

CHAPTER 5

DISCUSSION

5.1 Acid Dissociation Constants

The pK_{a2} value determined for PDA, 3.46 ± 0.04 , disagrees with the values reported in the literature (Table 5.1). The value reported in the literature was fit with a diprotic acid model. The potentiometric data from this study was analyzed using both a diprotic model and a triprotic model of PDA to examine the effect on the second acid dissociation constant value. The first and second pK_a values of the triprotic model agree with values determined using the diprotic model within 2 standard deviations. The H_3PDA^{+1} molecule is a minor species under the conditions of the potentiometric study and so the inclusion of this proton results in only a minor change in the data fitting. The literature pK_{a2} value is similar to the value determined by 1H NMR titrations, 2.74 ± 0.24 , which is the average of the second and third acid dissociation constant values as discussed in section 4.1. PDA is an analog of iminodiacetic acid (IDA) which has three reported pK_a values (Table 5.2). The similarity between the acid dissociation constants of nitrilotriacetic acid (NTA) and its analog DPA, discussed in the following paragraph, would suggest that IDA and PDA should also have similar acidic behavior and would support the use of a triprotic model for PDA. The difference of pK_{a2} values of PDA and IDA is caused by the additional electron donating aliphatic groups of the piperidine ring¹⁰⁰.

The pK_{a1} and pK_{a3} values, 9.42 ± 0.05 and 1.4 ± 0.3 , respectively, determined for DPA are within 2 standard deviations of the values reported in the literature (Table 5.1). The pK_{a2} value of DPA determined in this study was slightly higher than the value reported in the literature, 2.98 ± 0.05 versus 2.71. The difference may be due to the ionic media of the two studies, potassium nitrate versus sodium perchlorate ionic of this work.

The acid dissociation constant values determined for CA, 10.75 ± 0.04 , 3.02 ± 0.06 and 1.3 ± 0.3 in 0.1 M sodium perchlorate, are within 2 standard deviations of the previously determined values (Table 5.1). A direct comparison is difficult due to the different ionic media and temperatures in the different studies. The pK_a values of dipicolinic acid (Table 5.2) are significantly different from those of CA despite the structural similarity. The pK_{a1} value of CA more closely resembles the value listed for 4-hydroxybenzene (Table 5.1), indicating that the acidity of the CA amine is strongly affected by the phenolic resonance form.

5.2 Lanthanide(III) Stability Constants

5.2.1 PDA

The stability constants of PDA and lanthanide(III) ions could not be determined from potentiometry as discussed previously in section 4.2. The values reported in the literature (Tables 5.3 and 5.4) indicate that a moderately strong complex forms with lanthanide(III) ions; these values are similar to the values reported for IDA, listed in Table 5.5. The discrepancies of the values from this work and those in the literature are discussed in section 5.8.1.

5.2.2 DPA

The previously determined lanthanide(III) stability constants of DPA are listed in Tables 5.3 and 5.4. The stability constants values of DPA have a similar trend across the lanthanide(III) series but a direct comparison of the values can not be made due to the different ionic strength and media. The first stability constants determined in this study are within 2 standard deviations of the reported values except for the values determined with La(III) at 0.5 M ionic strength. The second stability constants determined by this work tend to be slightly higher than the values from the literature. The nitrate ionic media of the literature study could compete with the ligand, lowering the value compared

to the value determined in a non-complexing ionic media. The stability constants of DPA are lower than the values reported for the coordination analog NTA (Table 5.5). The stability constants of DPA and NTA values tend to have a smaller difference as the ionic radius of the lanthanide(III) ion decreases. The lower stability constant values of DPA are a result of the piperidine ring structure which can undergo an inversion of the coordination site due to interchange of boat conformations similar to cyclohexane. This geometric transition of the piperidine is referred to as ring flip as discussed in section 1.4. The ring flip would invert the amine and cause a lengthening of the Ln-N bond, reducing the stability of the complex.

5.2.3 CA

The previously reported stability constant of CA with lanthanum(III) (Table 5.6) is significantly lower than the value reported in this study, (Tables 5.3 and 5.4). The very low ionic strength and the lack of experimental details of the previous study make further comparison difficult. For the reported set of values, the first and second stability constant values of CA ($\log \beta_1$ ranging from 6.92 ± 0.12 to 7.18 ± 0.15 and $\log \beta_2$ 14.24 ± 0.13 to 14.97 ± 0.07 across the lanthanide(III) series) are an order of magnitude lower than the values for dipicolinic acid, listed in Table 5.5. The non-aromatic piperidine ring structure of CA causes the amine to change the coordination site geometry as the nitrogen atom orbitals alternate from planar “sp²” character to nonplanar “sp³” character, discussed in section 1.4. The non-aromatic amine would not be expected to be planar and would alternate being above and below the plane of the ring. The non-aromatic amine rearrangement would also affect the position of the carboxylic acid groups, decreasing their planarity. The alternating nitrogen position should introduce a longer solution Ln-N coordination distance, while the alternating position of the coordination groups should displace additional water molecules around the inner hydration sphere of the lanthanide(III) ion upon coordination and slightly decrease the affinity of the ligand for the coordinated metal compared to dipicolinic acid^{66,101}. This agrees with results from the laser fluorescence of Eu(III) that indicate that the first complex of CA displaces more water molecules from the Eu(III) inner hydration sphere than the dipicolinic acid complex. CA also shows a decreased lanthanide(III) ion size dependency relative to the

variation of dipicolinic acid stability constants across the lanthanide series. The smaller size dependency may be explained by the longer Ln-N coordination bond, the alternating coordination group geometry and the slightly increased bite size of the CA coordination site due to the non-aromatic resonance form. The decreased stability constants can also be explained by a reorientation of the proton and coordination sites of the imino atom of the non-aromatic CA molecule, called nitrogen inversion. The nitrogen inversion inverts the tetrahedral orbital configuration of the imino atom and breaks the coordination bond until inversion occurs again or the ligand reorients to allow the lanthanide(III) ion access to the lone pair of electrons on the nitrogen atom. The nitrogen inversion would weaken the Ln-N coordination bond and decrease the stability of the complex compared to dipicolinic acid.

5.3 Calorimetry

5.3.1 Ligand Protonation

5.3.1.1 DPA

The values for the change in entropy and enthalpy for the first protonation of the free ligand for DPA, IDA and NTA at $25.000 \pm 0.001^\circ\text{C}$ and 0.5 M sodium perchlorate media are listed in Table 5.7. Comparison of IDA and NTA indicates that the change of enthalpy of protonation decreases with increasing size of the molecule. ^1H NMR experiments indicate that the DPA molecule adapts different conformations as the pH is varied as seen in the behavior of the peak corresponding to the protons in the para position, discussed in section 4.6.3. The proton is localized on the amine but can also be associated with one or more of the carboxy groups, either directly or through one or more water molecules. The added proton would change the hydration sphere around the amine site. This increase in the organization of the DPA molecule would result in a net increase of entropy as water molecules are released. The decrease of the ΔH observed in the series IDA, NTA and DPA may be related to a decreased polarity of the amine site caused by the presence of additional electron donating alkyl groups.

5.3.1.2 CA

The ΔH and ΔS values for the first protonation, listed in Table 5.7, of CA cannot be directly compared to dipicolinic acid due to the different functionality associated with

the first protonation of the molecules. The aromatic amine of dipicolinic acid is much more acidic than the phenol or the aliphatic amine of the CA tautomers as can be observed in the pK_{a1} values of dipicolinic acid and CA, 4.51 and 10.75 ± 0.04 , respectively. The first acid dissociation constant of CA is more similar to the aliphatic amine of NTA or the phenol of hydroxybenzene than to that of dipicolinic acid (Table 5.1). The ΔH and ΔS of protonation values, $-23.7 \text{ kJ mole}^{-1}$ and $127.3 \text{ J mole}^{-1} \text{ K}^{-1}$, are also more similar to the values reported for NTA or hydroxybenzene (Table 5.5). Both the potentiometry and calorimetry studies indicate that the first acid protonation constant corresponds to either the phenol or aliphatic structure of the CA tautomers.

5.3.2 Change of Enthalpy

5.3.2.1 PDA

The heat of complexation of PDA is below the limit of detection of the calorimeter used in these experiments. The low heat of complexation is due to the weak lanthanide(III)-PDA complex, observed in the inability to measure the stability constants by potentiometry.

5.3.2.2 DPA

The first DPA complexes of Ho(III) or Nd(III) have an endothermic change of enthalpy and a large, positive change in entropy ($11.5 \pm 2.9 \text{ kJ mole}^{-1}$ and $221 \pm 10 \text{ J mole}^{-1} \text{ K}^{-1}$ for Ho(III) and $11.8 \pm 3.0 \text{ kJ mole}^{-1}$ and $242 \pm 11 \text{ J mole}^{-1} \text{ K}^{-1}$ for Nd(III)), indicating that the complex formation is an entropy driven process. The second DPA complex with Ho(III) or Nd(III) forms with a small, endothermic ΔH and a large, positive ΔS ($0.6 \pm 3.1 \text{ kJ mole}^{-1}$ and $109 \pm 10 \text{ J mole}^{-1} \text{ K}^{-1}$ for Ho(III) and $1.0 \pm 3.3 \text{ kJ mole}^{-1}$ and $203 \pm 11 \text{ J mole}^{-1} \text{ K}^{-1}$ for Nd(III)). The complexes of NTA form with an exothermic ΔH except in the case of the Ho-NTA that has a slightly endothermic enthalpy (Table 5.6). Previous work has shown a trend relating the residual enthalpy, $\delta\Delta H$, of aminopolycarboxylate complexation of Nd(III) ions and the sum of the pK_a values of the amine functional groups of the ligand, Figure 5.1¹⁴. The $\delta\Delta H$ is a value corresponding to the amine-lanthanide(III) interaction and is calculated from ΔH . The values of $\delta\Delta H$ is calculated by:

$$\delta\Delta H = \Delta H - n 6.5 \text{ kJ mole}^{-1} \quad \text{Eq. 5.1}$$

complexation where n is the number of coordinating carboxylate groups and each carboxylate coordination is assumed to have a similar enthalpy change as an acetate coordination. The $\delta\Delta H$ value increases as the amine or amines of an aminopolycarboxylate have decreased acid character. The values of dipicolinic acid, IDA and N,N'-ethylenediaminediacetic acid (EDDA) show significant deviations from the $\delta\Delta H$ - $\Sigma pK_a(N)$ trend. The dipicolinic acid deviation has been explained by a shorter bond distance between the lanthanide(III) ion and the nitrogen atom due to the more polar nature of the aromatic amine⁴. The IDA and EDDA deviations are due to longer lanthanide(III) amine bond distances⁴. The DPA molecule does not have an imino site but can undergo a ring flip as discussed in section 5.2.2. The ring flip would cause the coordination site to fluctuate as the carboxy groups convert between axial and equatorial positions. Then ring flip could also induce a nitrogen inversion as the N-acetate group reorients to coordinate to the lanthanide(III) ion. If the carboxylate coordinations of DPA behave similarly to acetate coordination, then the lower $\delta\Delta H$ values of the Nd-DPA complex suggests that the Nd-N bond distance of the DPA complex is longer than the typical bond distance of the selected aminopolycarboxylate ligands. The apparent decreased Nd-N interaction of DPA can be related to the ring structure that restricts the geometry of the coordination site. The aminopolycarboxylate ligands included in Figure 5.1 are straight chain aliphatic molecules except α -picolinic acid, dipicolinic acid and trans-1,2-diaminocyclohexanetetraacetic acid (DCTA). DCTA does not have a cyclic structure involved in the molecular geometry of the acetate groups. Dipicolinic acid and α -picolinic acid also have ring structures directly attached to the carboxy groups but cannot be directly compared to DPA due to the aromatic nature of both the ring structure and the amine of these ligands. The carboxylic acid groups of DPA may have longer coordination bonds and weaker interactions with the lanthanide(III) ions than acetate due to restricted molecule geometry of the piperidine ring. If the carboxy coordinations are weaker, the method used to calculate $\delta\Delta H$ would not represent the Ln-N interaction and meaningful comparisons to other aminopolycarboxylate ligands cannot be made.

5.3.2.3 CA

The ΔH values determined in this study for Ho(III) and Nd(III) complexation with CA, $20.1 \pm 3.8 \text{ J mole}^{-1} \text{ K}^{-1}$ for Ho(III) and $14.7 \pm 3.8 \text{ J mole}^{-1} \text{ K}^{-1}$ for Nd(III), do not agree with the literature values listed in Table 5.6. The values are difficult to compare due to the different ionic strengths, 0.001 M versus 0.50 M. The change of enthalpy of CA also does not agree with the values reported for dipicolinic acid even though a tautomer of CA and dipicolinic acid have an identical coordination site. The dipicolinate complex formation reactions are exothermic while the CA complex formation reactions are endothermic. The ΔH of CA would be expected to be lower than dipicolinic acid due to the increased aliphatic nature of the amine which typically are less exothermic complexes formation reactions with lanthanide(III) ions. The increased ΔH of aromatic amine coordination has been explained by a decreased distance between the lanthanide(III) ion and the amine⁴ but there is not a significant difference in the Gd-N distance reported in the crystal structures of CA¹⁰² and dipicolinic acid¹⁰³. The average Gd-O bond of dipicolinic acid is slightly shorter than the Gd-O bond distance of CA, 2.395 \AA^6 versus 2.447 \AA^5 , and is caused by increased interligand repulsion of the $[\text{Gd}(\text{CA})_3]^{3-}$ species versus the $[\text{Gd}(\text{Hdipic})(\text{dipic})]^0$ species. The solid state bond distances may not represent the aqueous lanthanide(III) coordination distances as the complexes would be expected to fluctuate more in an aqueous environment. Assuming the carboxylic acid coordinations of dipicolinic acid and CA are similar, the low $\delta\Delta H$ of CA, Figure 5.1, must indicate an increased Ln-N bond distance. Unlike dipicolinic acid, CA has both a phenolic aromatic and a keto-diene resonance form^{2,3}. The imino group in the non-aromatic keto form of CA can undergo nitrogen inversion and can cause elongation of the Ln-N bond, discussed in section 5.2.3. The carboxylic acid groups of CA and dipicolinic acid may not coordinate similarly. The hybridization of the amine orbitals changes in these resonance forms from “sp²” in the aromatic form to “sp³” in the diene form. The geometry of the N bonds would change from a planar confirmation (“sp²” = trigonal planar) to a non-planar confirmation (“sp³” = tetrahedral) as discussed in 5.2.3. The tetrahedral imino alters the geometry of the carboxylic acid groups on the CA molecule and could cause them to reorient out of the plane of the molecule and change the interaction of the carboxy groups with the lanthanide(III) ion. The reoriented carboxy

coordinations may not be similar to acetate and so the $\delta\Delta H$ value would not represent a Ln-N interaction.

5.3.3 Change of Entropy

5.3.3.1 PDA

The heat of complexation of PDA is below the limit of detection of the calorimeter used in these experiments. The low heat of complexation is due to the weak lanthanide(III)-PDA complex, observed in the inability to measure the stability constants by potentiometry.

5.3.3.2 DPA

NTA and DPA have similar ΔS values for the formation of the first Ho(III) complexes while DPA has a larger change of entropy than NTA upon formation of the first Nd(III) species (Table 4.6 and 5.5). The ΔS value of the first complex between Nd(III) and a series of aminopolycarboxylate ligands has been shown to be related to the number of inner sphere water molecules displaced during by complexation, Figure 5.2¹⁴. The value for DPA fits the general trend of increased ΔS with increased number of carboxylate bonds but is slightly higher than other tricarboxylic acid aminopolycarboxylate ligands. The slightly larger ΔS values of the first complex of DPA versus NTA indicates that DPA displaces a larger number of water molecule than NTA upon coordination to Nd(III). This agrees with results from fluorescence experiments that noted increased water displacement from the Eu(III) inner hydration sphere upon coordination of DPA compared to NTA.

The additional water molecules are displaced by fluctuations of the coordination site caused by the piperidine ring flip. The ring flip causes reorientation of the carboxylate and amine coordinations.

The ΔS value of the second complex formation of DPA and NTA agree well for Ho(III). The second complex of Nd-DPA has a significantly higher ΔS value than the corresponding NTA complex, indicating that additional water molecules are displaced from the Nd(III) inner hydration sphere upon DPA complex formation. The increased dehydration of Nd(III) during the second complex formation is caused by the piperidine ring flip as discussed for the first complex formation. The significant difference between

the values of Nd(III) and Ho(III) are probably related the inter-ligand charge repulsion which would be greater for the smaller Ho(III) ion. The repulsion would increase the Ho-DPA coordination distances and so displace fewer inner sphere water molecules than the Nd(III) ion complex.

5.3.3.3 CA

The La-CA ΔS value, Table 4.7, does not agree with the value previously reported (Table 5.6), but comparison is difficult due to the different ionic strengths. The ΔS values of complex formation are larger for CA than those of dipicolinic acid but follow the same trend of increased entropy as the lanthanide(III) radii decrease³⁰. The ΔS value for the Nd-CA complex formation is higher than typical dicarboxylic acid aminopolycarboxylate ligands, shown in Figure 5.2. This indicates that CA displaces an additional water upon complex formation when compared to dipicolinic acid. This agrees with results from laser fluorescence which indicate that CA displaces additional water molecules from the Eu(III) inner coordination sphere compared to the number displaced by complexation by dipicolinic acid. The additional waters are displaced from the inner hydration sphere of the lanthanide(III) ions because CA has varying carboxy and amine coordination geometry due to the keto tautomer and possible nitrogen inversion, discussed in section 5.2.3.

The formation of the second complexes of Nd(III) and Ho(III) have ΔS values similar to the formation of the first complex and are much higher than the values observed with dipicolinic acid, Table 5.8. The fluorescence results indicate that a similar number of water molecules are displaced from the Eu(III) inner hydration sphere by the second complexation of both the CA and dipicolinic acid, discussed in section 5.5. The higher ΔS values for the second CA complex formation can be explained by additional reorganization caused by the phenol-keto functional group. Upon coordination, the deprotonated phenol would reorganize water molecules in the secondary lanthanide(III) hydration sphere as well as the primary phenol hydration sphere to stabilize the charge of the functional group. These additional displaced water molecules can contribute to both the first and second ΔS values for CA coordination.

5.4 Hypersensitivity Spectroscopy

5.4.1 PDA

The change in the oscillator strength caused by complexation of PDA was too weak to allow the determination of a P_{ML} value.

5.4.2 DPA

The values of the oscillator strengths determined in this study are listed in Table 4.10. Previously measured oscillator strengths of IDA, NTA, dipicolinic acid and CA are listed in Table 5.9. The oscillator strength of the Nd(III) and Ho(III) aquo ions are considered to have values of 9.68×10^{-6} and 6.12×10^{-6} , respectively⁵³. The oscillator strengths of the aquo ions determined in this study are within 2 or 3 standard deviations of these values.

The oscillator strength values determined for the first complexes of DPA are within 1 standard deviation of the values reported for the first complex of NTA, molecules with a similar coordination site. The P_{ML_2} of DPA are higher than those reported for NTA and are similar to the value seen for IDA. The reported oscillator strength values of NTA show similar values for the first and second complex, indicating that the formation of the ML_2 species significantly decreases the amount of covalent interaction between the ligands and the lanthanide(III) ion.

The plots of P versus $[L] : [M]$, Figures 4.1 and 4.2, have 3 distinct regions. The oscillator strength increases linearly with the concentration of the species, showing the formation of ML and ML_2 complexes. After the ML_2 species forms, the oscillator strength becomes constant, indicating that either any ML_3 species does not form in significant concentrations or that the covalency term of the ML_3 does not affect the hypersensitive transition as is observed with NTA⁵³. Since an ML_3 complex is not expected to form with the tetradentate DPA ligand, the lack of this species seem reasonable and confirms the coordination model used in stability constant determination.

5.4.3 CA

The P_{ML} values of CA determined in this work do not agree with the values found in the literature. The oscillator strength values of dipicolinic acid and IDA are much higher in the Devlin *et al.* and Stephens *et al.* studies compared to the values reported by Fellows *et al.* as listed in Table 5.9. It is not readily apparent why the dipicolinic acid

and IDA values of these studies have such large differences since similar values were determined for the aquo ions. Since the Devlin *et al.* and Stephens *et al.* studies were performed by the same scientific group but reported significantly different oscillator strength values for IDA and dipicolinic acid, use of these values for comparison seems unreliable. Most of the CA oscillator strengths agreed, within 1 standard deviation, with the values reported Fellows *et al.* for dipicolinic acid, a molecule with a similar coordination sites as CA. The value determined for Ho-CA was lower than the value reported for Ho-dipicolinic acid, 12.15 ± 0.21 versus 14.26. The value of the Ho-dipicolinic acid from Fellows *et al.* appears to be higher than would be expected as oscillator strengths of Nd(III) are higher than those of Ho(III) for oscillator strength values below 20 and may reflect an increased hypersensitivity between Ho(III) and dipicolinic acid^{52,53}.

The plots of P versus [L] : [M], Figures 4.1 and 4.2, have different profiles for Nd(III) and Ho(III). Figure 4.1 shows 3 regions with positive slope, indicating the formation of 3 different complexes with Nd(III) which are most probably ML, ML₂ and ML₃ species. Figure 4.2 has 2 regions with positive slope and one region of constant values, indicating that Ho(III) forms two complexes with CA and the third species either forms in low concentrations or that the covalency term of that species does not affect the hypersensitive transition as discussed with DPA in section 5.4.1. The different ML₃ profiles indicates that the size of the lanthanide(III) ion may prevent formation of the third CA complex due to increased steric crowding and inter-ligand charge repulsion.

5.5 Eu(III) Laser Fluorescence

5.5.1 PDA

The Eu(III) fluorescence peaks, coordination number of the ligand and the number of water molecules in the inner hydration sphere of the Eu(III) ion for the various species of this study and other ligands of interest are listed in Table 5.10. The number of water molecules was calculated assuming that the inner coordination sphere of the aquo Eu(III) ion is occupied by 9 water molecules^{89,104}. A single peak was observed at 17273 cm⁻¹ for PDA complexation throughout all studies including varying pH from 2 to 6 and from ligand to metal concentration ratios of 0.1 to 5. The peak position of the PDA

species is the same as the value reported for the first acetate complexation (Table 5.8). This indicates that PDA is forming only a weak complex through a single carboxylic acid which displaces a single water from the inner coordination sphere of the Eu(III) ion. The number of water molecules in the inner hydration sphere of the Eu(III) ion could not be determined because the PDA peak was too weak under all conditions.

5.5.2 DPA

The Eu(III) fluorescence spectra of the previously reported NTA complex was performed on solid material and so comparisons to solution systems have to be made with the consideration that the aqueous system has a less rigid coordination system in which the coordinated ligands can still rapidly exchange. The ML species of DPA exists in two different environments (Table 5.10). The first Eu-DPA environment has a similar peak position as NTA (Table 5.10). The number of water molecules in the inner hydration sphere of Eu(III) of DPA is slightly lower than the value reported for NTA and the ligand coordination number of DPA is slightly higher than the value reported for NTA. The difference in number of water molecules and ligand coordination number indicates that the DPA complex occupies a larger area in the inner coordination sphere of Eu(III) than the NTA complex due the piperidine ring flip. The ring flip would cause the carboxy and amine coordination groups to reorganize around the metal ion. This reorientation corresponds to the hump that was always observed on the peak of the first complex that represents the conversion from one ring form to another.

5.5.3 CA

The peak positions of the CA complexes with Eu(III), listed in Table 4.11, agree the values reported previously within 1 or 2 cm^{-1} (Table 5.8). The calculated ligand coordination number is within 1 standard deviation of the values reported in the literature. The peak positions values of dipicolinic acid from previous studies generally vary within 1 or 2 cm^{-1} . The ligand coordination numbers are similar to the values reported for CA. The first dipicolinic acid complex has a Eu(III) hydration number of 3.2, indicating that only 3 waters are displaced. The number of water molecules in the inner sphere of the Eu(III) ion are slightly lower than those predicted in the literature which assumed the tridentate CA molecule would displace 3 water molecules. The CA molecule displaced 4

to 5 water molecules upon forming the first complex due to the keto tautomer. As the molecule switches between the keto and phenol tautomers, the coordination sites would change geometric positions and additional water molecules are displaced. The second CA complex has an average of 3 water molecules displaced per ligand. The decrease in the number of displaced water molecules indicates that the CA molecules of the second complex have a slightly longer coordination bonds due to inter-ligand charge repulsion, causing each ligand to occupy a smaller area in the inner coordination sphere of the Eu(III) ion.

5.6 NMR

5.6.1 PDA

The ^1H NMR of Eu-PDA system was performed at varying pH and did not exhibit the shift in the peaks expected upon the complexation of the paramagnetic Eu(III) ion. Previous work has studied the lanthanide(III) complexes of dipicolinic acid¹⁰⁵ and CA¹⁰⁶ by NMR and PMR. Diamagnetic lanthanide(III) ion shift the position of the ^1H NMR peaks of the complexed ligands¹⁰⁷. This shift was not observed in the Eu-PDA system. Additionally, the PDA peaks did not show significant ^1H NMR peak broadening that would have been expected if the paramagnetic Eu(III) complexed the ligand¹⁷. This indicates that the Eu-PDA complex was only a minor species that was not detected by the NMR measurement.

5.6.2 DPA

The ^1H NMR spectra of La(III) and Lu(III) DPA complexes have very different (Appendix C). The La(III)-DPA spectrum has very broad peaks while the 1:1 and 1:2 Lu(III)-DPA spectra have sharp peaks that retain their multiplicity. The spectra of DPA and the 1:1 [Lu(III)]:[DPA] system had the same number of peaks but all peaks had different chemical shifts. The sharpness of the peaks indicates that Lu-DPA kinetics were faster than the NMR time scale. The broadness observed in the peaks of the 1:1 [La(III)]:[DPA] spectrum indicates that this complex is undergoing an equilibrium on the NMR time scale with the broad peaks representing the average of two or more systems. This suggests that DPA complex formation is sensitive to changes in the size of the lanthanide ion with larger lanthanide(III) ions having slower reaction rates. The 1:1

[La]:[DPA] system was studied temperatures as low as 5.0°C but the peaks remained coalesced. The equilibrium may be the DPA piperidine ring flip with the broad peaks representing the transition from one chair form of DPA to the other chair form, involving boat and twist boat configurations of the ring.

The ^1H NMR peaks of 1:2 [Lu]:[DPA] systems are sharp and retain their multiplicity but have peaks that are also in the 1:1 [Lu]:[DPA] systems as well as additional peaks. The similar peaks in the 1:1 and 1:2 [Lu]:[DPA] system indicates that one of the DPA ligands in the ML_2 complex is similar to the DPA in the ML species while the additional peaks in the 1:2 [Lu]:[DPA] system indicates that the second DPA ligand in the ML_2 species must be in a different coordination environment. The steric bulk and inter-ligand charge repulsion of the second complexed DPA must cause this molecule to have a different orientation around the metal ion.

5.6.3 CA

^{13}C NMR experiments were performed on CA as well as on the Ca complexes of La(III) and Lu(III). The ^{13}C NMR peaks of the carbon shifted slightly. The alkene and aromatic carbon peaks are located at similar chemical shift and any effects on the tautomer speciation of CA could not be discerned using this technique.

5.7 Crystallography

The crystal structure of CA has been previously determined⁷⁰. The molecule was observed as a monohydrate zwitterion with a protonated amine and a deprotonated carboxylic acid. The other carboxylic acid and the phenol were also protonated. The crystal structure of the Gd-CA complex¹⁰² has also been determined and shown to exist as a $\text{Na}_5\text{Gd}(\text{CA})_2(\text{HCA})$ complex with 16 waters of hydration. Two CA molecules are completely deprotonated while one complex has a phenolic hydrogen. The authors fail to mention how the hydrogen atom position was assigned and also state that the water molecules were disordered. The phenolic proton could be reassigned as a proton of a water molecule that was hydrogen bonded to the CA, linking the $\text{Eu}(\text{CA})_3$ units.

Several studies report coordination distances for metal ion and the amine and carboxy oxygen atoms for CA^{18,108} and dipicolinic acid^{20,109,110}. The coordination distances of $\text{Fe}(\text{III})\text{OH}(\text{L})$, when $\text{L} = \text{CA}$ or dipicolinic acid, have values that agree

within 2 standard deviations²⁰. The coordination distance of $[\text{Gd}(\text{H}_x\text{L})_3]^{-n}$ species, where $\text{L} = \text{CA}$ or dipicolinic acid, are slightly longer for the CA^{18} system than the values calculated for dipicolinic acid¹⁸. The Gd(III) coordination distances reported in [18] were calculated from data reported in [19]. Although errors are not reported for the dipicolinic acid values, the coordination distances probably agree within 2 standard deviation values. The bond lengths reported for $[\text{Ho}(\text{Hdpic})(\text{dipic})]$ species²¹ agree with the bond lengths reported for the $[\text{Gd}(\text{dipic})_3]^{2-}$ species¹⁹ within 0.5%. The CA ring structure is more strained than the dipicolinate ring, observed by a ~3% lengthening of the bonds to the carbon in the para position relative to the amine.

The crystal structures determined for PDA exhibited ~30% zwitterion behavior, calculated from the relative proton density as calculated by least square refinement where one carboxylic acid was founded to only account for ~70% of a proton. The DPA molecule was founded exclusively as the zwitterion with full deprotonation of a carboxylic acid group.

5.8 Conclusions

5.8.1 PDA

The acid dissociation constants determined by this work indicate that PDA is triprotic instead of a diprotic acid as reported in the literature^{63,64}. The results from this work strongly disagree with the results reported by Thompson⁶⁴ for the lanthanide(III) stability constants of PDA. The PDA of this study was identified as the cis form of the compound by diffractometry. The ligand of the previous study might be suspect as it was not synthesized by the author and was characterized using elemental analysis. All techniques used in this work reported weak, monodentate complexation of lanthanide(III) ions by PDA. The coordination structural analog, IDA, has first stability constants of ranging between $10^{5.31}$ to $10^{6.71}$ for the lanthanide(III) series. The dissimilarity in complex strength of IDA and PDA can be explained by the PDA piperidine ring flip that reorients the coordination site, preventing chelate formation. The imino atom of the PDA molecule would also have a nitrogen inversion during the ring flip that would destabilize and lengthen any Ln-N coordination bonds.

5.8.2 DPA

The acid dissociation constants and lanthanide(III) stability constants show good agreement with the values previously reported for DPA. The DPA stability constants increase as the size of the lanthanide(III) radii decrease for both the first and second complexes. The complex formation is entropy driven and displaces 5 and 8 water molecules as DPA coordinates in tetradentate fashion to form first and second complexes, respectively. The larger number of water molecules displaced by the first complex and the decreased lanthanide(III) complex stability can be explained by the DPA piperidine ring flip which would reorient the coordination groups, causing the coordination groups to displace additional water molecules from the inner coordination sphere of the metal ion. Larger lanthanide(III) ions appear to have slower ring reorientation as observed in ^1H NMR experiments, indicating that smaller lanthanide(III) ions are a better fit for the coordination site of DPA. The endothermic ΔH values also indicate that the average coordination distances may be longer than in straight chain aminopolycarboxylate ligands. The longer coordination distances would be caused by the coordination site reorientation caused by the piperidine ring flip. This ring flip reorientation kinetics may explain the improved the lanthanide(III) size selectivity of DPA compared to a straight chain molecule NTA.

5.8.3 CA

The acid dissociation constants show general agreement with those found in the literature. The CA stability constants are slightly lower and have less change across the lanthanide(III) series compared to dipicolinic acid. The formation of the first complex is entropy driven and displaces 4 to 5 water molecules from the inner hydration sphere. The additional water molecules displaced during the complexation of the first ligand can be explained by the keto tautomer that removes the planar geometry of both the amine and the carboxy groups. The formation of the second complex is entropy driven and each ligand displaces 3 water molecules from the inner hydration sphere. The size of the lanthanide(III) ion is important in the formation of the ML_3 species. The hypersensitive spectrum of Nd clearly indicates the formation of a ML_3 complex while this species is not observed for the Ho(III) system (Figure 4.1 and 4.2). The tautomer forms of CA appear

to create a larger, fluctuating coordination site that reduces the lanthanide(III) size selectivity compared to dipicolinic acid.

5.8.4 Steric Hindrance of Aminopolycarboxylic Ligands

5.8.4.1 Piperidine Ring

Aminopolycarboxylate ligands with carboxy groups directly attached to the piperidine ring appear to decrease the complexation stability. The ring flip of the piperidine ring can reorient the coordination groups. In the case of PDA, the ring flip dominates the lanthanide(III) coordination chemistry and reduces the ligand to the formation of very weak complexes similar to those observed with acetate. DPA forms stable complexes but displaces additional water molecules upon formation of the first complex compared to the coordination structure analog NTA. The additional displaced water molecules can be observed both by the decreased Eu(III) waters of hydration of the complex measured by fluorescence and the increased change of entropy of complex formation measured by calorimetry. DPA does not follow the trend of increasing $\delta\Delta H(N)$ with increasing $\Sigma pK_a(N)$ that has been noted for straight chain aliphatic aminopolycarboxylate ligands. The deviation from $\delta\Delta H(N)$ is most likely related to the piperidine ring flip that would weaken the carboxylate coordinations and the Ln-N coordination by increased coordination bond lengths, as observed in the change of enthalpy determined by calorimetry. NMR experiments indicate that the piperidine ring flip appears to be less significant for smaller lanthanide ions like Lu(III) and may be the cause of the increased size selectivity of DPA compared to NTA.

5.8.4.2 CA

The tautomerization of CA causes the lanthanide(III) complexes to be less stable than with dipicolinic acid. The non-aromatic tautomer introduces non-planar alignment of both the amine and the carboxylic acid groups. The fluctuation of the coordination sites causes additional water molecules to be displaced from the inner hydration sphere as observed in both number of waters in the inner coordination sphere of Eu(III) as determined by fluorescence and the change of entropy determined by calorimetry. The fluctuation of the coordination groups increases the lanthanide(III) coordination bond lengths as seen in the change of enthalpy determined by calorimetry. The size of the

lanthanide(III) ions appears to have more influence on the formation of ML_3 complex with CA than with dipicolinic acid due to the increased steric crowding caused by fluctuation of the coordinating groups of the CA molecule.

5.9 Future Work

The coordination bond lengths of PDA, DPA and CA appear to be longer due to effects caused by the ring structures. CA appears to have different coordination geometry in solution than in solid state. Experiments using EXAFS techniques could measure the coordination bond lengths and examine the CA geometry to confirm any differences from the values of the solid state materials. Synthesis of a methoxy form of chelidamic acid may eliminate the tautomerization and the resulting compounds should behave more similarly to dipicolinic acid. Although 5.0 °C NMR experiments were not able to resolve the coalesced La-DPA peaks, low temperature studies might give insight into the kinetics of the ring flip and the influence of the ring flip on the coordination chemistry of DPA and PDA. Ring structures could be incorporated into future ligand design if the enhanced size lanthanide(III) selectivity of DPA over NTA is related to the kinetics of the DPA piperidine ring flip. Additional studies of the lanthanide(III) coordination chemistry with ligands such as piperidine-2-carboxylic acid and 2-carboxypiperidine-N-acetic acid may establish trends in the thermodynamic values for structurally hindered aminopolycarboxylic ligands