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Synthesis, characterization and solution ^{113}Cd NMR analysis of Cd(II) 1,4,7,10,13-pentaazacyclopentadecane complexes[1]

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Contents

Abstract

Two new cadmium(II) complexes of the macrocyclic ligand, 1,4,7,10,13-pentaazacyclopentadecane **5**, have been prepared and characterized. The crystal structure of dichlorocadmium(II) complex **3** was determined and reveals that the Cd(II) is coordinated in a pentagonal bipyramidal array of the five nitrogens of the macrocyclic ring and capped by two *trans*-chloro ligands. Crystal data for $Cd(C_{10}H_{25}N_5)Cl_2–0.5H_2O$ are as follows: monoclinic at 20 °C, space group $C2/c-C^6_{2h}$ (No. 15) with $a = 22.165(5)$ Å, $b = 11.439(3)$ Å, $c = 14.6788(4)$ Å, $\beta = 118.75(2)°$, $V = 3262(2)$ Å^3 and $Z = 8$ [$d_{calcd} = 1.660$ g cm^{-3};

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[1] Dedicated to Professor Daryle Busch on the occasion of his 70th birthday.

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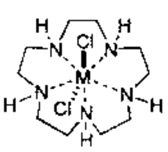
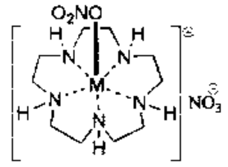
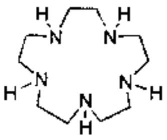
μ_a(Mo Kα)$=1.66\ \mathrm{mm}^{-1}$]. Solution ^{1}H, ^{13}C and ^{113}Cd NMR studies of complex **3** suggest that in non-polar solvents, such as $CDCl_3$, the seven-coordinate structure is maintained, while in aqueous media dissociation of one axial chloride ligand affords a macrocyclic ligand-folded six-coordinate species. This is analogous to the dichloromanganese(II) complex **1**. Folding of the pentaazamacrocyclic ligand **5** is confirmed as a relevant structural motif for this series of complexes by the X-ray structure determination of the bis(nitrate) derivative. Complex **4** $[Cd(C_{10}H_{25}N_5)NO_3]NO_3$ reveals a six-coordinate structure with a folded conformation of the macrocyclic ligand. Crystal data for $[Cd(C_{10}H_{25}N_5)NO_3]NO_3$ is as follows: orthorhombic at 20 °C, space group $P2_12_12_1-D_2^4$ (No. 19) with $a=9.627(2)$ Å, $b=12.858(2)$ Å, $c=14.003(2)$ Å, $V=1733.3(6)$ Å^3 and $Z=4$ [$d_{\mathrm{calcd}}=1.731\ \mathrm{g\,cm}^{-3}$; μ_a(Mo Kα)$=1.30\ \mathrm{mm}^{-1}$]. Solution ^{1}H, ^{13}C and ^{113}Cd NMR studies of complex **4** suggest six-coordinate structures in both $CDCl_3$ and D_2O, again with the macrocyclic ligand in a folded conformation. Again, this is entirely analogous to the Mn(II) bis(nitrate) complex **2**. ^{113}Cd NMR shifts are consistent with literature predictions for the types and numbers of coordinating ligands in complexes **3** and **4** in both NMR solvents.



1 M = Mn(II)
3 M = Cd(II)



2 M = Mn(II)
4 M = Cd(II)



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Keywords: Cadmium complexes; Macrocyclic ligand

1. Introduction

We have recently shown that Mn(II) complexes of 1,4,7,10,13-pentaazacyclopentadecanes are highly active functional mimics of the macromolecular human SOD enzymes [1]. Complex **1**, [Mn([15]aneN_5)Cl_2], catalyzes the dismutation of superoxide to oxygen and hydrogen peroxide with a k_{cat} value at pH$=7.4$ of $4.40(\pm 0.08)\times 10^7\mathrm{M}^{-1}\,\mathrm{s}^{-1}$. This class of macrocyclic Mn(II) complexes displays high kinetic stability toward dissociation and pronounced beneficial effects in animal models where tissue injury has been correlated with the overproduction of superoxide ion [2–8]. Our most recent work has focused on the development of a mechanistic paradigm for the conformational analysis of our more substituted catalysts as a function of the stereochemistry of the ligand system [9,10]. The goal is to use computer modeling along with experimental results to guide our synthetic and medicinal chemistry efforts for the concerted optimization of catalytic activity and complex stability.

As a starting point for this work we have reported the X-ray crystal structures of the parent complex **1** which crystallized as the seven-coordinate dichloro derivative [1] in comparison to the bis(nitrato) derivative **2** which crystallized in a ligand-folded form as the six-coordinate nitrato nitrate complex [9]. Our desire to study these species in solution by NMR spectroscopy prompted us to prepare the dichloro **3** and bis(nitrato) **4** Cd(II) analogues. ^{113}Cd NMR spectroscopy has been widely used as a probe of metal ion binding sites in molecules which range from metalloproteins to transition metal complexes [11–20]. In cases where the substitution of Cd for the metal ion of interest makes chemical sense, very interesting information can be obtained, as the ^{113}Cd chemical shift has been shown to be remarkably sensitive to the types of donor atoms, coordination number and geometry. The Cd(II) and Mn(II) ions possess filled and half-filled d-shells, respectively, and thus the coordination geometries of complexes **1–4** are not subject to ligand field effects [11,21]. While Cd(II) has a slightly larger ionic radius than Mn(II) [22], the structures of the dichloro complexes **1** and **3** and the bis(nitrato) complexes **2** and **4** are very similar in the solid state.

Herein we report our efforts to understand how macrocyclic ligand-folding in the solid state relates to the solution state, where catalysis takes place, and describe two new crystal structures, that of the dichlorocadmium(II) complex **3**, and the bis(nitrato)cadmium(II) complex **4**. In addition we report the solution ^{1}H, ^{13}C and ^{113}Cd NMR data for these new cadmium complexes and its relevance to the conformational tendencies of ligand **5**.

2. Experimental

2.1. General section

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer at resonance frequencies of 399.9 and 100.6 MHz, respectively. ^{113}Cd NMR spectra were recorded on the same spectrometer at 88.7 MHz. The ^{113}Cd chemical shifts are referenced to $CdSO_4$ in D_2O ($\delta = -3.0$). 1,4,7,10,13-Pentaazacyclopentadecane was prepared by a literature procedure [23].

2.2. Dichloro(1,4,7,10,13-pentaazacyclopentadecane)cadmium(II) (3)

A solution of 1,4,7,10,13-pentaazacyclopentadecane (2.0 g, 9.3 mmol) in methanol (50 ml) was treated with $CdCl_2$ (1.71 g, 9.3 mmol) and the mixture was heated to reflux for 2 h, allowed to cool to room temperature and concentrated. The residue was taken up into 1:1 ethanol/ethyl ether (20 ml), filtered through Celite and concentrated. Recrystallization from isopropyl alcohol/ether afforded 3.19 g (86% yield) of complex **3** as white single crystals suitable for X-ray crystallographic studies: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (ABq of doublets, $J = 10.4$, 3.2 Hz, $\Delta\nu = 17.5$ Hz, 2 H), 3.01 (d, $J = 12.4$ Hz, 2 H), 2.82–2.99 (complex m, 8 H), 2.72–2.81 (complex m, 2 H), 2.56–2.69 (complex m, 2 H), 2.51 (ABq, $J = 11.4$ Hz, 4 H), 2.39 (ABq of doublets, $J = 12.4$, 2.8 Hz, $\Delta\nu = 21.5$ Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.0, 47.8, 47.7, 47.0, 45. ^{113}Cd NMR (88.7 MHz, $CDCl_3$) δ 277. ^{113}Cd NMR (88.7 MHz, D_2O) δ 293. HRMS: m/z calculated for $C_{10}H_{25}N_5CdCl$, 364.0834; found 364.0864 $(M-Cl)^+$.

2.3. *Cadmium(II) 1,4,7,10,13-pentaazacyclopentadecane bis(nitrate)* **(4)**

To a mixture of $Cd(NO_3)_2 \cdot 4H_2O$ (2.87 g, 9.3 mmol) in methanol (50 ml) was added 1,4,7,10,13-pentaazacyclopentadecane (2.0 g, 9.3 mmol) and the reaction was heated at reflux for 3 h, cooled and concentrated. The residue was recrystallized from ethanol to afford 4.0 g (95% yield) of complex **4** as white needles (single crystals for X-ray crystallographic studies were obtained from aqueous ethanol): ^1H NMR (400 MHz, $CDCl_3$) δ 3.18–3.26 (complex m, 4 H), 3.18–2.98 (complex m, 4 H), 2.81–2.99 (complex m, 6 H), 2.81 (ABq of doublets, $J = 12.6$, 2.7 Hz, $\Delta\nu =$ 21.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.2, 48.1, 47.8, 47.3, 45.9. ^{113}Cd NMR (88.7 MHz, $CDCl_3$) δ 169. ^{113}Cd NMR (88.7 MHz, D_2O) δ 267.

2.4. *X-ray crystal structures*

Single crystals of $[Cd(C_{10}H_{25}N_5)Cl_2]$–$0.5H_2O$, **3**, are, at 20 °C, monoclinic, space group $C2/c - C^6_{2h}$ (No. 15) with $\boldsymbol{a} = 22.165(5)$ Å, $\boldsymbol{b} = 11.439(3)$ Å, $\boldsymbol{c} = 14.6788(4)$ Å, $\beta = 118.75(2)°$, $V = 3262(2)$ Å^3 and $Z = 8$ [$d_{\text{calcd}} = 1.660$ g cm^{-3}; μ_a(Mo Kα) = 1.66 mm^{-1}]. A total of 3754 independent absorption-corrected reflections having 2Θ(Mo Kα) < 55.0° (the equivalent of 1.0 limiting Cu Kα spheres) were collected on a computer-controlled Nicolet autodiffractometer using full (1.00°-wide) ω scans and graphite-monochromated Mo Kα radiation. The structure was solved using "Direct Methods" techniques with the Siemens SHELXTL-PC software package as modified at Crystalytics Company. The resulting structural parameters have been refined to convergence [$\boldsymbol{R}_1$ (unweighted, based on F) = 0.026 for 2989 independent absorption-corrected reflections having 2Θ(Mo Kα) < 55.0° and $I > 3\sigma(I)$] using counter-weighted full-matrix least-squares techniques and a structural model which incorporated anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for all hydrogen atoms. Water molecule and amine hydrogen atoms (H_{1w}, H_{1n}, H_{2n}, H_{3n}, H_{4n} and H_{5n}) were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were fixed at idealized sp^3-hybridized positions using a C–H bond length of 0.96 Å and their isotropic thermal parameters were fixed at values 1.2 times the equivalent isotropic thermal parameter of the carbon atoms to which they are covalently bonded.

Single crystals of $[Cd(C_{10}H_{25}N_5)(ONO)_2][NO_3]$, **4**, are, at 20 °C, orthorhombic, space group $P2_12_12_1 - D^4_2$ (No. 19) with $\boldsymbol{a} = 9.627(2)$ Å, $\boldsymbol{b} = 12.858(2)$ Å, $\boldsymbol{c} =$ 14.003(2) Å, $V = 1733.3(6)$ Å^3 and $Z = 4$ [$d_{\text{calcd}} = 1.731$ g cm^{-3}; μ_a(Mo Kα) = 1.30 mm^{-1}]. A total of 2264 independent absorption-corrected reflections having 2Θ(Mo Kα) < 55.0° (the equivalent of 1.0 limiting Cu Kα spheres) were collected on a computer-controlled Nicolet autodiffractometer using full (1.00°-wide) ω scans and graphite-monochromated Mo Kα radiation. The structure was solved using "Direct Methods" techniques with the Siemens SHELXTL-PC software package as modified at Crystalytics Company. The resulting structural parameters have been refined to convergence [$\boldsymbol{R}_1$ (unweighted, based on F) = 0.028 for 1955 independent absorption-corrected reflections having 2Θ(Mo Kα) < 55.0° and $I > 3\sigma(I)$] using counter-weighted full-matrix least-squares techniques and a structural model which incorporated anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for all hydrogen atoms. Amine hydrogen atoms (H_{1n}, H_{2n}, H_{3n}, H_{4n} and H_{5n}) were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were fixed at idealized sp^3-hybridized positions using a C–H bond length of 0.96 Å and their isotropic thermal parameters were fixed at values 1.2 times the equivalent isotropic thermal parameter of the carbon atoms to which they are covalently bonded.

3. Results and discussion

3.1. *X-ray diffraction and crystal structures*

The dichloro Cd complex **3**, ([Cd([15]aneN$_5$)Cl$_2$], was shown by single-crystal X-ray diffraction to possess the *trans*-dichloro seven-coordinate structure (Fig. 1) analogous to that observed with the Mn(II) complex, **1**, of the same ligand [1]. The bis(nitrato) Cd complex **4**, (Cd([15]aneN$_5$)NO$_3$]NO$_3$), was shown by X-ray diffraction studies to possess a different coordination geometry, a six-coordinate pseudo-octahedral geometry similar to that observed for the corresponding bis(nitrato) Mn(II) analogue, **2** (Fig. 2) [9]. Some pertinent bond lengths and bond angles for these two new Cd complexes are listed in Tables 1 and 2, respectively. Additional supporting data (atomic coordinates, all bond lengths and bond angles, and anisotropic thermal parameters) are available from the authors and will be filed with the Cambridge Crystallographic Database.

The structure of the complex **3** is very similar to that of its Mn(II) analogue,

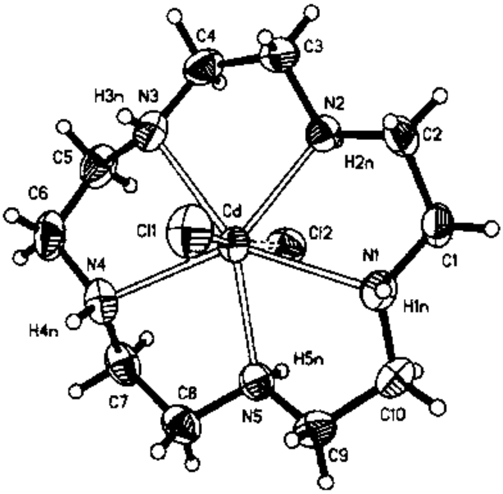

Fig. 1. ORTEP drawing of dichlorocomplex 3, showing the labeling scheme and the 50% probability ellipsoids for non-hydrogen atoms.

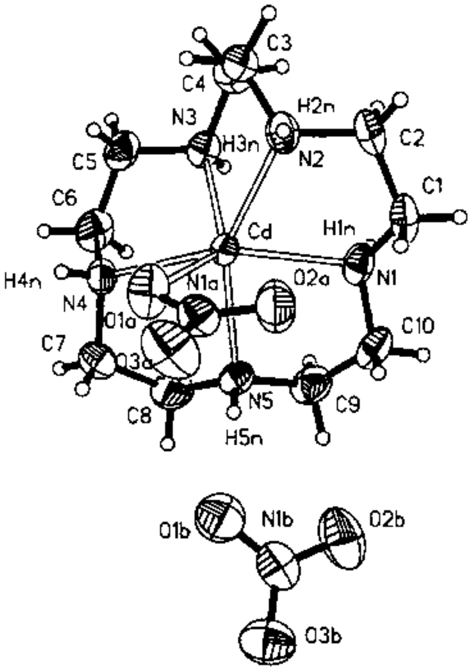

Fig. 2. ORTEP drawing for bis(nitrato) complex **4**, showing the labeling scheme and the 50% probability ellipsoids for non-hydrogen atoms.

Table 1
Selected bond lengths (Å) for complexes **3** and **4**

Complex **3**		Complex **4**	
Type[a]	Length[b]	Type[c]	Length[b]
Cd1–N1	2.484(2)	Cd–N1	2.359(5)
Cd–N2	2.349(3)	Cd–N2	2.327(6)
Cd–N3	2.413(3)	Cd–N3	2.402(5)
Cd–N4	2.450(3)	Cd–N4	2.339(5)
Cd–N5	2.359(3)	Cd–N5	2.350(5)
Cd–Cl$_1$	2.571(1)	Cd–O1a	2.409(4)
Cd–Cl$_2$	3.262(1)	Cd–O2a	2.866(5)

[a] Atoms labeled in agreement with Fig. 1.

[b] The numbers in parentheses are the estimated standard deviations in the last significant digit.

[c] Atoms labeled in agreement with Fig. 2.

although differences do arise owing to the inherently larger size of the Cd(II) ion relative to Mn(II). For example the Cd–Cl bond distances are 2.571 and 3.262 Å, whereas the Mn–Cl bond distances for the Mn(II) complex, **1**, are 2.56 and 2.63 Å. Similarly, the bis(nitrato) Cd complex, **4**, exhibits a longer metal–oxygen bond (2.409 Å) than that observed in the corresponding six-coordinate bis(nitrato) Mn(II)

Table 2
Selected bond angles (deg) for complexes **3** and **4**

Complex **3**		Complex **4**	
Type[a]	Angle[b]	Type[c]	Angle[b]
Cl1CdCl2	175.8(1)	N1CdO1a	127.9(2)
Cl1CdN1	88.2(1)	N2CdO1a	95.5(2)
Cl1CdN2	106.4(1)	N3CdO1a	132.1(2)
Cl1CdN3	95.3(1)	N4CdO1a	78.6(2)
Cl1CdN4	93.4(1)	N5CdO1a	92.3(2)
Cl1CdN5	113.9(1)		
Cl2CdN1	90.9(1)	N1CdN2	76.3(2)
Cl2CdN2	69.4(1)	N2CdN3	74.9(2)
Cl2CdN3	83.2(1)	N3CdN4	75.7(2)
Cl2CdN4	89.9(1)	N4CdN5	77.0(2)
Cl2CdN5	69.6(1)	N5CdN1	75.7(2)
N1CdN2	72.6(1)	N1CdN3	95.9(2)
N2CdN3	73.8(1)	N3CdN5	119.7(2)
N3CdN4	72.2910	N2CdN4	133.2(2)
N1CdN5	71.3(1)	N1CdN4	142.3(2)
N4CdN5	73.1(1)	N2CdN5	149.6(2)
	N1CdN3	145.8(1)	
	N1CdN4	141.6(1)	
	N2CdN4	141.9(1)	
	N2CdN5	123.8(1)	
	N3CdN5	135.4(1)	

[a] Atoms are labeled in agreement with Fig. 1.

[b] The numbers in parentheses are the estimated standard deviations in the last significant digit.

[c] Atoms are labeled in agreement with Fig. 2.

analogue, **2**, (2.222 Å). Even more indicative of the larger size of the Cd(II) ion are the observed bond lengths for the Cd–N bonds. The average Cd–N bond distance for the dichloro complex **3** is 2.411 Å compared to the 2.328 Å average value observed for the Mn(II) analogue, **1**. Similarly, the average Cd–N bond distance observed for the bis(nitrato) Cd complex, **4**, is 2.355 Å, while that of the Mn(II) analogue, **2**, is 2.283 Å. From these data it appears that the covalent radius of Cd(II) in this ligand framework is approximately 0.08–0.10 Å larger than Mn(II).

Another difference between the structures of the dichloro Cd complex, **3**, and that of the dichloro Mn(II) complex, **1**, which appears to be due to the larger size of Cd(II), is reflected in the degree to which the Cd(II) ion is out of the plane of the macrocyclic ring. The bond angle between the short chlorine (Cl_1) and the ring nitrogens is greater than in the Cd(II) analogue by several degrees. This is further reflected in the large elongation of the second Cd(II) chlorine bond to 3.26 Å. In any event, the average $\angle Cl_1MnN$ for **1** is about 91.6° while for the Cd(II) complex, **3**, this average angle is 99.4°.

Conformationally the structures of the Mn(II) and Cd(II) complexes are very similar, e.g. the NH pattern in all four complexes is identical in that the geometry of the N–H's relative to the plane of the macrocyclic ligand alternates so that the pattern is three N–H's on one side of the plane of the ring with two non-adjacent N–H's *cis* on the other side of the plane of the macrocyclic ring. An even more striking similarity in the structures of these complexes is observed for the structures of the six-coordinate bis(nitrato) complexes **2** and **4**. In these two complexes the coordination geometry can be specified by the five unique angles generated by the bound nitrato-O_{1a}–metal–nitrogen combination. For the Mn(II) complex, **2**, this set of five angles are 128.6°, 93.3°, 78.0°, 132° and 92.5°. For the corresponding Cd complex, **4**, the five $\angle$OMnN angles are virtually identical: 127.9°, 92.3°, 78.6°,132.1° and 95.5°. The same extent of folding of the macrocyclic ligand about these two spherically symmetric +2 metal ions indicates that the ligand itself dictates the magnitude and precise geometry of the folding in this pentaaza crown family of macrocyclic ligands.

3.2. ^{1}H and ^{13}C NMR studies

Complexes **1–4** are somewhat amphiphilic and are all readily soluble in either chloroform or water. The ^{13}C NMR spectra of complexes **3** and **4** in both D_2O and $CDCl_3$ at 25 °C are shown in Fig. 3. All spectra show five resonances which is consistent with the alternating N–H configuration observed in both crystal structures. A plane of symmetry, which bisects the one chelate ring with *syn* orientation of both N–H's, and the distal N–H (which is also on the same face of the macrocyclic framework), produces five different carbon atoms. The interesting feature of this series of spectra is that complexes **3** and **4** afford notably different 5 line patterns in $CDCl_3$. In the non-polar solvent $CDCl_3$, the ^{13}C NMR spectra suggest solution structures of **3** and **4** that are similar to their crystal structures (seven-coordinate pentagonal bipyramid with one long chloride bond for **3** and six-coordinate with an inner-sphere nitrato and an intimate ion-paired nitrate for **4**). This is in sharp contrast to the nearly identical spectra for **3** and **4** obtained in D_2O where solvolysis occurs and both complexes exist in very similar folded six-coordinate structures. It is also interesting to note that the chemical shift range decreases on going from dichloro complex **3** in $CDCl_3$ to bis(nitrate) complex **4** in $CDCl_3$ to **3** and **4** in D_2O. This trend is also indicative of the change from a seven-coordinate pentagonal bipyramidal structure in non-polar solvents to folded pseudo-octahedral structures in water. In the pentagonal bipyramidal structure of **3** in $CDCl_3$, macrocyclic ligand **5** rigidly occupies the equatorial plane which emphasizes the 5 distinct chemical shift environments. On going to D_2O, where solvolytic dissociation of axial ligands (with subsequent charge separation) is favorable, folded pseudo-octahedral structures in water predominate (which serve to average out chemical shift differences between ring carbons, thus narrowing the range).

The ^{1}H NMR spectra for **3** and **4** in D_2O and $CDCl_3$ are presented in Fig. 4. Once again in the $CDCl_3$, complexes **3** and **4** display distinctly different and somewhat complicated splitting patterns. The alternating NH pattern and plane of symmetry, as described above, generates pseudo-axial and pseudo-equatorial proton positions in each ethylenediamine bridge. Thus vicinal coupling is observed as well as geminal

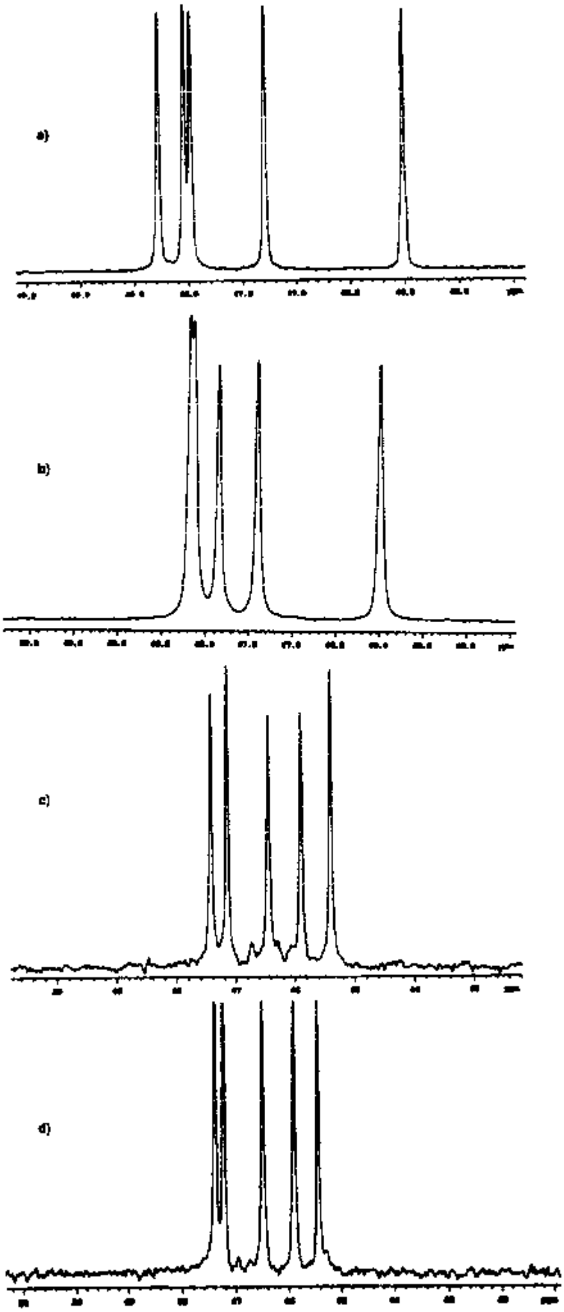

Fig. 3. ^{13}C NMR spectra of complexes **3** and **4**. (a) Dichloro complex **3** in $CDCl_3$. (b) Bis(nitrato) complex **4** in $CDCl_3$. (c) Complex **3** in D_2O. (d) Complex **4** in D_2O.

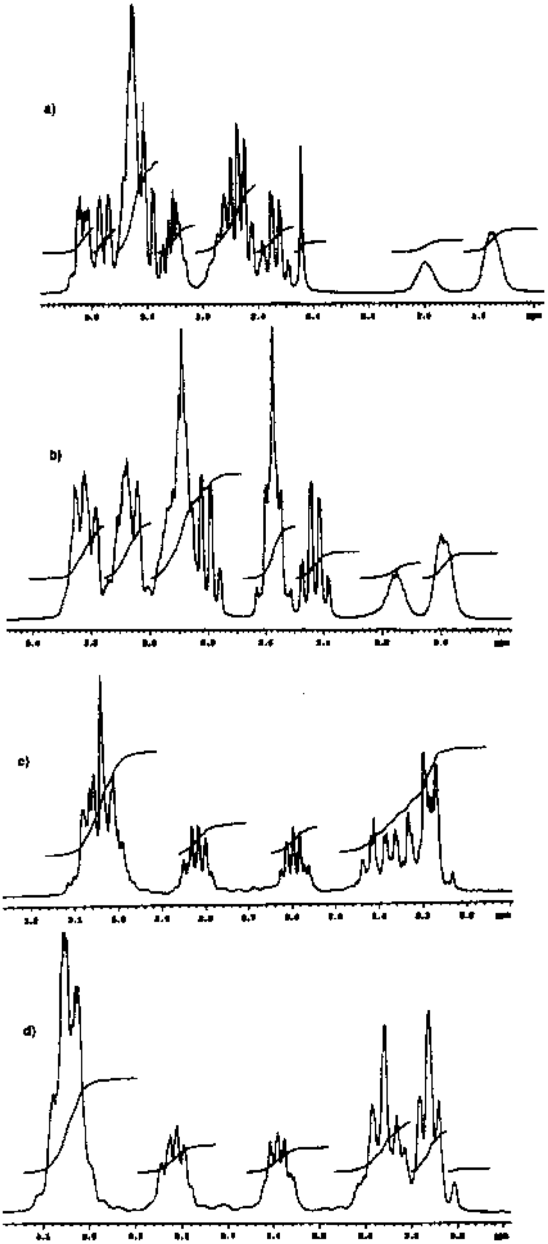

Fig. 4. ^1H NMR spectra of complexes **3** and **4**. (a) Dichloro complex in **3** in $CDCl_3$. (b) Bis(nitrato) complex **4** in $CDCl_3$. (c) Dichloro complex **3** in D_2O. (d) Dichloro complex **4** in D_2O.

AB systems for certain individual methylenes. Upon going to D_2O, very similar and significantly simplified spectra are afforded.

3.3. ^{113}Cd NMR studies

Because ^{113}Cd has received so much attention as an NMR metallobioprobe, in addition to many studies reported for coordination complexes of Cd and organocadmium species, there is a wealth of information in the literature regarding the relationship of chemical shift versus ligand environment [11–20]. Cadmium chemical shifts are dependent upon the type and number of ligands, as well as the geometry of the complex, but are not significantly affected by outer-sphere ligands (e.g. bulk solvent, spectator ions) [13,14]. Ligand dependent ^{113}Cd chemical shift trends, specifically those ligands of interest to this work, appear in Table 3. The ^{113}Cd chemical shifts of complexes **3** and **4** in $CDCl_3$ and D_2O are presented in Table 4 and may be interpreted as follows. The dichloro complex **3** in $CDCl_3$ affords a ^{113}Cd shift of 277 ppm. If one assumes that this is the shift for the seven-coordinate pentagonal bipyramidal structure, then it is possible to calculate remarkably accurate chemical shifts of the other three proposed species given the trend information in Table 3. For example, if the pentagonal bipyramidal form of **3** is represented as $LCdCl_2$ (where L = ligand **5**), then we calculate the chemical shift of complex **4** in $CDCl_3$ as the proposed six-coordinate nitrato (nitrate) by subtraction of 25 ppm for loss of the first chloride, subtraction of 85 for loss of the second chloride, subtraction of 50 ppm for addition of an inner-sphere nitrato and addition of 50 ppm for loss

Table 3
Ligand chemical shift trends

Ligand	Shift, δ (ppm)	Notes	Ref.
H_2O	+50		[15]
NO_3^-	−50		[16–19]
Cl^-	+85	First addition	[18]
	+25	Second addition	
Aliphatic amines	75p+51s+31t−50	"p" represents primary amines "s" represents secondary amines "t" represents tertiary amines	[15,16]
Coordination number	−50	Increase in coordination number	[20]

Table 4
^{113}Cd chemical shifts

Complex	δ (ppm) ^{113}Cd ($CDCl_3$)[a]	δ (ppm) ^{113}Cd (D_2O)[a]
3	277	293
4	169	267

[a] Spectra acquired at a concentration of 0.1N at 25 °C.

of 1 coordination site on going from seven to six-coordinate. As summarized in Eq. (1)

$$\mathrm{LCdCl_2} - \mathrm{Cl}^- - \mathrm{Cl}^- + \mathrm{NO_3^-} - 1 \text{ coordination} \tag{1}$$

$$277 - 25 - 85 - 50 + 50 = 167 \text{ ppm calc. [169 ppm experimental } (1\%\Delta)]$$

the chemical shift for complex **4** in $CDCl_3$ was calculated to be 167 ppm and we observed a shift of 169 ppm experimentally. Furthermore, the shift of complex **3** in D_2O can be calculated from its shift in $CDCl_3$ as described in Eq. (2). This is done by subtraction of 25 ppm for loss of the first chloride and addition of 50 ppm for loss of a

$$\mathrm{LCdCl_2} - \mathrm{Cl}^- - 1 \text{ coordination} \tag{2}$$

$$277 - 25 + 50 = 302 \text{ ppm calc. [293 ppm experimental } (3\%\Delta)]$$

coordination site on going from seven-coordinate in $CDCl_3$ to six-coordinate pseudo-octahedral in D_2O. And finally for the sake of consistency, one can calculate the shift of complex **4** in D_2O once again from complex **3** in $CDCl_3$ as described in Eq. (3).

$$\mathrm{LCdCl_2} - \mathrm{Cl}^- - \mathrm{Cl}^- + \mathrm{H_2O} - 1 \text{ coordination} \tag{3}$$

$$277 - 25 - 85 + 50 + 50 = 267 \text{ ppm calc. [267 ppm experiment } (0\%\Delta)]$$

Subtraction of 25 ppm for loss of the first chloride from $LCdCl_2$, followed by subtraction of 85 for loss of the second chloride, addition of 50 ppm for an inner-sphere water and addition of 50 ppm for loss of a coordination site. The calculated values are remarkably consistent with experiment and further reinforce our analysis of the solution speciation of cadmium complexes **3** and **4**.

In conclusion, the X-ray crystal structures of cadmium(II) complexes **3** and **4** are remarkably similar to the manganese (II) complexes **1** and **2**, respectively. The only differences arise from the larger covalent radius of cadmium, which is manifested in longer metal–Cl and metal–N bond distances and a greater displacement out of the plane of the macrocycle relative to the manganese complexes. The dichloro complexes **1** and **3**, and bis(nitrato) complexes **2** and **4** are conformationally analogous with respect to the ligand system. The alternating N–H stereochemistry is preserved in the cadmium structures relative to the manganese structures and the folding pattern of the six-coordinate bis(nitrato) complexes **2** and **4** is very similar. We believe that folding of the ligand system to afford six-coordinate structures similar to **2** is important in the catalytic SOD mechanism [9,10].

Recently, we have presented evidence that two pathways exist for catalytic dismutation of superoxide ion by manganese(II) complexes such as **1** and **2** [9]. These are as follows: (1) hydrogen atom transfer from a bound water on Mn(II) to $HO_2^{\cdot}$ to yield a Mn(III) hydroxo intermediate and (2) the dissociative pathway in which superoxide anion binds as a ligand to a vacant coordination site on Mn(II) followed by protonation/oxidation to yield a Mn(III) hydroperoxo species.

Subsequent reduction of the intermediate Mn(III) with superoxide anion completes the catalytic cycle. The ability of the macrocyclic ligand to fold and adopt a pseudo-octahedral conformation around Mn(II) that is similar to the geometric requirements of the transient Mn(III) species provides for facile electron-transfer from Mn(II) to superoxide in the catalytic mechanism. Owing to the structural and conformational similarity of the related spherically symmetric cadmium(II) complexes within the pentaazacyclopentadecane ligand environment, which we have now established, it is possible that solution NMR analysis may provide additional insight concerning catalytically relevant conformational speciation.

In non-polar, non-hydrogen bonding solvents, such as $CDCl_3$, the structures of complexes **3** and **4** are similar to their structures determined by X-ray crystallography. Complex **3** is a seven-coordinate pentagonal bipyramid with two *trans*-axial chlorides and the macrocyclic ligand array occupying an expanded equatorial plane. The ^{113}Cd NMR supports this analysis and this is entirely analogous to the crystal structure of manganese complex **1** [1]. The structure of six-coordinate complex **4**, which lies somewhere between a pentagonal pyramid and a distorted octahedron, is also maintained in $CDCl_3$. The ^{113}Cd shift supports this six-coordinate structure with an inner-sphere nitrato. In water both complexes solvolyze to six-coordinate monocationic species and this process is driven by ligand folding. ^{1}H and ^{13}C NMR spectra of **3** and **4** in D_2O are almost identical supporting very similar solution structures. Under apparently slow exchange conditions with respect to a $Cd(L)^{2+} + Cl^- = [Cd(L)Cl]^+$ process, the ^{113}Cd shift at 25 °C in D_2O supports a six-coordinate structure for complex **3** with an inner-sphere chloride and a six-coordinate structure for complex **4** with an inner-sphere D_2O.

We have synthesized related pentaazacyclopentadecane ligand systems which have been designed to enhance or prevent this type folding through stereochemical interaction of carbon-substituent groups [9,10]. We believe that this study may lay the groundwork for further solution state conformational analysis of more highly substituted pentaazacyclopentadecane ligand systems on spherically symmetric divalent metal ions via ^{1}H, ^{13}C and ^{113}Cd NMR spectroscopy.

4. Supplementary data section

Crystallographic details for complexes 3 and **4** (including atomic coordinates, anisotropic thermal parameters, bond lengths and bond angles for non-hydrogen atoms) (23 pages) are available from the authors.

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