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ARTICLES

Direct Determination of NMR Correlation Times: Analysis of the Cd−CyDTA Complex by the Relaxation Rate Ratio Method

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The relaxation rate ratio method (RRR) has been used to calculate molecular correlation times, τ_c, from the ^{13}C and ^{113}Cd relaxation rates of cadmium−cyclohexanediamine tetraacetate (CyDTA). The ratio of spin−spin (R_2) relaxation rates to spin−lattice (R_1) relaxation rates (R_2/R_1) is used to determine the relative motion of specific nuclei within the Cd−CyDTA complex. Formation of the Cd−CyDTA complex results in an increase in the measured NMR rotational correlation times compared with the values obtained for the CyDTA ligand alone. ^{13}C chemical shifts, evidence of ^{113}Cd−^{14}N coupling and NMR rotational correlation times provide information concerning the geometry of the Cd−CyDTA complex. The NMR experimental results correlate with anhydrous, hydrated, and hydroxylated ab initio structures of the Cd−CyDTA complex.

Introduction

NMR relaxation measurements often provide useful information about the dynamics and structure of complex molecular systems in both liquid and solid phases. This information includes such properties as rotational correlation times, internuclear distances, and where appropriate, quadrupolar coupling constants. In particular, NMR rotational correlation times can be useful in studies of molecular complex formation. NMR rotational correlation times have been calculated using NOE measurements in the region of extreme narrowing ($\omega\tau \ll 1$). Investigators have also used low-temperature studies outside of the region of extreme narrowing ($\omega\tau > 1$), where the appropriate spectral density equation passes through a minimum and can be solved directly.[1,2] The term "extreme narrowing" is typically used to describe rapid molecular rotation (ps correlation times) which simplifies the rotational correlation equations ($\omega\tau_c \ll 1$, where $\omega = 2\pi\upsilon$ and τ_c = the effective correlation time). In theory, the rotational correlation time may be thought of as the time required for a molecule to rotate a distance of 1 rad. More accurately, the correlation time is the integral with respect to time from 0 to ∞ of the normalized autocorrelation function. The correlation equations that are useful to the investigator include those developed by Abragam and others that describe rotational molecular motion and its relationship with intramolecular events.[3−5] In particular, quadrupolar and dipolar relaxation can be directly related to rotational motion with the use of spherical harmonic functions. Solution of the resulting autocorrelation functions produces correlation time dependent spectral density functions at a set frequency, assuming exponential decay.[3−5c] The spectral density equations describe spin−lattice (longitudinal $= R_1 = 1/T_1$) and spin−spin (transverse $= R_2 = 1/T_2$) relaxation mechanisms that include dipole−dipole, chemical shift anisotropy, spin rotation and scalar and quadrupolar relaxation.

Despite the increased complexity of the spectral density functions, it is often more useful to investigate the region of

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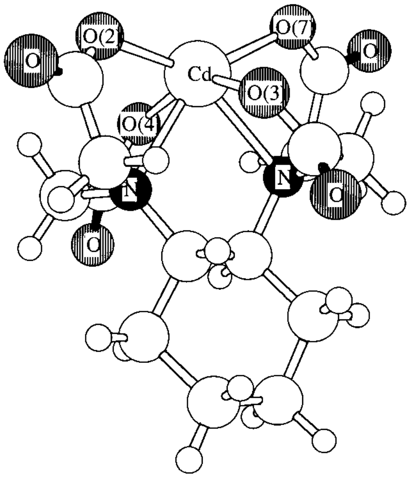

Figure 1. 321-G optimized structure of Cd−CyDTA^{2-} (GAUSSIAN 94).

reduced molecular motion outside the region of extreme narrowing ($\omega\tau > 1$), than to investigate the region of extreme narrowing ($\omega\tau \ll 1$). In particular, viscous solutions (i.e., proteins, nucleic acids, organometallic complexes, molten salts, etc.) provide an opportunity to determine NMR rotational correlation times using the NMR relaxation ratio method in both quadrupolar and dipolar relaxing systems.

A method for the calculation of NMR rotational correlation times that requires differing values of spin−lattice (longitudinal) and spin−spin (transverse) dipolar relaxation rates has recently been developed for the nuclei ^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{31}P, and ^{113}Cd at field strengths of 4.7, 6.35, 7.05, 9.4, 11.75, and 14.1 T.[6,7] In this study, ^{13}C and ^{113}Cd NMR relaxation rates are used to determine rotational correlation times of the metal−ligand complex, Cd−CYDTA (cadmium cyclohexanediamine tetraacetate), shown in Figure 1.

The monohydrate and OH^{-} liganded versions of Cd−CyDTA will be discussed in this report. Proposed structures and relaxation properties of the cadmium complexes of both CyDTA and its simpler precursor, EDTA, have been reported.[8−11] CyDTA and EDTA act as strong complexing agents of metal ions; however, this study indicates that cadmium−CyDTA complexes are stronger and more rigid than cadmium−EDTA complexes.

Experimental Section

Materials. The ligand, (±)-*trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid monohydrate (CyDTA), was purchased from the Aldrich Chemical Co. (Milwaukee, WI). Cadmium nitrate, certified ACS grade, was obtained from Fisher Scientific (Fair Lawn, NJ). Deuterated water (D_2O, 99.8% d) was purchased from Fluka (Buch, Switzerland). A capillary containing a 20% solution of dioxane in D_2O was used as a chemical shift reference for the ^{13}C spectra, and cadmium perchlorate (0.1 M), obtained from Aldrich, was used as the chemical shift reference in the ^{113}Cd spectra. The solution of CyDTA was prepared[11] by adding D_2O and NaOD (Isotec Inc.) to CyDTA until the ligand dissolved, achieving a final concentration of approximately 0.7 M and a pD of 6.3.

The cadmium complex was prepared by adding $Cd(NO_3)_2$ to the CyDTA solution, resulting in a concentration of approximately 0.7 M Cd−CyDTA with a slight excess of free ligand,[11] as indicated by the proton chemical shift data for these species. The resulting solution was adjusted to pD 6.3 with NaOD. The measured pH was corrected for the deuterium isotope effect using the relationship pD = pH + 0.4.[12]

The chemical shift D_2O reference solutions (20% dioxane and 0.1 M $Cd(ClO_4)_2$) were contained in sealed glass capillary tubes and placed in 5 mm NMR tubes containing solutions of either the CyDTA ligand or the Cd−CyDTA complex. The NMR tubes were triply degassed on a vacuum line to remove dissolved oxygen and sealed immediately with a torch.

Computational Methods. The GAUSSIAN 94 package[13] of programs was used to perform ab initio calculations on the VAX 4000 and the DEC 3000 Model 600/700 AXP systems at Wichita State University. The Cd−CyDTA structures were surveyed initially using the semiempirical MOPAC 6 program[14] and refined using ab initio methods. The semiempirical structures were used to compute a Z matrix for input into the GAUSSIAN programs for ab initio computations. For all structures, the 3-21G basis set was used. This basis set is resident in the GAUSSIAN 94 package.

NMR Chemical Shift and Relaxation Measurements. The ^{13}C and ^{113}Cd NMR experiments were carried out using a Bruker AM-500 MHz spectrometer equipped with a 5 mm broad band probe. All carbon FIDs were acquired with a spectral width of 31 250 Hz and 64k data points. Carbon chemical shifts are reported relative to the internal dioxane standard ^{13}C chemical shift value of 66.66 ppm. Longitudinal (spin−lattice) relaxation times, T_1's, were obtained using the inversion−recovery pulse sequence with delay times of 19 and 80 s for ^{13}C and ^{113}Cd, respectively. For the ^{13}C measurements, a set of 18 τ values ranging from 0.02 to 20 s was used for each T_1 measurement. At each τ value, 16 transients were coadded in order to achieve an adequate signal-to-noise ratio. A set of 10 values ranging from 0.5 to 20 s plus 30 s for τ^{∞} were used for the ^{113}Cd T_1 measurements, with 24 transients coadded at each value. The T_1 relaxation times were calculated using a nonlinear least-squares fit of the resulting data to a single exponential since no evidence of biexponential behavior was observed. Transverse, T_2 (spin−spin), relaxation times were determined from the peak widths at half-height ($\Delta\nu_{1/2} = 1/\pi T_2^*$, where $1/T_2^* = 1/T_2 + \gamma\Delta B_0/2$). The true T_2 relaxation times were calculated by correcting the measured T_2^* for magnetic field inhomogeneity using the T_2 of dioxane measured with the CPMG pulse sequence.

Results and Discussion

***Ab Initio* Structural Results.** *Molecular Structures of Cd−CyDTA Complexes.* Previous evidence suggests that water does not penetrate the inner coordination sphere of the Cd−CyDTA complex.[11] This is not the case for the crystal structure of the $Cd_3(EDTA)_2{\cdot}(H_2O)_6$ complex where the central cadmium ion is surrounded by water molecules.[15] However, the remaining two cadmium ions in $Cd_3(EDTA)_2{\cdot}(H_2O)_6$ maintain their inner coordination sphere with only a slight penetration by a single water molecule in each case.[15] As an alternative method of investigation, the ab initio (321-G) structures of the cadmium complex, Cd−CyDTA, its monohydrate, Cd−CyDTA·H_2O, and its hydroxylated form, Cd−CyDTA(OH)$^{-}$ were determined.

Molecular Structure of Cd−CyDTA^{2-}. The gas-phase structure of Cd−CyDTA (Figure 1) indicates both tight binding of the carboxyl groups and close proximity of the nitrogen atoms to cadmium as expected. Calculated cadmium−oxygen bond lengths are 2.214 (Cd−O(2)), 2.214 (Cd−O(7)), 2.327 (Cd−O(3)), and 2.328 Å (Cd−O(4)) and the cadmium−nitrogen distances are both 2.423 Å. The monohydrate of Cd−CyDTA is shown in Figure 2.

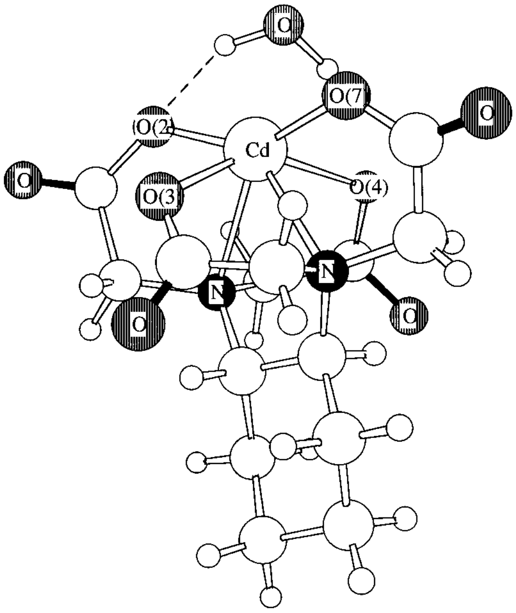

Figure 2. 321-G optimized structure of Cd−CyDTA·H_2O^{2-} (GAUSSIAN 94).

Molecular Structure of Cd−CyDTA·H_2O^{2-}. The addition of a water molecule to Cd−CyDTA results in only minor changes to the basic structure of the cadmium complex. The cadmium−oxygen bond lengths have lengthened slightly to 2.237 (Cd−O(7)), 2.302 (Cd−O(3)), 2.308 (Cd−O(2)), and 2.394 (Cd−O(4)) Å. The cadmium−nitrogen distances have also increased slightly to 2.469 (Cd−N(5)) and 2.509 (Cd−N(6)) Å. The cadmium−oxygen distance for water is 2.498 Å and the hydrogen(water)−oxygen distances are 1.74 (H(46)−O(2)) and 1.84 (H(45)−O(4)) Å. The combination of cadmium oxygen (water) interactions and hydrogen bonds between the water hydrogens and the carboxylate oxygens provide a strong stabilizing force for this hydrated complex. However, there is no ab initio evidence that water is able to penetrate the inner coordination sphere of the Cd−CyDTA complex. All attempts to add a second water of hydration to Cd−CyDTA were unsuccessful.

Molecular Structure of Cd−CyDTA·OH^{3-}. At high pHs, hydroxyl ion penetrates the inner coordination sphere of Cd−EDTA.[10] This result suggested a third calculation (Figure 3) in which the water of hydration is replaced by OH^-. Unlike the Cd−EDTA complex, where high pHs produce structural changes in the Cd complex,[10] the addition of a OH^- to Cd−CyDTA results in only minor changes to the basic structure of the cadmium complex. The cadmium−oxygen bond lengths are 2.595 (Cd−O(7)), 2.371 (Cd−O(3)), 2.408 (Cd−O(2)), and 2.432 (Cd−O(4)) Å. The cadmium−nitrogen distances have increased slightly to 2.683 (Cd−N(5)) and 2.680 (Cd−N(6)) Å. The cadmium−oxygen distance for Cd−OH^- is 2.130 Å and there is evidence of a hydrogen bond between the hydroxyl H(44) and O(7) (H(44)−O(7) distance is 2.31 Å) which is also bound to Cd. It is apparent from these three forms of Cd−CyDTA (Figures 1−3) that the tight binding between cadmium and CyDTA excludes the addition of water or OH^- to the inner coordination sphere of the Cd−CyDTA complex.

NMR Analysis of the Cd−CyDTA Complex. *NMR Chemical Shifts.* The ^{1}H and ^{13}C chemical shift data obtained for the CyDTA ligand and its Cd complex are given in Table 1. The proton chemical shift values are in agreement with those published previously for the CyDTA ligand[8] and the cadmium complex.[9] The carbon chemical shifts for Cd−CyDTA are similar to those published for the cadmium complex of EDTA.[10]

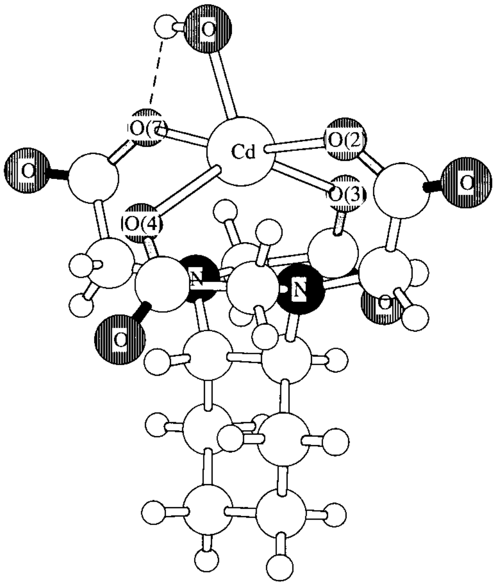

Figure 3. 321-G optimized structure of Cd−CyDTA·OH^{3-} (GAUSSIAN 94).

TABLE 1: ^{13}C and ^{1}H Chemical Shift Data for the CyDTA Ligand and the Cd−CyDTA Complex

group	^{13}C chemical shift	^{1}H chemical shift
	CyDTA Ligand	
CH_2 cyclohexane	23.56 ppm	1.272, 1.833 ppm
CH_2 cyclohexane	23.80	1.473, 2.146
CH_2 acetate	54.12	3.513, 3.795
CH methine	61.93	3.350
COO^-	174.03	
	Cd−CyDTA	
CH_2 cyclohexane	24.21	1.871, 1.273
CH_2 cyclohexane	24.55	2.202, 1.382
CH_2 acetate:axial	52.39	3.374, 3.169
CH_2 acetate:equatorial	56.81	3.535, 3.027
CH methine	60.92	2.589
COO^-	178.6, 178.4	

The ^{1}H and ^{13}C chemical shifts of individual species provide considerable information about the formation of the Cd−CyDTA complex. The CyDTA and Cd−CyDTA species have separate and distinct chemical shifts, indicating that any possible chemical exchange is slow on the NMR time scale. In particular, ^{1}H chemical shifts are used to indicate the formation of the Cd−CyDTA complex from CyDTA described in an earlier section.

In particular, the two ^{1}H resonances and the ^{13}C resonance of the ligand acetate groups undergo chemical shift changes and are doubled upon formation of the Cd−CyDTA complex. These results are supported by the ab initio calculations. As shown in Figures 1−3, the side chains of the ligand are quite rigid in the complex relative to their positions in the free ligand. In the complex (Figures 1−3), the acetate protons are axial and equatorial with respect to the plane of the nitrogen atoms and are nonequivalent, giving rise to resonances with distinct chemical shifts. The same situation occurs for the ^{13}C resonance of the carboxylate groups. The ^{13}C NMR spectrum of the CyDTA ligand contains only one CO_2^- resonance reflecting an averaged local environment for this group due to its greater mobility. However, as shown in Figures 1−3, the complex contains two distinct CO_2^- environments in which the carboxylate groups are oriented axially and equatorially with respect to the plane of the nitrogen atoms. Consequently, carboxylate groups in the Cd−CyDTA complex produce two resolved resonances in the ^{13}C NMR spectrum. This observation is in contrast to the single $^{13}CO_2^-$ resonance reported for the Cd−EDTA complex, with this difference again attributed to the greater lability of the EDTA complex.[10]

R_2/R_1 Ratios as Predictors of Relative Rotational Motion. The spectral density functions that describe intramolecular dipolar spin−spin (tranverse) relaxation rates contain a zero frequency spectral density term that is not present in the equations that describe intramolecular dipolar spin−lattice (longitudinal) relaxation rates for various nuclei. The inclusion of this term in addition to the evaluation of spherical harmonic functions effectively guarantee that intramolecular dipolar R_2/R_1 ratios are >1 outside the region of "extreme narrowing" (i.e., where $\omega\tau > 1$). Evaluation of these ratios[6,7] for various dipolar nuclei including ^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{31}P, and ^{113}Cd further establishes that as the intramolecular dipolar R_2/R_1 ratio increases, the rotational correlation time, τ_c, decreases. It is apparent that these ratios can be used to "map" relative motion within a given molecule or molecular complex.

Calculation of Rotational Correlation Times. The calculation of ^{13}C rotational correlation times, τ_c, from the ratio of nuclear spin−spin and spin−lattice relaxation rates ($R_2 = 1/T_2$, $R_1 = 1/T_1$) has been demonstrated in slightly viscous solutions.[6] This approach is applicable when either (a) dipolar relaxation is the major contributing relaxation mechanism (as is often the case with ^{1}H−^{1}H relaxation[16−19] and relaxation between directly bonded ^{13}C-^{1}H nuclei[20−25]) or (b) when the fraction of the dipolar contribution to the spin−lattice and spin−spin relaxation mechanisms is essentially the same for a specific nucleus. Previous studies[6,7] suggest that condition (b) is often the case, subject to the pitfalls of scalar relaxation and chemical exchange. In any case, the dipolar relaxation ratio equations have been solved by iterative methods, assuming a range of values for R_2/R_1. The solutions of these equations are represented by separate polynomials at various field strengths (eq 1).[6,7]

$$\tau_c(\text{ns}) = a_0 + a_1(R_2/R_1) + a_2(R_2/R_1)^2 + a_3(R_2/R_1)^3 + a_4(R_2/R_1)^4 \quad (1)$$

Knowledge of the above polynomial allows the investigator to determine rotational correlation times at a particular field strength from a limited number of measurements. Measurement of R_1 ($=1/T_1$) and R_2 ($=1/T_2$) values at a field strength of 11.75 T enables the calculation of molecular correlation times for the various resonances in the ^{13}C and ^{113}Cd spectra of both the free ligand and the Cd−CyDTA complex. These ^{13}C and ^{113}Cd rotational correlation times are given in Table 2, along with the values obtained for T_1 and T_2.

Comparison of R_2/R_1 Ratios. As indicated in a previous section, the R_2/R_1 ratios can be used to map the relative motion of nuclei within a given molecule. In the Cd−EDTA complex,[10] the ^{13}C R_2/R_1 ratios at 2.3 T increase from 1.74 to 8.80 (pH 6.55) and from 2.05 to 13.1 (pH 13.75) as one proceeds from CH_2 to CO_2^-. These values are comparable to ^{13}C R_2/R_1 ratios of 1.99, 2.15, 7.06, and 7.45 obtained for CH_2 acetate:equatorial, CH_2 acetate:axial, and carboxylate groups in the Cd−CyDTA complex (Table 2). The cyclohexane carbons in Cd−CyDTA have ^{13}C R_2/R_1 ratios of 1.45 and 1.32, consistent with their location furthest from the center of mass and their ability to undergo inversion.

CyDTA and Cd−CyDTA ^{13}C Rotational Correlation Times. Table 2 contains the ^{13}C rotational correlation times calculated for the CyDTA ligand from eq 1. As mentioned previously and indicated in Figures 1−3, the cyclohexane methylene carbons of CyDTA are not attached to other heavy atoms or groups of atoms and are more likely to undergo some inversion. The correlation times of the acetate methylene and carboxylate carbons are the longest, indicating a lesser degree of mobility when compared with the methylene carbons of the substituted cyclohexane.

TABLE 2: ^{13}C T_1, T_2, and Correlation Times for the CyDTA Ligand and the Cd−CyDTA Complex and ^{113}Cd T_1, T_2, and Correlation Times for the Cd−CyDTA Complex

group	^{13}C T_1	^{13}C T_2	correlation time
	CyDTA Ligand		
CH_2 cyclohexane	0.150 s	0.0927 s	1.1 ns
CH_2 cyclohexane	0.147	0.108	0.9
CH_2 acetate	0.170	0.0023	13
CH methine	0.313	0.131	1.8
COO^-	2.77	0.0401	13
	Cd−CyDTA		
CH_2 cyclohexane	0.135	0.0934	0.94
CH_2 cyclohexane	0.143	0.108	0.83
CH_2 acetate:axial	0.136	0.0633	1.6
CH_2 acetate:equatorial	0.161	0.0809	1.4
CH methine	0.262	0.0970	2.0
COO^-	1.82	0.244	4.3
	1.72		4.1

group	^{113}Cd T$_1$	^{113}Cd T$_2$	correlation time
^{113}Cd	4.8 s	0.025 s	26 ns[a]

[a] For an adjusted value, see text.

The values for the ^{13}C T$_1$ and T$_2$ relaxation times of the cyclohexane carbons in both the CyDTA free ligand and the Cd−CyDTA complex are similar to those of the Cd−EDTA complex.[10] The carboxylate ^{13}C T$_1$ values decrease in the order, free ligand > Cd−EDTA complex > Cd−CyDTA complex, suggesting that binding to Cd is strongest in the Cd−CyDTA complex. The ^{113}Cd T$_1$ and T$_2$ relaxation times measured for the Cd−CyDTA complex are considerably shorter than those reported for the cadmium complex of EDTA, consistent with Cd binding more tightly to CyDTA than to EDTA.

Cd−CyDTA ^{113}Cd Correlation Times. From the calculated structures for the cadmium complex (Figures 1−3), one would expect that the cadmium ion and its attached ligands occupy a center of both mass and motion, which it clearly does. The correlation time of ^{113}Cd in Cd−CyDTA may be considered as limiting the rotational motion of the complex. However, this correlation time is nearly 6 times that of the acetate carbons in Cd−CyDTA and is considerably longer than one might predict, in view of the close proximity of the carboxylate ^{13}C's to ^{113}Cd. This result is not consistent with the calculated structures shown in Figures 1−3 or with the evidence supporting the kinetic stability of metal−ligand bonding in the Cd−CyDTA complex. A more reasonable interpretation of the smaller carboxylate group rotational correlation times in the cadmium complex involves scalar coupling between quadrupolar ^{14}N and dipolar ^{113}Cd as discussed in the following sections.

^{113}Cd−^{14}N Interactions. Figure 4 contains the proton decoupled ^{113}Cd spectrum of Cd−CyDTA. The ^{113}Cd spectrum shows five lines which are somewhat broadened because of interaction with ^{14}N, a quadrupolar nucleus. The value of J (^{113}Cd−^{14}N) is 23.3 Hz and the line widths in Figure 4 indicate a scalar coupling between ^{113}Cd and the quadrupolar ^{14}N nucleus. As shown in Figures 1−3, the nitrogens in the calculated structures of Cd−CyDTA are close to the cadmium ion, with the nitrogen lone pairs providing the source of the ^{14}N−^{113}Cd interaction.

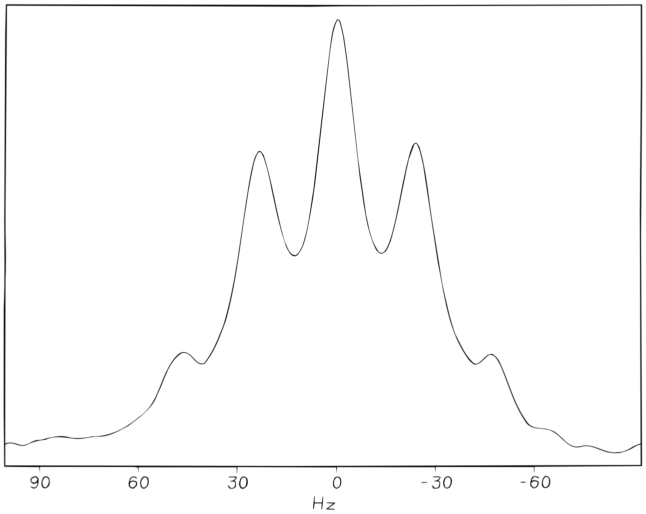

Figure 4. The ^{1}H decoupled ^{113}Cd Spectrum of Cd−CyDTA showing coupling to ^{14}N. The ^{113}Cd spectrum shows five lines which are broadened by scalar coupling with the quadrupolar ^{14}N nuclei. $J(^{113}\text{Cd}-^{14}\text{N})$ is 23.3 Hz.

Contribution of Scalar Coupling to ^{113}Cd T_2. The effect of scalar coupling with ^{14}N is to reduce the spin−spin relaxation time, T_2, such that the observed T_2 value is in the millisecond range, as given in Table 2 (T_2 for ^{113}Cd in Cd−CyDTA is 25 ms). Similar results are obtained for the Cd−EDTA complex,[10] where ^{113}Cd T_2 values obtained from ^{1}H decoupled ^{113}Cd spectra vary from approximately 100 to 160 ms (4.7 and 9.4 T) at pH < 11. There is no effect on ^{113}Cd T_1 in this case as the Larmor frequencies (^{113}Cd and ^{14}N) are sufficiently far apart.[4,26] Consequently, the measured ^{113}Cd spin−spin relaxation rate, R_2, is equal to the sum of the dipolar and scalar relaxation rates, while the ^{113}Cd spin−lattice relaxation rate, R_1, depends only on dipolar contributions to relaxation and is unaffected by the scalar interactions.[4]

$$R_2 = R_2^{\text{dipolar}} + R_2^{\text{scalar}} = 41\ \text{s}^{-1} \tag{2}$$

where $R_2^{\text{scalar}} = (4\pi^2 J^2_{\text{IS}}/3)(S)(S+1)T_2^{\text{S}}$; and $T_2^{\text{S}} = T_2$ of the faster relaxing nucleus, ^{14}N.[4]

In liquids, the contribution of ^{14}N scalar relaxation to spin $^{1}/_{2}$ nuclei is often small when compared with dipolar relaxation due to neighboring ^{1}H or ^{19}F nuclei because of the small magnetic moment of the ^{14}N nucleus.[27,28] However, an indication of the contribution of ^{14}N scalar relaxation to the spin−spin relaxation of ^{113}Cd in Cd−CyDTA is found in Figure 4, where the ^{113}Cd spectrum is consistent with significant scalar coupling between ^{113}Cd and ^{14}N nuclei from the CyDTA ligand.[28]

Calculation of an "Adjusted" ^{113}Cd Correlation Time. Typical values for ^{14}N T_2 relaxation times in ^{14}N bonded to methylene or methyl carbons vary from 1 to 4 ms.[28] The upper value for ^{14}N T_2 in the Cd−CyDTA complex is 3.0 ms, at which point all of the ^{113}Cd R_2 is scalar. Assuming an "average" value of 2.5 ms for T_2^{S} and using the experimental value of 23.3 MHz for J_{IS} results in a R_2^{scalar} value of 36 s^{-1}. This results in an "adjusted" value of 5.0 s^{-1} for R_2^{dipolar} and 0.020 s for ^{113}Cd T_2. The adjusted R_2/R_1 ratio of 24.1 produces (eq 1) a correlation time of 8.8 ns for ^{113}Cd in the Cd−CyDTA complex. This value of 8.8 ns is at best an approximate value; however, it is only twice the value of the carboxylate ^{13}C rotational correlation time and provides a reasonable fit with the other ^{13}C nuclei as well.

Decrease in ^{13}C Correlation Times. The rotational correlation times for the acetate CH_2 carbon atoms decrease from 13 ns in the CyDTA ligand to 1.6 and 1.4 ns for the Cd−CyDTA complex. The correlation times of the carboxylate carbons similarly decrease from 13 ns in the free ligand to 4.3 and 4.1 ns in the cadmium complex. This difference in correlation times may be explained on the basis that the correlation times of the carbon atoms in the complex no longer represent the rotational correlation time of the ligand. In fact, the rotational correlation times of the acetate CH_2 and carboxylate carbons are due to both rotation of the Cd-centered complex and the individual rotational motions of each carbon-containing group. The correlation times of these groups in the complex can be thought of as a sum of rates of rotational motion, or more simply,

$$1/\tau_{\text{COO}^-(\text{complex})} \approx 1/\tau_{\text{Cd(complex)}} + 1/\tau_{\text{COO}^-(\text{free})} \tag{3}$$

In the case of the carboxylate carbons, the correlation time calculated for the free ligand was 13 ns while the adjusted correlation time of the cadmium metal center of the complex is approximately 8.8 ns. Using eq 3, one calculates a correlation time for the carboxylate of the complex, $\tau_{\text{COO}-(\text{complex})}$, of 5.2 ns which may be compared with the values of 4.3 and 4.1 ns determined from our experimental results. Admittedly, there is no particular reason $\tau_{\text{COO}^-(\text{complex})}$ and $\tau_{\text{COO}^-(\text{free})}$ should be identical in view of the changes in the center of rotation that occurs upon formation of the cadmium complex. However, one would expect some similarity between $\tau_{\text{COO}^-(\text{complex})}$ and $\tau_{\text{COO}^-(\text{free})}$. Finally, the ^{13}C correlation times of the nuclei or groups involved in binding are expected to decrease in the metal complex compared with the free ligand (Table 2).

Conclusions

The relaxation rate ratio method[6,7] of calculating molecular correlation times, which requires only the measurement of T_1 and T_2 relaxation times, has been used here to calculate rotational correlation times for the metal−ligand complex Cd−CyDTA and its free ligand, CyDTA. Using these correlation times, one may conclude that cadmium and its attached carboxylate ligands occupy the center of mass and motion. It has also been shown here that the nitrogen atoms in Cd−CyDTA are in close proximity to the cadmium in the calculated structure. This is supported by the observed coupling between ^{113}Cd and ^{14}N as well as line-broadening effects that provide evidence for an interaction between the nitrogen lone pairs and the cadmium ion. Finally, the hypothesis that CyDTA−metal complexes are less labile than those of EDTA because of the absence of water in the inner coordination sphere is supported by the ab initio structures and rotational correlation times consistent with tight binding of carboxyl groups and the close proximity of nitrogen atoms to cadmium.

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