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Solution and Solid State Characterization of a Cadmium Octaazacryptand Complex

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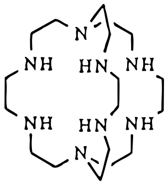
The constant for cadmium binding by octaazacryptand L = $N(CH_2CH_2NHCH_2CH_2NHCH_2CH_2)_3N$ was determined by potentiometry; log β_{ML} =18.3(1). Calculation of pM values (pM = −log [M]) show that L has the highest reported binding affinity for cadmium relative to other [2.2.2] polyoxa−polyaza cryptates. Two cadmium cryptate complexes, $[CdL](BF_4)_2$ (**1a**) and $[CdL](OAc)_2{\cdot}2H_2O$ (**1b**), were synthesized by metalation of the free cryptand. The molecular structures of compounds **1a** and **1b** were determined by X-ray diffraction. Crystallographic data for **1a**: trigonal, $P\bar{3}1c$, $Z = 2$, $a = 9.581(2)$ Å, $c = 17.003(4)$ Å, $V = 1351.2(5)$ Å^3. Crystallographic data for **1b**: monoclinic, $C2/c$, $Z = 4$, $a = 10.500(2)$ Å, $b = 14.782(3)$ Å, $c = 19.395(4)$ Å, $\beta = 99.30(2)°$, $V = 2971(1)$ Å^3. The cadmium ions in both complexes are eight-coordinate and display similar coordination geometries but different ligand conformations, designated as parallel and oblique. The cadmium coordination sphere is best described as a bicapped octahedron. Through 2D NMR experiments we have found that the Cd is in a symmetric environment and the conformation of the ligand in solution is consistent with the parallel conformation observed in one of the solid state structures. The ^{113}Cd NMR shift of this eight-coordinate amine complex is 75 ppm relative to 0.1 M aqueous $Cd(ClO_4)_2$, which correlates with shifts observed for other [2.2.2] cadmium polyoxa−polyaza cryptates.

Introduction

Cryptands are three-dimensional cage ligands that can form selective and highly stable metal complexes.[1−4] Metal selectivity is adjusted by varying the donor atom type, the number of donor atoms, and the size of the cavity, while the macrobicyclic effect often leads to enhanced complex stability.[2,5] We are studying the receptor properties of the octaazacryptand, L = $N(CH_2CH_2NHCH_2CH_2NHCH_2CH_2)_3N$. The synthesis of this ligand was first reported by Dietrich,[6] and we recently reported a simple, two-step synthetic route to L.[7]



L

The first report of ion-binding by L was the crystal structure of $[FLH_6]^{5+}$,[6] and it was subsequently found that the overall magnitude of fluoride binding in aqueous solution is $10^{11.2}$ and that the fluoride/chloride selectivity is $10^{7.6}$.[8] Subsequent work shows that L also binds strongly to metal cations. Martin and co-workers[9] recently reported the X-ray structure of the $[PbL]^{2+}$ complex and solution NMR data for $[CdL]^{2+}$ and $[PbL]^{2+}$. Solution thermodynamic work in our laboratory has shown that L has a high affinity for large metal ions, especially Hg(II), Pb(II), and Cd(II).[10,11] Smaller metal cations do not optimally fit in the binding cavity of L but, nonetheless, can display interesting chemistry. Copper, for example, forms an electron-delocalized bis(copper) complex of L, with both copper ions inside the macrobicycle.[12−16]

The work presented in this paper is motivated by the desire to improve our basic understanding of the structure and dynamics of cryptand−metal binding. Lehn and Montavon explored the stability and selectivity of toxic heavy metal complexation by polyoxa−polyaza macrobicycles. In these studies, it was found that increasing the number of nitrogen binding sites generally leads to decreased stability of alkali-metal and alkaline-earth-metal [2.2.2] cryptates and increased stability of toxic heavy metal cryptates like those of Cd, Pb,

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and Hg.[17] This study of the all-nitrogen cryptand supplements the previous work and forms a basis for the further investigation into potential uses of these cryptands in detoxification and environmental remediation. In this report, we present the results of our structural and binding studies of the cadmium complex of L. The binding constant for cadmium with the cryptand in water was determined by potentiometric titration, and comparisons are made to the binding affinity of other [2.2.2] cryptands. We have obtained crystal structures of $[CdL]^{2+}$ with BF_4^- and $CH_3CO_2^-$ counterions. In both cases, the cadmium is coordinated in a bicapped octahedral geometry, but the cryptand adopts different conformations. ^1H, ^{13}C, ^{15}N, and ^{113}Cd NMR studies confirm that cadmium binds inside the cryptand in solution, and we propose a solution structure of $[CdL]^{2+}$ consistent with one of the conformations observed in the solid state.

Experimental Section

NMR spectra were recorded in D_2O on a Bruker WM300 or a Bruker AMX-500 spectrometer. Chemical shifts for ^1H and ^{13}C are reported relative to TSP (3-(trimethylsilyl)-1-propanesulfonic acid, sodium salt), for ^{113}Cd relative to 0.1 M $Cd(ClO_4)_2$, and for ^{15}N relative to saturated $NaNO_3$. The ^{15}N spectrum was obtained on a Bruker WM300 using a 40 μs (~35°) pulse width and a 5.5 s recycle time. The ^{113}Cd spectrum was obtained on a Bruker WM300 using a 2 μs (~17°) pulse width and a 2.4 s recycle time. All 2D experiments were performed using a Bruker AMX-500 spectrometer and a probe temperature of 300 K. $^1H-^{13}C$ HMQC (heteronuclear multiple quantum coherence) data were collected using a phase-sensitive pulse sequence and $1/2J = 3.4$ ms; each FID consisted of 256 blocks of 1024 points with 16 scans per block. WALTZ 16 decoupling was employed with the water resonance presaturated. NOESY data were acquired using a standard phase-sensitive (TPPI) pulse sequence (2674 Hz spectral width, 512 blocks of 1024 points with 8 scans per block); the mixing time used was 800 ms. COSY data were acquired using a standard phase-sensitive (TPPI) pulse sequence with 256 blocks of 1024 points employing a sweep width of 3125 Hz; each block consisted of 8 scans. The HMQC data set was processed using an unshifted sine-bell-squared window applied over 256 points and zero-filled to 1024 points in both dimensions. The NOESY data set was processed using an unshifted sine-bell-squared window applied over 512 points and zero-filled to 1024 points in both dimensions. The COSY data set was processed using a 69°-shifted sine-bell-squared apodization over 256 points and zero-filled to 1024 points in both dimensions. An Orion EA 920 pH meter and an Ingold combination electrode for NMR tubes were used to make pH measurements. Standard buffers in H_2O with pH values of 4.01, 7.00, and 10.00 were used to calibrate the electrode. Uncorrected pH meter readings in D_2O are designated pH*. Elemental analyses were obtained on a Perkin-Elmer PE2400 analyzer.

Materials Preparation. L was synthesized using the previously reported procedure, and its purity was verified by ^1H NMR, elemental analysis, and potentiometric titration.[7] $CdCO_3$ precipitate was formed by combining aqueous solutions of $Cd(NO_3)_2$ and Na_2CO_3. $Cd(BF_4)_2$ was prepared by treatment of the resulting $CdCO_3$ with HBF_4. The resulting white solid (81 mg) was dissolved in 30 mL of EtOH, and 100 mg of L was dissolved in 10 mL of EtOH. The two solutions were combined, and a white precipitate formed immediately. The product was collected by vacuum filtration and recrystallized from 4 mL of hot water. Upon cooling, crystals formed and 29 mg of $[CdL](BF_4)_2$, **1a**, was collected. Anal. Calcd for $C_{18}H_{42}N_8B_2F_8Cd$: C, 32.93; H, 6.45; N, 17.07. Found: C, 32.99; H, 6.50; N, 16.93.

Crystals of $[CdL](OAc)_2 \cdot 3H_2O$, **1b**, were obtained from stoichiometric amounts of $Cd(OAc)_2$ and a tribenzylated aminal derivative of L in methanol.[18] Hydrolytic cleavage of this derivative resulted in the formation of L, and $[CdL](OAc)_2 \cdot 3H_2O$ was the only crystalline material recovered from the evaporated solution.

Titration Experiments. KOH (carbonate free) and HNO_3 titrants were prepared from concentrates and ultrapure water to give approximately 0.1 M solutions. The KOH titrant (0.1009(4) M) was standardized against potassium hydrogen phthalate, and the HNO_3 titrant (0.1011(1) M) was then standardized against the KOH. A stock solution of 0.096(2) M $Cd(NO_3)_2$ in 0.1012 M HNO_3 was prepared, and the molarity of Cd(II) was determined by ICP (inductively coupled plasma) analysis.

Potentiometric titrations were carried out in a water-jacketed cell, at 25.0 ± 0.1 °C, under ultrapure argon. A pK_w of 13.78 (0.10 M ionic strength, 25 °C) was used in all calculations.[19] Titrations were performed using a Radiometer ABU93 Triburette pH/pX meter and were controlled by a PC-386, which allows automated data collection using software developed in this laboratory. Combination pH electrodes were calibrated before each titration to measure p[H] (−log [H]) directly.[8]

L, ca. 0.005 M in 0.1 M KNO_3, was titrated with HNO_3 while p[H] was measured to determine the exact concentration of ligand in solution.[20] A stoichiometric amount of $Cd(NO_3)_2$ was added and the solution titrated with KOH. Three titrations were performed, and approximately 300 data points were collected in each data set in the p[H] range of 2−11. This p[H] range corresponds to 0−6.5 equiv of base for each data set. Overall formation constants (log β) for CdL and CdLH were determined from nonlinear least-squares analysis using the program BETA[21] and previously determined protonation constants for L.[8] Cadmium hydrolysis constants[19] were included in the equilibrium calculations but did not significantly affect the cadmium cryptand equilibria over the pH range studied. The weighted average values of log β_{ML} and log K^H_{MLH} were calculated by using the equation

$$\log K = \{\sum_{i=1}^{n}[(\log K)_i/\sigma_i^2]\}/\{\sum_{i=1}^{n}(1/\sigma_i^2)\}$$

where values of σ were obtained from BETA and the sum is over the number of experiments. The error in log K is reported as the standard deviation of $(\log K)_i$ values and represents the reproducibility of titration results.

NMR Sample Preparation. For the ^1H spectra, NMR samples of L and $[CdL]^{2+}$ in D_2O were made from stock solutions of 10 mM L (0.2 M KNO_3) and 10 mM $Cd(NO_3)_2$ to give samples (5 mM in ligand and 0.1 M ionic strength) that mimic the potentiometric titration conditions. For the 2D ^1H and ^{13}C spectra, a sample of 18 mM $[CdL]^{2+}$ was prepared from stock solutions of 228 mM L and 20 mM $CdCl_2$ in D_2O. The counterion of the cadmium salt did not show any effect on any of the NMR spectra. For the natural-abundance ^{15}N and ^{113}Cd spectra, a 0.47 M sample was prepared. The pH of all samples was adjusted with 1 M NaOD or 1 M DNO_3 as necessary to achieve the desired pH.

X-ray Structure Determinations. Crystals of **1a** were grown by slow evaporation from water, and a colorless, hexagonal plate with dimensions of 0.20 × 0.29 × 0.09 mm was selected for data collection. Crystals of **1b** were grown by slow evaporation from methanol, and a colorless, rhombic crystal with dimensions of 0.27 × 0.36 × 0.37 mm was selected for data collection. Preliminary photographic examinations and data collections were performed on a four-circle Siemens R3m/V diffractometer with graphite-monochromated Mo $K\alpha$ radiation at 203 K. Cell constants were obtained from least-squares refinement of 20−25 reflections, and the crystal systems were confirmed by axial photographs. The intensities of two check reflections were monitored during each data collection and showed no significant decay. For **1a**, a face-indexed numerical absorption correction was applied to the data with 001 as the major face and 100, 010 as side faces, and the structure

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(18) Barr, M. E.; Smith, P. H. Unpublished results.

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(20) L is recrystallized from water, and its hydration state varies somewhat. In all experiments, a solution of L was first titrated with acid in the absence of cadmium. The concentration of L was then determined by taking the derivative and assuming that the highest peak corresponds to 4 equiv of added acid.

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Table 1. Selected Crystallographic Data

compd	$Cd(C_{18}H_{42}N_8)(BF_4)_2$ **(1a)**	$Cd(C_{18}H_{42}N_8)(CH_3CO_2)_2 \cdot 3H_2O$ **(1b)**
empirical formula	$C_{18}H_{42}N_8B_2F_8Cd$	$C_{22}H_{54}N_8O_7Cd$
fw	656.6	655.1
space group	$P\bar{3}1c$	$C2/c$
a, Å	9.581(2)	10.500(2)
b, Å		14.782(3)
c, Å	17.003(4)	19.395(4)
β, deg		99.30(2)
V, Å^3	1351.2(5)	2971(1)
Z	2	4
2θ range, deg	5−55	4−45
d_{calc}, g/cm^3	1.614	1.465
μ, cm^{-1}	8.87	7.88
transm coeff (min/max)	0.714/0.887	0.517/0.757
no. of reflcns collcd	2491	2678
no. of indep reflcns	1053 (R(int) = 0.0165)	1953 (R(int) = 0.0187)
no. of obsd reflcns ($F > 4\sigma(F)$)	938	1554
R(obsd data)	R1^a = 0.0321 wR2^b = 0.0420	R1^a = 0.0425 wR2^b = 0.0496

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = [\sum[w(F_o^2 - F_c^2)^2]/\sum[wF_o^4]]^{1/2}$.

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients (Å^2 $\times$ 10^3) for the Cation of **1a**

	x	y	z	U(eq)^a
Cd	6667	3333	7500	31(1)
N1	6667	3333	5868(3)	44(1)
N2	6792(4)	5817(4)	6925(2)	46(2)
C1	7080(8)	4958(6)	5592(3)	52(2)
C2	6282(6)	5668(6)	6093(3)	55(2)
C3	8433(6)	7216(4)	7074(2)	64(2)
N2′	9055(24)	5824(25)	6949(10)	57(9)
C1′	7938(48)	5039(44)	5632(15)	70(17)
C2′	9360(36)	5702(34)	6075(16)	88(13)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

Table 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Coefficients (Å^2 $\times$ 10^3) for the Cation of **1b**

	x	y	z	U(eq)^a
Cd	5000	6863(1)	2500	36(1)
N1	7246(5)	6880(6)	3527(3)	75(3)
N2	5259(5)	5490(3)	3266(3)	43(2)
N3	7036(5)	6965(5)	2024(3)	70(3)
N4	5144(11)	8145(5)	3344(6)	117(5)
C1	7134(8)	6142(7)	4022(4)	77(4)
C2	6561(8)	5321(6)	3639(4)	67(3)
C3	4759(9)	4710(4)	2848(3)	62(3)
C4	8359(7)	6739(9)	3170(4)	124(6)
C5	8202(9)	7228(10)	2494(5)	145(6)
C6	6810(9)	7532(9)	1397(5)	125(6)
C7	7302(12)	7766(9)	3892(6)	136(6)
C8	5995(14)	8049(7)	4001(8)	143(7)
C9	3868(16)	8390(8)	3470(8)	175(8)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

was solved by direct methods.[22] Data for **1b** were corrected using a semiempirical absorption correction (ψ scan), and the structure was solved using a Patterson map.[22] Structures were refined with full-matrix least-squares methods with all non-hydrogen atoms refined anisotropically. Hydrogen atom positions for the ligand and the counterions were calculated (C−H = 0.96 Å) and added to the structure factor calculations without refinement. Crystal data are given in Table 1. Final positional parameters are given in Tables 2 and 3. Additional crystallographic data, atomic coordinates and equivalent isotropic displacement parameters, additional bond lengths and angles, anisotropic displacement parameters, and hydrogen atom coordinates and isotropic displacement parameters are available as Supporting Information.

(a) [CdL](BF$_4$)$_2$ (1a). The Cd and two independent B atoms occupy the $\bar{3}/m$ special positions with one-sixth of the molecule being unique. The $[CdL]^{2+}$ cation is disordered with roughly 85% of the cryptand having a “right-hand” twist and 15% having a “left-hand” twist as determined by refinement of the occupancy. This disorder mimics a vertical mirror plane, but refinement in the corresponding space group with the enforced 50:50 occupancy was unsatisfactory. The atoms exhibiting disorder are C1, C2, and N2 with the lower occupancy atoms being designated as C1′, C2′, and N2′. The BF_4^- anions also are disordered and are modeled as two superimposed, inverted tetrahedral species oriented with one B−F bond along the 3-fold axis and each tetrahedron with 0.5 site occupancy.

(b) [CdL](OAc)$_2$·3H$_2$O (1b). The $[CdL]^{2+}$ moiety sits on a crystallographic 2-fold axis with half of the cation being unique. The cation exhibits pseudo-3-fold geometry. The independent acetate anion is disordered in a ratio of ca. 50:50, with the two orientations slightly offset from one another. Two independent sites are occupied by water molecules with site occupancies of 1 and ca. $^1/_2$ (refined value of 0.62). The cation, acetate anion, and the two independent waters of hydration form an extensive hydrogen-bonding network.

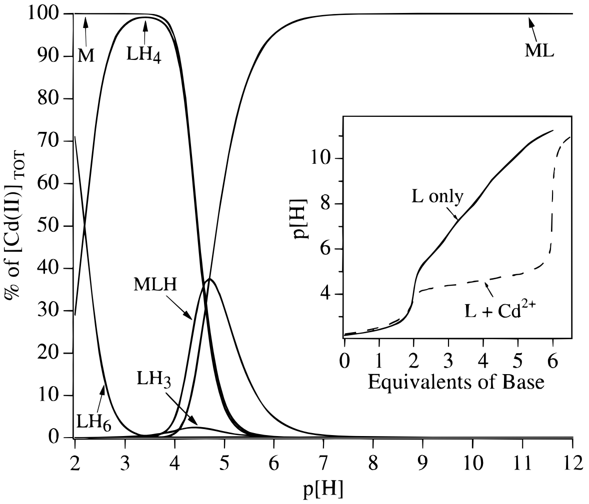

Figure 1. Species plot showing the L−Cd complexes as a function of p[H] where $[L]_{total} = [Cd]_{total} = 5$ mM. Inset: Potentiometric p[H] titration curves of L in the absence (solid line) and presence of cadmium (broken line).

Results

Titration Data. L was titrated with KOH in the presence of an equimolar amount of $Cd(NO_3)_2$ while the p[H] was monitored. The inset of Figure 1 illustrates the titration curves for L by itself and for L with 1 equiv of cadmium. The depression of the curve in the presence of 1 equiv of cadmium relative to the L-only curve illustrates the strong cadmium binding. The protonation constants for L were determined previously.[8] The cadmium−L titration curve was modeled using the previously determined ligand protonation constants and two cadmium species: ML and MLH. Equilibrium expressions for these two species are as follows:

$$Cd^{2+} + [L] \rightleftharpoons [CdL]^{2+} \quad \log K = 18.3(1)$$

$$[CdL]^{2+} + [H] \rightleftharpoons [CdLH]^{3+} \quad \log K = 4.7(3)$$

The stability constants derived from the titration curves predict the p[H]-dependent solution speciation of L and cadmium complexes shown in Figure 1. Below p[H] 4 the cryptand LH$_4$ species and free cadmium are the dominant species in solution. As the pH is increased, the MLH species reaches

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(22) *SHELXTL PLUS*; Siemens Analytical X-Ray Instruments, Inc.: Madison, WI, 1990.

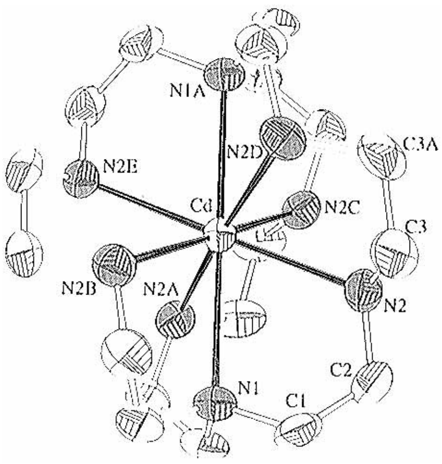
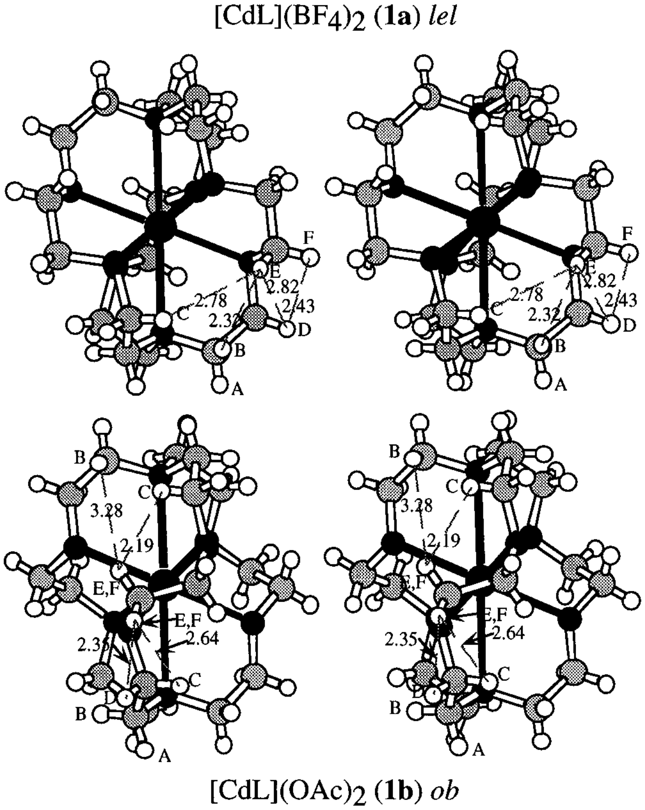


Figure 2. ORTEP diagram and labeling scheme of the $[CdL]^{2+}$ cation in $[CdL](BF_4)_2$ **(1a)** with hydrogen atoms omitted. Thermal ellipsoids are set at the 50% probability level.


$[CdL](BF_4)_2$ (**1a**) *lel*

$[CdL](OAc)_2$ (**1b**) *ob*

Figure 3. Ball and stick stereoviews of the cations of $[CdL](BF_4)_2$ (top) and $[CdL](OAc)_2$ (bottom). Note the orientation of the "central" C−C bond axis relative to the C_3 axis of the ligand which distinguishes the conformations as *lel* and *ob*, respectively.

a maximum concentration at p[H] 5 and then decreases with further increase in pH as the ML species grows in. From p[H] 7 to 12 the ML species dominates the distribution diagram, and there is no unbound cadmium or free ligand present.

Structure Descriptions. The structure of **1a** with the labeling scheme is illustrated in Figure 2. Both structures consist of a complex cation with cadmium bound inside L and discrete anions, BF_4^- or OAc^-. Stereoviews of the structures of the cations for **1a** and **1b** are illustrated in Figure 3. A list of values of selected bond distances and angles appears in Table 4.

Table 4. Selected Bond Distances (Å) and Angles (deg) for **1a** and **1b**

	1a	**1b**
Cd−N2 (2° N)	2.519(4)	2.49(2)[a]
Cd−N1 (3° N)	2.775(4)	2.832(6)
3° N−3° N	5.55(1)	5.66(1)
N2−Cd−N2D	70.3(2)	71.3(6)[a]
N2−Cd−N2A	105.9(1)	104.0(6)[a]
N2−Cd−N2E	175.3(2)	174(1)[a]
N2−Cd−N2C	78.1(2)	81.1(3)[a]
N1−Cd−N2	67.2(1)	65.5(5)[a]
dihedral angle C2−N2−C3−C3A	180	96

[a] Average values.

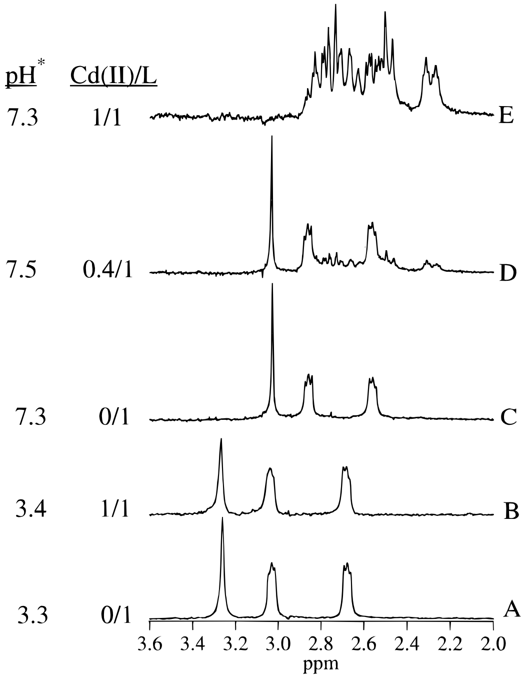


Figure 4. ^1H NMR spectra of 5 mM L in the presence of 0, 0.4, and 1.0 equiv of cadmium at pH* ~3.4 and ~7.5 measured at 300 MHz and 300 K. The similarity of spectra A and B shows that the cadmium does not bind at pH* 3.4 as predicted by the species plot in Figure 1. Spectrum E represents the NMR spectrum of the $[CdL]^{2+}$ complex at pH* 7.3. Addition of 0.4 equiv of cadmium to a solution of L at this pH* gives rise to spectrum D, which is a combination of spectra C (ligand only at pH 7.3) and E illustrating slow exchange in the reaction $ML + L' \rightleftharpoons ML' + L$.

The ligand in both structures exhibits 3-fold geometry with the axis of symmetry running through the two tertiary amines and the cadmium ion. The geometry of the cryptand ligand differs in that the "central" ethylene bridge is parallel to the 3-fold axis in **1a** and oblique to it in **1b**. These arrangements are best characterized by the dihedral angle around the secondary amine defined by the atoms C2−N2−C3−C3A in Figure 2. This dihedral angle has a value of 180° in **1a** and 96° in **1b**.

The coordination spheres of cadmium are very similar in these two compounds and are best described as bicapped octahedrons. The six 2° amines coordinate to cadmium in a distorted octahedral geometry with a Cd−N bond length of 2.52 Å in **1a** and an average bond length of 2.49 Å in **1b**. The tertiary amines cap two triangular faces, and the Cd−3° amine distances are 2.78 Å for **1a** and 2.83 Å for **1b**. These Cd−N distances correspond to 3°−3° amine distances of 5.55 and 5.66 Å, respectively. The distorted octahedral geometry of the secondary amines can be described as a compression along the 3-fold axis of a regular octahedron. This distortion is shown by the increase in the 2°N−Cd−2°N angle in the basal plane (e.g. N2−Cd−N2A) from 90 to 106° for **1a** and to 104° for **1b**. The angle between amines in opposite basal planes (e.g. N2−Cd−N2C in Figure 2) is decreased by the compression from 90 to 67.2° for **1a** and to 65.4° for **1b**.

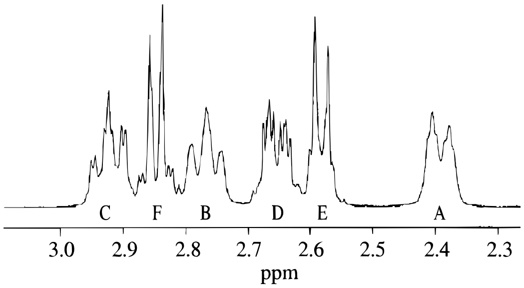
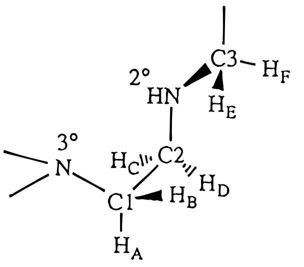


Figure 5. ^{1}H NMR spectrum of $[CdL]^{2+}$ at pH* 7.6 taken at 500 MHz and 300 K.

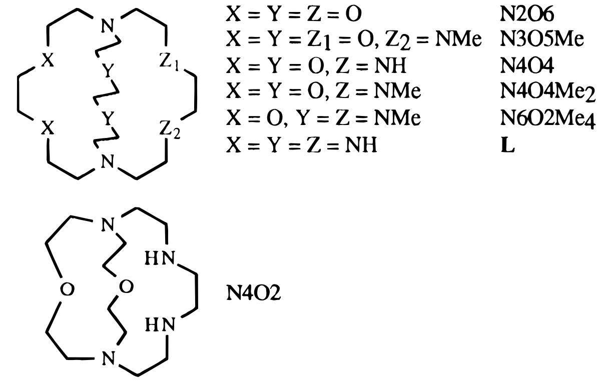
NMR. ^{1}H spectra of L in the presence of 0, 0.4, and 1 equiv of Cd at pH* ~3.5 and ~7.5 are presented in Figure 4. The spectrum of an equimolar mixture of Cd and L at pH* 3.4 (spectrum B) appears similar to the spectrum of L without Cd at pH* 3.3 (spectrum A). This observation agrees with the species plot generated from the potentiometric titration data which shows the LH_4 species dominating at pH* 3.4 and the absence of significant cadmium complexation (less than 1%). When pH* is adjusted to 7.3, a very complicated proton spectrum, spectrum E, corresponding to $[CdL]^{2+}$ is observed. A comparison of spectra C (the free cryptand at pH* 7.3) , D (cryptand in the presence of 0.4 mol of Cd), and E indicates that the Cd complex is in slow exchange with the free ligand ($ML + L' \rightleftharpoons ML' + L$) on the NMR time scale.

The spectrum of $[CdL]^{2+}$ at pH* 7.6 at a higher field (Figure 5) is resolved into six distinct patterns including two doublets (E and F), two pseudotriplets (B and C), and two complex doublets (A and D), all of which are of equal intensity. The ^{13}C spectrum has three resonances at 49.4, 45.3, and 43.4 ppm corresponding to C1, C3, and C2, respectively. Measurement of the C−H correlation spectrum showed a correlation between C1 and H_A and H_B, C2 and H_C and H_D, and C3 and H_E and H_F. Thus, there are three unique carbons and the protons on each carbon are chemically inequivalent as shown in the following diagram. These COSY and NOESY correlation experiments corroborate the proton assignments for $[CdL](ClO_4)_2$ in acetonitrile[9] which were based on 1D spectra alone. Keller reports shifts of C1 ≈ 52 ppm, C3 ≈ 46 ppm, and C2 ≈ 44.5 ppm for the analogous complex $[Cd(N4O4)]^{2+}$ (Chart 1).[23] Thus, the same trend in the chemical shifts is observed with C1 > C3 > C2 and C1 significantly deshielded relative to C2 and C3.



Inspection of the resolved 1D spectrum (Figure 5) shows that protons H_B and H_C exhibit strong vicinal coupling (~12 Hz) on the same order of magnitude as the geminal coupling (~13 Hz), resulting in a pseudotriplet pattern. However, H_A and H_D are complex doublets, implying that the vicinal coupling (~5 Hz) is significantly weaker than the geminal coupling (~13 Hz), and therefore, H_B and H_C must be anti to one another while H_A and H_D are gauche. Thus, we are able to assign protons H_A, H_B, H_C, H_D as shown in the prior diagram. From the NOESY spectrum, we know that proton H_E exhibits three relatively strong interactions with protons H_B, H_C, and H_D and that proton H_F strongly interacts with H_D. Using the two crystal structures as guides to provide us with distances between protons for the two conformations of the cryptand, we find that when the cryptand is in the parallel conformation, proton H_E is closest (<3 Å) to protons H_B, H_C, and H_D; see Figure 3. In this conformation, the crystal structure shows that proton H_F has only one close contact to proton H_D. This is consistent with the NOESY spectrum. When the cryptand is in the oblique orientation, neither proton H_E nor H_F is closer than 3.3 Å to proton H_B. Thus, we assign H_E and H_F on the basis of the observed crystal structures and conclude that the cryptand conformation in solution is similar to the parallel conformation found in the solid state structure of **1a**.

Chart 1



X = Y = Z = O	N2O6
X = Y = Z_1 = O, Z_2 = NMe	N3O5Me
X = Y = O, Z = NH	N4O4
X = Y = O, Z = NMe	N4O4Me$_2$
X = O, Y = Z = NMe	N6O2Me$_4$
X = Y = Z = NH	**L**

N4O2

The ^{113}Cd NMR signal for this compound at pH 7.6 exhibits a broad signal at 75.1 ppm, and the signal is not affected by dilution from 0.47 to 0.24 M. With the protons decoupled, the half-height line width is 33 Hz. With the protons coupled the signal broadens to 93 Hz without discrete ^{113}Cd−^{1}H coupling.

The ^{15}N spectrum for the $[CdL]^{2+}$ complex displays two signals at −346.7 (6N, secondary amines) and −354.5 ppm (2N, tertiary amines). These values fall in the normal range for 2° amines in Cd−amine complexes.[24] Both of these signals exhibit scalar couplings to cadmium of ca. 65 Hz for the 2° amines and 36 Hz for the 3° amines at 300 and 500 MHz. The cadmium−nitrogen couplings reported here are somewhat small compared to those of other reports in the literature of 80−210 Hz.[24,25] Jakobsen and Ellis suggested that small cadmium−nitrogen couplings may be due to exchange phenomena.[26] However, this explanation is not reasonable for our complex because we know that the $[CdL]^{2+}$ complex is in slow exchange on the proton NMR time scale, $ML + L' \rightleftharpoons ML' + L$. We suggest that the small couplings are due to the long cadmium−nitrogen bond distances observed in these complexes, 2.5−2.8 Å.

Discussion

We have determined that L forms a very strong complex with cadmium. In order to make comparisons of binding affinities of ligands with different pK_a values, we have calculated the pM (pM = −log [M]) values as a function of pH for [ligand] = [Cd(II)] = 5 mM. Data used to calculate the pM plots for ligands other than L were obtained from the NIST database.[19] A comparison of the pM plots of [2.2.2] polyoxa−polyaza

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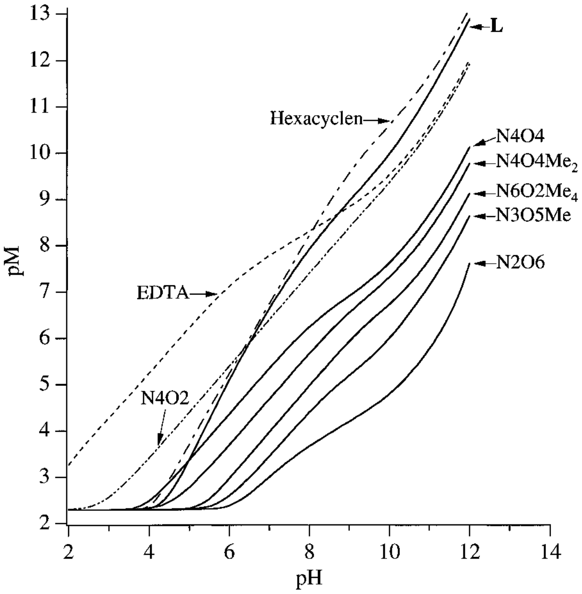

Figure 6. Plot of pM versus pH for a series of Cd [2.2.2] cryptates and a smaller Cd [2.1.1] N4O2 cryptate. See Chart 1 for cryptand abbreviations. Also shown for comparison are data for EDTA and hexacyclen (1,4,7,10,13,16-hexaazacyclooctadecane).

cryptates with cadmium is illustrated in Figure 6 by the solid lines. L has a higher pM value than any of the other [2.2.2] cryptands above pH 5; thus, it results in lower free cadmium concentrations in solution. We have included three other ligands for comparison: EDTA (ethylenediaminetetraacetic acid), N4O2 (see Chart 1), and hexacyclen (1,4,7,10,13,16-hexaazacyclooctadecane). While EDTA is a more effective chelator than L for cadmium below pH 9, the pM plot shows that L is a stronger chelator for cadmium above pH 9. However, the macrocycle hexacyclen binds cadmium more effectively than any of the [2.2.2] cryptands over the entire pH range shown in Figure 6. This is somewhat surprising, given that L has more donor atoms and is better "preorganized" than hexacyclen, and suggests that the cavity size of L is not ideal for cadmium. The cadmium-binding ability of the N4O2 cryptand,[17] especially at low pH, suggests that a smaller cavity size is more ideal for cadmium (see Figure 6). The apparent lack of a cryptate effect with cadmium has been observed for [2.2.2] N2O6[5] and for a heptaazacryptand[27] and, as in the case of L, is likely due to a cavity size mismatch with cadmium. Generally, cryptands show stronger metal-size/cavity-size correlations than macrocyclic complexes.[5,28]

For chelators to be effective at sequestering metals, they should show selectivity as well as high binding constants. We have preliminary data that show the ratio of $\beta_{\mathrm{ML(Cd(II))}}/\beta_{\mathrm{ML(Zn(II))}} \approx 10^6$ for L. This selectivity equals the best value measured for a mixed [2.2.2] polyoxa−polyaza macrobicycle.[17] Neither EDTA nor hexacyclen, each of which shows greater stability for cadmium, shows any selectivity for cadmium over zinc.[19] Thus, L shows more selectivity for cadmium over zinc that is likely due to a somewhat better cavity size match with cadmium compared to zinc.

The two structures for the Cd−cryptate complexes reported here exhibit different ligand geometries signified as the parallel (*lel*) or oblique (*ob*) orientation of the central ethylene (C3−C3A in Figure 1) bridge with respect to the 3-fold ligand axis. The ligand structure of complex **1a** is similar to that of the free ligand in that both are in the *lel* conformation as evidenced by comparison of the dihedral angles represented by the atoms C2−N2−C3−C3A in Figure 1: 176.49° for the cryptand[7] and 180° for **1a**. In contrast, complex **1b** has an average dihedral angle of 96° and exhibits the oblique orientation. Similar conformations were observed in $[Cu_2L](OAc)_3$ (*lel*) and $[CuL](NO_3)_3$ (*ob*),[14] and in the crystal structure of $[PbL](ClO_4)_2{\cdot}H_2O$, the ligand appears to adopt the *ob* conformation.[9] However, solid state structures of $[Cd(en)_3]^{2+}$, en = ethylenediamine, complexes exhibit only the *lel* conformation.[29−33] Typically, the *lel* form is favored over the *ob* form due to less severe hydrogen−carbon van der Waals interactions.[34] Molecular mechanics calculations[35] of L strain energy for the two conformations predict that the *lel* form of the free ligand is 2.3 kcal/mol lower in energy than the *ob* form (*lel* = 29.1 and *ob* = 31.4 kcal/mol). The two X-ray crystal structures were used as starting points in the minimizations after removing the cadmium ion. The cadmium cryptate appears to adopt the energetically favored *lel* conformation in both protic (H_2O) and aprotic (CH_3CN) solvents as shown by the similar ^1H proton spectra reported in this work and by Martin.[9] In either case, the ligand geometry does not significantly affect the Cd coordination sphere (Figure 3).

In both complexes, the cadmium coordination sphere is best described as a bicapped octahedron, and the secondary amines form a distorted octahedral geometry with compression along the 3-fold axis of the capping tertiary amines. In the uncomplexed L the distance from the 2°N to the centroid is 2.82 Å and the 3°N−centroid distance is 3.19 Å.[7] The introduction of cadmium into the ligand serves to contract L in toward the metal ion, resulting in average Cd−2°N distances of 2.5 Å and Cd−3°N distances of 2.8 Å. It is interesting to note that the average 2°N−Cd−2°N bite angle of ~70° and the approximate Cd−2°N bond lengths of ~2.5 Å compare very favorably with the ideal geometry for a five-membered ring such as a metal−ethylenediamine complex, N−M−N 69°, M−N 2.5 Å.[36,37] Using the effective ionic radii for cadmium and for three-coordinate nitrogen,[38] we calculate Cd−N bond distances of 2.41 Å for six-coordinate and 2.56 Å for eight-coordinate cadmium complexes. The average of all Cd−N bonds is ~2.6 Å for **1a** and **1b**. This distance is similar to those observed in other eight-coordinate cadmium−amine complexes[39,40] and is significantly longer than the <2.4 Å Cd−N distances for six-coordinate Cd−N complexes.[29−33,41−43]

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The cadmium complex of an analogous diazacryptand, [Cd(N2O6)][$CdCl_4$] (where N2O6 = N($CH_2CH_2OCH_2CH_2OCH_2CH_2$)$_3$N), exhibits nearly cubic geometry with Cd−3°N distances of 2.43 Å, which are slightly shorter than the average Cd−O distance of 2.47 Å.[44] This cryptand also forms a cubic, eight-coordinate complex with Mn(II).[45] The shorter Cd−3°N bond observed in the [Cd(N2O6)]$^{2+}$ complex is indicative of cadmium's preference for "soft" donors like nitrogen over oxygen. Thus, in the N2O6 cryptand we see shorter Cd−3°N bond lengths compared to those in L, where the cadmium already has six soft-donor secondary amines coordinated to it.

^{113}Cd NMR studies of Cd complexed with the N4O4 cryptand showed ^{3}J(^{113}Cd−C) coupling,[23] which indicates a significant bonding interaction between Cd and the tertiary amines. The broadness of the ^{13}C signals and the use of natural-abundance Cd instead of enriched ^{113}Cd precluded the observation of any ^3J(Cd−C) coupling for [CdL]$^{2+}$. However, Cd−N coupling is quite distinct in the natural-abundance ^{15}N NMR spectrum, where the coupling to the secondary amines is much stronger than that to the tertiary amines, ^1J(^{15}N−Cd) = 65 vs 36 Hz. We conclude from this scalar coupling that there is bonding of the cadmium to the tertiary amines.

The chemical shifts for Cd are affected by ligand type, coordination geometry, coordination number, ligand basicity, and ligand orientation.[46−49] The typical δ_{Cd} for six-coordinate cadmium−amine complexes is 200−450 ppm.[50,51] The δ_{Cd} of the eight-coordinate [CdL]$^{2+}$ is 75 ppm, which is significantly upfield compared to that of six-coordinate cadmium−amine complexes. The effect of coordination number on cadmium chemical shifts is not well understood mostly due to the inability to differentiate various effects. For example, increasing the coordination number usually leads to larger metal−ligand distances and may lead to a less favorable ligand geometry for coordination to the metal. It has been suggested that shielding roughly increases with increasing coordination number.[23,48,52] There have been several reports wherein lengthening of the Cd−N bond in complexes with strong steric demands leads to increased shielding of the ^{113}Cd nucleus.[46,47,49] The shielding observed in [CdL]$^{2+}$ is probably due to the higher coordination number of 8 and the corresponding longer Cd−N bond lengths averaging 2.5 Å to the secondary amines and 2.8 Å to the tertiary amines. The inherent steric demands in a cryptand may also shift the resonance upfield by affecting orbital overlap.

Comparing our δ_{Cd} to those of other cryptand complexes, we find that δ([Cd(N2O6)]$^{2+}$) = −78 ppm, δ([Cd(N4O4)]$^{2+}$) = 46 ppm,[23] and δ([CdL]$^{2+}$) = 75 ppm. In six-coordinate complexes, as the number of amine donors around cadmium increases, the cadmium resonance shifts downfield because nitrogen is generally more deshielding than oxygen. This trend is confirmed in these eight-coordinate cryptand complexes, where there is no ambiguity as to the coordination number for these structures.

Summary

L has a high affinity for cadmium, log K_{ML} = 18.3. Comparison to other [2.2.2] polyoxa−polyaza cryptands shows that the pM values for cadmium are higher in the presence of L above pH 5, and thus, the amount of free cadmium is lower compared to the case of other cryptands. In the solid state, L can adopt one of two conformations, parallel or oblique, and in solution the ligand geometry is similar to that of the parallel form observed in the crystal structure. The cadmium metal ion is eight-coordinate in solution and the solid state and adopts a bicapped octahedral geometry. The chemical shift of the ^{113}Cd NMR signal is 75 ppm and is significantly upfield compared to six-coordinate cadmium amine complexes.

Acknowledgment. We greatly appreciate the technical assistance of Dr. Cliff Unkefer and Dr. Griselda Hernandez-Duarte, and we especially thank Professor David LeMaster for helpful discussions regarding the NMR data and interpretation. Funding for this research was provided by the Department of Energy under the Laboratory Directed Research and Development Program. J.A.T. acknowledges the Director's Office for a Director's funded Postdoctoral Fellowship. Los Alamos National Laboratory is operated by the University of California for the U.S. Department of Energy under Contract W-7405-ENG-36.

Supporting Information Available: Tables of atomic coordinates, anisotropic displacement coefficients, bond distances, bond angles, and idealized H atom coordinates and isotropic displacement coefficients for both compounds and Figure S1, showing the ^{1}H−^{1}H NOESY spectrum of [CdL]$^{2+}$ (14 pages). Ordering information is given on any current masthead page.

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