 mL of concentrated sulfuric acid cooled to 10 °C. The initial green color changed to orange-gold. Bromine was liberated when the Br_3^- salt was used for this stage. The solution was stirred at room temperature for 2 h and then poured over ice (160 g). After the ice had melted, excess ammonium hexafluorophosphate (ca. 5 g) was added to precipitate the porphyrin. The solid was collected by filtration and washed twice with 10 mL portions of water, followed by 20 mL of 1:1 diethyl ether−2-propanol. The green solid was dried in vacuo overnight to give 75% yield of crude porphyrin based on the [H_2T(4-*N*-MePy)P](4-toluenesulfonate)$_4$ starting material. Slow evaporation of an acetone−water solution produced lustrous tinsel green crystals (56% yield). The porphyrin so prepared is in its triprotonated form, [H_3OBT(4-*N*-MePy)P](PF_6)$_5$. This salt could be metathesized with tetrabutylammonium chloride in acetone to form the water-soluble Cl^- salt. UV−visible data (Cl^- salt, H_2O solvent) [λ/nm (log ϵ)]: 317 (3.14), 498 (3.78), 671 (2.82), 752 (2.44). ^{1}H NMR (250 MHz, dmso-d_6), δ/ppm: 9.54 (d, 8H, *m*-H), 9.19 (d, 8H, *o*-H), 4.65 (s, 12H, $^+$NCH_3), 1.42 (b, (2+*x*)H, core H). A sample of the PF_6^- salt was recrystallized from 1:1 acetone−water and subjected to elemental analysis. ^{1}H NMR showed that the sample contained acetone of crystallization. The sample analyzed as [H_3OBT(4-*N*-MePy)P](PF_6)$_5$·$2(CH_3)_2CO$. Anal. Calcd for $C_{44}H_{31}N_8Br_8P_5F_{30}$·$2C_3H_6O$: C, 27.91; H, 2.01; N, 5.21; Br, 29.70. Found: C, 28.63; H, 2.09; N, 5.53; Br, 30.10.

Solution Studies. Aqueous solutions of the porphyrin were titrated with concentrated solutions of NaOH, NaCl, or LiCl, keeping the ionic strength at 0.1, 0.2, or 1.0 M with NaOH, KOH, or KCl. All titrations were performed at 25.0 °C with minimal exposure to air. Spectrophotometric measurements were made with a Milton-Roy Spectronic 3000 diode array spectrophotometer. pH measurements were made using an Orion 501 pH meter calibrated with commercial buffers (Fisher). Plots of the absorbance changes with Li^+ concentration were fitted to binding isotherms using the nonlinear least-squares fitting routines in Kaleidagraph 3.0 (Synergy, Reading, PA). Measurements of ^{7}Li NMR spectra were made using a Bruker 270 MHz spectrometer and were referenced to 1.1 M LiCl in D_2O.

Results

The bromination method chosen is based on a synthesis of copper octabromotetraphenylporphyrin reported by Bhyrappa and Krishnan.[5] Preliminary experiments suggested that their recommendation of using a copper porphyrin as the bromination substrate gave higher yields than the free base porphyrin. We have continued to synthesize the octabrominated porphyrin via the copper derivative since demetalation of the copper porphyrin is readily achieved by dissolution in concentrated sulfuric acid. Experiments using solvents such as methanol or dimethyl sulfoxide, or addition of pyridine to the bromination mixture, lead to incomplete bromination. Use of dimethylformamide as solvent leads to rapid and complete octabromination of the porphyrin.[35] Addition of water to the resulting solution leads to the precipitation of a green product which is presumably the tribromide salt. This assignment is strengthened by the observation that if the solution is allowed to stand, the porphyrin redissolves, and it can then be reprecipitated by the addition of a small amount of elemental bromine. This solid was not characterized, but was instead demetalated by dissolution in cold concentrated sulfuric acid. Aqueous hydrochloric acid or neat

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trifluoroacetic acid was not able to remove the copper. The demetalated porphyrin was isolated as the PF_6^- salt upon cautious addition of the acidic solution to ice, followed by the addition of solid NH_4PF_6. This salt was sparingly soluble in water, but it was soluble in acetone, acetonitrile, and dmso. The water-soluble chloride salt of the porphyrin was insoluble in these solvents so that metathetical interchange between PF_6^- and Cl^- salts was readily achieved.

The ^1H NMR spectrum of the nonmetalated porphyrin in dmso-d_6 shows no residual pyrrole β resonances and has a signal at 1.42 ppm which we assign to the core protons. This assignment is based on the position of the resonance and on the fact that it exchanges with D_2O. The position of this peak is unusual, since most porphyrins have their core proton resonances between -2 and -4 ppm, and reflects the electron-deficient nature of this porphyrin. This shift can be regarded either as due to an inductive electron withdrawal or as an effect of a reduced ring current in this porphyrin.

The bromine substituents of 2,3,7,8,12,13,17,18-octabromo-5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)porphyrin, H_2OBT-(4-*N*-MePy)P^{4+}, have a marked effect on its physical and chemical properties. This porphyrin is the most acidic porphyrin reported to date and is fully deprotonated by pH 11. The diprotonated porphyrin is the major species in solution only between pH 2 and 6, in contrast to most other porphyrins, for which this is the dominant species over most of the aqueous pH range. The visible spectrum of this porphyrin shows that five different species are present between strongly acidic conditions and pH 12, Figure 2, corresponding to the porphyrin having zero to four inner protons. These species are related by acid dissociation equilibria

$$H_4\text{OBT(4-}N\text{-MePy)}P^{6+} = H_3\text{OBT(4-}N\text{-MePy)}P^{5+} + H^+ \qquad pK_{a1} < 1$$

$$H_3\text{OBT(4-}N\text{-MePy)}P^{5+} = H_2\text{OBT(4-}N\text{-MePy)}P^{4+} + H^+ \qquad pK_{a2} \approx 2$$

$$H_2\text{OBT(4-}N\text{-MePy)}P^{4+} = \text{HOBT(4-}N\text{-MePy)}P^{3+} + H^+ \qquad pK_{a3} = 6.5 \pm 0.1$$

$$\text{HOBT(4-}N\text{-MePy)}P^{3+} = \text{OBT(4-}N\text{-MePy)}P^{2+} + H^+ \qquad pK_{a4} = 10.2 \pm 0.1$$

where the values for pK_{a3} and pK_{a4} were measured at an ionic strength of 0.1 M. These values can be compared with the acid dissociation equilibria of H_xT(4-*N*-MePy)$P^{(2+x)+}$ for which pK_{a3} $\approx$ 12.9.[37] The increased acidity (or decreased basicity) of this porphyrin is due to the combined electron-withdrawing effect of the bromine substituents[5] and the methylpyridiniumyl substituents.[38]

The two most basic forms of this porphyrin, OBT(4-*N*-MePy)$P^{2+}$and HOBT(4-*N*-MePy)P^{3+}, have distinctive bands at long wavelength, with the band for OBT(4-*N*-MePy)P^{2+} having a λ_{max} >1000 nm in acetone-water solutions.

The fully deprotonated porphyrin has a strong affinity for lithium and forms a lithium complex in basic aqueous solution. This is the first observation of a lithium porphyrin that is stable in aqueous solution. Figure 3a shows the result of titrating a solution of OBT(4-*N*-MePy)P^{2+} in 0.01 M NaOH + 0.09 M NaCl with Li^+. The porphyrin Soret band moves from 579 to 533 nm, a blue shift of 46 nm. This result differs from the behavior for the water-soluble porphyrin H_xT(4-*N*-MePy)$P^{(2+x)+}$ (x = 0 or 1), Figure 3b, where addition of lithium to a basic aqueous solution decreases the apparent value of pK_{a3} but the spectrum of the basic form of the porphyrin remains relatively unperturbed.

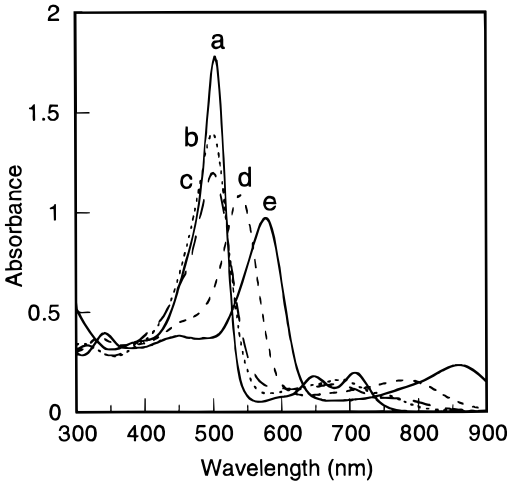

Figure 2. UV−visible spectra of aqueous solutions of H_xOBT(4-*N*-MePy)$P^{(2+x)+}$ (concentration = 1.2×10^{-5} M) in (a) 11 M HCl (x = 4), (b) 1 M HCl (x = 2), (c) pH 4 (x = 2), (d) pH 8 (x = 1), and (e) pH 11 (x = 0).

Aqueous lithium binds in a 1:1 ratio with OBT(4-*N*-MePy)-P^{2+} with a binding constant K_1 of $(9.6 \pm 0.5) \times 10^2$ M^{-1} (0.1 M KOH, 25.0 °C), inset to Figure 3a.

$$\text{OBT(4-}N\text{-MePy)}P^{2+} + Li^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{LiOBT(4-}N\text{-MePy)}P^{3+} \qquad K_1$$

Attempted fits for two Li^+ ions binding were unsatisfactory, and fits with two sequential bindings gave a second binding constant of less than 50, with a large error (80−100%), suggesting that only one Li^+ binds over the range $[Li^+] = 10^{-4}$−10^{-1} M. The calculated binding constants (K_1) are given in Table 1. Addition of Na^+ to the solutions causes a decrease in the effective binding constant for Li^+. Thus, in 0.1 M NaOH the binding constant is reduced to $(8.4 \pm 0.4) \times 10^2$ M^{-1} while in 0.1 M NaOH + 0.1 M NaCl the binding constant is $(5.2 \pm 0.7) \times 10^2$ M^{-1}. Separate analysis for the binding of Na^+ using K^+ salts for the supporting electrolyte gave an upper limit for Na^+ binding of 1.0 ± 0.3 M^{-1} (0.1 M KOH). This suggests that the decrease in Li^+ binding observed in 0.1 M NaOH + 0.1 M NaCl includes an additional term reflecting the change in ionic strength or the increase in $[Cl^-]$, since competitive Na^+ binding is not sufficient to account for the decrease in the lithium binding constant. No evidence for the binding of K^+ was observed in aqueous solution. The effective binding constant for Li^+ binding decreases to $(4.3 \pm 0.3) \times 10^2$ M^{-1} at pH 9.83 (μ = 0.11 M; 0.025 M $NaHCO_3$ + 0.025 M Na_2CO_3) and 65 $\pm$ 4 M^{-1} at pH 9.05 (μ = 0.11 M; 0.1 M NaCl + 0.01 M $Na_2B_4O_7$), in accord with lithium binding only to the fully deprotonated porphyrin.

^{7}Li NMR spectra of solutions containing similar amounts of OBT(4-*N*-MePy)P^{2+} and Li^+ are shown in Figure 4a−c. The resonance at ca. −0.14 ppm is assigned to free Li^+, while the peak at ca. −10.25 ppm is assigned to bound lithium.[23,24] The separate resonances show that exchange between free and bound lithium is slow on the NMR time scale at 279 K. At 299 K the signals are broadened markedly, Table 2, showing that exchange of Li^+ between the two environments is occurring. Analysis

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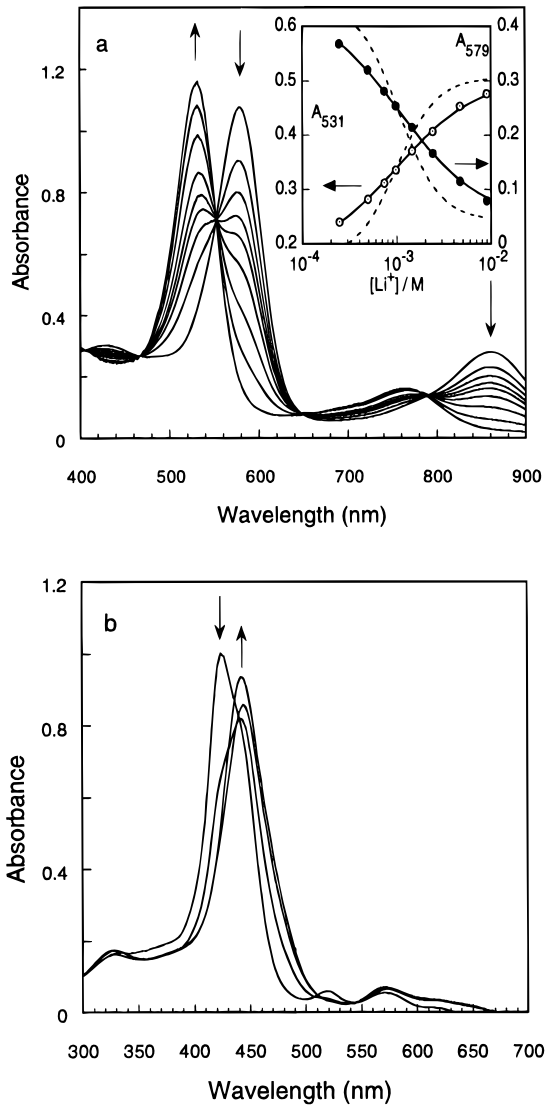

Figure 3. (a) Titration of OBT(4-*N*-MePy)P^{2+} (1.14×10^{-5} M) in 0.01 M NaOH + 0.09 M NaCl with Li^+ at 25 °C. [Li^+] = 0, 0.26, 0.52, 0.77, 1.0, 1.5, 3.0, 6.8, 44 mM. Inset: Binding of Li^+ by OBT-(4-*N*-MePy)P^{2+} in 0.1 M KOH at 25 °C. Solid curves are least-squares fits for a 1:1 (Li^+:porphyrin) binding stoichiometry while broken lines correspond to a 2:1 stoichiometry. (b) Titration of H_xT(4-*N*-MePy)-$P^{(x+2)+}$ ($x = 1-2$; pK_{a3} is ca. 12.9) in 1 mM KOH with Li^+ at 25 °C. [Li^+] = 0, 1.1, 10.6, 95 mM.

Table 1. Calculated Binding Constants for the Interaction of Li^+ with H_xOBT(4-*N*-MePy)$P^{(2+x)+}$ in Aqueous Solution at 25.0 °C

supporting electrolyte	K_1 (Li^+ binding constant)/M^{-1}
0.1 M KOH	$(9.6 \pm 0.5) \times 10^2$
0.1 M NaOH	$(8.4 \pm 0.4) \times 10^2$
0.1 M NaOH + 0.1 M NaCl	$(5.2 \pm 0.7) \times 10^2$
0.025 M $NaHCO_3$ + 0.025 M Na_2CO_3, pH = 9.83	$(4.3 \pm 0.3) \times 10^2$
0.1 M NaCl + 0.01 M $Na_2B_4O_7$, pH = 9.05	65 ± 4
0.1 M KOH	$K_{Na} = (1.0 \pm 0.3)$

of the line broadening, Table 2, gives the estimated relaxation times τ_1 ($=1/k_1$) and τ_{-1} ($=1/k_{-1}$) for incorporation and loss of Li^+, respectively. The temperatures used for the NMR study were limited by the freezing point of D_2O and by the tendency for the OBT(4-*N*-MePy)P^{2+} to decompose at elevated temperatures in highly basic conditions. The tabulated values of τ_1 and τ_{-1} are based on estimates of unperturbed line widths for solutions of Li^+_{aq}, and low-temperature measurements of

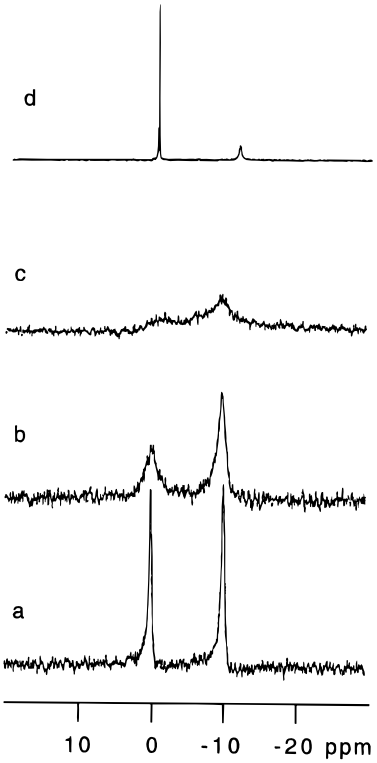

Figure 4. ^{7}Li NMR of 7.0 mM OBT(4-*N*-MePy)P^{2+} + 6.8 mM Li^+ in D_2O at (a) 279 K, (b) 299 K, and (c) 314 K. Spectrum d is the ^{7}Li NMR of 7.6 mM H_xT(4-*N*-MePy)$P^{(2+x)+}$ ($x = 1-2$) + 7.6 mM Li^+ + 11 mM KOH in D_2O at 298 K.

slow-exchanging lithium porphyrins. The data presented in this paper show significantly faster exchange than previous reports of other Li^+−porphyrin interactions, where the signals show insignificant broadening at 298 K.[23−26] However, this result is in accord with observations that the octabrominated porphyrins metalate at an increased rate compared to their nonbrominated analogs, presumably because the bromines cause some distortion of the porphyrin macrocycle.[39−41] The analogous ^{7}Li NMR spectrum for H_xT(4-*N*-MePy)$P^{(2+x)+}$ is shown in Figure 4d, with the bound Li^+ signal at −11.5 ppm, and clearly shows that at pH >12 this porphyrin also binds Li^+ ions. The LiT(4-*N*-MePy)P^{3+} resonance is at higher frequency than the signal for LiOBT(4-*N*-MePy)P^{3+}, in accord with the reduced ring current of the latter porphyrin.[5] The NMR results demonstrate that OBT(4-*N*-MePy)P^{2+} is binding Li^+ even in the presence of the good donor solvent water (Gutmann donor number 18 in dilute solution, 33 in bulk)[42] as opposed to the interaction being ion-pairing between the porphyrin and a solvated lithium ion.

The basic species OBT(4-*N*-MePy)P^{2+} and LiOBT(4-*N*-MePy)P^{3+} are stable for hours at pH 10, but in the presence of excess OH^- there is a slow subsequent reaction ($t_{1/2}$ = 1.5 h at pH 12) that causes the porphyrin to precipitate as a blue-purple solid which is insoluble in all common solvents. However, all measurements reported here were obtained at times much shorter than required for this reaction.

Discussion

The octabrominated porphyrin OBT(4-*N*-MePy)P^{2+} is the most acidic (least basic) porphyrin so far reported in aqueous

(39) This argument assumes that the Li^+ binding involves more than a solvent-separated ion pair or purely Coulombic interaction with no associated porphyrin accommodation. This is in agreement with observations by Arnold and co-workers.[23−25]

(40) Bhyrappa, P.; Nethaji, M.; Krishnan, V. *Chem. Lett.* **1993**, 869−872.
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(42) Gutmann, V. *Coord. Chem. Rev.* **1976**, *18*, 225−255.

Table 2. ^{7}Li NMR Data for the Interaction of Li^+ (6.8 mM Total) with OBT(4-*N*-MePy)P^{2+} (7.0 mM Total) in D_2O

T, K	$\delta(Li^+_{aq})$ ppm[a]	fwhm, Hz[b]	τ_1, ms[c]	δ(LiOBT(4-*N*-MePy)P^{3+}), ppm[a]	fwhm, Hz[b]	τ_{-1}, ms[c]
279	−0.14	46.15	8.0	−10.25	55.9	
299	−0.33	247	1.3	−9.98	145	3.4
314	−1.5	834	0.38	−9.28	400	0.91
298[d]	−0.26[d]	5.73[d]		−11.6[d]	50.0[d]	

[a] Measured at 104.9 MHz, referenced to 1.1 M LiCl in D_2O. [b] Full width at half-maximum height, calculated using the Lorentzian line shape analysis in the NMR processing software Nuts32. [c] $\tau = (\pi(\text{fwhm} - \text{fwhm}_0))^{-1}$ where fwhm_0 is the estimated fwhm in the absence of exchange. $\tau_1 = 1/k_1$ and $\tau_{-1} = 1/k_{-1}$ where k_1 and k_{-1} are the first-order relaxation rates for addition and loss of Li^+, respectively. [d] Data for a solution of 7.6 mM Li^+ + 7.6 mM H_xT(4-*N*-MePy)$P^{(2+x)+}$ in D_2O.

solution. The low pK_a values, the red-shifted spectra, and the unusual position of the core proton ^{1}H NMR resonance all indicate the large perturbation of the porphyrin electronic structure caused by the combination of the octabromination and the presence of the four *N*-methylpyridiniumyl groups. The acidity of this porphyrin means that at pH >10 protons do not compete for the inner nitrogen sites, so that metal ions which usually are considered as weak binders to porphyrins can form stable complexes in aqueous solution. Thus, the porphyrin binds Li^+ reversibly in a 1:1 stoichiometry in the physiological concentration range. Binding only occurs above pH 9, corresponding to reaction with the fully deprotonated porphyrin. The binding of Li^+ causes a visible change in the solution color from blue-purple (pH >10) to red at Li^+ concentrations $>1 \times 10^{-3}$ M. The reaction can be followed at 532, 579, or 862 nm, all regions that are comparatively free of interferences by other porphyrinic materials, since transition metal complexes of this octabrominated porphyrin have Soret bands between 450 and 480 nm,[39] while natural porphyrins have Soret absorbances near 400 nm.[21,43] The binding of Li^+_{aq} to the porphyrin is both strong ($K_1 = 960$ M^{-1}) and selective ($K_{1,Li^+}/K_{1,Na^+} = 960$) and is accompanied by a visible color change, suggesting that this compound could be used as a colorimetric complexant for Li^+ in aqueous solution.

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