Coordinatively Unsaturated Metallates of Cobalt(II), Nickel(II), and Zinc(II) Gated by a Rigid and Narrow Void

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Abstract: Both natural enzymatic systems and synthetic porous material catalysts utilize well-defined and uniform channels to dictate reaction selectivities on the basis of size or shape. Mimicry of this design element in homogeneous systems is generally difficult owing to the flexibility inherent to most small molecular species. Herein, we report the synthesis of a tripodal ligand scaffold which orients a narrow and rigid cavity atop accessible metal coordination space. The permanent void is formed through a macrocyclization reaction whereby the 3,5-dihydroxyphenyl arms are covalently linked through methylene bridges. Deprotonative metallation leads to anionic and coordinatively unsaturated complexes of divalent cobalt, nickel, and zinc. An analogous series of trigonal monopyramidal complexes bearing a non-macrocyclized variant of the tripodal ligand are also reported. Physical characterization of the coordination complexes has been carried out using multiple spectroscopic techniques (NMR, EPR, UV-Vis), cyclic voltammetry, and X-ray diffraction. Complexes of the macrocyclized \([L_{\text{OCH}_2\text{O}}]^3–\) ligand retain a rigid cavity upon metallation, with this cavity gating entrance to the open axial coordination site. Through a combination of spectroscopic and computational studies, it is shown that acetonitrile entry into the void is sterically precluded, disrupting anticipated coordination at the intracavity site.
Introduction

Synthetic inorganic chemistry has witnessed an increasing focus on the secondary coordination sphere as a means to control reaction outcomes at ligated metal centers.\(^1\)–\(^5\) Specific efforts are often guided by the finely-tuned microenvironments designed by nature to govern substrate binding and product formation at metallocofactors.\(^3\),\(^6\) Indeed, carefully tailored ligands incorporating H-bond donors/acceptors,\(^7\)–\(^15\) Lewis acids,\(^16\)–\(^21\) or electrostatic charges\(^22\)–\(^25\) are now often used to stabilize transition states or products as a means to alter reaction outcomes of metal complexes with small molecules.

In order to regulate the arrival of exogenous species and control substrate conformation, nature frequently buries metalloenzymes within protein structure with access for exogenous substrates accessible only through well-defined channels. Mimicry of this property in synthetic complexes can be approached by housing metal-binding chelators within channels defined by macrocyclic motifs.\(^26\)–\(^29\) Provided the channel serves as the sole point of ingress for substrates, metal-based reactivity becomes dependent upon the kinetic feasibility of passage through the channel. Similar considerations guard reactivity within crystalline porous materials, as substrates must diffuse into a crystallite to access non-surface active sites.\(^30\),\(^31\) Industrial heterogeneous catalysis often exploits this approach on enormous scales to realize selectivities on the basis of size/shape.\(^32\) In principle, such a design strategy likewise could effect interesting selectivities in synthetic homogeneous catalytic schemes, although realization has often proven elusive using known systems.\(^33\)

Pioneering work from Breslow demonstrated that cyclodextrins appended with chelating motifs could localize a hydrophobic channel adjacent to a metal center.\(^26\),\(^34\) Subsequent approaches in ligand design have expanded the diversity of macrocyclic systems – most
frequently employing calixarenes and resorcinarenes – and have focused on spatially controlling the macrocycle’s orientation with respect to the metal center (Figure 1a).35–41 Macrocycles bearing judiciously designed chelating groups can result in the macrocycle interior serving as the sole access point to the enshrouded metal center (Figure 1b). However, synthetic routes to these systems can be laborious, as the macrocycle must be synthesized, chemically modified, and then covalently linked to the metal binding motif. As an alternative approach, the groups of Lu42 and Schrock43 have demonstrated macrocyclization reactions upon tris(2-aminoethyl)amine (TREN) based scaffolds to orient either a 45-membered ring or an arene-capped organic cavity above the metal binding pocket (Figure 1c). These procedures obviate the separate synthesis of macrocyclic species that is subsequently decorated with chelating motifs, and theoretically could enable construction of a library of proligands with varying cavity dimensions. However, no follow up reports have appeared for either system, perhaps signalling synthetic difficulties unique to those particular scaffolds.

We have endeavored to develop a short and modular synthetic route to a ligand that orients a narrow and rigid channel above accessible metal coordination space. Starting with a TREN-derived tris-amide platform bearing 3,5-dihydroxyphenyl arms, we demonstrate the construction of a rigid and narrow macrocycle-defined channel that is oriented directly atop the metal-binding pocket. This simple three-step procedure employs macrocyclization as the final step and evokes the rigidification of resorcinarenes to form cavitands through linking adjacent phenol groups via a methylene bridge.44,45 Deprotonation and metallation with cobalt(II), nickel(II), and zinc(II) sources leads to anionic four-coordinate complexes containing an open coordination site that is housed inside the rigid cavity. A control series of complexes bearing a ligand variant that lacks a rigid cavity is also presented for comparison. It is shown that the
narrow channel profile in the macrocyclized ligand precludes acetonitrile binding to the open site in the cobalt(II) congener, while nitrile coordination readily occurs in the non-macrocyclized cobalt(II) complex. Computational investigations indicate that intracavity acetonitrile binding is precluded by the narrow dimensions of the void.

**Figure 1.** Examples of synthetic cavity-bearing ligand systems.

**Results and Discussion**

A tripodal tris-amide bearing 3,5-dihydroxyphenyl arms was targeted as a precursor to a macrocyclized proligand (Figure 2a). Benzyl protection of the phenolic groups in 3,5-dihydroxybenzoic acid allowed for smooth amide bond formation with TREN using 1,1’-carbonyldiimidazole (CDI) as a coupling mediator. Deprotection of \( \mathbf{H_3L^{Obn}} \) with 1,4-cyclohexadiene (1,4-CHD) and catalytic Pd/C resulted in formation of desired \( \mathbf{H_3L^{OH}} \) as a
hygroscopic colorless solid. Taking inspiration from the rigidification of resorcinarenes to form cavitands,\textsuperscript{44,45} it was endeavored to covalently tether adjacent aromatic rings to one another through methylene bridges. A variety of dihalomethane reagents (CH\textsubscript{2}BrCl; CH\textsubscript{2}Br\textsubscript{2}; CH\textsubscript{2}BrI; CH\textsubscript{2}I\textsubscript{2}) were found capable of producing the desired macrocyclized species H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} upon heating with H\textsubscript{3}L\textsuperscript{OH} in the presence of a Bronsted base as assayed by \textsuperscript{1}H NMR spectroscopy and electrospray ionization-mass spectrometry (Figure 2).

It should be noted that macrocyclization must compete with oligomerization processes which link multiple tris-amide species together through a methylene unit.\textsuperscript{47} Optimization of the macrocyclization conditions was pursued by varying parameters such as dihalomethane source and rate of addition, base, temperature, and dilution. These studies revealed that a slow addition of CH\textsubscript{2}BrI to H\textsubscript{3}L\textsuperscript{OH} (12 mM) and K\textsubscript{2}CO\textsubscript{3} in N,N-dimethylformamide (DMF) at room temperature, with subsequent heating to 60 °C, produces H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} in satisfactory yields (Figure 2). By removing aliquots of known volume from reaction mixtures and analyzing them by \textsuperscript{1}H NMR with an internal standard, it was determined that H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} was produced in approximately 10% yields. Isolation of macrocyclized H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} from these combined crude products is accomplished via Soxhlet extraction with CHCl\textsubscript{3}. Serial triturations of the obtained extractant with water, methanol, and hexane yields spectroscopically pure H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} as a colorless solid.
Figure 2. Synthesis (a) and two views of the solid-state structure (b) of $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$.

Single crystals of $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$ were obtained from a dilute methanol solution. Solid-state structure determination by X-ray diffraction confirms the formation of an 18-membered ring that defines the crest of a narrow cavity, which is bounded by the faces of three aromatic rings (Figure 2b). The methylene bridges give rise to a pair of doublets in the $^1\text{H}$ NMR spectrum that correspond diastereotopic H-atoms bearing an endo or exo relationship to the cavity (Figure S1.5). Although the solid-state structure depicts two distinct methylene orientations (two point upward atop the crest while the third is rotated downward), these bridges hinge rapidly and display equivalence by $^1\text{H}$ NMR spectroscopy at temperatures as low as -80 °C (Figure S1.15). The covalent linkages defining the macrocycle endow $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$ with excellent thermal stability, as heating to 100 °C in dry DMSO-$d_6$ for 1 week leaves $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$ unchanged. Notably,
exposure of $H_3L^{\text{OCH}_2\text{O}}$ to wet DMSO-$d_6$ at this temperature results in substantial decomposition over the course of several days (Figure S1.16), potentially owing to hydrolysis of the acetal linkages.

Despite the conformationally constrained nature of $H_3L^{\text{OCH}_2\text{O}}$, metallation to form monometallic complexes can be carried out following deprotonation of the amide N-H bonds. Treatment with KH in $N,N$-dimethylacetamide (DMA) followed by addition of $\text{M(OAc)}_2$ (M = Co, Ni, Zn) yields the four-coordinate complexes $[\text{ML}^{\text{OCH}_2\text{O}}^-]$ (Figure 3). Crystallographic characterization of these metallates as their $[\text{K(18-crown-6)}]^+$ salts revealed conservation of a tight void space bounded by the faces of the tethered aromatic rings. This void encapsulates the open axial coordination site, with the metal center buried beneath the rim of the cavity by approximately 6 Å. All three complexes crystallize as infinite one-dimensional chains, with $[\text{K(18-crown-6)}]^+$ cations each bridging two metallate species through contacts with amide or acetal O atoms (Figures S5.9-11). Both $[\text{CoL}^{\text{OCH}_2\text{O}}^-]$ and $[\text{ZnL}^{\text{OCH}_2\text{O}}^-]$ adopt nearly idealized trigonal monopyramidal geometries; all equitorial N-M-N bond angles fall between 117-121° while the complexes’ $\tau_4$ parameters$^{48}$ lie squarely in the range expected for trigonal monopyramidal geometries (Co = 0.86; Zn = 0.84). The nickel(II) congener $[\text{K(18-crown-6)}][\text{NiL}^{\text{OCH}_2\text{O}}]$ contains two formula units in the asymmetric unit (Figure S5.13). The primary coordination spheres of both crystallographically independent nickel complexes show a distortion from trigonal symmetry, with each complex bearing one large equitorial N-Ni-N angle (130.09(12)° and 141.78(7)°$^{49}$ and $\tau_4$ values describing geometries intermediate between trigonal monopyramidal and sawhorse ($\tau_4 = 0.80$ and 0.72, respectively). While a high-spin $d^8$ complex in a (pseudo) trigonal monopyramidal geometry is susceptible to Jahn-Teller distortion,$^{50}$ the magnitude of distortion seen for the $[\text{NiL}^{\text{OCH}_2\text{O}}^-]$ unit with $\tau_4 = 0.72$ is
surprising. Of the previously reported four-coordinate nickel(II) complexes bearing TREN-derived ligands, the largest equatorial N-Ni-N angle occurs within Cummins’ and Nocera’s Ni$_2$ metallocryptand (133.83(17)$^\circ$). Accordingly, while the large N-Ni-N angle of 141.78(7)$^\circ$ observed here is likely not representative of the average geometry present in solution, it does provide a snapshot of equatorial distortions that are conformationally accessible in complexes of the [L$^{\text{OC}2\text{H}}$]$^{3-}$ ligand.

Figure 3. (a) Synthesis of the metallates K[ML$^{\text{OC}2\text{H}}$] (M = Co, Ni, Zn). (b) Solid-state structure of [CoL$^{\text{OC}2\text{H}}$]$^\text{-}$ as viewed along the equatorial coordination plane. (c) Solid-state structures of [CoL$^{\text{OC}2\text{H}}$]$^\text{-}$ (left), [NiL$^{\text{OC}2\text{H}}$]$^\text{-}$ (center), and [ZnL$^{\text{OC}2\text{H}}$]$^\text{-}$ (right) as viewed through the macrocycle-defined cavity. For all solid-state structures, [K(18-crown-6)]$^+$ cation and co-crystallized solvent molecules are omitted for clarity.
Figure 4. Synthesis of K[ML\text{OME}] (top) and solid-state structure of [CoL\text{OME}]^{-} (bottom). The [K(18-crown-6)]\textsuperscript{+} cation and co-crystallized solvent molecules omitted for clarity. The nickel and zinc congeners pack in an isomorphous fashion.

To facilitate analysis of the structural effects of arene ring tethering on the resultant complexes, metallation of the 3,5-dimethoxy substituted tris-amide\textsuperscript{55} H\textsubscript{3}L\text{OME} was carried out in a similar fashion as for H\textsubscript{3}L\text{OCH}_2\text{O}. The corresponding four-coordinate cobalt(II), nickel(II), and zinc(II) metallates were crystallographically characterized as their [K(18-crown-6)]\textsuperscript{+} salts and adopt isomorphous structures (Figures 4 and S5.6-7). Infinite one-dimensional chains arise through contacts of each [K(18-crown-6)]\textsuperscript{+} cation with amide O atoms on two adjacent [ML\text{OME}]\textsuperscript{-} units (Figure S5.12). As for the complexes of [L\text{OCH}_2\text{O}]\textsuperscript{3-}, [CoL\text{OME}]^{-} (\tau_4 = 0.85) and [ZnL\text{OME}]^{-} (\tau_4 = 0.84) exhibit nearly idealized trigonal monopyramidal geometries, while [NiL\text{OME}]^{-} distorts toward a sawhorse conformation (\tau_4 = 0.78, largest N-Ni-N angle =
127.81(5)°. In each structure, the edge of one arene ring points inward toward the metal site and sits between the other two rings, which orient their faces inward (Figure 4, bottom right). However, the $^1$H NMR spectra of all three $[ML^{OMe}]^-$ congeners are consistent with a $C_{3v}$ symmetric structure in solution, indicating conformational fluxionality on the NMR timescale (Figures S1.11-14). Accordingly, while both ligands capably promote a trigonal coordination environment about the metal and the presence of an open axial coordination site, macrocyclized $[L^{OCH_2O}]^3-$ alone enforces a rigid, unoccupied channel that leads into the primary coordination sphere.

As is common for TREN-derived LX$_3$-type ligands,$^{56,57}$ both $[L^{OCH_2O}]^3-$ and $[L^{OMe}]^3-$ promote high-spin electronic configurations, with Evans method measurements yielding values consistent with $S = 3/2$ and $S = 1$ configurations for the Co and Ni complexes, respectively (Table 1). Cyclic voltammograms of $[CoL^{OCH_2O}]^-$ and $[NiL^{OCH_2O}]^-$ reveal electrochemically irreversible waves that we attribute to formal Co$^{3+/2+}$ and Ni$^{3+/2+}$ redox events (Figures 5a-b and S4.1-2). The EPR spectrum of $[CoL^{OCH_2O}]^-$ in frozen CH$_2$Cl$_2$ solution (10 K) displays axial symmetry, with $g$ values of 4.49 and 2.01 (Figure 5c). An eight line pattern due to hyperfine coupling with $^{59}$Co ($I = 7/2$, 100% abundance) is evident for the latter feature. The axial nature of this spectrum indicates that $[CoL^{OCH_2O}]^-$ in solution maintains the trigonally symmetric coordination geometry seen in the solid state by X-ray diffraction. These EPR spectral parameters are consistent with those seen for other trigonal monopyramidal cobalt complexes with $S = 3/2$ ground states,$^{11-13,51,55}$ and additionally are nearly identical to those for $[CoL^{OMe}]^-$ (Table 1 and Figure 5c).
Table 1. Solution state magnetic moments and selected EPR fitting parameters.

<table>
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<tr>
<th>Compound</th>
<th>Effective Magnetic Moment$^a$</th>
<th>$g_1$</th>
<th>$g_2$</th>
<th>$A$ ($^{59}$Co)</th>
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<tr>
<td>[CoL$^{\text{OCH}_2\text{O}}$]$^-_1$</td>
<td>4.2 $\mu_B$</td>
<td>4.49</td>
<td>2.01</td>
<td>271.4 MHz</td>
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<tr>
<td>[CoL$^{\text{OMe}}$]$^-_1$</td>
<td>4.2 $\mu_B$</td>
<td>4.48</td>
<td>2.01</td>
<td>257.0 MHz</td>
</tr>
<tr>
<td>[NiL$^{\text{OCH}_2\text{O}}$]$^-_1$</td>
<td>3.7 $\mu_B$</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>[NiL$^{\text{OMe}}$]$^-_1$</td>
<td>3.3 $\mu_B$</td>
<td>–</td>
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$^a$Measured in solution using Evans method at 23 °C.

Figure 5. Portions of the cyclic voltammograms (scan rate = 0.1 V/s) for [CoL$^{\text{OCH}_2\text{O}}$]$^-_1$ (a) and [NiL$^{\text{OCH}_2\text{O}}$]$^-_1$ (b) in CH$_2$Cl$_2$ ([N((n-Bu)$_4$]PF$_6$ electrolyte). c) X-band EPR spectra of [CoL$^{\text{OCH}_2\text{O}}$]$^-_1$ (black line) and [CoL$^{\text{OMe}}$]$^-_1$ (blue line) recorded at 10 K in frozen CH$_2$Cl$_2$. 
We hypothesized that the rigid apertures guarding coordination space in $[\text{ML}^{\text{OCH}_2\text{O}}]^{-}$ could gate access of exogenous substrates into the cavity interior. Barring entry in the equatorial plane, substrate binding to the open coordination site relies on penetration through the aperture defined by the three aromatic rings and their acetal linkages. Notably, dissolution of turquoise $[\text{CoL}^{\text{OCH}_2\text{O}}]^{-}$ in the coordinating solvent acetonitrile does not result in any noticeable color changes, and UV-visible spectra at both 23 °C and -40 °C show exclusively $d$-$d$ bands that correspond to a trigonal monopyramidal high-spin Co center, indicating that acetonitrile does not coordinate to the open axial site (Figure 6a,c). In contrast, dissolution of green $[\text{CoL}^{\text{OMe}}]^{-}$ in acetonitrile gives a deep purple solution, and the electronic spectra of these solutions show peaks corresponding to both trigonal monopyramidal and trigonal bipyramidal Co centers. Variable-temperature measurements evidence that acetonitrile binding to $[\text{CoL}^{\text{OMe}}]^{-}$ becomes increasingly favored at lower temperatures (Figure 6b,d). Cooling concentrated acetonitrile solutions of $\text{K}[\text{CoL}^{\text{OMe}}]$ to -35 °C precipitates both green crystals of $\text{K}[\text{CoL}^{\text{OMe}}]^{-}$ and purple crystals of $\text{K}[\text{Co(NCMe)L}^{\text{OMe}}]^{-}$. Structural determination of the latter by X-ray diffraction (Figure 7) reveals an axially bound acetonitrile ligand (Co–N$_{\text{NCMe}}$ = 2.113(2) Å) and an elongation of the $\text{trans}$ Co–N$_{\text{amine}}$ bond (2.299(2) Å vs. 2.1605(19) Å for the trigonal monopyramidal complex). Space for the bound acetonitrile to reside within the coordination sphere is created by rearrangement of the arene rings compared to the structure of $[\text{CoL}^{\text{OMe}}]^{-}$ (vide supra), which rotate such that all three orient their faces inward and surround the nitrile.
Figure 6. Exclusion of MeCN from the coordination sphere of $[\text{CoL}^{\text{OCH}_2\text{O}}]^{-}$ (a), while binding to $[\text{CoL}^{\text{OMe}}]^{-}$ occurs readily at ambient and low temperatures (b). c) UV-visible spectra of $[\text{CoL}^{\text{OCH}_2\text{O}}]^{-}$ in MeCN at 23 ºC and -40 ºC. d) UV-visible spectra of $[\text{CoL}^{\text{OMe}}]^{-}$ in acetonitrile at temperatures between -40 ºC and 70 ºC (spectra were obtained at intervals of 10 ºC).

Figure 7. Solid-state structure of $[\text{Co(NCMe)}\text{L}^{\text{OMe}}]^{-}$. Hydrogen atoms, the countercation, and co-crystallized acetonitrile molecules have been omitted for clarity.
In accord with experimental observations, dispersion-corrected Density Functional Theory (DFT) calculations indicate a substantial difference in the thermodynamics of acetonitrile binding between the two cobalt complexes (Figure 8). At the OLYP$^{60}$ level (def2-TZVP(-f) basis set on Co; def2-SVP basis set on light atoms), acetonitrile binding to $S = 3/2$ [CoL$^{\text{OMe}}$]$^-\,$ to give [Co(NCMe)L$^{\text{OMe}}$]$^-$ at standard temperature (273.15 K) is computed to be exothermic ($\Delta H = -14.7$ kcal/mol) with a Gibbs free energy of reaction that is nearly thermoneutral ($\Delta G = -1.0$ kcal/mol). In contrast, binding of acetonitrile to [CoL$^{\text{OCH}_2\text{O}}$]$^-$ is computed to be endothermic ($\Delta H = +8.1$ kcal/mol) and accordingly strongly endergonic ($\Delta G = +22.7$ kcal/mol). The metrical parameters about cobalt in the optimized structure of [Co(NCMe)L$^{\text{OCH}_2\text{O}}$]$^-\,$ do not differ substantially from those in [Co(NCMe)L$^{\text{OMe}}$]$^-\,$ with the exception of the bond length between Co and the axial tertiary amine (Tables S6.2 and S6.5); this is both a reflection of the increased conformational flexibility possessed by the [L$^{\text{OMe}}$]$^{3^-}\,$ ligand, and the very shallow potential energy surface along the Co-N$_{\text{amine}}$ coordinate for [Co(NCMe)L$^{\text{OMe}}$]$^-\,$ (see the Supporting Information section S6.2).$^{61}$ Rather, it seems apparent that the rigid steric profile of the narrow void in [CoL$^{\text{OCH}_2\text{O}}$]$^-\,$ precludes MeCN binding. Support for this hypothesis was obtained via computationally exploring intracavity binding of the smaller and rigorously linear nitrile HCN. The primary coordination spheres in the optimized geometries of [Co(NCH)L$^{\text{OCH}_2\text{O}}$]$^-\,$ and [Co(NCH)L$^{\text{OMe}}$]$^-\,$ are readily comparable with significant discrepancies only seen on comparing the Co-N$_{\text{amine}}$ distances (Tables S6.3 and S6.6). Importantly, however, the calculated enthalpy and free energy of HCN binding exhibit only very minor differences between these cobalt complexes and are similar in magnitude to those computed for MeCN binding to [CoL$^{\text{OMe}}$]$^-\,$
This observation suggests that intracavity binding of very small ligands in $[ML^{OCH_2O}]^-$ complexes is sterically feasible.

**Figure 8.** Density functional theory (DFT) investigations into the coordination of nitrile ligands to the axial sites in $[CoL^{OCH_2O}]^-$ and $[CoL^{OMe}]^-$. Top: Calculated enthalpy and Gibbs free energy values for acetonitrile (left) and hydrogen cyanide (right) coordination to the cobalt complexes at standard temperature. Bottom: Relaxed surface scans along the Co-N$_{nitrile}$ coordinate for acetonitrile (left) and hydrogen cyanide (right) cavity penetration and coordination. Energy values are relative to the summed single-point energies of $[CoL^{OCH_2O}]^-$ and the free nitrile.
An interesting aspect of cavity-gated complexes is the potential for cavity penetration to serve as the rate-limiting event in a metal-based reaction. While ligand-binding events at unsaturated metal centers often have small activation barriers associated with coordination sphere rearrangements, the rate-limiting event for intracavity coordination could plausibly be penetration of the void by the incoming ligand. To explore this notion, relaxed surface scans were performed to investigate the energetics of MeCN and HCN ingress/egress through the narrow void (Figure 8, bottom). In both cases, a significant increase in ΔE (i.e. ΔH at 0 K) occurs as the nitrile progresses through the void, with maxima for both ligands occurring at Co-N\textsubscript{nitirle} distances outside of van der Waals contact. Indeed, it seems intuitive that these distances would maximize steric pressures given both the slightly convex profile of the arene-defined void and the potential for clashing of the nitrile with the methylene groups lining the cavity crest. The methyl group of an intracavity-ligated MeCN must reside near the narrowest region of the void, and the attendant steric clashing offsets the stabilization afforded by a weak Co-N\textsubscript{nitirle} coordinative bond. However, HCN is apparently small enough that steric pressures subside enough at shorter Co-N\textsubscript{nitirle} distances to yield a net energetically favorable binding event. Note that attempts were made to synthesize [Co(NCH)\textsubscript{L OCH\textsubscript{2}O}]\textsuperscript{−} by exposing [CoL\textsubscript{OCH\textsubscript{2}O}]\textsuperscript{−} to HCN (Caution: hydrogen cyanide is a highly toxic gas), but were hampered by competitive demetallation to yield H\textsubscript{3}L\textsuperscript{OCH\textsubscript{2}O} along with unidentified cobalt-containing species.

The inaccessibility of the void within [CoL\textsuperscript{OCH\textsubscript{2}O}]\textsuperscript{−} to MeCN likely reflects a high degree of rigidity and a low proclivity for the cavity to undergo guest-responsive conformational changes. In this way, the [L\textsuperscript{OCH\textsubscript{2}O}]\textsuperscript{3−} ligand differs from the calix[6]arene-bearing “funnel
complexes” championed by Reinaud, which generally display guest-adaptive cavities.\textsuperscript{29,63} Indeed, it is well known that calix[6]arenes display conformational flexibility enabled by rotations about the C\textsubscript{sp3}-C\textsubscript{arene} bonds.\textsuperscript{64,65} In contrast, the macrocyclic motif within the [L\textsuperscript{OCH2O}\textsubscript{3}]\textsuperscript{3–} ligand more closely approximates the structure of Cram’s cavitands,\textsuperscript{44} wherein each arene is linked to its neighboring rings through two points of attachment, embuing the macrocycle with greatly enhanced rigidity and less conformational adaptibility.

Conclusions

In summary, we have shown that macrocyclization of a TREN-derived proligand with methylene dihalides can engender a rigid and narrow void that is oriented atop the metal binding pocket. Despite its rigidity, H\textsubscript{3}L\textsuperscript{OCH2O} can undergo deprotonative metallation to yield four-coordinate complexes which localize an open coordination site within the ligand cavity. The cavity’s narrow profile tightly regulates the arrival of substrates at the open coordination site, and precludes the binding of acetonitrile on the basis of size, as clashing of the nitrile with atoms near the cavity rim thermodynamically outweigh the formation of a weak M-N\textsubscript{nitrile} bond. Additionally, calculations demonstrate that entry of even small-profile species into the void space must overcome a significant kinetic barrier that is likely to slow substrate ingress. We envision that localization of reactive metal-bound motifs within the cavity of complexes bearing the [L\textsuperscript{OCH2O}\textsubscript{3}]\textsuperscript{3–} ligand will allow for kintetic stabilization and characterization of metal-bound species that have traditionally proven elusive.
**Experimental Section**

**General Considerations.** All manipulations were carried out under an atmosphere of purified dinitrogen using standard Schlenk and glovebox techniques. Unless otherwise stated, reagent-grade starting materials were purchased from commercial sources and either used as received or purified by standard procedures. Unless otherwise stated, organic solvents were deoxygenated and dried using a Pure Process Technologies solvent purification system. *N,N*-dimethylacetamide (DMA) and dimethylsulfoxide-*d*$_6$ were stored over activated 3 Å molecular sieves, transferred via cannula into a separate flask, sparged with N$_2$ for 1 h, and stored over fresh 3 Å molecular sieves in the glovebox prior to use. Chloroform-*d* was stirred with CaH$_2$, distilled into a separate flask, degassed via freeze-pump-thaw cycles, and stored over activated 3 Å molecular sieves in the glovebox prior to use. Methanol was neither deoxygenated nor dried and was used as received. Molecular sieves (3 Å) and Celite were separately pre-activated in a 180 °C oven overnight, then transferred into a round bottom flask and heated under vacuum (*P* < 100 mTorr) at a temperature in excess of 200 °C for at least 12 h, and then stored in the glovebox. Tetra(n-butylammonium) hexafluorophosphate for electrochemical measurements was recrystallized three times from ethanol, and then dried under vacuum with P$_2$O$_5$ at 120 °C until the pressure reached 50 mTorr.

Solution $^1$H and $^{13}$C{ootnotesize{1}$^1$H} nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX-400 or DPX-500 spectrometer locked on the signal of deuterated solvents. $^1$H and $^{13}$C{ootnotesize{1}$^1$H} chemical shifts are reported in ppm relative to SiMe$_4$ ($^1$H and $^{13}$C δ = 0.0 ppm) with reference to residual solvent resonances. Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier transform infrared spectrometer. Electronic absorption measurements were recorded using either an Agilent Cary 60 UV–Vis spectrometer (ambient temperature
measurements) or an Agilent Cary 6000i UV-Vis-NIR spectrometer (variable temperature measurements). Samples were prepared in the glovebox and sealed in a quartz cuvette (1 cm pathlength). X-band electron paramagnetic resonance (EPR) measurements were carried out on a Bruker EMXplus spectrometer (microwave frequency of 9.382 GHz). Samples were prepared as solutions in CH₂Cl₂ in the glovebox, glassed via flash-cooling in liquid nitrogen, and loaded into the spectrometer. Electrochemical measurements were performed using a CH Instruments 620 D potentiostat with a three electrode setup, including a Ag/AgNO₃ (1 M) reference electrode (CHI111), a Pt wire counter electrode (CHI115, surface area in solution of 0.14 cm²), and a glassy carbon working electrode (CHI104, 3 mm diameter). Solutions were prepared using dry and degassed CH₂Cl₂ at a concentration of 1 mM metal complex. The [NBu₄]PF₆ electrolyte concentration was 1 M. Voltammograms were referenced to the Cp₂Fe⁺/⁰ couple using ferrocene as an internal standard. Solution phase effective magnetic moments were determined using the Evans method. A dried solid analyte sample was dissolved in 0.800 mL of 9:1 v/v CH₂Cl₂/PhCF₃. This solution was added to a borosilicate NMR tube, along with a flame-sealed glass capillary containing a 4:1 v/v CH₂Cl₂/PhCF₃ internal standard. Elemental analyses were performed on a PerkinElmer 2400 Series II Analyzer at the CENTC Elemental Analysis Facility, University of Rochester.

**Preparation of anhydrous cobalt(II) acetate.** A flame-dried three-necked round bottom flask outfitted with a reflux condensor was evacuated and then backfilled with nitrogen a total of three times. The flask was charged with acetic anhydride (76 mL, 805 mmol) and sparged with N₂ for 1 h. Cobalt(II) acetate tetrahydrate (20 g, 79.6 mmol) was then added to the flask under N₂ purge, and the solution was heated to reflux for 12 h. After cooling, the solution was filtered using a Schlenk frit, and while maintaining an inert atmosphere the light pink solid was
transferred into the glovebox and washed with 5 x 50 mL portions of Et₂O. The solid was then dried under vacuum and was confirmed to be anhydrous via FT-IR spectroscopy (KBr pellet). Yield = 13.7 g, 77.4 mmol, 96%.

**Preparation of anhydrous nickel(II) acetate.** A flame-dried three-necked round bottom flask outfitted with a reflux condensor was evacuated and then backfilled with nitrogen a total of three times. The flask was charged with acetic anhydride (76 mL, 805 mmol) and sparged with N₂ for 1 h. Nickel(II) acetate tetrahydrate (20 g, 79.7 mmol) was then added to the flask under N₂ purge, and the solution was heated to reflux for 12 h. After cooling, the solution was filtered using a Schlenk frit, and while maintaining an inert atmosphere the light green solid was transferred into the glovebox and washed with 5 x 50 mL portions of Et₂O. The solid was then dried under vacuum and was confirmed to be anhydrous via FT-IR spectroscopy (KBr pellet). Yield = 13.8 g, 78.1 mmol, 97%.

**Synthesis of H₃L⁰Bn.** Note: All water used in this preparation was 18.2 MΩ nanopure water. All glassware used in this preparation was soaked in a KOH/iPrOH bath, rinsed with water three times, and dried prior to use. Neglecting these precautions led to reaction mixtures that were darkened in color and resulted in difficulties purifying the subsequently synthesized H₃L⁰CH₂O. We attribute these observations to the proclivity of TREN-derived tris-amides to act as very strong chelators of halides and small inorganic anions.⁶⁷ A 1 L three-necked round bottom flask was charged with 3,5-di(benzyloxy)benzoic acid (39.0 g, 117 mmol, 3.3 eq.) and 300 mL of CH₂Cl₂. Solid 1,1’-carbonyldiimidazole (18.9 g, 117 mmol, 3.3 eq.) was added slowly, and the reaction was then stirred for 1 h. After purging the headspace with N₂ to ensure liberation of evolved CO₂, tris(2-aminoethyl)amine (5.30 mL, 35.3 mmol) was then added in a single portion via syringe and the reaction was allowed to stir for 12 h. The reaction mixture was then washed
with water five times in a separatory funnel. The organic layer was dried under vacuum ($P = 30$ mTorr) to afford a colorless powder. Yield = 31.6 g, 29.0 mmol, 82%. $^1$H NMR (400.1 MHz, DMSO-$d_6$): $\delta = 8.41$ (br s, 3H, -NH), 7.39 (br s, 30H, -Ph), 7.10 (br s, 6H, o-Ar), 6.78 (br s, 3H, p-Ar), 5.07 (br s, 12H, -C$_2$H$_5$Ph), 3.35 (br s, 6H, -NHCH$_2$CH$_2$N), 2.71 (br s, 6H, -NHCH$_2$CH$_2$N) ppm. $^{13}$C{$^1$H} NMR (125.8 MHz, DMSO-$d_6$) $\delta = 165.74$, 159.33, 136.77, 136.64, 128.44, 127.89, 127.71, 106.19, 104.48, 69.46, 37.93 ppm. Calculated elemental analysis for C$_{69}$H$_{66}$H$_4$O$_9$: C, 75.66%; H, 6.07%; N, 5.11%. Found: C, 74.82%; H, 6.17%; N, 5.26%.

**Synthesis of H$_3$L$^{\text{OH}}$.** Note: All water used in this preparation was 18.2 MΩ nanopure water. All glassware used in this preparation was soaked in a KOH/iPrOH bath, rinsed with water three times, and dried prior to use. Neglecting these precautions led to reaction mixtures that were darkened in color and resulted in difficulties purifying the subsequently synthesized H$_3$L$^{\text{OCH$_2$O}}$. We attribute these observations to the proclivity of TREN-derived tris-amides to act as very strong chelators of halides and small inorganic anions.$^{67}$ In a three-necked round bottom flask equipped with a reflux condenser and under an N$_2$ atmosphere, a solution of H$_3$L$^{\text{OBn}}$ (22.6 g, 20.6 mmol) in methanol (550 mL) was added under an N$_2$ purge. Subsequently added under an N$_2$ purge were Pd/C (10 wt% Pd; 2.20 g, 2.07 mmol Pd, 0.1 eq.), and then 1,4-cyclohexadiene (19.6 mL, 207 mmol, 10 eq.). The reaction was then heated to 60 °C for 16 h. The resulting black suspension was filtered and the filtrate was then dried in vacuo to yield a hygroscopic colorless solid. Yield: 9.79 g, 17.6 mmol, 85 %. $^1$H NMR (400.1 MHz, DMSO-$d_6$) $\delta = 9.40$ (s, 6H, -OH), 8.19, (t, $J = 3$ H, -NH), 6.65 (d, $J = 2$ Hz, 6H, o-Ar), 6.33 (t, $J = 2$ Hz, 3H, p-Ar), 3.28 (q, $J = 7$ Hz, 6H, -NHCH$_2$CH$_2$N), 2.65 (t, $J = 7$ Hz, 6H, -NHCH$_2$CH$_2$N) ppm. $^{13}$C{$^1$H} NMR (125.8 MHz, DMSO-$d_6$) $\delta = 166.54$, 158.31, 136.94, 105.45, 105.04, 53.47, 37.79 ppm. Calculated analysis
Synthesis of $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$. A three-necked 2 L round bottom flask (which had been previously soaked in a KOH/iPrOH bath, washed with nanopure water, and dried) was equipped with a 500 mL addition funnel was purged with N$_2$ for 30 min, and then charged with $\text{H}_3\text{L}^{\text{OH}}$ (9.79 g, 17.7 mmol) and K$_2$CO$_3$ (43.9 g, 318 mmol, 18 eq.). To the flask was added 1 L of dry and deoxygenated DMF via cannula transfer. The addition funnel was charged with a solution of CH$_2$BrI (5.32 mL, 70.6 mmol, 4 eq.) in dry and deoxygenated DMF (500 mL) using a cannula. The CH$_2$BrI solution was then added dropwise into the reaction mixture with stirring over the course of 13 h at 23 ºC, and then stirred for an additional 9 h. Subsequently, the temperature was increased to 60 ºC and the reaction was stirred for another 24 h. Upon cooling, the reaction mixture was concentrated under reduced pressure. The resulting pink/red residue was placed in a glass coarse fritted filter thimble and extracted with chloroform using a Soxhlet extractor over the course of two weeks. The resulting suspension was then dried in vacuo, and the off-white solid was serially triturnated at 50 ºC with water, methanol, and hexanes, yielding $\text{H}_3\text{L}^{\text{OCH}_2\text{O}}$ as a colorless solid after drying in vacuo. Yield: 0.880 g, 1.49 mmol, 8.4%. $^1$H NMR (400.1 MHz, DMSO-d$_6$): $\delta$ = 7.25 (d, J = 2 Hz, 6H, o-Ar), 7.23 (br s, 3H, -NH), 6.61 (t, J = 2 Hz, 3H, p-Ar), 6.18 (d, J = 7.7 Hz, 3H, -OCH$_2$O-), 5.45 (d, J = 7.7 Hz, 3H, -OCH$_2$O-), 3.47 (m, 6H, -NHCH$_2$CH$_2$N), 2.60 (t, J = 6 Hz, 6H, -NHCH$_2$CH$_2$N) ppm. $^{13}$C{$^1$H} NMR (125.8 MHz, DMSO-d$_6$): $\delta$ = 165.39, 157.39, 135.85, 112.55, 112.01, 92.71, 50.23, 35.51 ppm. Calculated elemental analysis for C$_{30}$H$_{30}$N$_4$O$_9$: C, 61.01%; H, 5.12%; N, 9.49%. Found: C, 59.55%; H, 5.08%; N, 9.32%.
**Synthesis of H$_3$L$^{OMe}$**. A 1 L Schlenk flask was charged with a 500 mL CH$_2$Cl$_2$ solution of 3,5-dimethoxybenzoic acid (82.3 g, 452 mmol, 3.3 eq.) and then purged with N$_2$. While under N$_2$ purge, 1,1’-carbonyldiimidazole (77.7 g, 475 mmol, 3.5 eq.) was added as a solid. The reaction was then allowed to stir for 1 h under N$_2$. After purging the headspace with N$_2$ to ensure liberation of evolved CO$_2$, tris(2-aminooethyl)amine (20.5 mL, 137 mmol). After washing the reaction mixture five times with H$_2$O using a separatory funnel, the organic layer was dried in vacuo. The resulting pale yellow residue was recrystallized from THF to yield H$_3$L$^{OMe}$ as colorless crystals. Yield: 81.4 g, 93%. The $^1$H NMR spectrum of this compound matched that reported previously.$^{55}$

**Synthesis of [K(18-crown-6)][CoL$^{OCH_2O}$]**. In the glovebox, a scintillation vial was charged with H$_3$L$^{OCH_2O}$ (0.100 g, 0.169 mmol) and KH (0.027 g, 0.677 mmol, 4 eq.). DMA (2 mL) was added, and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Co(OAc)$_2$ (0.046 g, 0.254 mmol, 1.5 eq.) and stirred for 12 h. After filtering through Celite and washing the filter cake with additional DMA (4 mL), Et$_2$O was added to the filtrate to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et$_2$O/DMA solution. The resulting greenish residue was then dissolved in a solution of 18-crown-6 (0.054 g, 0.203 mmol, 1.2 eq.) in CH$_2$Cl$_2$ (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried in vacuo, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 ºC for 3 d yielded turquoise crystals, which were harvested
and washed with Et$_2$O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in CH$_2$Cl$_2$ and then dried *in vacuo* at 60 °C to yield [K(18-crown-6)][CoL$_{2}$OCH$_2$O] that is free from residual MeCN. Yield: 0.063 g, 0.066 mmol, 39%. $^1$H NMR (400.1 MHz, DMSO-d$_6$): $\delta$ = 75.4, 3.6 (18-c-6), -0.2, -10.3 ppm. $\mu_{\text{eff}}$ = 4.2 $\mu_B$ (Evans method, $^{19}$F NMR, CH$_2$Cl$_2$/PhCF$_3$, 23 °C). Material for elemental analysis was prepared by recrystallization of crude and crown ether-free material from a DMA solution upon vapor diffusion of Et$_2$O. Calculated analysis for C$_{30}$H$_{27}$N$_4$O$_9$CoK: C, 52.56%; H, 3.97%; N, 8.17%. Found: C, 52.77%; H, 4.12%; N, 8.56%.

**Synthesis of [K(18-crown-6)][NiL$_{2}$OCH$_2$O].** In the glovebox, a scintillation vial was charged with H$_3$L$_{2}$OCH$_2$O (0.100 g, 0.169 mmol) and KH (0.027 g, 0.677 mmol, 4 eq.). DMA (2 mL) was added, and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Ni(OAc)$_2$ (0.045 g, 0.254 mmol, 1.5 eq.) and stirred for 12 h. After filtering through Celite and washing the filter cake with additional DMA (4 mL), Et$_2$O was added to the filtrate to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et$_2$O/DMA solution. The resulting light orange residue was then dissolved in a solution of 18-crown-6 (0.054 g, 0.203 mmol, 1.2 eq.) in CH$_2$Cl$_2$ (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried *in vacuo*, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 °C for 3 d yielded orange/pink crystals, which were harvested and washed with Et$_2$O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in CH$_2$Cl$_2$ and then dried *in vacuo* at 60 °C to yield [K(18-crown-6)]
6)[NiL^{OCH2O}] that is free from residual MeCN. Yield: 0.082 g, 0.086 mmol, 51%. \(^1\)H NMR (400.1 MHz, DMSO-\(d_6\)): \(\delta = 27.6, 11.4, 11.2, 5.31, 3.5 \) (18-c-6) ppm. \(\mu_{\text{eff}} \) = 3.7 \(\mu_B\) (Evans method, \(^1\)F NMR, CH\(_2\)Cl\(_2\)/PhCF\(_3\), 23 °C). Material for elemental analysis was prepared by recrystallization of crude and crown ether-free material from a DMA solution upon vapor diffusion of Et\(_2\)O. Calculated analysis for C\(_{34}\)H\(_{36}\)N\(_5\)O\(_{10}\)NiK(K[NiL^{OCH2O}] • DMA): C, 52.86%; H, 4.70%; N, 9.07%. Found: C, 51.74%; H, 5.09%; N, 9.49%.

**Synthesis of [K(18-crown-6)][ZnL^{OCH2O}].** In the glovebox, a scintillation vial was charged with H\(_3\)L\(^{OCH2O}\) (0.100 g, 0.169 mmol) and KH (0.027 g, 0.677 mmol, 4 eq.). DMA (2 mL) was added, and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Zn(OAc)$_2$ (0.047 g, 0.254 mmol, 1.5 eq.) and stirred for 12 h. After filtering through Celite and washing the filter cake with additional DMA (4 mL), Et\(_2\)O was added to the filtrate to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et\(_2\)O/DMA solution. The resulting colorless residue was then dissolved in a solution of 18-crown-6 (0.054 g, 0.203 mmol, 1.2 eq.) in CH\(_2\)Cl\(_2\) (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried *in vacuo*, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 °C for 3 d yielded colorless crystals, which were harvested and washed with Et\(_2\)O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in CH\(_2\)Cl\(_2\) and then dried *in vacuo* at 60 °C to yield [K(18-crown-6)][ZnL^{OCH2O}] that is free from residual MeCN. Yield: 0.063 g, 0.066 mmol, 39%. \(^1\)H NMR (400.1 MHz, DMSO-\(d_6\)): \(d = 6.62 \) (d, \(J = 2 \) Hz, 6H, o-Ar), 6.33 (t, \(J = 2 \) Hz, 3H, p-Ar), 6.04 (d, \(J = 2 \) Hz, 6H, o-Ar), 5.31 (d, \(J = 2 \) Hz, 3H, p-Ar), 3.5 (t, \(J = 2 \) Hz, 3H, p-Ar), 2.7 (d, \(J = 2 \) Hz, 6H, o-Ar), 1.4 (s, 6H, o-Ar).
= 7 Hz, 3H, -OCH₂O-), 5.36 (d, \( J = 7 \) Hz, 3H, -OCH₂O-), 3.53 (s, 24H, 18-c-6), 3.39 (t, \( J = 7 \) Hz, 6H, ), 2.68 (t, \( J = 7 \) Hz, 6H) ppm. \(^{13}\text{C}\}^{1\text{H}}\) NMR (125.8 MHz, DMSO-\(d_6\)): \( \delta = 174.26, 156.27, 145.52, 111.09, 108.96, 91.95, 69.38, 49.99, 42.97 \) ppm. Material for elemental analysis was prepared by recrystallization of crude and crown ether-free material from a DMA solution upon vapor diffusion of Et₂O. \( \text{C}_{34}\text{H}_{36}\text{N}_5\text{O}_{10}\text{ZnK} (\text{K}[\text{ZnL^{OCH2O}}] \cdot \text{DMA})\): C, 52.49%; H, 4.66%; N, 8.99%. Found: C, 51.73%; H, 4.94%; N, 8.99%.

**Synthesis of \([\text{K}(18\text{-crown-6})][\text{CoL^{OMe}}]\).** In the glovebox, a scintillation vial was charged with \( \text{H}_3\text{L^{OMe}} \) (0.200 g, 0.314 mmol) and KH (0.050 g, 1.24 mmol, 4 eq.). DMA (2 mL) was added, and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Co(OAc)\(_2\) (0.083 g, 0.470 mmol, 1.5 eq.) and stirred for 3 h. After filtering through Celite, Et₂O was added to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et₂O/DMA solution. The resulting green residue was then dissolved in a solution of 18-crown-6 (0.099 g, 0.376 mmol, 1.2 eq.) in \( \text{CH}_2\text{Cl}_2 \) (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried in vacuo, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 °C for 3 d yielded a mixture of green and purple crystals (the latter corresponding the to the acetonitrile adduct), which were harvested together and washed with Et₂O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in \( \text{CH}_2\text{Cl}_2 \) and then dried in vacuo at 60 °C to yield \([\text{K}(18\text{-crown-6})][\text{CoL^{OMe}}]\) that contains no acetonitrile. Yield: 0.147 g, 0.147 mmol, 47%. \(^1\text{H}\) NMR (400.1 MHz, DMSO-\(d_6\)): \( \delta = 13.5, 3.6 \) (18-c-6), 0.0, -4.3 ppm. \( \mu_{\text{eff}} = 4.2 \) \( \mu_B \) (Evans method, \(^{19}\text{F}\)
NMR, CH$_2$Cl$_2$/PhCF$_3$, 23 ºC). Calculated combustion analysis for C$_{45}$H$_{63}$N$_4$O$_{15}$CoK: C, 54.15%; H, 6.36%; N, 5.61%. Found: C, 54.36%; H, 6.47%; N, 5.59%.

**Synthesis of [K(18-crown-6)][NiL$^{OMe}$].** In the glovebox, a scintillation vial was charged with H$_3$L$^{OMe}$ (0.200 g, 0.314 mmol) and KH (0.050 g, 1.24 mmol, 4 eq.). DMA (2 mL) was added, and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Ni(OAc)$_2$ (0.083 g, 0.470 mmol, 1.5 eq.) and stirred for 3 h. After filtering through Celite, Et$_2$O was added to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et$_2$O/DMA solution. The resulting light orange residue was then dissolved in a solution of 18-crown-6 (0.099 g, 0.376 mmol, 1.2 eq.) in CH$_2$Cl$_2$ (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried in vacuo, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 ºC for 3 d yielded dichroic pink/orange crystals which were harvested together and washed with Et$_2$O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in CH$_2$Cl$_2$ and then dried in vacuo at 60 ºC to yield [K(18-crown-6)][NiL$^{OMe}$] that contains no acetonitrile. Yield: 0.152 g, 0.152 mmol, 49%. $^1$H NMR (400.1 MHz, DMSO-d$_6$): $\delta$ = 21.4, 9.2, 6.4, 3.5 (18-c-6) ppm. $\mu_{\text{eff}}$ = 3.3 $\mu_B$ (Evans method, $^{19}$F NMR, CH$_2$Cl$_2$/PhCF$_3$, 23 ºC). Calculated combustion analysis for C$_{45}$H$_{63}$N$_4$O$_{15}$NiK: C, 54.17%; H, 6.36%; N, 5.62%. Found: C, 53.29%; H, 6.15%; N, 5.56%.

**Synthesis of [K(18-crown-6)][ZnL$^{OMe}$].** In the glovebox, a scintillation vial was charged with H$_3$L$^{OMe}$ (0.200 g, 0.314 mmol) and KH (0.050 g, 1.24 mmol, 4 eq.). DMA (2 mL) was added,
and the effervescent solution was stirred for 1 h during which time bubbling ceased. This solution was filtered through Celite to remove residual KH, and then added to solid Zn(OAc)$_2$ (0.086 g, 0.470 mmol, 1.5 eq.) and stirred for 3 h. After filtering through Celite, Et$_2$O was added to precipitate the desired complex. This suspension was stirred for 30 min and then filtered through a fine porosity fritted funnel. The crude complex remaining on the funnel was washed five times with a 5:1 Et$_2$O/DMA solution. The resulting colorless residue was then dissolved in a solution of 18-crown-6 (0.099 g, 0.376 mmol, 1.2 eq.) in CH$_2$Cl$_2$ (2 mL) and stirred for several minutes before filtering through Celite. The filtrate was dried in vacuo, and then taken up in a minimum amount of MeCN. Storage in a glovebox freezer at -35 ºC for 3 d yielded colorless crystals which were harvested together and washed with Et$_2$O to remove a small amount of co-crystallized 18-crown-6. The crystals were re-dissolved in CH$_2$Cl$_2$ and then dried in vacuo at 60 ºC to yield [K(18-crown-6)][ZnL$^{OMe}$] that contains no acetonitrile. Yield: 0.107 g, 0.107 mmol, 34%. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ = 6.42 (s, 6H, o-Ar), 6.16 (s, 3H, p-Ar), 3.54 (s, 24H, 18-c-6), 3.42 (s, 18H, -OCH$_3$), 3.30 (br s, 6H, -NHCH$_2$CH$_2$N), 2.61 (br s, 6H, -NHCH$_2$CH$_2$N) ppm. $^{13}$C{$^1$H} NMR (128.7 MHz, DMSO-d6): $\delta$ = 171.84, 159.40, 144.46, 104.12, 101.05, 69.48, 55.12, 54.43, 42.13 ppm. Calculated combustion analysis for C$_{45}$H$_{63}$N$_4$O$_{15}$ZnK: C, 53.80%; H, 6.32%; N, 5.58%. Found: C, 53.24%; H, 6.41%; N, 5.42%.

**Associated Content**

**Supporting Information**

The Supporting Information is available free of charge.

Nuclear Magnetic Resonance (NMR) data for all newly reported compounds; additional UV-Visible Absorption Spectroscopy data; fitting of all Electron Paramagnetic Resonance
(EPR) spectra; additional cyclic voltammetry data; details of crystallographic data collection and refinement; details of Density Functional Theory (DFT) calculations. (PDF)

**Accension Codes**

CCDC 2256935–2256942 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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The authors declare no competing financial interests.

Acknowledgements

The authors gratefully acknowledge the American Chemical Society Petroleum Research Fund (66140-DNI3) and the University of Rochester for financial support of this work. J.G.B. was supported by the University of Rochester Department of Chemistry through the iScholar summer research program. Prof. Michael Neidig and Dr. Aleksa Radovic are thanked for assistance with variable temperature UV-visible spectroscopic and EPR spectroscopic measurements. Prof. Kara Bren and Alison Samatian are thanked for assistance with electrochemical measurements.

References


(46) Attempts to directly form $\text{H}_3\text{L}^{\text{OH}}$ from three equivalents of 3,5-dihydroxybenzoic acid with TREN using various amide bond-forming coupling reagents consistently led to either incomplete conversion or intractable mixtures.


(48) Yang, L.; Powell, D. R.; Houser, R. P. Structural Variation in Copper(I) Complexes with

(49) The crystallographically independent nickel complex bearing the smaller N-Ni-N angle exhibits disorder of one equatorial N and the axial N atoms, and accordingly the angle of 130.09(12)\(^\circ\) should be interpreted with caution.


(51) As ascertained from a search of the Cambridge Structural Database Version 5.43 (updated September 2022).


(61) A previous study found that the tripodal vanadium complexes $[(Me_3Si)NCH_2CH_2]_3N)V$ and $[(Me_3Si)NCH_2CH_2]_3N)VO$ similarly have shallow potential energy surfaces along the axial V-N$_{amine}$ coordinate. See: Majumdar, S.; Stauber, J. M.; Palluccio, T. D.; Cai, X.; Velian, A.; Rybak-Akimova, E. V.; Temprado, M.; Captain, B.; Cummins, C. C.; Hoff, C. D. *Inorg. Chem.* 2014, 53 (20), 11185–11196.


