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# Peripheral Metal-Ion Binding to Tris(thia–oxo crown) Porphyrazines

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We report the preparation and solution properties of metal-free [**1b(H$_2$)**] and cobalt [**1c(Co)**] porphyrazines (pz's), where three pyrroles are functionalized with a $S_2O_3$ crown ether for metal-ion binding and the fourth pyrrole is appended with two long-chain alcohols (bis((11-hydroxyundecyl)thio)) for potential use as surface anchors. Compounds **1b(H$_2$)** and **1c(Co)** exhibit ion-specific optical changes in the presence of $Ag^+$ and $Hg^{2+}$. Binding of $Ag^+$ to **1b(H$_2$)** is described by a 1:1 binding isotherm, with $K_D \sim 147$ $\mu$M, whereas binding of $Hg^{2+}$ to **1b(H$_2$)** appears more complex. For **1c(Co)**, binding of $Ag^+$ and $Hg^{2+}$ also can be fit to a 1:1 isotherm, with $K_D \sim 109$ and 83 $\mu$M, respectively. All four titrations show nonisosbesticity, including those apparently describable by the 1:1 isotherm, which indicates that there are intermediate stages as multiple ions bind. Neither **1b(H$_2$)** or **1c(Co)** gives optical responses to $Ni^{2+}$, $Zn^{2+}$, $Pb^{2+}$, or $Cu^{2+}$ or to alkali ($Li^+$, $Na^+$, $K^+$, and $Cs^+$) and alkaline earth ($Mg^{2+}$, $Ca^{2+}$, and $Ba^{2+}$) metal ions. Nonetheless, "hard" ions are sensed electrochemically: $Na^+$ and $Li^+$ strongly shift the pz/pz$^-$ couple of **1b(H$_2$)** and $Co^{III}/Co^{II}$ couple of **1c(Co)**. For the addition of 4 equiv of $Li^+$ to **1c(Co)**, the $Co^{III}/Co^{II}$ shifts +40 mV, and for the addition of 4 equiv of $Na^+$ to **1c(Co)**, the shift is +155 mV. The shifted redox waves of **1c(Co)** all retain their reversibility. In contrast, for the addition of either 4 equiv of $Li^+$ or $Na^+$ to **1b(H$_2$)**, the shifts of the pz/pz$^-$ couple are essentially the same, ~170 mV, and the shifted redox waves become broadened and less reversible, due to ion-induced aggregation. For **1c(Co)** the shape of the titration curves [M]/[**1b(H$_2$)**] versus $E_{1/2}$ is concave to the *x*-axis, implying cooperative binding of multiple $M^+$ ions as part of the redox/binding system of equilibria.

## Introduction

Considerable progress has been made in the synthesis of molecules which exhibit optical *or* electrochemical responses to specific analytes,[1−11] but molecules which combine these two modes of detection are less common.[12,13] Heteroatom-functionalized porphyrazines (pz's) have the potential to act in this dual fashion. The peripheral groups of such pz's can be tailored to bind specific classes of ions,[14−17] and the ion binding to the peripheral heteroatoms strongly perturbs the intense, visible-to-near-IR, pz optical transitions.[18−20] For example, thia−oxo crown pz's show distinct optical changes when they bind $Ag^+$ and $Hg^{2+}$ ions,[15,21,22] while aza-crown pz's are well suited to binding first and second row transition

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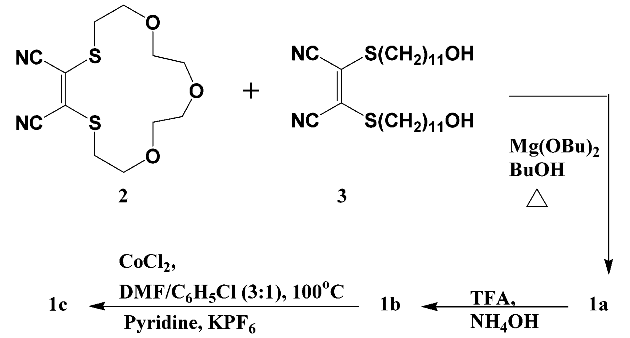
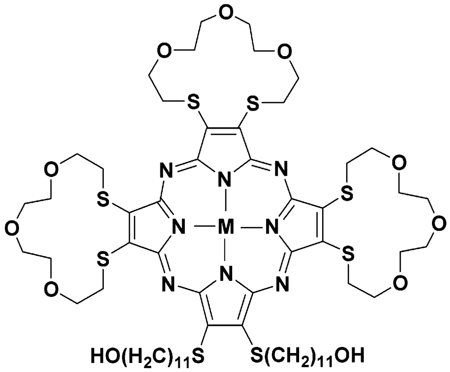
metal ions and Pb$^{2+}$.[16] In addition, heteroatom-functionalized porphyrazines also exhibit rich redox chemistry,[14,23−27] and reduction potentials should shift aniodically when ions bind at the periphery due to electrostatic interactions between the pz redox center and the bound ions,[28−30] as with cation binding to crown ethers attached to ferrocene (Fc)[31−33] and tetrathiafulvalene (TTF).[34,35] Compounds that can sense analytes in a dual mode offer not only the possibility of differential responses within the individual reporting modes but the additional prospect of differentially detecting ions with one mode which are not detectable with the other.

We report here the preparation and solution properties of **1**, whose pz core is encircled by three $S_2O_3$ crown ethers for metal-ion binding,[36] along with two long-chain alkyl hydroxy groups (bis((11-hydroxyundecyl)thio)) for potential use as surface anchors.[37−39] We find that compounds **1b(H$_2$)** and **1c(Co)** exhibit ion-specific optical changes in the presence of Ag$^+$ and Hg$^{2+}$ but give no optical responses to Ni$^{2+}$, Zn$^{2+}$, Pb$^{2+}$ or Cu$^{2+}$ or to alkali (Li$^+$, Na$^+$, K$^+$, and Cs$^+$) and alkaline earth (Mg$^{2+}$, Ca$^{2+}$, and Ba$^{2+}$) metal ions. Nonetheless, "hard" ions are sensed electrochemically: Na$^+$ and Li$^+$ strongly shift the pz/pz$^-$ couple of **1b(H$_2$)** and Co$^{III}$/Co$^{II}$ couple of **1c(Co)**. Numerous studies have shown phthalocyanines,[40−51] porphyrins,[52−57] and also pz's[15−17,21,22,58,59] exhibit potentially useful optical changes upon metal-ion binding; however, to our knowledge, this is the first investigation that examines *both* differential electrochemical and optical perturbations of a pz macrocycle.

**Scheme 1**





**1a. M = Mg**
**1b. M = H$_2$**
**1c. M = Co$^{III}$(Py)$_2$**

## Results and Discussion

**Synthesis.** Porphyrazine **1a** was prepared according to Scheme 1 by a Mg−butoxide templated cross-macrocyclization of 1,2-dicyano-3,15-dithia-6,9,12-trioxacylopentadecane ("$S_2O_3$ crown mnt)[36] (**2**) with 1,2-dicyano-1,2-bis((11-hy-

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droxyundecyl)thio)ethylene (**3**)[60] followed by demetalation with trifluoroacetic acid. We have shown that the mixed cyclization of two different substituted dinitriles to prepare pz's of the form M[pz($\mathbf{A}_n\mathbf{B}_{4-n}$)], where **A** and **B** represent two different types of functionalization, in this case the hydroxyalkane and crown, respectively, can be directed toward a selected product or products in a variety of ways.[24,26,27] Often this requires no more than carefully controlling the stoichiometry. We find that, in most efforts to prepare $n = 3$ porphyrazines where **A** represents the crown, yields are improved by using a stoichiometric excess of the partner dinitrile;[14] however, for the synthesis of **1b(H$_2$)**, a simple stoichiometric ratio of 1 equiv of **3** for 3 equiv of **2** gave optimal yields. This likely is attributable to the fact that the two maleonitriledithiolates are evenly matched cyclization partners. This reaction produced three major products, the desired product **1b(H$_2$)** plus the fully symmetrical isomers, H$_2$[pz(**A$_4$**)] and H$_2$[pz(**B$_4$**)]. The crude mixture was separated into components by column chromatography, with **1b(H$_2$)** being isolated in yields of ~17%. The cobaltic pz **1c(Co)** was prepared by reacting **1b(H$_2$)** with $CoCl_2$ and then with pyridine to exchange the axial ligands.[15,61] The absorption spectra of **1b(H$_2$)** and **1c(Co)** (Figures 1 and 3) are similar to those reported for other sulfur-appended pz's:[15,61] **1b(H$_2$)** has a B (soret) band at 346 nm, a broad, intense n → $\pi$* transition at 504 nm, and a split Q-band at 644 and 712 nm; **1c(Co)** exhibits a B-band at 336 nm, a weaker n → $\pi$* transition at 442 nm, and a single Q-band at 664 nm.

**Spectroscopic Heavy-Metal Ion Titrations.** The sulfur groups of thioether crowns generally coordinate "soft" metals, i.e., low-valent transition metals and group Ib and IIB metals;[62] in particular, $S_2O_3$ crown dinitriles coordinate $Pd^{2+}$, $Ag^+$, and $Hg^{2+}$.[36,63] Both **1b(H$_2$)** and **1c(Co)** exhibit optical changes, indicative of metal-ion binding, when titrated with $Ag^+$ and $Hg^{2+}$ ions. The $Cd^{2+}$ ion also binds strongly but causes precipitation of the pz, precluding further solution studies with this ion. No optical changes are observed when the pz's are titrated with $Pd^{2+}$, $Ni^{2+}$, $Zn^{2+}$, $Pb^{2+}$, and $Cu^{2+}$.

The titration of **1b(H$_2$)** with $Ag^+$ is shown in Figure 1. $Ag^+$ binding causes marked effects on the macrocycle's B- and Q-bands and on the n → $\pi$* transitions (transitions attributed to the nonbonding sulfur electron (n) to the $\pi$* pz orbital).[20] The n → $\pi$* band involves lone pairs on the sulfur atom, and the loss of this transition can be directly attributed to coordination of $Ag^+$ by the sulfur atoms.[20] The peripheral sulfur atoms can coordinate metal ions either in a bidentate S–S coordination mode through two sulfur atoms on the same pyrrole unit or in a tridentate S–N–S coordination mode through binding to sulfur atoms on adjacent pyrroles plus the intervening *meso* nitrogen atom.[61,64] The latter type of coordination strongly blue-shifts the B-band out of the visible region,[61,65] but no such shift is seen for **1b**, Figure 1. Thus, **1b(H$_2$)** does not bind $Ag^+$ in the tridentate mode. Instead, the split Q-band observed for the parent pz coalesces into a single Q-band as the $Ag^+$ ion concentration is increased, as might occur upon irreversible insertion of $Ag^+$ into the central cavity of the pz. However, addition of $NH_4Cl$ to the pz/$Ag^+$ solution immediately precipitates AgCl and regenerates the parent pz spectrum. Together, these results implicate the crown as the site of $Ag^+$ binding.

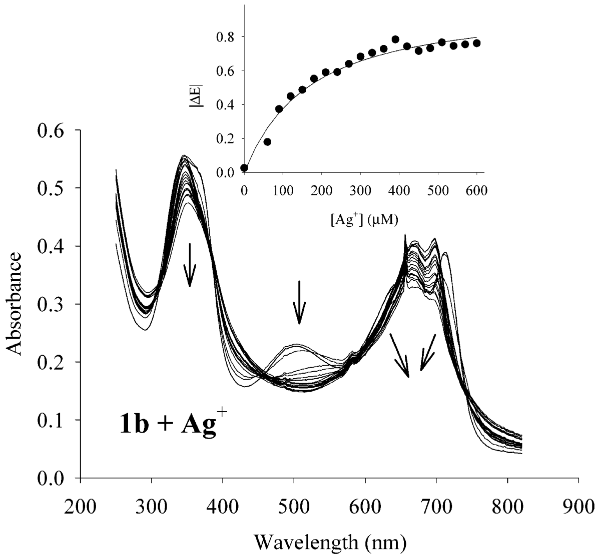

**Figure 1.** UV–visible spectra during titration by $Ag^+$ of **1b(H$_2$)** (30 $\mu$M) in $CH_2Cl_2$/MeOH (70:30). Each spectrum, after that of **1b(H$_2$)** itself, follows the addition of 1 molar equiv of $Ag^+$. Inset: Plot of the change in the absolute value of the change in the sum of the extinction coefficients ($\epsilon/10^3$) at $\lambda = 320$, 360, 500, 620, and 700 nm in response to $Ag^+$ addition, along with a fit to a 1:1 binding isotherm, with resulting dissociation constant, $K_D = 147$ $\mu$M.

Figure 1 shows the spectroscopic changes during $Ag^+$ ion titration, and the inset plots the sums of the extinction coefficient changes at several wavelengths ($\lambda = 320$, 370, 496, 514, 620, 720, and 738 nm) along with a fit to a 1:1 binding isotherm; the fit gives a dissociation constant, $K_D = 147$ $\mu$M. Such a description implies that the $Ag^+$ ions which bind to **1b(H$_2$),** presumably one/crown or three in all, bind independently of one another. However, the overall behavior of the system likely is more complex: although the optical spectra exhibit isosbestic points at 306, 450, and 744 nm during the titration, clearly nonisosbestic behavior occurs around 600 and 650 nm, consistent with sequential metal-ion binding steps.

The titration of **1b(H$_2$)** with $Hg^{2+}$ is shown in Figure 2. The optical changes are qualitatively the same as those observed for the $Ag^+$ titration. As with the $Ag^+$ titration, the absence of a B-band blue shift during the titration precludes tridentate coordination of $Hg^{2+}$ in solution, while the addition of $NH_4Cl$ to the solution immediately regenerates the parent pz spectrum, indicating both that the binding of $Hg^{2+}$ is reversible and that $Hg^{2+}$ is not binding in the central

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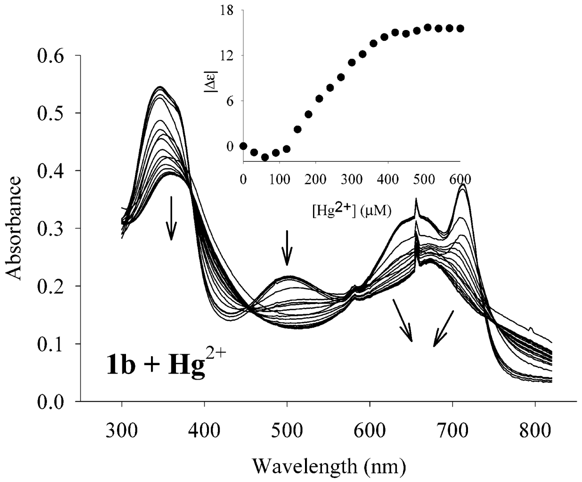

**Figure 2.** UV−visible spectra during titration by $Hg^{2+}$ of **1b(H$_2$)** (30 μM) in $CH_2Cl_2$/MeOH (70:30). Each spectrum, after that of **1b(H$_2$)** itself, follows the addition of 1 molar equiv of $Hg^{2+}$. Inset: Plot of the change in the absolute value of the change in the sum of the extinction coefficients ($\epsilon/10^3$) at $\lambda = 320$, 360, 500, 620, and 700 nm in response to $Hg^{2+}$ addition.

cavity of the pz. However, Figure 2 reveals that the response of **1b(H$_2$)** to $Hg^{2+}$ is quite different from the response to $Ag^+$, with the strongly nonisosbestic behavior in the $Hg^{2+}$ titration indicating that binding of multiple metals proceeds through partially saturated intermediates. Moreover, the spectra show little if any response to $Hg^{2+}$ additions until ∼100 μM (inset of Figure 2). This may indicate that the first $Hg^{2+}$ ion binds to the oxygens of a crown and thus does not influence the optical behavior. Subsequent additions of $Hg^{2+}$ do change the optical spectra, indicative of interactions at sulfur, until the binding saturates at $[Hg^{2+}] \sim 350$ μM. Overall, these data show that $Hg^{2+}$ binds in a complicated fashion but more strongly than $Ag^+$.

Titrations of Co(py)$_2$pz, **1c(Co)**, with either $Ag^+$ or $Hg^{2+}$, cause comparable optical changes, in contrast to the behavior of **1b(H$_2$)**. Figure 3 thus shows only the titration of **1c(Co)** with $Hg^{2+}$. Binding of either ion causes a decrease in the absorbance of the already weak $n \rightarrow \pi^*$ transition but no blue shift of the Soret band. The parent spectrum again is regenerated by addition of $NH_4Cl$, and thus, as for **1b(H$_2$)**, $Ag^+$ and $Hg^{2+}$ bind to **1c(Co)** via reversible coordination to the crowns. The single Q-band of **1c(Co)** changes smoothly upon metal-ion binding but not as much as does the split Q of **1b(H$_2$)**. The observed changes in extinction coefficient also can be fit to a 1:1 binding isotherm (Figure 3, inset); the fit gives dissociation constants, $K_D \sim 109$ μM for $Ag^+$ and $K_D \sim 83$ μM for $Hg^{2+}$, reasonably similar to the dissociation constant for $Ag^+$ binding to **1b(H$_2$).** Again, however, the model of independent metal-ion binding to the crowns is contradicted by nonisosbestic behavior during the titrations.

**Spectroscopic Titrations with Alkali and Alkaline Earth Metal Ions.** Alkali and alkaline earth metals are expected to bind primarily to the oxygen atoms of the crown,[66] which are not coupled to the pz core, rather than to the sulfur atoms, which are. Thus, binding these ions to

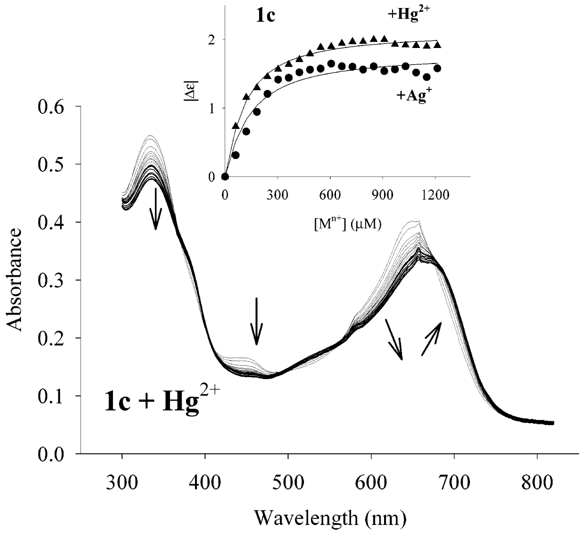

**Figure 3.** UV−visible spectra during titration by $Hg^{2+}$ of **1c(Co)** (61 μM) in $CH_2Cl_2$/MeOH (70:30). Each spectrum, after that of **1c(Co)** itself, follows the addition of 1 molar equiv of $Hg^{2+}$. Inset: Plot of the change in the absolute value of the sum of the extinction coefficients at $\lambda = 622$ and 688 nm, in response to both $Hg^{2+}$ and $Ag^+$ addition, along with the fits to a 1:1 binding isotherm, with resulting dissociation constant, $K_D = 83$ μM for $Hg^{2+}$ and $K_D = 109$ μM for $Ag^+$.

**1b(H$_2$)** and **1c(Co)** would not be expected to result in substantial optical changes. In fact, *none* of the alkali metal ions, $Li^+$, $Na^+$, $K^+$, and $Cs^+$, or alkaline earth ions, $Mg^{2+}$, $Ca^{2+}$, and $Ba^{2+}$, change the optical spectra of **1b(H$_2$)** and **1c(Co)** when added in concentrations of ∼5 mM.

**Electrochemistry.** The porphyrazine ring often can be reduced to the mono- and dianionic states or oxidized to the monocationic state. In addition, pz's with redox-active metal ions typically show an additional metal-based redox couple.[14] The cyclic voltammograms of **1b(H$_2$)** and **1c(Co)** are shown in Figure 4. Compound **1b(H$_2$)** exhibits two sequential one electron ring reductions, pz/pz$^-$ ($E_{1/2} = -1000$ mV) and pz$^-$/pz$^{2-}$ ($E_{1/2} = -1460$ mV), and a single reversible one electron ring oxidation, pz/pz$^+$ ($E_{1/2} = 540$ mV). The cyclic voltammogram of cobaltic pz, **1c(Co)**, shows only two reversible waves within the solvent window, one with $E_{1/2} = -660$ mV and assigned to the $Co^{III}/Co^{II}$ redox couple,[67,68] and with $E_{1/2}$ at −1560 mV due to the pz/pz$^-$ process. All $E_{1/2}$ values were calculated from $(E_{pa} + E_{pc})/2$ at a scan rate of 110 mV s$^{-1}$ with no correction for junction potentials and are referenced versus ferrocene.

To examine the effect of metal-ion binding at the periphery on the cyclic voltammetry of **1b(H$_2$)** and **1c(Co)**, we isolated and monitored the pz/pz$^-$ couple for **1b(H$_2$)** ($E_{1/2} = -1000$ mV) and the $Co^{III}/Co^{II}$ couple for **1c(Co)** ($E_{1/2} = -660$ mV) for study while metal salts were added. With these pz's, one cannot use $Ag^+$ or $Hg^{2+}$, as they are reduced at less negative potentials, so experiments were carried out by adding $Li^+$ or $Na^+$. As can be seen in Figure 4, and more clearly in Figure 5, these waves are electrochemically reversible,

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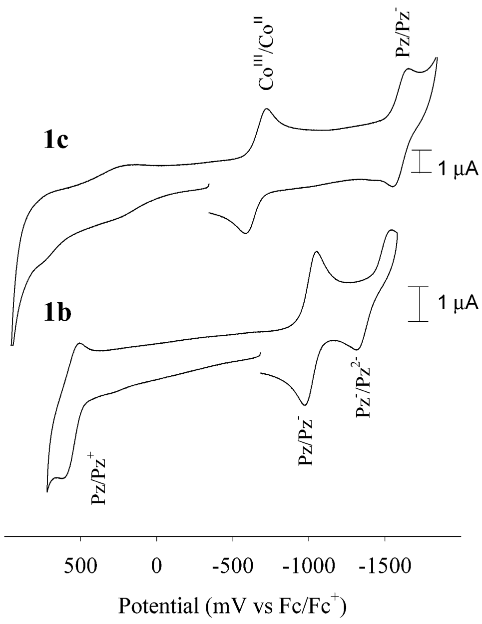

**Figure 4.** Cyclic voltammograms for **1b(H$_2$)** and **1c(Co)** (1.4 mM) in $CH_2Cl_2$ with 0.1 M (TBA)$PF_6$, referenced versus $Fc^+$/Fc. For **1b(H$_2$)** the following couples are noted: pz/pz$^-$ ($E_{1/2} = -1000$ mV); pz$^-$/pz$^{2-}$ ($E_{1/2} = -1460$ mV); pz$^+$/pz ($E_{1/2} = 540$ mV). For **1c(Co)** the couples are pz/pz$^-$ ($E_{1/2} = -1560$ mV) and Co$^{III}$/Co$^{II}$ ($E_{1/2} = -600$ mV).

approaching the expected 59 mV peak to peak separation. The experiments were limited to the addition of ~4 equiv of Li$^+$ or Na$^+$, because, at the concentrations used for the electrochemistry experiments ([pz] ~ 1.4 mM), the pz's precipitate upon further additions, presumably through coordination-induced aggregation.

As a control, H$_2$[pz($n$-pr$_8$)] (**4**) and Co(py)$_2$[pz($n$-pr$_8$)] (**5**), which have no peripheral ion binding sites, such as sulfur atoms, were titrated with up to 4 equiv of Na$^+$ or Li$^+$ and studied by cyclic voltammetry. These two compounds have cyclic voltammograms that are correspondingly similar to those of **1b(H$_2$)** and **1c(Co)**. In particular, **4** has a reversible pz/pz$^-$ wave of $-1370$ mV[25] and **5** has a reversible Co$^{III}$/Co$^{II}$ wave at $-25$ mV. Neither compound exhibited a significant change in cyclic voltammogram, in particular, to the "reporter" couples, during the titrations. This demonstrates that ion pairing of the Na$^+$ or Li$^+$ cations with the reduced pz is not important and that any shifts observed during a titration of **1b(H$_2$)** or **1c(Co)** can be attributed to cation binding to the crowns.

Figure 5 shows the effects on the reporter couples caused by the addition of 4 equiv of Na$^+$ and of Li$^+$ to **1c(Co)** and **1b(H$_2$)**, while Figure 6 plots $E_{1/2}$ for these couples during the titrations up to 4 equiv. The Co$^{III}$/Co$^{II}$ potential of **1c(Co)** shifts by +40 mV after the addition of 4 equiv of Li$^+$, while the addition of 4 equiv of Na$^+$ to **1c(Co)** causes a far greater overall shift, +155 mV. In both cases, the couple remains electrochemically reversible, as these shifts occur without ancillary broadening. The distinct differences between Li$^+$ and Na$^+$ are attributed to differences in the affinities of Li$^+$ and Na$^+$ for the thia−oxo crowns of **1c(Co)**. They are consistent with the behavior of $S_2O_3$ crowns linked to TTF.[34,35] During the progressive addition of the 4 equiv of the two M$^+$ ions to **1c(Co)**, the shifts in potential, which are concave to the [M$^+$] axis (see below), do not approach saturation (Figure 6).

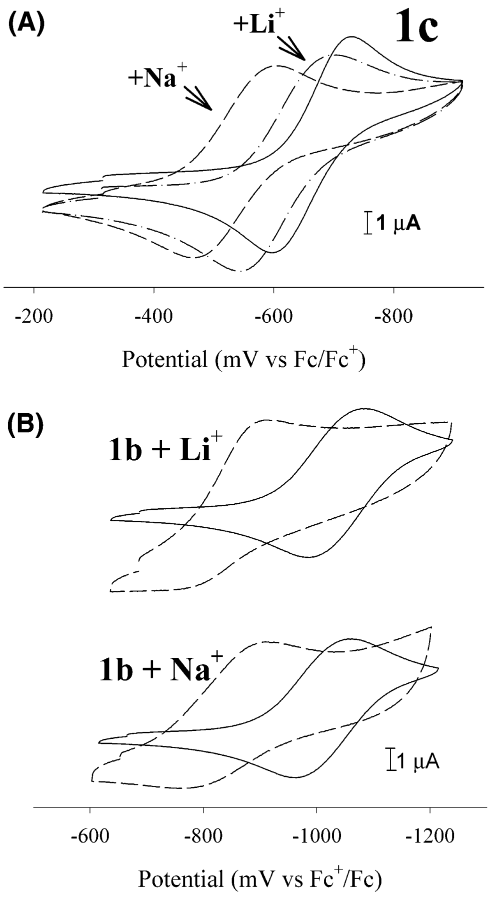

**Figure 5.** (A) Cyclic voltammogram of **1c(Co)** (1.4 mM) in $CH_2Cl_2$ with 0.1 M (TBA)$PF_6$ as the electrolyte and the CV's of **1c(Co)** after the addition of 4 equiv of Na$^+$ and 4 equiv of Li$^+$, shown as the dashed lines. (B) Cyclic voltammogram of **1b(H$_2$)** (1.4 mM) in $CH_2Cl_2$ with 0.1 M (TBA)$PF_6$ as the electrolyte and the CV's of **1b(H$_2$)** after the addition of 4 equiv of Na$^+$ and 4 equiv to **1c(Co),** shown as the dashed lines.

For **1b(H$_2$)**, the shifts of the pz/pz$^-$ couple in response to the addition of 4 equiv of Na$^+$ and Li$^+$ ions both are large, ~170 mV, but in this case they are accompanied by marked broadening of the wave, Figure 5B. Again, the plot of $E_{1/2}$ is concave for low [M$^+$], but after the addition of ~3 equiv of [M$^+$], particularly for Li$^+$, the potential appears to approach a saturation value. We suggest that the broadening and anomalous shape of the plot of $E_{1/2}$ for **1b(H$_2$)** primarily reflects the effects of ion-induced pz aggregation that is occurring as the precursor to the precipitation seen with further additions of salt. Thus, we interpret the similarity in the shifts that accompany the titration of **1b(H$_2$)** with Na$^+$ and Li$^+$ as implying that aggregation processes overshadow the binding differences. The contrasting behavior of the Co$^{III}$/Co$^{II}$ redox wave for **1c(Co),** which remains essentially reversible and does not broaden with the addition of [M$^+$], Figure 5A, likely indicates that the axial pyridine ligands enhance solubility and suppress aggregation. The differential electrochemical response of **1c(Co)** to Na$^+$ and Li$^+$ thus likely reflects an intrinsic difference in the affinity of the two ions for the $S_2O_3$ crown.

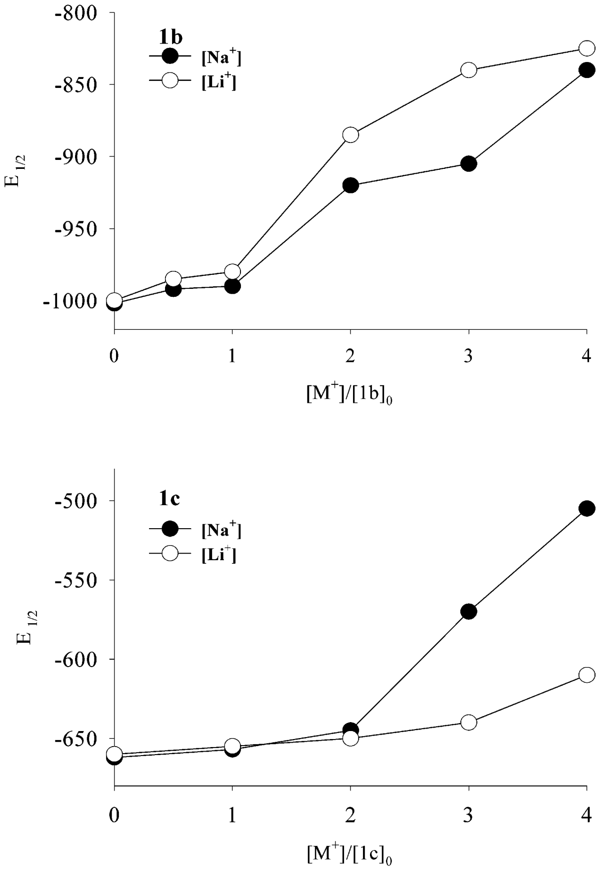

**Figure 6.** Reduction potentials ($E_{1/2}$) of **1b(H$_2$)** and **1c(Co)** during titrations with Na$^+$ and Li$^+$.

Because the Co$^{III}$/Co$^{II}$ redox wave for **1c(Co)** appears to remain essentially reversible during the M$^+$ titrations, it is legitimate to discuss the shape of the titration curves for **1c(Co)**, Figure 6, and to note that this shape implies the occurrence of cooperative binding of multiple M$^+$ ions as part of the redox/binding system of equilibria. To see this, consider ion binding by a pz according to eq 1,

$$P + qM^+ \rightleftharpoons PM^+_q \quad K_{ox}; \quad K_{red}/K_{ox} > 1 \tag{1}$$

$$P^- + qM^+ \rightleftharpoons P{-}M^+_q \quad K_{red}$$

with the association constant, $K$, being greater for binding to the reduced pz than the oxidized one. Here, $q$ is the number of ions that bind in a single step. If only one M$^+$ binds to a pz, or if multiple ions bind independently, then $q = 1$, whereas $q > 1$ implies cooperative binding of multiple ions. As a result of the differential binding to the two pz redox states, $E_{1/2}$ varies with [M$^+$], the free ion concentration, according to the expression[69]

$$E_{1/2} = E_0 + RT/nF\{\ln(1 + K_{red}[M^+]^q)/(1 + K_{ox}[M^+]^q)\} \tag{2}$$

At the beginning of a titration, when [M$^+$] is suitably small, the equation reduces to

$$E_{1/2} \sim E_0 + 0.059K_{red}[M^+]^q \tag{2a}$$

and $E_{1/2}$ should increase linearly with the initial additions of M$^+$ for independent ion binding, $q = 1$ (eq 2a). However in the case of the binding of Li$^+$ and Na$^+$ to **1b(H$_2$)**, the curves in Figure 6 are nonlinear, corresponding to $q > 1$, indicating that multiple ions bind cooperatively. If, instead, two or more ion-bound pz's associate upon reduction of a pz, this would form an alternate type of "cooperative" binding, and one might also expect a curve like those in Figure 6.

## Conclusions

The thia−oxo crown pz's **1** discussed here show the essential features of a *dual* opto-electrochemical sensor, with optical and electrochemical measurements complementing each other. Metal-ion binding to **1b(H$_2$)** and **1c(Co)** elicits extensive absorbance changes in the visible-to-near-IR region. Importantly, these changes are intrinsic to the pz's themselves and will occur when the pz's are surface confined, unlike the optical changes upon metal binding to pc crowns,[40−51] which are dominated by aggregation. Further, of the optical experiments, Figures 1−3, three of the four titration curves are well described by a 1:1 binding isotherm, although all four show nonisosbesticity, which indicates that more than one ion binds and that there are intermediate stages in the process. Such favorable optical changes do not occur for such well-studied electrochemical sensors as crown-derivatized ferrocene[31−33] and tetrathiafulvalene.[34,35]

Pz's **1b(H$_2$)** and **1c(Co)** also show large changes in $E_{1/2}$ upon ion binding to the peripherally fused crowns, even for the central Co$^{III}$/Co$^{II}$ redox couple of **1c(Co)**. The Co$^{III}$/Co$^{II}$ redox couple remains reversible during a titration, although the ring reduction of **1b(H$_2$)** does not. The benefits of a dual approach are illustrated as well: binding of Na$^+$ and Li$^+$ to **1** gives no optical response but is readily detectable electrochemically.

These particular molecules are not themselves actual candidates as dual sensors because the $E_{1/2}$ values of their reporter couples are too low. Thus, the electrochemical examination of Ag$^+$ and Hg$^{2+}$ could not be carried out because the metal ions are reduced before the pz's are. However, variation in the core metal ion and at the periphery will allow us to tailor $E_{1/2}$ as well as ion selectivity.[15−17,21,22,58,59] These molecules are nonetheless an important first step in toward the goal of preparing surface-confined porphyrazine with dual sensing properties.

## Materials and Methods

**Procedures.** All starting materials were purchased from Aldrich Chemical and used as received, with the exception of lithium tetrakis(pentafluorophenyl)borate etherate and sodium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate, which were purchased from Boulder Scientific Co. and used as received. All solvents were used as purchased without additional purification with the exception of the methylene chloride used for electrochemistry, which was HPLC grade, purchased from Burdick and Jackson, and further dried over 4 Å molecular sieves. Chromatography used Baxter silica gel 60 Å (230−400 mesh).

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Electronic absorption spectra were recorded using a Hewlett-Packard HP8452A diode-array spectrophotometer. All measurements were in made a 1 mL quartz cuvette sealed with a septum. During the titration, metal salts were added from a stock solution (typically 6 mM) with a microliter syringe, and after each addition the solution was shaken for 2 min to ensure proper mixing. Corrections for volume were made in all data analysis.

Cyclic voltammetry experiments were done at room temperature under nitrogen in dry, dearated methylene chloride with 0.1 M recrystallized tetrabutylammonium hexafluorophosphate as the supporting electrolyte using a Cypress Systems 2000 electroanalytical system. The experiment used a Pt working electrode, a Ag wire quasi reference electrode, and a Pt mesh auxiliary electrode, with ferrocene as an internal reference ($E_{1/2} = 459$ mV). All $E_{1/2}$ values were calculated from $(E_{pa} + E_{pc})/2$ at a scan rate of 110 mV s$^{-1}$ with no correction for junction potentials. The scan range was 600 mV, and the scan was done starting from the anodic (+) to the cathodic (−) direction.

$^1$H and $^{13}$C NMR spectra were obtained using a Varian Mercury 400 spectrometer. Fast atom bombardment mass spectra (FAB-MS) were recorded at the Mass Spectrometry Laboratory, School of Chemical Sciences, at the University of Illinois using a Micromass ZAB-Se instrument. Atmospheric phase chemical ionization mass spectra (APCI-MS) were recorded locally by Dr. Fenghe Qiu using a Micromass Quattro II RCMS triple quadrupole (APCI-MS) instrument

**General Methods.** 1,2-Dicyano-3,15-dithia-6,9,12-trioxacylopentadecane (**2**)[36] and $H_2$[pz(pr$_8$)], pr = propyl (**4**),[25] were prepared by literature methods, and 1,2-dicyano-1,2-bis((11-hydroxyundecyl)thio)ethylene was prepared by a modification of the literature method **(3)**—we found that using acetone as the solvent instead of propanol improved yields (83% compared to 68%).[60]

**Synthesis of $H_2$[pz($A_3B$)] [A = ($S_2O_2$ crown)$_3$; B = ($CH_2$)$_{11}$)$_2$ (1b($H_2$))].** Magnesium metal (11 mg, 0.40 mmol) and *n*-BuOH (7 mL) were heated to reflux under $N_2$. At reflux, a small chip of iodine was added to facilitate the formation of magnesium butoxide. After 12 h at reflux, 200 mg (0.7 mmol) of 1,2-dicyano-3,15-dithia-6,9,12-trioxacylopentadecane **(2)** and 107 mg (0.22 mmol) of 1,2-dicyano-1,2-bis((11-hydroxyundecyl)thio)ethylene **(3)** were added to the butoxide mixture; the solution turned a dark green color over the course of 6 h. After 24 h the reaction was stopped and the BuOH was removed under reduced pressure; the remaining dark green residue was dissolved in $CH_2Cl_2$ (30 mL) to which $CF_3COOH$ (20 mL) was added. In the dark, the solution was stirred for 15 min and then poured onto crushed ice and neutralized with concentrated $NH_4OH$ resulting in a purple solid which was extracted with $CH_2Cl_2$. The organic layers were combined and dried over $Mg_2SO_4$. Purification by column chromatography (silica gel, $CH_2Cl_2$/MeOH, 93:7) gave **1b($H_2$)** as a purple solid (50 mg, 0.036 mmol, 17%): $^1$H NMR (400 MHZ, $CDCl_3$) $\delta$ 4.21 (m, 12H), 3.93 (m, 12H), 3.58 (m, 4H), 3.57 (m, 4H), 3.56 (m, 4H), 1.89 (m, 4H), 1.61 (m, 4H), 1.32 (m, 28H); $^{13}$C NMR (100 MHZ, $CDCl_3$) $\delta$ 26.09, 29.34, 29.67, 29.74, 29.87, 29.89, 29.92, 30.10, 30.86, 33.12, 35.30, 35.56, 39.58, 61.98, 63.24, 64.64, 66.21, 66.52, 70.83, 70.91, 70.98, 71.12, 71.17, 128.98, 131.09, 139.51, 140.10, 140.19, 151.44, 154.45; UV−vis ($CHCl_3$) [$\lambda_{max}$, nm (log $\epsilon$)] 346 (4.38), 504 (4.00), 644 (4.18), 712 (4.31); MS (FAB-MS) *m/z* 1385.4 (M + H$^+$), calcd for $C_{62}H_{96}N_8S_8O_{11}$ *m/z* 1384.5.

**Synthesis of Co$^{III}$Cl[pz($A_3B$)] [A = ($S_2O_2$ crown)$_3$; B = ($CH_2$)$_{11}$)$_2$ (1c(Co))].** Macrocycle **1b($H_2$)** (0.025 g, 0.018 mmol) and $CoCl_2$ (0.024 g, 0.18 mmol) were dissolved in DMF/chlorobenzene (75:25) and heated to 100 °C for 8 h under nitrogen. The solvent was removed, and the pz was chromatographed on silica gel using $CH_2Cl_2$/MeOH (95:5) as the eluant. The major bright green band was collected (0.024 g, 92% yield): UV−vis ($CH_2Cl_2$) [$\lambda_{max}$, nm (log $\epsilon$)] 336 (3.96), 442 (3.56), 664 (3.92); FAB-MS *m/z* 1442.6 (M + H$^+$), calcd for $C_{62}H_{94}N_8S_8O$, **1c(Co),** *m/z* 1441.4.

**Optical Titrations.** For the optical and electrochemical titrations with **1c(Co)**, 20 equiv of pyridine was added to a solution of **1c(Co)** to exchange the axial ligand. A 1 equiv amount of $KPF_6$ was then added, and the solution was filtered to remove the KCl precipitate.

**1b($H_2$) + Ag$^+$ or Hg$^{2+}$.** A 30 $\mu$M solution of **1b($H_2$)** in $CH_2Cl_2$/MeOH (70:30) was prepared, and its absorbance spectra was recorded in a 1 mL quartz cuvette fitted with a septa. During the titration molar equivalents of Ag$^+$ or Hg$^{2+}$ from a 3 mM stock solution were added and their absorbance spectra reported. To fit the binding of Ag$^+$ to a 1:1 isotherm, the sums of the extinction coefficients at $\lambda = 320$, 370, 496, 514, 620, 720, and 738 nm were used. To plot the change in extinction coefficient as a response to Hg$^{2+}$ binding, the sums of the extinction coefficients at $\lambda = 320$, 360, 500, 620, and 700 nm were used.

**1c(Co) + Ag$^+$ or Hg$^{2+}$.** A 61 $\mu$M solution of **1c(Co)** in $CH_2Cl_2$/MeOH (70:30) was prepared, and its absorbance spectra was recorded in a 1 mL quartz cuvette fitted with a septa. During the titration molar equivalents of Ag$^+$ or Hg$^{2+}$ from a 6 mM stock solution were added and their absorbance spectra reported. To fit the binding to a 1:1 isotherm, the sums of the extinction coefficients at $\lambda = 622$ and 688 nm were used.

**Electrochemical Titrations: 1b($H_2$) + Na$^+$ or Li$^+$.** A 1.4 mM solution of **1b($H_2$)** in $CH_2Cl_2$ was prepared and the cyclic voltammogram was recorded for a scan over a potential range of 600 mV (−600 to −1200 mV vs Fc$^+$/Fc). During the titration molar equivalents of Na$^+$ or Li$^+$ from a stock solution (0.14 M) were added and their cyclic voltammograms recorded. Ferrocene was added as an internal reference after the final scan.

**1c(Co) + Na$^+$ or Li$^+$.** A 1.4 mM solution of **1c(Co)** in $CH_2Cl_2$ was prepared, and the cyclic voltammogram was recorded for a scan over a potential range of 600 mV (−200 to − 800 mV vs Fc$^+$/Fc). During the titration molar equivalents of Na$^+$ or Li$^+$ from a stock solution (0.14 M) were added and their cyclic voltammograms recorded. Ferrocene was added as an internal reference after the final scan.

**Synthesis of Co$^{III}$Cl[pz(pr$_8$)] (pr = Propyl) (5).** Macrocycle **4** (0.100 g, 0.152 mmol) and $CoCl_2$ (0.201 g, 1.53 mmol) were dissolved in DMF/chlorobenzene (75:25) and heated to 100 °C for 8 h under nitrogen. The solvent was removed, and the pz was chromatographed on silica gel using $CH_2Cl_2$/MeOH (95:5) as the eluant. The major bright green band was collected (0.096 g, 68% yield): UV−vis ($CH_2Cl_2$) ($\lambda_{max}$, nm) 338, 446, 648; APCI-MS *m/z* 708.5 (M + H$^+$), calcd for $C_{40}H_{56}N_8Co$ *m/z* 707.4.

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