ASSESSING MEDIUM EFFECTS IN TALSPEAK-LIKE SYSTEMS VIA CALORIMETRIC ENTROPY TITRATIONS

By

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A dissertation submitted in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

WASHINGTON STATE UNIVERSITY
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MAY 2017

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Acknowledgements

To properly thank everyone who has contributed to my success would probably double the length of this dissertation. First and foremost, I must thank Dr. Ken Nash for the opportunity to work in his lab, and the many lessons he has imparted to me. I would not be the scientist I am without his support, patience, and passion for teaching. I must thank the other members of my committee, Drs. Paul Benny, Zach Heiden, and Scot Wherland for their invaluable support and the opportunity to complete my work. The discussions I have had with each of them have improved me as a scientist, and expanded my view of the scientific enterprise.

I also have to thank both the current and former members of the Nash group for the laughs, the support, and the many insightful discussions. Dr. Jessica Drader introduced me to the Nash lab, and trained me in the proper use and inventory of radioactive materials. Dr. Nic Uhnak was always ready to listen to whatever scientific thoughts crossed my mind, no matter how outlandish. Dr. Ben Tokheim always had a smile, and offered me considerable advice as I was starting out in writing this dissertation.

Current members of the Nash group have kept me going, even when I most wanted to give up. I could not have succeeded without all their support. Dr. Joey Lapka provided invaluable assistance in interpreting the luminescence data, and offering alternative explanations for the results of my experiments with considerable patience. Ashleigh Kimberlin, Thibaut Martin, Ian Hobbs, and Guy Dutech have all provided encouragement, laughs, and many a fascinating discussion. I have to acknowledge the lab of Dr. Nathalie Wall, which allowed me to use several of their instruments for my work, and the input of Lindsey Neill and Kevin Swearingen who helped with the experiments and the data analysis.
I would be remiss in not mentioning the support of my family. My father Greg Berry has encouraged me in all my endeavors over the years, and has supported me when I’ve been down. My mother Beverly Cayford has been a source of encouragement and convinced me that I will be a success. My brothers Mark and David have offered encouragement for me to keep working hard, and to emulate them in their success. Shaun and Recie Tyson have opened their home to me and given me every opportunity to escape from Pullman when I needed one. Alan Tyson has given me pointers in how to use my computer to greatest effect, and grudgingly fixed my computer when I break it. And finally, Katherine Tyson has been with me through every step of the way, good times and bad. I never could have made it without you. You are my rock.
ASSESSING MEDIUM EFFECTS IN TALSPEAK-LIKE SYSTEMS VIA CALORIMETRIC ENTROPY TITRATIONS

Abstract

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This study investigated the application of calorimetric entropy titrations to the light lanthanides in TALSPEAK-like systems. Since TALSPEAK operates in an unusual ionic medium, this work was expanded to probe medium effects of the buffer by investigating three separate buffer systems. The work includes the determination of complexation of lactate with the light lanthanides at 2.0 M ionic strength, to provide internally consistent thermodynamic data for accurately modeling titration experiments. Luminescence titrations were conducted to validate the models for the titration experiments, and determine the stability constant for the metal-DTPA formation in these systems. Based on modeling using literature values, the reaction of DTPA with the lanthanides reaches an equilibrium with 80% of the metal complexed to DTPA in the 2.0 M total lactate and glycolate media under the specific conditions investigated. To corroborate these results, and predict changes in the hydration of the metal center in each of the buffers, luminescence lifetime measurements were conducted. These titrations suggest possible coordination modes for europium in these different media. Calorimetric entropy titrations were conducted to determine whether there are medium effects associated with the high concentrations
of the buffer. A model defining a 1:1 metal-DTPA complex was developed to calculate the enthalpy, stability constant, Gibbs energy and entropy in the different buffers under the same conditions of pH, ionic strength, and metal concentration. An alternative model accounting for competing complexation equilibria was developed to determine the stability constant for metal-DTPA complex formation comparable to literature in the buffer medium. Comparison of this value to literature suggests the light lanthanides exhibit an increase in the stability constant for the metal-DTPA complex in the buffer systems relative to the constants determined in 2.0 M sodium perchlorate. The work presented here suggests the potential benefit of calorimetric entropy titrations to study these complex systems. Calorimetry offers a new way to directly probe the influence of the medium in systems that could not be measured previously, due to limitations in other experimental techniques.
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Chapter 1

Introduction

Nuclear Energy

Due to increasing concern about global climate change and the environmental impacts from burning fossil fuels, there is a greater incentive to produce power by means that do not generate large quantities of greenhouse gases or other pollutants. This is a global concern, principally due to the rapid industrialization that is in progress in a number of developing nations. China and India have a particular interest in developing a high technology sector of the economy, and these enterprises are generally energy intensive. To support this objective, methods of power generation using indigenous technology and resources and a corresponding diversification of the energy sector have become a specific goal.\textsuperscript{1-3} Generating electricity via techniques such as wind and solar power, the staples of the green movement in the United States, are dependent on intermittent sources which limits their applicability for base-load power generation. Implementation of these energy sources requires significant research into energy storage technologies to supplement the base-load requirements during off-peak generation times. The sources of green energy that meet the needs for base-load power generation, particularly hydroelectric, depend on specific environmental conditions such as access to a river and geology favorable to the construction of a dam.

However, nuclear reactors are capable of producing power reliably and have proven to be a comparatively safe source of electrical energy.\textsuperscript{4} Nuclear power is also a mature technology with considerable experience in commercial application reducing the need for further research prior to implementation, though significant improvements have been made since the initial expansion of this technology. Most currently operating reactors are categorized as generation II
reactors, which are based on technology developed for commercial application in the late 1960s and early 1970s. Many of these reactor types require active cooling and operator intervention to maintain safe operation and generation of power. Since the initial development and expansion of commercial nuclear power, a series of advances in implementing passive safety systems, i.e. systems that would allow the reactor to shut down without any intervention from plant operators, have improved the safety and reliability of new reactors. The latest generation of reactors, classed as generation III and III+, are being built utilizing these evolutionary designs. Further research and development based on the experience gained through the years of reactor operation are leading toward implementation of even more advanced systems. The more advanced systems include multiple passive safety features and greater utilization of fuel resources, even using the spent fuel from earlier generations of reactors. These features suggest that expanding the use of nuclear power has significant potential to address the future power needs of both industrialized and developing societies. An additional benefit to the expansion of nuclear power is the ability to destroy excess nuclear weapons material that was produced by the United States and the Soviet Union during the Cold War. However, there are several issues that must be addressed if nuclear power is to be expanded. The most pressing of these problems is the final disposal of nuclear fuel after irradiation and discharge from a nuclear reactor.

The Nuclear Fuel Cycle

The nuclear fuel cycle describes the life of the constituents of the reactor fuel from mining through final disposal. The cycle can be divided into a front end, which describes the mining of uranium, enrichment if necessary, conversion to fuel rods, and power production, and the back end, which concerns the management of the fuel after discharge from the reactor. Because the majority of nuclear reactors in operation today utilize uranium oxide enriched to
2-5% in $^{235}\text{U}$ in fuel pellets, policies governing the front end of the fuel cycle are well established. The policies determining the back end of the fuel cycle, and the final management of spent nuclear fuel, generally fall into two categories – open fuel cycles and closed fuel cycles. In an open fuel cycle, after discharge from the reactor the spent nuclear fuel is allowed to cool thermally and radiolytically in a spent fuel pond, and the intact fuel elements are then directly sent to a geological repository. This is currently the policy of the majority of countries that utilize nuclear power, including the United States.

In a closed cycle, the fuel is allowed to cool in spent fuel ponds, the rod cladding is removed and the used fuel matrix (predominantly $\text{UO}_2$) is dissolved in acid. The uranium plutonium and other actinides are separated from the fission products and recycled back into fuel rods. The remaining components that cannot be reused are isolated and placed in a geological repository. There are several potential advantages to closing the fuel cycle, including: greater utilization of the uranium resources contained in the fuel, decreasing the volume of waste in the geological repository, reducing long term radiotoxicity and the need for extended isolation of the fuel, and reduction in the heat production of the waste. These advantages allow for greater predictability of the geological repository, and consequently greater confidence in the proper isolation of the most dangerous of the waste products. To accomplish this, the fuel needs to be separated into the active (i.e., fissionable) components, uranium and plutonium in particular, and the matrix elements as well as the fission fragments that are responsible for a decrease in the efficiency of the fuel.

**Handling and Processing of Nuclear Fuel**

In current thermal nuclear reactors, a fissile nucleus such as $^{235}\text{U}$ or $^{239}\text{Pu}$ will absorb a thermalized neutron and undergo fission. The reaction generates a substantial amount of energy
as well as two fission products and several additional neutrons that can sustain further fissioning.\textsuperscript{8} Several fission products, such as \textsuperscript{83}Kr (\(\sigma_\gamma 180\) b) or \textsuperscript{135}Xe (\(\sigma_\gamma 2,665,000\) b), have neutron absorbing characteristics that reduce the number of neutrons available for further nuclear reactions.\textsuperscript{11} To compensate for the decrease of available neutrons, a greater number of fissions is necessary to maintain the stable neutron flux in the reactor, leading to a buildup in the concentration of neutron absorbing nuclei. This is a well-established concern of using nuclear power; to compensate for the expected increase in neutron-absorbing fission products the amount of initial uranium loaded into the reactor is greater than is needed for criticality. The excess reactivity of the fuel is controlled either by adding rods containing neutron absorbing elements or neutron absorbing compounds to the neutron moderator. In any particular quantity of fuel, there is a finite amount of increased reactivity that can compensate for the loss of neutrons from fission products, which limits the amount of power that can be economically generated. The buildup of neutron capturing fission products is the reason that in the light water reactors used by the United States, the fuel is generally discharged from the reactor after approximately 18 months. Despite this increase in neutron poisons, upon discharge the fuel primarily consists of unused uranium (95\% of heavy metal) and plutonium (1\% of heavy metal), which can be further exploited for energy production after reprocessing. Upon the initial discharge, this fuel is transferred to a temporary storage pool where the fuel is actively cooled by circulating water and the short-lived radionuclides are allowed to decay. Following this cooling period of five to ten years, the fuel can be transferred to either a reprocessing plant or dry cask storage. During operation of the nuclear power plant, additional neutron activation reactions can occur in structural materials such as the steel pressure vessel, but they are not the dominant reactions of
concern in the spent nuclear fuel. Neutron capture in the actinide elements is the only other mechanism that will be discussed here.

In addition to fissioning, some of the elements present in the fuel capture neutrons and subsequently undergo decay into heavier actinides. A representative reaction, in which the predominant isotope of uranium present in the fuel, $^{238}\text{U}$, captures a thermal neutron and undergoes beta decay resulting in the isotope of neptunium $^{239}\text{Np}$ is shown in equation 1. This product can undergo further decays to $^{239}\text{Pu}$ which can also undergo fission, neutron capture, or decay. This results in both an increased energy yield and an increase in the concentration of heavier actinides.

$$^{238}_{92}\text{U} + ^{1}_{0}\text{th} \rightarrow ^{239}_{92}\text{U} \rightarrow ^{239}_{93}\text{Np} \quad (1)$$

It is these actinides, notably $^{237}\text{Np}$, $^{238,239,240,242}\text{Pu}$, $^{241,243}\text{Am}$, and $^{245,246,247,248}\text{Cm}$, that are the major contributors to the long-term (greater than 400 years) radiotoxicity of spent nuclear fuel as several of them have half-lives on the order of thousands to millions of years. Figure 1 shows the ingestion toxicity of one ton of used nuclear fuel versus time after discharge. The solid black line represents purely the fission products, while the individual dashed lines represent the differing amount of activity depending on the residual actinides in the fuel, assuming reprocessing removes the majority of the actinides. The line marked “total” refers to the activity, assuming there is no transmutation of the actinides present in the waste. The horizontal dashed line represents the reference activity of natural uranium in equilibrium with its daughter products. The activity of the actinides can be further reduced if they are either transmuted in a
specialized facility, or recycled back into power reactors of several different types to generate additional power.\textsuperscript{10,13,14}

Figure 1-1 Ingestion toxicity of one ton of used nuclear fuel. Reprinted from.\textsuperscript{13}

Figure 1 suggests that it may be desirable to remove and transmute the transuranium actinides that are the most significant contributors to the long-term activity of the spent nuclear fuel, while simultaneously reducing the total amount of high level nuclear waste. The reprocessing of nuclear fuel is complicated, however, as a consequence of the neutron capture and fission processes described above. Spent nuclear fuel contains elements from approximately one third of the periodic table, with isotopes representing every group and a range of chemistries.\textsuperscript{15} This severely complicates the process of separating the most radioactive compounds from those that can be disposed of as much lower hazard low level waste. Despite such a complex environment, methods for the isolation of plutonium and uranium from the rest of the fuel constituents have been developed and demonstrated on the industrial scale. Currently,
the dominant method for separation of complex mixtures such as these is through selective solvent extraction; advanced research for more complete recycling and waste minimization also focuses on solvent extraction methods.

**Solvent Extraction**

A solvent extraction process entails contacting two immiscible phases, generally a lighter organic phase containing a species-selective extractant molecule with an aqueous phase containing the compounds or metals of interest. Once the compound is extracted into the organic phase, the two phases are separated and the enriched organic phase is sent to additional processing, while the aqueous raffinate is either disposed of as waste or recycled to an earlier stage of the process. The enriched organic phase is contacted with a fresh aqueous phase that changes the conditions to back-extract, or strip, the compound of interest – in the current set of studies this is a metal ion. At this point, the metals in this process can then be converted into the form needed for either fuel fabrication or disposal, and the organic phase recycled for further processing of dissolved fuel. Equation 2 describes the distribution ratio, which describes the efficiency of isolating the metal, while equation 3 describes the separation factor between two metals. The bar over the symbol refers to the organic phase, while the absence indicates the concentration of the metal or volume is referring to the aqueous phase.

\[
D = \frac{[\text{Metal}]_o}{[\text{Metal}]_a} \cdot \frac{V}{V}
\]

(2)

\[
SF = \frac{D_{M1}}{D_{M2}}
\]

(3)
In the case of the closed nuclear fuel cycle, each of the individual stages of the process are solvent extraction steps, usually conducted using either centrifugal contactors or pulse columns, depending on the chemical kinetics of the reactions driving and/or limiting the phase transfer reaction. Those metals that have multiple accessible oxidation states, e.g., plutonium and uranium, are separated by means of controlling and changing on command these states. In the early stages of the PUREX process, the plutonium and uranium are in the hexavalent state, where they can be selectively extracted from the aqueous phase using TBP. Following the extraction, contact with a reducing agent changes the oxidation state to the non-extractable trivalent state, where the elements can be isolated. However, in the course of these separations the minor actinides Am and Cm follow the lanthanides through these stages, due to the similarity in chemistry between these groups. Because several of the high fission-yield lanthanides have such large thermal neutron capture cross sections, e.g. $^{149}\text{Sm}$ ($\sigma_\gamma 40,000$ b) or $^{157}\text{Gd}$ ($\sigma_\gamma 255,000$ b), the transmutation of the minor actinides requires separation from these elements as the final step in this process. A number of separation schemes have been developed to achieve the separation between the lanthanides and minor actinides. Among the earliest and most thoroughly developed of these is the Trivalent Actinide-Lanthanide Separations by Phosphorus reagent Extraction from Aqueous Komplexes (TALSPEAK) process.

**TALSPEAK**

Separating the lanthanides from the minor actinides americium and curium is necessary for the transmutation via neutron capture or fission to be an efficient process. The lanthanides are significant yield fission products, and consequently the concentrations of the lanthanides are large relative to the minor actinides in spent fuel. In addition, the large neutron capture cross sections of the lanthanides (particularly Sm, Eu, and Gd) significantly reduces the number of
neutrons available for transmutation resulting in a significant decrease in the efficiency of this process.\textsuperscript{8,11} Unfortunately, the separation of the minor actinides from the lanthanides is a very complex process because the two groups have very similar chemistry. Both groups are categorized as hard acids, have a single trivalent oxidation state in acidic solution, and have similar ionic radii.\textsuperscript{19} However, there is a slightly greater radial extension of the 5f/6d orbitals in the actinides relative to the lanthanides, which allows for a 5-8 percent increase in covalency in binding to molecules that contain softer donors, such as nitrogen.\textsuperscript{20,21} To effect a separation between the groups, Weaver and Kappelmann took advantage of this behavior when developing the TALSPEAK process.

Due to the chemical similarity of the lanthanides and actinides, the liquid cation exchanging extractant that was used for the TALSPEAK process, bis(2-ethylhexyl)phosphoric acid (HDEHP, Figure 1-2a), shows very little selectivity between the ions of the lanthanides and the minor actinides of similar ionic radius in the absence of a holdback reagent. To facilitate the group separation, the polyaminopolycarboxylate diethylenetriaminepentaacetic acid (DTPA, Figure 1-2c) was incorporated in the aqueous medium as an actinide-selective holdback reagent.\textsuperscript{15,18,22} The addition of the softer nitrogen in the holdback reagent improves the stability of the actinide complex relative to the lanthanides, and thus enables the separation between the 4f and 5f elements. The chemical equations governing the extraction reaction and the metal ligand complex formation reactions are represented in equations 3 and 4.\textsuperscript{23,24}

$$M^{3+} + 3(\text{HA})_{2} \rightleftharpoons M(\text{AHA})_{3} + 3H^{+}$$ (3)

$$M^{3+} + H_{3}\text{DTPA}^{2-} \rightleftharpoons M\text{DTPA}^{2-} + 3H^{+}$$ (4)
where the bar over the complex represents the species is in the organic phase, (HA)$_2$ represents HDEHP as a dimer, and M(AHA)$_3$ represents the extracted metal complex.$^{25}$ The cation exchanging ligand releases protons upon complexing the metal, and consequently may alter the pH of the aqueous phase. To minimize the change of pH, a carboxylic acid buffer was added.$^{18}$

The choice of carboxylic acid buffer, lactic acid (Figure 1-2b), was determined in a series of studies by Weaver and Kappelmann.$^{26}$ Several additional effects were found upon this significant modification of the aqueous phase, and will be discussed below.

![Chemical structures](image)

- **a.** bis-(2-ethylhexyl)phosphoric acid (HDEHP)
- **b.** 2-hydroxypropanoic acid (lactic acid)
- **c.** diethylenetriamine-N,N',N'',N'''-pentaacetic acid (DTPA)

Figure 1-2 Structures of the major components of TALSPEAK: a.) bis-(2-ethylhexyl)phosphoric acid (HDEHP), b.) 2-hydroxypropanoic acid (lactic acid), c.) diethylenetriamine-N,N',N'',N'''-pentaacetic acid (DTPA).

The series of carboxylic acids initially studied by Weaver and Kappelmann are shown in Table 1-1.$^{27}$ This particular study was conducted to examine the influence of the carboxylic acid on the distribution ratio of the metal, and therefore there was no additional holdback reagent.
Under the process conditions described, the most extracted actinide is californium while the least extracted lanthanide is neodymium. Californium is not a major contributor to the actinide inventory in unrecycled spent nuclear fuel, but neodymium is a high yield fission product with a moderate thermal neutron capture cross section \( ^{145}\text{Nd} \sigma_\gamma 45 \text{ b} \). For 1.0 M lactic acid, the value of the distribution ratio of Nd at pH 1.8 was 6.4, while at pH 3.0 the distribution ratio had a value of 22. This corresponds to a separation factor of 1.8 under the lower pH conditions, and 2.3 under the higher pH conditions. The larger the separation factor, the fewer process stages are needed to allow decontamination of one metal from the other. Based on the separation factors between the selected lanthanide and americium, there is little improvement with only the incorporation of a buffer. The choice of lactic acid as the carboxylic acid for the process is made more clear in the studies that incorporated DTPA as the actinide-selective holdback reagent (Table 1-2).
Table 1-1 Extraction of americium and lanthanides from various 1.0 M carboxylic acid solutions by 0.2 M HDEHP in 1,4-diisopropylbenzene (no DTPA present). Reproduced from.\textsuperscript{27} pK\textsubscript{a} values are at 1.0 M ionic strength, and were reproduced from the Martell and Smith database.\textsuperscript{28}

<table>
<thead>
<tr>
<th>Acid</th>
<th>pK\textsubscript{a}</th>
<th>Distribution coefficient for americium</th>
<th>La/Am</th>
<th>Ce/Am</th>
<th>Eu/Am</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(at pH 1.8)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formic</td>
<td>3.53</td>
<td>150</td>
<td>0.14</td>
<td>0.55</td>
<td>3.1</td>
</tr>
<tr>
<td>Acetic</td>
<td>4.55</td>
<td>33</td>
<td>0.24</td>
<td>1.0</td>
<td>6.7</td>
</tr>
<tr>
<td>Propionic</td>
<td>4.73</td>
<td>180</td>
<td>0.41</td>
<td>1.0</td>
<td>11</td>
</tr>
<tr>
<td>Glycolic</td>
<td>3.60</td>
<td>0.94</td>
<td>0.74</td>
<td>1.9</td>
<td>39</td>
</tr>
<tr>
<td>Diglycolic</td>
<td>2.82, 3.76</td>
<td>0.0025</td>
<td>4</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td><strong>Lactic*</strong></td>
<td><strong>3.62</strong></td>
<td><strong>3.5</strong></td>
<td><strong>1.2</strong></td>
<td><strong>2.1</strong></td>
<td><strong>27</strong></td>
</tr>
<tr>
<td>Tartaric</td>
<td>2.74, 3.69</td>
<td>0.16</td>
<td>1.1</td>
<td>2.8</td>
<td>45</td>
</tr>
<tr>
<td>Citric</td>
<td>2.79, 4.10, 5.23</td>
<td>0.36</td>
<td>0.9</td>
<td>2.4</td>
<td>45</td>
</tr>
<tr>
<td>Malonic</td>
<td>2.58, 5.05</td>
<td>20</td>
<td>0.31</td>
<td>1.1</td>
<td>10</td>
</tr>
<tr>
<td>α-Hydroxyisobutyric</td>
<td>3.78</td>
<td>18</td>
<td>0.7</td>
<td>1.4</td>
<td>6.3</td>
</tr>
<tr>
<td>Glycine-HNO\textsubscript{3}</td>
<td>2.44, 9.66</td>
<td>26</td>
<td>0.23</td>
<td>1.0</td>
<td>5.7</td>
</tr>
<tr>
<td><strong>(at pH 3.0)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycolic</td>
<td>3.60</td>
<td>1.9</td>
<td>4.6</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td><strong>Lactic*</strong></td>
<td><strong>3.62</strong></td>
<td><strong>9.4</strong></td>
<td><strong>5.4</strong></td>
<td><strong>48</strong></td>
<td></td>
</tr>
<tr>
<td>Citric</td>
<td>2.79, 4.10, 5.23</td>
<td>0.47</td>
<td>3.8</td>
<td>41</td>
<td></td>
</tr>
</tbody>
</table>

\*Note: D\textsubscript{Nd} was 6.4 at pH 1.8 and 22 at pH 3.0

As can be seen in Table 1-2, addition of both DTPA and the carboxylic acid buffers substantially improves the separation factor between the selected lanthanides and americium, which is used as representative of the actinide series. An additional feature of the incorporation of the carboxylic acid buffer is a change in the order of extractability (Figure 1-3).
Figure 1-3 Order of extractability of the lanthanides and actinides by HDEHP. $E^0_a$ is the distribution ratio for the respective metal. Conditions: Org: 0.3 M HDEHP in 1,4-diisopropylbenzene, Aq:1.0 M Na⁺/H⁺ lactate, 0.05 M DTPA, pH 3.0. Reprinted from.²⁷

At high concentrations of the lactic acid, the lanthanide that is least extracted (Nd) is not the same as the least extracted lanthanide from mineral acid solutions (La).²⁷ This is one of several influences of the carboxylic acid buffer that are poorly understood, though the origin of this particular effect is most likely due to the competition between the formation of metal-lactate complexes, and metal-DTPA complexes. As indicated in the speciation plots in Figure 1-4, when traversing the lanthanide series, the stability of the lactate metal complexes increases due to the predominantly ionic character of the bonding, while the DTPA complexes reach a maximum
stability around Gd.\textsuperscript{22} The speciation plot for americium is chosen as a representative actinide, and for comparison to those values in the tables.

Table 1-2 Extraction of americium and lanthanides from mixtures of DTPA and carboxylic acids. Organic phase: 0.2 M HDEHP in 1,4-diisopropylbenzene; Aqueous phase: 0.05 M DTPA in 1.0 M carboxylic acid at pH 3.0. Reprinted from.\textsuperscript{27}

<table>
<thead>
<tr>
<th>Acid</th>
<th>Distribution coefficient for americium</th>
<th>La/Am</th>
<th>Ce/Am</th>
<th>Eu/Am</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formic</td>
<td>0.0102</td>
<td>270</td>
<td>147</td>
<td>19</td>
</tr>
<tr>
<td>Acetic</td>
<td>0.0086</td>
<td>430</td>
<td>163</td>
<td>24</td>
</tr>
<tr>
<td>Propionic</td>
<td>0.0052</td>
<td>770</td>
<td>190</td>
<td>29</td>
</tr>
<tr>
<td>Butyric</td>
<td>0.0009</td>
<td>--</td>
<td>190</td>
<td>10</td>
</tr>
<tr>
<td>Glycolic</td>
<td>0.0124</td>
<td>145</td>
<td>97</td>
<td>84</td>
</tr>
<tr>
<td><strong>Lactic</strong></td>
<td><strong>0.0085</strong></td>
<td><strong>380</strong></td>
<td><strong>140</strong></td>
<td><strong>91</strong></td>
</tr>
<tr>
<td>Citric</td>
<td>0.0102</td>
<td>73</td>
<td>84</td>
<td>105</td>
</tr>
<tr>
<td>Malonic</td>
<td>0.0087</td>
<td>290</td>
<td>184</td>
<td>57</td>
</tr>
<tr>
<td>$\alpha$-Hydroxyisobutyric</td>
<td>0.0132</td>
<td>370</td>
<td>144</td>
<td>62</td>
</tr>
<tr>
<td>Glycine-HNO\textsubscript{3}</td>
<td>0.0111</td>
<td>270</td>
<td>144</td>
<td>16</td>
</tr>
</tbody>
</table>

Comparison of the separation factors in the presence and absence of DTPA indicates the need for the holdback reagent for an efficient process. However, a second factor that can be seen in Figure 1-4 is the pH dependence of the metal-DTPA complex formation. To maximize the formation of the actinide-holdback, while minimizing the formation of the lanthanide-holdback complex, pH 2 appears to be ideal. But, an additional consideration when studying these effects is the influence of pH on the extractant. Under low pH conditions, the equilibrium for the cation exchanging extractant molecule favors the protonation of the extractant, reducing the distribution of the metal into the organic phase. This suggests that a higher pH is preferable, reducing the number of contacts necessary to separate the metal species. To balance these competing factors,
and to run the process under conditions within the buffering capacity of lactic acid, Weaver and Kappelmann selected a pH of 3.0.\textsuperscript{27}

Figure 1-4 Representative TALSPEAK speciation diagrams. Conditions: 0.001 M metal, 1.0 M Na\textsuperscript{+}/H\textsuperscript{+} lactate, I = 2.0 M in sodium nitrate, 0.05 M DTPA. Lanthanide stability constants and protonation constants from.\textsuperscript{29} Am stability constants from.\textsuperscript{28}

The addition of lactic acid at moderate to high concentration has shown a variety of effects in the TALSPEAK process. In addition to providing buffering during the extraction
process, incorporating lactic acid resulted in: increased solubility of the DTPA, improved phase
disengagement kinetics between the organic and aqueous phase prior to phase separation,
substantial increase in the phase transfer kinetics in particular with respect to the heavy
lanthanides, and improved resistance to radiolysis. The ultimate origin of these effects is
not well understood at present, despite the significant number of studies that have been
conducted investigating these unexpected changes. While many of the characteristic
improvements upon addition of the carboxylic acid into the system are desirable, the system has
proven difficult to model accurately using the thermodynamic data found in literature. This
complicates the ability to address issues if the industrial process should encounter sub-optimal
operating conditions during implementation.

Developing a model to determine the extraction behavior for the TALSPEAK process
requires accounting for all of the species present in the system, as well as all of the equilibria that
can influence the distribution ratio for the metal. In this case, the species that influence the
extraction are the extracted metal species, identified by the equilibrium in equation 2, and any
species that acts as a holdback for the metal in the aqueous phase. Nilsson and Nash utilized the
following equilibria to develop the model that is represented in equation 8. Since the holdback
reagent is a polyprotic acid, competition with the hydrogen ion is factored into the equations.
This is represented by equation 5. A protonated metal complex has been reported for trivalent
metals and DTPA, which is represented by equation 6.

\[ M^{3+} + H_nR^{n-5} \rightleftharpoons MR^{2-} + nH^+ \]  

(5)

\[ M^{3+} + H_nR^{n-5} \rightleftharpoons MHR^- + (n - 1)H^+ \]  

(6)
where $M$ is the trivalent lanthanide or actinide, and $R$ indicates DTPA. These equilibria clearly show the pH dependence of the interaction between the DTPA and the metal. These two equilibria only refer to the interaction between the metal and the holdback reagent; however, there are additional interactions between the anionic form of the lactic acid and the metal in the aqueous phase, seen in Figure 1-4 and represented by equation 7.

$$M^{3+} + nL^- \rightleftharpoons ML_n^{3-n} \quad (7)$$

where $L^-$ refers to the lactate anion, and complexes for the 1:1, 1:2, and 1:3 metal:ligand have been reported.\textsuperscript{22} Combining equation 2 and 5-7 generates equation 8, which is the model that, combined with thermodynamic parameters taken from the literature, generated the solid-line trends seen in Figure 1-5.

$$D = \frac{[M(AHA)_3]}{[M^{3+}] + [ML^2+]+[ML_2^+] + [ML_3^3+] + [MR^{-2}] + [MHR^{-}]} \quad (8)$$

Attempts at modeling the distribution ratio of the metal with equation 8, and using the known thermodynamic parameters taken from the literature, indicate a predicted increase in the extraction at higher pH.\textsuperscript{35} This prediction is inconsistent with the results found in experiment.

The experimental results, as seen in Figure 1-5, predict an increase in extraction at higher pH values; clearly this is a different trend from the distribution ratios that are predicted by the model. Due to this clear deviation from the expected behavior, extensive studies have been
conducted to determine possible sources of these differences. An initial consideration was that the thermodynamic data used for the model may not be internally consistent, as the data were acquired by differing methods and research groups. Consequently, a new set of thermodynamic data were determined for the conditions in TALSPEAK.\textsuperscript{29,35} Alternative sources for the deviations were explored, such as the formation of a less-extractable ternary complex in the organic phase, or formation of a stronger ternary complex in the aqueous phase between the basic form of the buffer and the metal species.\textsuperscript{34,36–39} Despite this significant research the studies concluded that, while the formation of these species is possible, the expected concentration of competing species is not sufficient to completely explain the results. Due to the continued resistance of classical TALSPEAK to thermodynamic modeling, more advanced forms of the TALSPEAK process have been developed.

Figure 1-5 Distribution ratios of americium, lanthanum, neodymium and europium as a function of p[H$^+$]. Aqueous phase: 1 M Na$^+$, 1 M Lactic acid, 0.05 M DTPA, 1 mM (total) Ln + Y; Organic phase: 0.5 M HDEHP in 1,4-DIPB, extractions were carried out at room temperature. The lines in the figure were calculated using equation 8 and the relevant stability constants were used from.\textsuperscript{28} Reprinted from.\textsuperscript{35}
An alternative approach, beyond attempting to determine why deviations occurred in the original TALSPEAK process, looked into modifying TALSPEAK into a system that could be modeled accurately.\textsuperscript{40} These advanced TALSPEAK studies made changes to various components of the system, such as switching the organic phase extractant to a more basic extractant, pairing this extractant with an alternative aqueous holdback reagent, and modifying the aqueous phase buffer.\textsuperscript{38,40–43} The advanced TALSPEAK systems incorporating the changes noted above have proven much more amenable to modeling using a combination of thermodynamic values taken from the literature and equation 8, suggesting a fundamental difference between advanced TALSPEAK and its conventional sibling.

The simplest modification of the TALSPEAK system changed the acidic cation exchanging extractant from HDEHP to the more basic (2-ethylhexyl)phosphonic acid mono(2-ethylhexyl) ester (HEH[EHP], Figure 1-6a), reasoning that the more basic extractant was less likely to extract compounds that compete with the metal of interest, such as water, sodium ions, or lactic acid.\textsuperscript{40}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{advanced_talspeak_modifications.png}
\caption{Advanced TALSPEAK modifications. a.) Extractant (2-ethylhexyl)phosphonic acid mono(2-ethylhexyl) ester (HEH[EHP]), b.) holdback reagent N-(2-hydroxyethyl)ethylenediamine-N,N',N'-triacetic acid (HEDTA)}
\end{figure}

The new extractant does allow the model to predict the behavior of the system accurately, but the increase in basicity of HEH[EHP] corresponds with a weakening of the extractant resulting in a
decrease in the distribution ratio. To maintain reasonable distribution ratios in a separation step requires changes to the aqueous phase holdback as well. The initial choice for the holdback reagent in this pairing was the substitution of the pentadentate N-(2-hydroxyethyl)ethylenediamine-N,N’,N’-triacetic acid (HEDTA, Figure 1-6b) for the DTPA in traditional TALSPEAK. This resulted in a flat pH profile over the range that was tested, and the experimental data are in agreement with the model calculations made using equation 8. The extraction of sodium ion, water, and lactic acid into the organic phase in the HEH[EHP] containing system is considerably suppressed relative to the HDEHP containing system. However, the incorporation of a pentadentate ligand does not completely saturate the coordination environment of either the lanthanides or the actinides in the aqueous phase. One aspect of this is the possible formation of additional ternary complexes in the aqueous phase, which also must be accounted for in the course of modeling the system. Ternary complexes between the metal, buffer, and complexant have been observed in studies of at least one form of the advanced TALSPEAK system. In addition to the modification of the extractant and the holdback reagent, changes to the buffer offer some opportunities to operate the process under more acidic conditions, where the behavior is more predictable and modification of the aqueous raffinate from previous stages of the process (e.g. PUREX) is less necessary.

As noted in the tables above, Weaver and Kappelmann explored a wide variety of carboxylic acids, and tested the separation factors between the lanthanides and Am using DTPA over a range of pH values. When DTPA is the aqueous holdback reagent, the separation factor improved significantly as the pH value increased, leading the authors to suggest operating at a pH of approximately 3.0. This is optimized for the balance between extractant and DTPA holdback, and also governs the choice of buffer used in the process. Since the Advanced
TALSPEAK processes have changed both the holdback reagent and the extractant, there is an opportunity to optimize the system at a lower pH, which has the advantage of reducing the amount of solvent conditioning between the preceding steps of the PUREX process and the TALSPEAK process. To operate at a lower pH, an alternative buffer is needed, as the buffering window for lactic acid ($pK_a = 3.60$) extends from approximately 2.6 to 4.6 pH units.\textsuperscript{41,45,48} The advanced TALSPEAK systems substitute both the buffer, and the lower-denticity holdback reagent HEDTA. A consequence of this is the possibility of ternary complexes between the metal, holdback reagent, and the buffer in the aqueous phase. The effect of ternary complexes may be advantageous from the perspective of binding kinetics, but requires further study to determine how these interactions can improve the system. Determining all of the interactions in a system as complex as this is very difficult, and attempting a new method for direct determination of process applicable thermodynamic parameters lead to the project presented here.

**Scope of the work**

Investigating the thermodynamics of systems as complex as TALSPEAK can be accomplished by separating the components into aqueous phase chemistry, organic phase chemistry, and the partitioning process. Subsequently, the system is broken further into the component species, such as individual protonation enthalpies and complexation stability constants. This is the classic approach to modeling of systems, and potentially offers benefits to address problems as they arise in operation of the system. One consequence of this analytical method for a system with as many species and individual compounds as TALSPEAK, is the possibility of neglecting interactions that may occur between components of the system, such as differences in the solvation interactions. Directly probing these medium effects is challenging, but has potentially large impacts on process operation. However, isothermal titration calorimetry
offers the potential to determine the aqueous phase thermodynamics directly, including all aqueous phase components in solution in a single experiment. Preliminary studies of the aqueous phase components using isothermal titration calorimetry have been conducted by Travis Grimes and Gabriel Johnson in the Nash group. These results suggested some possible changes to the characteristics of the aqueous phase, as well as the utility of calorimetry for studying these reactions, and were the origin of the work reported here.

In the course of this project, the reaction-specific enthalpy and stability constant of the aqueous phase complexation between DTPA and the early lanthanides in an environment representative of the TALSPEAK process was investigated primarily by isothermal titration calorimetry. The combination of these data allow direct determination of the conditional entropy for these reactions, which is potentially useful in formulating and implementing the final process. There were some unforeseen complications with utilizing the technique for the later lanthanides, which limited the studies to those of lanthanum through europium. As these are the lanthanides that have the highest fission yield, this is not a limitation to applying this technique to further development of the TALSPEAK or advanced TALSPEAK processes. In addition, three separate carboxylic acid buffers were studied for insights into traditional TALSPEAK, as well as potential future forms of this process using modified buffers.

These studies were to determine the conditional enthalpy, conditional Gibbs free energy via direct determination of the stability constant of the complex in high concentrations of the buffer, and the conditional entropy of the formation of these complexes. The combination of these data can provide insight into the nature of the complexes, as well as information directly applicable to process implementation. Additionally, a model that takes into account all competing equilibria which allows determination of the reaction-independent stability constants
was developed and applied to the lactate and glycolate systems. To determine the conditions in which calorimetry will provide the most useful data, some initial modeling studies were conducted, and the stability constants of the lanthanides with the lactate were determined using potentiometry for the purposes of a complete set of consistent thermodynamic data. These data were combined with the previously determined protonation constants and stability constants determined by Travis Grimes for the purposes of modeling.\(^{29}\)

An additional question that has arisen in the course of similar experiments is whether the complex that is formed in the TALSPEAK aqueous phase is exclusively a 1:1 complex between the metal and DTPA, or whether ternary metal complexes may participate in the behavior of these solutions.\(^{49,50}\) To determine whether there are more species than the 1:1 complex forming in the course of these experiments, luminescence titrations were performed under conditions similar to the calorimetric studies using europium as a representative lanthanide. The method required using a lower concentration of lanthanide to prevent saturation of the photomultiplier tubes in the instrument, and the concentration of the DTPA was altered accordingly. The total concentration of the buffer was held at either 1.0 M or 2.0 M in all cases, and the pH was fixed at the same value as in the calorimetry experiments. These studies suggest that the only contributing species to the solution are those predicted by the modeling: the initial metal-buffer complexes, and the metal-DTPA complex forming during the course of the titration.

As was noted earlier, several of the advanced TALSPEAK systems utilize different buffer systems in an attempt to improve the performance of the system. This gave rise to the variation of the buffer systems studied here, with interest in the lactate system as the prototypical TALSPEAK system, and a simpler carboxylic acid, glycolate, and the more complex carboxylic acid, malonate. These two were selected as indicative of possible other coordination behaviors,
as well as potential future application. Glycolate, being the simplest α-hydroxy acid, provides some interesting clues into the influence of the structure on the thermodynamics of the complexes, and how this related to the more complex lactic acid. Malonate, while not an α-hydroxy acid, was selected as representative of the possible future directions of the TALSPEAK system. For the sake of comparison between all the data sets, the conditions of pH and ionic strength were maintained as constant between each buffer system, ensuring the speciation of the DTPA and the terminal metal-DTPA complex remains the same across each system that was studied.
References


Weaver, B.; Kappelmann, F. A. TALSPEAK: A New Method of Separating Americium and Curium from the Lanthanides by Extraction from an Aqueous Solution of an Aminopolyacetic Acid Complex with a Monoacidic Organophosphate or Phosphonate; ORNL 3559; Oak Ridge National Laboratory: Oak Ridge, TN (United States), 1964.


Chapter 2

Application of Calorimetric Entropy Titrations for Determination of $\Delta G$, $\Delta H$, and $\Delta S$ in Lactate-containing TALSPEAK-like Systems

Abstract

The high concentration of the lactic acid buffer that must be used in the conventional TALSPEAK process as a phase-transfer catalyst and pH-control buffer could have an adverse impact on the reliability of thermodynamic modeling predictions of process performance. The 0.5 M to 2.0 M concentration of a pH 3.5 lactate solution in the aqueous phase constitutes a very unconventional ionic medium. As a result, thermodynamic data from the literature used to predict the thermodynamics of the complexation and ligand protonation reactions occurring in the solution may provide totally inadequate speciation predictions. Common techniques used to study the effects of the medium on important reactions, such as absorption spectroscopy or potentiometry, are of limited utility when applied to the lanthanides in systems as complex as the TALSPEAK medium. In the present work, the stability constants of the lanthanides with lactate are determined at 2.0 M ionic strength in sodium nitrate by potentiometry for accurate modeling of titration simulations. This was followed by determination of the stability constant for the formation of the metal-holdback reagent complex in the TALSPEAK system in two high-lactate media aqueous solutions via luminescence spectroscopy. Finally, a new method for the determination of the stability constants and enthalpies, calorimetric entropy titrations, is applied to the overall system. The results suggest an apparent effect associated with the lactate medium, possibly correlated to changes in the dehydration energy of the lanthanide metal.
Introduction

The influence of the aqueous medium on thermodynamic parameters of a system can have significant implications for accurately modeling solute-solute interactions under operational conditions. An example of this influence is changes in the value of the acid dissociation constant ($pK_a$) as a function of the concentration of a background electrolyte. In addition to the concentration, the composition of that background electrolyte can also significantly influence thermochemical behaviors, i.e., the measured value for the $pK_a$ of a weak acid is not necessarily the same in 1.0 M potassium nitrate as it is in 1.0 M sodium perchlorate. Direct measurement of these medium effects can be done in a variety of ways for simple systems, but is much more complicated for a system such as TALSPEAK where a variety of species may interfere with accurate measurements.

Previous work has suggested that there are changes in the values of thermodynamic parameters, depending on the medium. Zalupski et al. investigated the changes in enthalpy for the protonation of lactic acid in a background electrolyte of 1.0 M of the sodium salts of perchlorate, nitrate, trifluoromethanesulfonate (triflate), and methylsulfonate.\textsuperscript{1} When determining the enthalpy of protonation for lactate in these media relative to protonation in 1.0 M sodium lactate, the relative change in enthalpy, $\Delta(\Delta H)$, ranged from 0.05 kJ/mol (in sodium triflate) to 1.28 kJ/mol (in sodium perchlorate). Such a large change in the enthalpy values based purely on the background electrolyte suggests there may be additional influences on other measured parameters. From these data, Grimes used sodium triflate as a background electrolyte to determine the $pK_a$ values of the holdback reagent used in the TALSPEAK process, diethylenetriaminepentaacetic acid (DTPA); the stability constant for the formation of the 1:1 DTPA: Eu complex and the protonated HDTPA: Eu complex via potentiometric titrations were
also reported. The results suggest there is a slight lowering of the stability constant for the metal-ligand species and the pKₐ values in triflate media, relative to the same experiments in sodium perchlorate. Further probing the effects of the medium offers potential insight into the complexity of the TALSPEAK system.

Unfortunately, for methods of direct measurement the large number of components of TALSPEAK make characterizing thermochemical data more difficult. Directly determining the stability constant for the lanthanide-DTPA complexes via potentiometry in the high concentration lactate media is not possible, due to the overwhelming concentration of the buffer. Other methods, such as absorption spectroscopy, are limited by the characteristics of the lanthanides; only a few of the lanthanides, e.g. Nd, Ho, and Er, exhibit useful hypersensitivity in their UV-Vis spectra. Luminescence spectroscopy is similarly limited to only a couple of lanthanides (Eu and Tb). Techniques such as NMR offer characterization of the species in solution, and information regarding the exchange dynamics; however, much less information regarding the stability constants of the species can be determined. Therefore, an alternative series of experiments to determine both the equilibrium constants for reactions in the lactate medium, as well as the enthalpy and entropy for these reactions using calorimetric entropy titrations has been conducted.

Calorimetric entropy titration is a technique that has been used to determine the binding between metal centers and ligands and the enthalpy and entropy of these reactions in a single experiment. The method as applied to TALSPEAK has several advantages over the methods mentioned previously for determining medium effects in these solutions. First, most chemical reactions either generate or absorb some measureable heat during the course of the reaction. Modern calorimetric instruments can measure this heat directly, and fitting the resulting data can
accurately determine the enthalpy for the reaction. Second, the reaction is a physical change that is independent of the spectral characteristics of the lanthanide, and therefore can in principle be applied to all of the lanthanides, so long as the reaction being measured produces or absorbs heat. And finally, the method can determine multiple thermodynamic parameters- the enthalpy, entropy, and Gibbs free energy- simultaneously in a single experiment. In this study, calorimetric entropy titrations have been applied to the reaction of the DTPA holdback reagent with the lanthanides under the conditions of high lactate concentration, at a fixed pH and high ionic strength. The high ionic strength was selected to minimize possible changes in the activities of the reacting species.

**Experimental**

**Reagents**

The lanthanide nitrate stocks used were prepared from 99.999% lanthanide oxides from Arris International Co. The oxides were mixed with HNO$_3$ (70%, Omnitrace nitric acid, Fisher Scientific) and gently heated to promote dissolution of the oxide. The pH of the stock solutions was adjusted to 2–3. The stocks were standardized to determine metal concentration, nitrate concentration, and acidity using ICP-MS, cation ion exchange chromatography (Dowex 50x beads, H$^+$ form), and potentiometric titrations using a Mettler-Toledo DL-50 Graphix autotitrator and a Ross Semi-micro electrode with the internal reference solution switched to 3.0 M sodium chloride. The base was a solution of approximately 0.10 ± 0.01 M sodium hydroxide prepared by diluting a known amount of 50% NaOH (Sigma Aldrich, 50% used to minimize carbonate contamination) with degassed 18 MΩ-cm water, and standardized by titration against potassium hydrogen phthalate (KHP) that was dried in a 110°C oven overnight. The endpoint
was determined by the color change in phenolphthalein, and a minimum of five replicates was performed to improve confidence.

Sodium nitrate (NaNO$_3$, 95+%, Oakwood Chemical) crystals were dissolved in deionized water, passed through a fine frit filter, and recrystallized from hot water. The crystals were then dissolved in the minimum amount of DI water possible to create concentrated stock solutions of sodium nitrate. The concentration of the resulting NaNO$_3$ solution was then standardized by weighing a sample of the solution and using ion exchange chromatography (Dowex 50x beads, H$^+$ form). The eluent was then titrated against standardized sodium hydroxide to a phenolphthalein endpoint. A minimum of three replicate standardization titrations were performed, and the NaNO$_3$ concentration was determined with high confidence in mol/kg solution. This stock solution could be added by mass, and was used to prepare the high ionic strength background for all solutions.

Diethylenetriaminepentaacetic acid, (DTPA 98%, Sigma Aldrich), was purchased in the fully protonated form, and used as received with no further purification.

Sodium DL-lactate (60% w/w aqueous solution, Alfa Aesar) was purchased as the sodium salt and standardized by weighing a sample of the solution and using ion exchange chromatography (Dowex 50x beads, H$^+$ form). The eluent was then titrated against standardized sodium hydroxide to a phenolphthalein endpoint. Five replicate samples were titrated, and the concentration of the sodium lactate was determined to be 5.077 ± 0.020 mol/kg solution. The sodium salt was used because concentrated solutions of lactic acid will form lactides and other esterification products, leading to variability and uncertainty in the concentration of lactate in solutions prepared from the concentrated stock solution.\textsuperscript{8} Because the esterification reaction requires the presence of the protonated species, this side reaction is inhibited in the sodium salt.
The sodium lactate was used as received, with no further purification. A 1.000 ± 0.60 L stock solution of 0.200 ± 0.002 M sodium lactate, 1.80 ± 0.010 M sodium nitrate was prepared for the lanthanide-lactate stability constant studies to minimize differences between runs. Stock solutions of 1.00 ± 0.010 M and 2.00 ± 0.010 M total lactate at an ionic strength of 2.0 M maintained by sodium nitrate and acidified to a pH of 3.60 with concentrated nitric acid were prepared for the dilutions of the lanthanide metals for calorimetric experiments. Stock solutions of 50.00 ± 0.10 mL, 50.9 ± 0.2 mM DTPA and either 1.00 ± 0.010 M or 2.00 ± 0.010 M total lactate, ionic strength 2.0 M were prepared for the calorimetry titration experiments and dilution heats. All solutions were prepared using 18 MΩ-cm water.

Sodium hydroxide solutions for potentiometric titrations were prepared from a 50% w/w stock (Sigma Aldrich) to minimize carbonate contamination. The stock was centrifuged to ensure no suspended sodium carbonate solids were pipetted, enough of the sodium nitrate stock solution was added to attain the necessary ionic strength, and was then diluted using boiled degassed and deionized water. Gran titrations were performed to calibrate the electrode and establish whether there was significant carbonate contamination. If the carbonate concentration was higher than 1.5%, the solution was rejected, and remade. The base standardizations were performed against oven-dried potassium hydrogen phthalate allowed to cool in a vacuum desiccator and dissolved in a solution of sodium nitrate to the corresponding ionic strength.

Methods

Potentiometric Titrations

Potentiometric titrations were performed using a Mettler-Toledo DL50-Graphix autotitrator and a Ross Orion semi-micro glass electrode, with the internal reference solution switched from 3.0 M potassium chloride to 3.0 M sodium chloride. Other experiments conducted
in this research lab using this electrode included perchlorate, which is known to precipitate in the glass frit when potassium is present in the reference solution.\textsuperscript{11} The temperature was maintained at 25.0 ± 0.1 °C by a circulating water bath and a jacketed beaker. The electrode was calibrated for the 2.0 M ionic strength by titrating nitric acid (~0.10 M) with a standardized sodium hydroxide (ca. 0.30 M) at 2.0 M ionic strength with sodium nitrate as the background electrolyte, and using the Gran method to determine the standard potential and the slope factor.\textsuperscript{9,10} To determine the acid dissociation constant ($K_a$) at 2.0 M ionic strength in nitrate media, a solution of 0.010 ± 0.001 M sodium lactate acidified with three equivalents of nitric acid was titrated with a freshly prepared and standardized 0.300 ± 0.05 M solution of sodium hydroxide. For replicate data, two 100.0 ± 0.1 mL samples of the 0.010 ± 0.001 M lactic acid solutions were prepared, and 20.0 ± 0.1 mL aliquots were titrated with the sodium hydroxide solution. Sodium hydroxide solutions were standardized against oven-dried KHP. The accumulated data provided ten replicate samples, and the data were fit using the Hyperquad2008 software.\textsuperscript{12}

Stability constants for the lanthanide lactate species were determined via potentiometric titrations of a solution containing 0.010 ± 0.001 M of the respective lanthanide with a known amount of nitric acid and enough sodium nitrate to give an ionic strength of 2.0 M. The base (titrant) used in these experiments was a solution of 0.200 ± 0.002 M sodium lactate fixed at an ionic strength of 2.0 M using sodium nitrate. This method was selected to improve visibility of changes in the pH profile in solution with a high buffering capacity.\textsuperscript{13} To minimize differences between runs, 1.000 ± 0.60 L of a stock solution of 0.200 ± 0.002 M sodium lactate prepared by mass with 1.80 ± 0.010 M sodium nitrate background electrolyte. Each 100.0 ± 0.1 mL lanthanide solution was prepared from the standardized lanthanide stock solutions by mass and acidified with 3 equivalents of nitric acid. The ionic strength was fixed at 2.0 M with sodium
nitrate. Twenty mL aliquots of the solution were titrated with the 0.200 ± 0.002 M lactate stock solution. The stability constants were fit using Hyperquad2008. This program uses mass balance equations, known stability constants, and a Newton-Raphson method to minimize the error between a calculated value and the measured values of the pH. Nitrate lanthanide stability constants were included in the model, and were taken from the literature.

**Luminescence Measurements**

All luminescence titration experiments were conducted at room temperature (22 ± 1°C). The only lanthanide studied via luminescence spectroscopy was europium, due to the accessibility of the hypersensitive peak in the $^5D_0 \rightarrow ^7F_2$ transition. For each of the 1.00 ± 0.010 M and 2.00 ± 0.010 M buffer concentrations, 10.00 ± 0.04 mL of a solution containing 1.00 ± 0.1 mM Eu$^{3+}$ was prepared by mass from the lanthanide stock solution, the sodium lactate stock solution, and enough sodium nitrate stock solution to ensure the final ionic strength is 2.0 M. At the pH used for these studies, the sodium lactate buffer is 50% protonated, so prior to pH control approximately 40% equivalent of concentrated nitric acid was added. The final pH of the solution was fixed at pH 3.60 by adding concentrated nitric acid and using a Ross semi-micro electrode calibrated with pH 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, and 4.0 nitric acid standards at 2.0 M ionic strength. After pH control, the solution was diluted to the mark using degassed, deionized water. The corresponding 10.00 ± 0.04 mL of 10.5 ± 0.2 mM DTPA titrant solution was prepared by mass, using solid DTPA, the high concentration stock sodium lactate solution, and enough sodium nitrate solution to ensure the final ionic strength is 2.0 M. The DTPA was allowed to dissolve in the sodium lactate and sodium nitrate solution, prior to pH control using nitric acid as above. The solution was then diluted to the mark using degassed deionized water.
A HORIBA Jobin Yvon FluoroMax-4 spectrophotometer was used for all luminescence experiments. The excitation source for the emission experiments was an ozone-free, continuous output 150 W xenon lamp with an excitation wavelength range of 200-950 nm (optimized in the UV). The excitation wavelength of 393 nm was used to directly excite the $4f$ electrons in the europium cation. The excitation source was coupled to a Czerny-Turner monochromator, with 1200 grooves/mm gratings. The emission was monitored through a second grating set at 90° relative to the excitation source. The emission slit width was set at 5 nm. Emission spectra were obtained using the software that accompanies the instrument, FluorEssence (HORIBA Scientific, version 3.5 for Windows). The emission spectra were recorded in the range 550-725 nm in increments of 0.25 nm and integration time of 1 second.

Luminescence lifetimes ($\tau$) of europium were measured using a pulsed diode light source (SpectraLED-390, peak wavelength = 394 nm, wavelength FWHM = 25 nm) to excite the europium $4f$ electrons. The emission lifetime was monitored at 615 nm corresponding to the $^5D_0 \rightarrow ^7F_2$ transition. This peak was selected, as there is increased splitting in the $^5D_0 \rightarrow ^7F_1$ peak occurring at 590 nm upon formation of the Eu-DTPA complex. Lifetime measurements were determined using a time-correlated single photon counting (TCSPC) accessory (FluoroHub, HORIBA Scientific) and collected using the accompanying software, DataStation (HORIBA Scientific, version 2.6). The analysis and fitting of the data was done using the Decay Analysis Software (DAS, HORIBA Scientific, version 6.6). The data were fit to one, two, or three exponentials, and the goodness of fit returned by the software ($\chi^2$ value) must be less than 1.2 for the fitting to be acceptable. Adding more species generally corresponds to an improved fit; however, there are additional parameters considered when determining the number of species in the solution. If the error in the lifetime is large compared to the measured value of the lifetime,
the measured value likely does not correspond to an actual species. The software also performs an approximate calculation of the contribution of each species to the fit; if this contribution is negative or less than approximately 5%, this species is neglected.

**Titration Calorimetry Experiments**

Calorimetric entropy titration experiments were performed on the light lanthanides using a Calorimetry Sciences Corporation Isothermal Titration Calorimeter (CSC ITC-4200). The temperature was fixed at 25.00 ± 0.01°C by the internal water bath. The internal water bath is maintained by a pulsed heater, and consequently must have an external circulating water bath (VWR) to act as a heat sink. The power compensation calorimeter measures heat changes with semiconductor thermocouples (Peltier modules) between a reference cell and a reaction vessel, both composed of Hastelloy C. The reference sample has a small heater adjacent to it that maintains a certain constant power; when an exothermic reaction occurs in the sample cell, the power to the reference-cell heater is increased until the thermocouples reach the same temperature. The change in the power output is measured using the accompanying RunITC software, and the areas of the peaks in the resulting thermogram were integrated using the BindWorks 3.1 software package. Calibration of the instrument was done by electrical calibrations from an internal heater, and complexometric titrations by titrating a solution of 0.0100 ± 0.005 M 18-Crown-6 ether (Sigma Aldrich, 99+% ) into a solution of oven-dried 0.100 ± 0.01 M BaCl₂ (Fischer Scientific, ACS Reagent Grade). The value for the enthalpy was compared to the literature value of -31.42 ± 0.20 kJ/mol for the reaction, and if necessary the calibration factor was adjusted until the two values are in agreement. The measured value for the enthalpy at the final calibration factor was -31.11 ± 0.14 kJ/mol.
To minimize differences between the lanthanide runs, stock solutions of each of the buffers, 1.00 ± 0.010 M total lactate and 2.00 ± 0.010 M total lactate, were prepared by mass by diluting the sodium lactate solution (60% w/w, Alfa Aesar) with enough sodium nitrate to ensure a final ionic strength of 2.0 M at a pH of 3.60, and diluted with DI water. Under the pH conditions of the experiments, half of the buffer is deprotonated and is therefore contributing to the ionic strength. To maintain ionic strength at 2.0 M, a sample 1.0 M buffer solution would have ionic strength contributions of: 1.0 M sodium from the sodium lactate, 0.5 M from the lactate anion, 0.5 M nitrate from the nitric acid used to neutralize the buffer, and 1.0 M sodium nitrate added. The buffer solution was pH controlled using nitric acid, and a Ross semi-micro glass electrode calibrated with nitric acid standards at pH 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, and 4.0 at 2.0 M ionic strength in sodium nitrate. The stock buffer solution was used to prepare 10.00 ± 0.01 mL samples of each of the lanthanides by taking the corresponding volume of the concentrated stock solution of lanthanide nitrate and diluting to the mark using the buffer solution. The buffer solutions were also used for the purposes of determining the heats of dilution that must be subtracted from the experimental reaction heats.

Stock solutions of 50.00 ± 0.10 mL 51.0 ± 0.2 mM DTPA were used to minimize differences between the lanthanide experiments. The solid DTPA was added by mass into a 50.00 ± 0.10 mL volumetric flask, the mass of sodium lactate needed for either the 1.00 ± 0.010 M or 2.00 ± 0.010 M total lactate solutions was added, the relevant mass of sodium nitrate solution to ensure an ionic strength of 2.0 M at the pH of 3.60 was added, and the solutions were pH controlled to 3.60. The DTPA solution dilution heats were determined by titrating the DTPA into the buffer solution in the absence of the metal.
The titration experiments were conducted by pipetting 1.000 ± 0.004 mL (Finnpipette) of the lanthanide solution into the reaction vessel (Hastelloy C calorimeter cup of 1.30 mL capacity), measuring both the mass and the density (Sigma 702 force tensiometer) of these solutions to ensure accurate determination of the volume. This leaves a headspace in the cell, and is used because the volumes must be known accurately to calculate changes in concentration upon dilution for the model to correctly fit the data. The DTPA titrant solution is pulled into a dispensing syringe (250 μL gastight syringe, Hamilton), and installed into the calorimeter. The stirring rate was set at 300 rpm, and the entire apparatus is allowed to thermally equilibrate for several hours. After the equilibration time, 50 injections of 5 μL are started with 5 minutes between injections, and a start time of 5 minutes to determine the baseline. Any drift in the instrument is subtracted from the baseline, dilution heats are determined in separate experiments and are subtracted from the data. The areas of the peaks in the thermogram generated by the instrument are integrated, and the data are fit according to a 1: 1 binding model in OriginPro2015.

Results and Discussion

Potentiometry

Determination of changes in the speciation in solution during the course of calorimetric titrations requires accurate values for each of the stability constants for all species present in the solution. When determining the stability constants of the metal-DTPA complex in these titrations, established competing equilibria include 1:1, 1:2, and 1:3 metal: lactate species, as well as the 1:1 and 1:2 metal: nitrate species; the stability constants for the formation of each of these complexes must be accounted for to accurately determine the medium-independent equilibrium constant. While there are several literature reports that suggest the possible
formation of a 1:4 metal: lactate species, these data are not conclusive, and recent literature does not include this species.\textsuperscript{18,19} Fitting of the measured potentiometric data acquired in the present work does not converge when a tetra-lactate complex is included in the model. The stability constants for the metal-DTPA complex are well established, as well as the pK\textsubscript{a} values for the DTPA molecule at 2.0 M ionic strength in several background electrolytes.\textsuperscript{2} However, the values for the stability constants for the formation of the lanthanide-lactate complexes reported in literature are less accurate. Initial experiments in the present work were conducted to determine the values of the pK\textsubscript{a} for lactic acid, a necessary parameter for accurately fitting the data, followed by the determination of the lanthanide-lactate stability constants.

The values listed for the pK\textsubscript{a} of lactic acid at 2.0 M ionic strength according to the Martell and Smith database are: 3.65 (in sodium chloride background electrolyte), 3.73 (in potassium chloride background electrolyte), and 3.80 (in sodium perchlorate background electrolyte).\textsuperscript{20} In the experiment to determine the lanthanide-lactate stability constants, a solution of the respective lanthanide at a pH of 1.50 was titrated using sodium lactate as the base. As the lactate is acting as the base in this titration, and the amount of lactate free for complexation to the metal must be known accurately, the value of the pK\textsubscript{a} of the lactate is a critical component. To determine the pK\textsubscript{a} of lactic acid and maintain internal consistency in the data, 100.0 ± 0.2 mL solutions of 10.0 ± 0.1 mM sodium lactate, 2.0 M ionic strength in sodium nitrate were acidified and titrated with a freshly prepared solution of 0.300 ± 0.050 M sodium hydroxide, 1.70 ± 0.05 M NaNO\textsubscript{3}. The data were then fit using the program HyperQuad2008.\textsuperscript{12} The pK\textsubscript{a} value in these experiments was determined to be 3.61 ± 0.01. This value was used during the fitting of the following lanthanide-lactate potentiometry experiments.
Literature values for the stability constants of the early lanthanides with lactate are shown in Table 2-1. Values seen in parentheses are considered unreliable according the criteria selected by the reviewers of the literature. Accurately interpreting calorimetric experiments requires including these competing species, particularly for determining reaction-independent thermodynamic parameters. To reduce the uncertainties, a new set of stability constants was determined by potentiometric titrations.

Table 2-1 Critically selected values for lanthanide-lactate stability constants for 1:1, 1:2, and 1:3 complexes at 2.0 M ionic strength. Taken from.

<table>
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<th>log β_{103}</th>
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<tr>
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<td>(4.38)</td>
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<tr>
<td>Sm</td>
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<td>(4.58)</td>
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*Praseodymium values are at 0.5 M ionic strength

Values determined via the potentiometric titrations in the present work are shown in Table 2-2. These values are close to those from literature, and show similar trends across the values (e.g. Nd has nearly the same values as Pr). The uncertainty reported in Table 2-2 is shown at ± 2σ. The data were used to simulate the luminescence and calorimetric titration experiments to determine the optimum experimental conditions. Luminescence experiments were conducted to validate the calorimetric model, and determine the stability constant for the europium-DTPA formation.
Table 2-2 Values of stability constants for the 1:1, 1:2, and 1:3 lanthanide-lactate complexes determined in 2.0 M ionic strength fixed with NaNO₃ in the present work. Fitting was performed using Hyperquad2008. Uncertainty is ± 2σ.

<table>
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**Luminescence Spectroscopy**

The significant acid dependence of extraction in the TALSPEAK process that was observed by Nilsson and Nash led to the suggestion that a ternary complex may form that acts as an additional holdback reagent at high concentrations of free lactate. This led several research groups to investigate whether ternary complexes involving lanthanide-lactate-DTPA may form at the high concentrations of lactate in these systems. Leggett and Jensen specifically targeted the formation of these complexes using spectrophotometric titrations, fluorescence spectroscopy, and thermometric titrations. They concluded that these complexes were not observed under the conditions of the experiments, even at concentrations of free lactate of 0.75 M. Griffiths’ doctoral work investigated the formation of these ternary complexes at high pH with both EDTA and DTPA. The NMR experiments conducted with DTPA and lactate with the lanthanides were inconclusive with respect to the formation of a ternary complex. Griffiths used concentrations of 1:1:1 for metal: lactate: DTPA, which is considerably lower in concentration than the systems studied in the present work. With the ambiguity in the literature, a set of luminescence spectroscopy studies using europium was conducted to validate the model used in the calorimetric titration experiments.
Several reviews of TALSPEAK chemistry have investigated the probable chemical speciation, and the interactions in these media. At the pH value selected for these studies, the dominant chemical equation for the reaction in both the calorimetric experiments and the luminescence spectroscopy is shown in equation 1.

\[
M(lac)_3 + H_3DTPA^{2-} \rightleftharpoons MDTPA^{2-} + 3Hlac
\]  

(1)

where M is the metal ion, lac refers to the lactate anion, and Hlac refers to lactic acid. Equation 1 assumes that the primary reacting species are H\(_3\)DTPA\(^{2-}\), which constitutes approximately 80% of the DTPA species at pH 3.60, and M\((lac)\)_3 which is approximately 90% of the metal species prior to the first injection. Luminescence titrations were completed to observe the formation of the metal-DTPA complex and to determine the stability constant for the formation of the M-DTPA complex in high concentration lactate media. Europium is the only lanthanide used in these experiments because the metal has an emission spectrum in the visible range and hypersensitivity in the spectroscopic transitions.

Figure 2-1 shows the expected speciation for the conditions of the 1.00 ± 0.010 M total lactate luminescence titration. Though calorimetric experiments require higher concentrations of metal during measurements, the concentration of the europium metal was reduced to 1.00 ± 0.1 mM to avoid overloading the photomultiplier tubes in the instrument. Consequently, the concentration of DTPA in the titrant was also reduced from 50.9 ± 0.2 mM to 10.5 ± 0.2 mM. The concentration of the buffer was maintained at either 1.00 ± 0.010 M total lactate or 2.00 ± 0.010 M total lactate, to minimize differences between the calorimetry and the luminescence experiments.
Figure 2-1 Titration simulation of luminescence experiments. Conditions: Titrand: 0.001 M Eu³⁺, 1.00 M H⁺/Na⁺ lactate, pH 3.60, I = 2.0 M. Titrant: 0.0105 M DTPA, 1.00 M H⁺/Na⁺ lactate, pH 3.60, I = 2.0 M. DTPA stability constants from. Eu-lactate stability constants at 2.0 M ionic strength from.⁵

Based on the predicted speciation in 1.0 M total lactate, the reaction nears completion at approximately 100 μL of titrant. The volume of injections in the experiment was 5.00 ± 0.06 μL, so the spectra should indicate almost exclusively dilution at approximately injection 19. The luminescence spectrum was recorded from 550 nm to 725 nm, and the spectra were fit in HypSpec2008. Figure 2-2 shows the full spectrum of the titration for the 1.00 ± 0.010 M total lactate solution at a fixed pH of 3.60. The instrument records the spectra in counts/second, and the values for the experiments conducted here are generally in the range of 10⁵ cps. These data cannot be fit by HypSpec, so the data are background subtracted, and divided by a value that brings the maximum of the intensity to near 1. The spectra in Figure 2-2 are also dilution corrected for the purposes of presentation. The value determined by the program returns a log β for EuDTPA²⁻ of 21.25 ± 0.01. The value found under these conditions is slightly larger than the log value determined by Grimes in 2.0 M sodium perchlorate of 21.03 ± 0.01. This value is also larger than the log β reported by Grimes in 2.0 M trifluoromethanesulfonate (triflate) media
(20.74 ± 0.01) used as a lactate analog.\textsuperscript{2} The combination of these two sets of data suggest that there may be an influence that initially increases the stability constant, followed by a decrease.

For comparison to the calorimetry results, a condition-dependent value for the stability constant was also determined by eliminating all competitive equilibria in the model, and fitting the data assuming “free” metal and “free” DTPA are the only reagents. The log value returned by HypSpec for this experiment is 4.75 ± 0.01, equivalent to a K of 56000 ± 600. This is equivalent to the conditional equilibrium constant in the calorimetry, discussed in the next section.

Discussion of the 2.00 ± 0.010 M total lactate luminescence experiments is below.

The majority of the lanthanides have spectra that are insensitive to changes in the ligand environment surrounding the metal, which complicates analysis. The hypersensitivity of the peak near 615 nm in Eu, however, is useful to indicate the formation of a complex as the titrant is added.\textsuperscript{26} An expanded view of the $^{5}D_{0} \rightarrow ^{7}F_{2}$ transition (the “hypersensitive peak”) is shown in

![Figure 2-2 Full spectrum of luminescence titration. 1.00 mL Eu$^{3+}$ solution, 5.00 µL injection volume. Titrand: 1.00 mM Eu$^{3+}$, 1.00 M Na$^{+}$/H$^{+}$ lactate, pH 3.60, I = 2.0 M. Titrant: 10.5 mM DTPA, 1.00 M Na$^{+}$/H$^{+}$ lactate, pH 3.60, I = 2.0 M. Spectrum shifts from black to red over the course of the titration.](image)
Figure 2-3. The spectra clearly indicate an isosbestic point, indicating the conditions for which the metal is transitioning from the europium-lactate complex to the DTPA complex. The final spectrum is consistent with the formation of the metal-DTPA complex.

![Graph showing intensity vs. wavelength for spectra from a titration experiment. The graph indicates the isosbestic point at 610 nm, with the spectrum shifting from black to red over the course of the titration.]

Luminescence titrations were also conducted in 2.00 ± 0.010 M total lactate. A set of titration simulations using stability constants from the literature at 2.0 M total lactate were performed to accurately interpret data from these luminescence studies. The titration simulation for the 2.0 M total lactate data is shown in Figure 2-4.
Figure 2-4 Titration simulation of luminescence experiments. Conditions: Titrand: 0.001 M Eu$^{3+}$, 2.00 M H$^+$/Na$^+$ lactate, pH 3.60, I = 2.0 M. Titrant: 0.0105 M DTPA, 2.00 M H$^+$/Na$^+$ lactate, pH 3.60, I = 2.0 M. DTPA stability constants from. Eu-lactate stability constants at 2.0 M ionic strength from. At the higher concentration of buffer there is an apparent increase in competition between the lactate and the DTPA for the metal center. A consequence of this is the DTPA does not completely displace all of the lactate molecules coordinated to the metal center. This effect can be seen in luminescence lifetime studies. Using the model developed from the literature and the luminescence titration data collected for the 2.00 ± 0.010 M total lactate data, HypSpec calculates the log of the stability constant for the formation of the metal-DTPA complex under these conditions as 20.85 ± 0.01. The reduction in the log of the stability constant is an effect that is also seen when changing the background electrolyte, as the value determined in 2.0 M sodium triflate was 20.75 ± 0.01. Sodium triflate was indicated as a thermochemical analog for lactate; agreement in the decrease in the log of the stability constant is further evidence of a medium effect. As with the above 1.00 ± 0.010 M total lactate data, a condition-dependent value of the equilibrium constant was also calculated for comparison to the calorimetric results. HypSpec returns a log K value of 3.44 ± 0.01, equivalent to a K of 2800 ± 30. To obtain some possible
structural information regarding these complexes, luminescence lifetime measurements were conducted on the initial metal-lactate medium and after addition of 2.6 equivalents of DTPA.

Time-Resolved Laser Fluorescence Spectroscopy (TRLFS) can be used to determine certain properties of the coordination environment. The emission of the excited europium ion is efficiently quenched by the presence of hydroxide oscillators, due to the similarity in the energy levels of the excited state and the vibrational modes OH oscillator. The energy is lost to the vibration of the O-H bond, and consequently coordinated water molecules contribute the equivalent of 2 OH oscillators to the energy loss. The number of coordinated OH groups can be determined to ± 1 OH group based on empirical correlations between the lifetime of the excited state and the known number of coordinated water molecules. The decay lifetime can be fitted with the number of exponentials that correspond to the number of species present; in general, the curves are fitted to 1, 2, or 3 exponentials, and the value of the $\chi^2$ in the resulting fit should be less than 1.2. While the uncertainty in the fit generally decreases as more species are included, there are several other criteria that may reduce the likelihood of additional species. The fitting equation can determine approximate percentage contributions from each species to the fitting; if this value is negative (or less than 5%), that contribution should be excluded. Additionally, if the error in the lifetime is larger than the measurement, the species can also be neglected. The average number of water molecules coordinated to the metal center can be approximated by determining the lifetime, and inserting this value, in $\mu$s, into equations 2 and 3.

$$k_{obs} = \frac{1}{t}$$  

(2)
\[ n(\text{H}_2\text{O}) = (1.05 \times 10^3)k_{\text{obs}} - 0.7 \]  

where \( n(\text{H}_2\text{O}) \) is the number of water molecules coordinated to the europium center, and \( \tau \) is the measured lifetime (in \( \mu \text{s} \)). This is an empirical equation, and consequently the error on the fit is approximately 0.5 water molecules. The energy of the excited state in the europium ion is lost to the vibrational modes of the OH oscillator. As a result, water is considered to contribute 2 OH oscillators, and a coordinated alcohol or hydroxide is equivalent to 1 OH. Consistent with a middle lanthanide, europium in aqueous solution has a coordination number of 8-9 with an average of 8.5. If lactate binds to the europium metal in a bidentate manner through the \( \alpha \)-hydroxyl group, as expected based on free energy diagram relationships, each of the lactate anions should/could displace 2 water molecules. If the \( \alpha \)-hydroxyl group remains protonated, then the net number of OH-oscillators coordinated to the metal center should be decreased by 3 for each lactate that binds. Therefore the expected number of coordinated water molecules in the lactate medium should be 3-4.5.

In the lifetime measurements of the 1.00 ± 0.010 M total lactate solution and using equation 2, the lifetime of 315.90 ± 2.23 \( \mu \text{s} \) corresponds to 2.7 water molecules on the europium center. There is an uncertainty of approximately one-half water molecule in the equation, so the range could extend to 3.2 water molecule equivalents. Three lactates coordinating through the protonated hydroxyl groups represent the equivalent of 1.5 water molecules, so there appears to be only one water molecule still coordinated to the europium center, which is fewer than expected. There are several possible explanations for this effect. In the high concentration of lactate, the kinetics of exchange may be faster than the lifetime studies, thereby reducing the apparent number of coordinated water molecules. The high nitrate concentration may displace an
additional two water molecules, giving a net anionic species, and indicating only a single water molecule is left. Or the assumed geometry is not reflected in the actual solution behavior.

Regardless of the origin of this effect, the terminal species of the luminescence titration, the Eu(DTPA) species, has the $618.77 \pm 20.39$ μs lifetime that is consistent with the monohydrate shown in Figure 2-5 and in the literature.$^{35}$

![Figure 2-5 Proposed EuDTPA structure.](image)

Based on these studies, the model describing the calorimetric titrations should describe the formation of a 1:1 metal-DTPA complex forming in the course of the titration, as described in Figure 2-1.

Measurements in the $2.00 \pm 0.010$ M total lactate luminescence lifetimes suggest several differences in the initial and final complexes. The lifetime measurement of the europium in the $2.00 \pm 0.010$ M total lactate with no DTPA present indicates a lifetime of $339.90 \pm 0.6$ μs. The slight increase in the lifetime relative to the $1.00 \pm 0.010$ M total lactate data suggests a slight decrease in hydration of the metal center, consistent with a minor increase in the concentration of the tris-lactate complex. Application of equation 2 gives a value of 2.5 water molecules. After addition of 2.6 equivalents of DTPA, the lifetime measurements suggest that the best fit occurs
with two major species with lifetimes of $341.11 \pm 11.67 \mu s$, and $650.87 \pm 2.18 \mu s$. The first species which represents $35\%$ of the measured value has the equivalent of 2.5 water molecules coordinated, while the second species that constitutes $65\%$ of the measured value has 1 water molecule. The first species is most likely the tris-lactate complex, as the lifetime is nearly identical to that measured when DTPA is absent. The second species is assigned to the metal-DTPA complex. As predicted in the titration simulation in Figure 2-4, even at large excesses the DTPA does not completely complex the europium metal (displace all lactates). The consistency of these predictions with the measurements supports the model developed for the calorimetric entropy titrations.

**Calorimetry**

To investigate whether there might be an effect associated with the medium of the TALSPEAK process, calorimetric entropy titrations were performed. The values of the enthalpy for the overall process and the Gibbs free energy for the binding of the DTPA molecule to the early lanthanide metals was studied by titrating the DTPA containing solution into the metal ion containing solution in the presence of a high concentration of the lactate buffer. Two solutions, one a $1.00 \pm 0.010$ M total lactate solution, the other a $2.00 \pm 0.010$ M total lactate solution, were studied to assess possible medium effects. Previous work has suggested changes in the thermodynamics of the formation of the metal-DTPA complex at high concentrations of lactate, possibly indicating an effect from this highly unusual ionic medium.

Based on the titration simulations and luminescence spectroscopy studies above, the lanthanide metals are only expected to form a 1: 1 metal: DTPA complex. Therefore, a binding model that includes only these species was considered. To isolate the stability constant of the
reaction, which corresponds to the reaction of the “free” DTPA molecule with the “free” metal, the following mass balance equations were considered.

\[
[M]_T = [M] + [ML] + [ML_2] + [ML_3] + [MR] \quad (4)
\]

\[
[R]_T = [R] + [HR] + [H_2R] + [H_3R] + [H_4R] + [H_5R] + [MR] \quad (5)
\]

where M refers to the metal, L refers to lactate, R refers to DTPA, H refers to the hydrogen ion, and MR refers to the metal-DTPA complex; all values are in terms of concentration, rather than activities, and charges are omitted for clarity. The values of [M], the free metal concentration, [R], the free DTPA concentration, and [MR] are unknown in the course of the reaction. Rearranging these equations yields equations 5 and 6.

\[
\frac{[M]_T - [MR]}{(1 + \beta_{110}[L] + \beta_{120}[L]^2 + \beta_{130}[L]^3)} = [M] \quad (6)
\]

\[
\frac{[R]_T - [MR]}{(1 + \beta_{101}[H] + \beta_{102}[H]^2 + \beta_{103}[H]^3 + \beta_{104}[H]^4 + \beta_{105}[H]^5)} = [R] \quad (7)
\]

where \( \beta \) refers to the overall stability constant for either the metal-lactate complex, or the protonation of DTPA. Formally, there are three other mass balance equations that should be considered, corresponding to the concentration of the nitrate, the concentration of the hydrogen ion, and the concentration of the buffer (particularly the free lactate anion). However, a simplifying assumption was made in these systems: due to the high concentration of the buffer,
the amount of free lactate remains very nearly constant over the course of the experiment, and
the concentration of the free hydrogen ion is constant to within the accuracy of the glass pH
probe. The nitrate forms complexes that are much weaker than the other complexing agents, and
was consequently neglected in the calorimetric model. The equilibrium constant for the
formation of the MR complex is given by equation 8.

$$K = \frac{[MR]}{[M][R]} \quad (8)$$

Substitution of equations 6 and 7 into equation 8 gives equation 9.

$$K([M]_{T} - [MR])([R]_{T} - [MR]) - [MR](1 + \beta_{101}[H] + \beta_{102}[H]^2 + \beta_{103}[H]^3 + \beta_{104}[H]^4 + \beta_{105}[H]^5)(1 + \beta_{110}[L] + \beta_{120}[L]^2 + \beta_{130}[L]^3) = 0 \quad (9)$$

This equation is quadratic in [MR]. The basic equation describing a 1:1 binding model in
calorimetry is given by equation 10.

$$q_i = \Delta H \ast V \ast \Delta[MR]_i \quad (10)$$

where $q_i$ is the heat produced at the $i^{th}$ injection, $\Delta H$ is the enthalpy for the formation of the M-
DTPA complex, $V$ is the volume of the cell, and $\Delta[MR]$ is the change in the concentration of the
M-DTPA complex. The change in the concentration of the metal-DTPA complex is described by
equation 11.
\[
\Delta [\text{MR}]_i = \left( \frac{(b + K[M]_T + K[R]_T)^2 - \sqrt{(b + K[M]_T + K[R]_T)^2 - 4K^2[M][R]_T^2}}{2K} \right)_i - \left( \frac{(b + K[M]_T + K[R]_T)^2 - \sqrt{(b + K[M]_T + K[R]_T)^2 - 4K^2[M][R]_T^2}}{2K} \right)_{i-1} \tag{11}
\]

where the value of the stability constant, \(K\), is a fitting parameter, and all other values are known.

The value for the constant \(b\) in equation 11 is given by equation 12.

\[
b = (1 + \beta_{101}[H] + \beta_{102}[H]^2 + \beta_{103}[H]^3 + \beta_{104}[H]^4 + \beta_{105}[H]^5)(1 + \beta_{110}[L] + \beta_{120}[L]^2 + \beta_{130}[L]^3) \tag{12}
\]

If the data are fit using equation 11 with the value of \(b = 1\), the resulting equilibrium constant, enthalpy, and the derived Gibbs free energy and entropy are apparent constants. This is a consequence of ignoring all the competing equilibria in solution. These can be useful for comparing between sets of data, where either the \(\beta\) values are unknown, or the stepwise enthalpy values cannot be determined. The combination of these equations, when applied to the calorimetry data, gives a stability constant for the formation of the M-DTPA complex, and an overall enthalpy value for the reaction. A sample power trace is shown in Figure 2-6. The negative values of the peaks indicate that the reaction is endothermic.
Any baseline drift in these experiments is corrected prior to analysis. Dilution heats of both the metal solution and the DTPA titrant are determined in separate experiments, and are subtracted from the integrated heat data. The area of each of the peaks is integrated, and the integrated areas of the peaks are fit using equation 11. When using known values for each of the metal-lactate stability constants and the protonation constants for the DTPA, condition-independent parameters can be determined. Figure 2-7 shows a sample of the fitted thermogram.
Figure 2-7 Fitting of the integrated heats for 5.0 mM Pr$^{3+}$, 1.00 M total lactate, pH 3.60, I = 2.0 M with NaNO$_3$ titrated with 50.9 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M with NaNO$_3$. The red line is the fit according to equation 10. The uncertainty is the average of three replicates.

The use of equation 11 directly provides data about the equilibrium constant and $\Delta H_{rxn}$ which can be useful for determining changes in the Gibbs free energy and the entropy for the overall reaction. Equations 13, 14, and 15 describe the determination of these other parameters from the fits.

$$\Delta G = -RT\ln(K)$$ (13)

$$\Delta G = \Delta H - T\Delta S$$ (14)

$$\Delta S = \frac{\Delta H - \Delta G}{T}$$ (15)

The values of the condition-independent Gibbs free energy is considered first, and compared to literature values. This is followed by consideration of the conditional constants for the reaction.
**Condition Independent ΔG**

The condition independent value of the stability constant is determined by applying equations 10 and 11 with the value of b according to equation 12. This takes account of the amount of “free” metal, i.e. metal that is not complexed to lactate, and “free” DTPA, i.e. the fully deprotonated form of the ligand. This provides a stability constant, and a derived Gibbs free energy, that can be compared to the values in literature.

Table 2-3 shows the values of the stability constants for the M-DTPA complex formation taken from the literature, as well as the values determined in the present work. The literature values were determined via potentiometry, and did not include any effects due to high concentration of lactate. The uncertainty presented in the tables for the values determined in the present work correspond to the percent uncertainty in the value of the stability constant. Reporting these values as percentages rather than propagating the errors yields larger uncertainties; however, as the calorimetric method is fitting multiple parameters simultaneously, larger errors can be expected. In Table 2-3, the column labels 1.00 M and 2.00 M refer to the total concentration of lactate at which the experiments were run. All data were measured at 2.0 M ionic strength.
Table 2-3 Values of the equilibrium constants for the formation of the LnDTPA complex. All data were acquired at 2.0 M ionic strength. Literature values in 2.0 M NaClO₄ from.¹ 1.00 M and 2.00 M refers to total concentration of Na⁺/H⁺ lactate. Uncertainty is reported at ± 1σ.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>Literature</th>
<th>1.00 M</th>
<th>2.00 M</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>18.02 ± 0.02</td>
<td>18.94 ± 0.53</td>
<td>18.48 ± 0.37</td>
</tr>
<tr>
<td>Ce</td>
<td>19.06 ± 0.02</td>
<td>19.56 ± 0.53</td>
<td>19.18 ± 0.38</td>
</tr>
<tr>
<td>Pr</td>
<td>19.64 ± 0.01</td>
<td>20.34 ± 0.41</td>
<td>20.17 ± 0.40</td>
</tr>
<tr>
<td>Nd</td>
<td>20.23 ± 0.01</td>
<td>20.09 ± 0.40</td>
<td>20.23 ± 0.40</td>
</tr>
<tr>
<td>Sm</td>
<td>20.79 ± 0.01</td>
<td>20.47 ± 1.49</td>
<td>20.72 ± 0.67</td>
</tr>
<tr>
<td>Eu</td>
<td>21.03 ± 0.01</td>
<td>21.30 ± 2.13</td>
<td>20.84 ± 0.41</td>
</tr>
</tbody>
</table>

Despite the large errors reported in the stability constants determined via calorimetry, there is an apparent effect for the light lanthanides associated with incorporating lactate. Converting these values into Gibbs free energies can provide a useful visual comparison, as is seen in Figure 2-8.

Figure 2-8 Gibbs energy data of the lanthanides binding to DTPA from the literature at 2.0 M NaClO₄ (squares), 1.00 M Na⁺/H⁺ lactate and 2.0 M ionic strength in NaNO₃ (triangles), and 2.00 M Na⁺/H⁺ lactate at 2.0 M ionic strength in NaNO₃ (circles). Uncertainties in the present work are percents, and reported at ± 1σ. Literature values from.²
These data suggest an apparent influence of the medium on the free energy of the lanthanides binding to DTPA. The greater effect of the lactate on the light lanthanides may be correlated to a decrease in the hydration of the lanthanide due to the displacement of water by the lactate, while this effect is harder to determine in the heavier lanthanides due to the large uncertainties in the data.

A significant source of the error in the heavy lanthanides is due to the change in the shape of the titration curve. The curve in Figure 2-7 is for praseodymium, and clearly shows a number of points along the equilibrium curve with relatively little uncertainty in the central points. Figure 2-9 is a representative plot of samarium, indicating larger uncertainties in the central points of the curve, from which data the value for the equilibrium constant is determined. Using experimental weighting for these fits results in large uncertainties for the equilibrium constant.

![Graph](image)

Figure 2-9 Integrated heats for 5.4 mM Sm$^{3+}$, 1.00 M total lactate, pH 3.60, I = 2.0 M fixed with NaNO$_3$ titrated with 50.9 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M fixed with NaNO$_3$. The uncertainty is the average of three replicates.

In the heavier lanthanides samarium and europium the titration curve becomes considerably sharper, leading to large differences in the central points of the curve, and is consequently not
well fit by the modeling equation generating the large errors seen in the Gibbs energy plot. A sample europium titration is shown in Figure 2-10.

![Graph showing a power trace over time](image)

**Figure 2-10** Representative power trace. Conditions: Initial volume = 1.017 mL Titrand: 5.0 mM Eu\(^{3+}\), 1.00 M Na\(^+\)/H\(^+\) lactate, pH 3.60, I = 2.0 M fixed with NaNO\(_3\). Titrant: 50.9 mM DTPA, 1.00 M Na\(^+\)/H\(^+\) lactate, pH 3.60, I = 2.0 M fixed with NaNO\(_3\), 5 μL injections.

The model used to calculate the equilibrium constant requires a sigmoid curve in which there are several points in the center. As the curve becomes sharper, the central points of the curve also become more sensitive to slight changes in the concentration of the metal or the initial volume dispensed into the sample cell. This leads to larger uncertainties in the curve, which are weighted differently than the initial and final points.\(^a\) To accurately determine large equilibrium constants such as those for the metal-DTPA complex formation, competing equilibria must contribute to the observed data trace, as in the case of the buffer competing with DTPA for the metal. Changes of the conditions can allow increases or decreases in the sharpness of the curve, but may also

---

\(^a\) The weighting of the data is according to an instrumental method. The average of the triplicate runs is used to calculate the value of the integrated data point, and the standard deviation of the triplicate runs is used as the uncertainty in each point. Points with large uncertainties contribute less to the fit.
change other parameters such as the ionic strength. To maintain internal consistency, all reactions in this study were run under the same conditions.

**Reaction ∆G, ∆H, and ∆S**

The above description of the Gibbs free energy and the equilibrium constant isolates the “free” metal and the “free” DTPA. This reaction is represented by equation 16.

\[
M^{3+} + \text{DTPA}^{5-} \rightleftharpoons \text{MDTPA}^{2-}
\]  

However, the reaction that was measured in the experiments was more accurately represented by equation 1. If all of the independent competing enthalpy and entropy values can be determined in separate experiments, then the values of the enthalpy and entropy that are not dependent on the specific reaction studied in the system can also be determined in these experiments. The experimental data acquired can, however, still provide information regarding changes in the reaction characteristics. Conditional values for the enthalpy, entropy, and Gibbs energy can be determined in these systems by neglecting the contribution of all competing equilibria within the reaction, and assuming that the overall complexation reaction occurs as a single 1:1 complex. Assuming the speciation predicted in Figures 2-1 and 2-4, approximate values for the enthalpy of complexation for the 1:1 metal-DTPA complex, are reported in Table 2-4. These calculations assume the equilibrium in chemical equation 1, weighting the enthalpies according to the predicted concentrations of metal-tris lactate and metal-bis lactate in both the 1.00 ± 0.010 M total lactate and 2.00 ± 0.010 M total lactate systems.
Table 2-4 Predicted values for the enthalpy of complexation assuming chemical equation 1 at 1.0 M total lactate and 2.0 M total lactate. Enthalpy values from.\textsuperscript{20}

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>1.0 M ΔH (kJ/mol)</th>
<th>2.0 M ΔH (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>32.9</td>
<td>33.0</td>
</tr>
<tr>
<td>Ce</td>
<td>34.9</td>
<td>36.5</td>
</tr>
<tr>
<td>Sm</td>
<td>35.9</td>
<td>38.3</td>
</tr>
<tr>
<td>Eu</td>
<td>20.0</td>
<td>20.5</td>
</tr>
</tbody>
</table>

The values for the praseodymium and neodymium enthalpies are not included in Table 2-4, because the literature does not include the enthalpy of formation for the bis- and tris-lactate species. Conditional constants are only useful for comparison when the conditions of two reactions are the same, i.e., when only a single parameter is changing, such as the lanthanide in these systems. All other constituents of the reaction remain the same meaning the ionic strength, pH, lactate concentration, etc. are the same, and therefore the reaction proceeds according to the same pathway.

The equation used to determine the enthalpy and the stability constant for these reactions is equation 11 with the value of “b” equal to 1. This corresponds to the equation assuming a 1:1 complex formation, which is consistent with the measured data. When the integrated heats are plotted against the ratio of the titrated ligand (DTPA) to the metal, the equivalence point falls near 1.0. This is a useful check on the concentration of the metal, and if the concentration of the metal is considered a semi-adjustable parameter can provide a means of reducing error between sample runs. In addition, a first derivative plot of this graph also indicates a 1:1 complex, as seen in Figure 2-9. With these checks on the concentration of the metal and the model, the conditional thermodynamic parameters can be determined for the enthalpy and conditional Gibbs energy, and from these the reaction entropy.
Figure 2-11 Graph of the first derivative plot. The data represent the change in heat/injection vs. the total volume of the cell. The lowest point occurring at 1.108 mL is the equivalence point for the metal-DTPA, and corresponds to the inflection point in Figure 2-7. Conditions: titrand: 5.0 mM Pr³⁺, 1.00 M Na⁺/H⁺ lactate, pH 3.60, I = 2.0 M fixed with NaNO₃; titrant: 50.9 mM DTPA, 1.00 M Na⁺/H⁺ lactate, pH 3.60, I = 2.0 M fixed with NaNO₃. Initial volume = 1.017 mL, 5 μL injections.

The values for the thermodynamic parameters for the formation of the metal-DTPA complex in 1.00 ± 0.010 M total lactate are presented in Table 2-4. The errors in the enthalpy values and the equilibrium constant are taken directly from the fitting, while the error in ΔG is found by calculating the percent uncertainty in K, and multiplying by the measured value of ΔG. The same procedure is used to evaluate the error in ΔS. Comparing the conditional values for the equilibrium constant measured in the calorimetry with those determined by luminescence in europium supports the application of this method, as the results are within 2σ of one another, despite to large errors in the calorimetric experiment. The luminescence experiments are only applicable to a couple of lanthanides with hypersensitivity in the spectrum, and accessible energy levels (Eu, Tb).³
Table 2-5 Values of ΔH, K, ΔG, and ΔS for the formation of the lanthanide-DTPA complex in 1.00 M total lactate solutions. The uncertainties are reported as percent uncertainty for ΔH, K, ΔG at ± 1σ, while the error was propagated for ΔS and is reported at ± 2σ.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH (kJ/mol)</th>
<th>K</th>
<th>ΔG (kJ/mol)</th>
<th>ΔS (J/mol-K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>43.8 ± 0.8</td>
<td>1200 ± 34</td>
<td>-17.58 ± 0.50</td>
<td>206 ± 6</td>
</tr>
<tr>
<td>Ce</td>
<td>45.8 ± 0.6</td>
<td>3100 ± 83</td>
<td>-19.93 ± 0.53</td>
<td>220 ± 6</td>
</tr>
<tr>
<td>Pr</td>
<td>43.0 ± 0.2</td>
<td>10000 ± 150</td>
<td>-22.83 ± 0.30</td>
<td>221 ± 3</td>
</tr>
<tr>
<td>Nd</td>
<td>49.4 ± 0.4</td>
<td>7000 ± 120</td>
<td>-21.95 ± 0.36</td>
<td>239 ± 11</td>
</tr>
<tr>
<td>Sm</td>
<td>47.0 ± 1.2</td>
<td>9600 ± 700</td>
<td>-22.73 ± 1.66</td>
<td>234 ± 34</td>
</tr>
<tr>
<td>Eu</td>
<td>37.0 ± 0.2</td>
<td>64000 ± 6600</td>
<td>-26.92 ± 2.53</td>
<td>216 ± 44</td>
</tr>
</tbody>
</table>

The entropy values of the reaction remain very nearly constant across the series, suggesting that the overall reaction, as expected, does not change from La to Eu. The increase in the competitive equilibrium constant, and the corresponding value of the Gibbs energy, mirrors the increases seen in Figure 2-8. Since the value of the entropy is not changing, the increase in the free energy is compensated for by an increase in the relative binding strength correlated to the greater exothermic character of the lanthanide-DTPA interaction. A similar trend is seen in the literature values for the binding of DTPA to the lanthanides.\textsuperscript{37} Actinides show a similar pattern, where the heavier actinides have a smaller ionic radius and therefore stronger ionic interaction with the ligand.\textsuperscript{38} Comparing the measurements to the predicted enthalpy in Table 2-4 indicates that the measured values are considerably more endothermic than suggested by the literature enthalpies. If the assumptions in the calculation of the predicted enthalpies are correct, the change in the enthalpy by approximately 10-20 kJ/mol indicates a significant medium effect. The data for the 2.00 ± 0.010 M total lactate samples are presented in Table 2-6, indicating some interesting changes in the system at the higher concentration of lactate.
Table 2-6 Values of ΔH, K, ΔG, and ΔS for the formation of the lanthanide-DTPA complex in 2.00 M total lactate solutions. The uncertainties are reported as percent uncertainty for ΔH, K, ΔG at ± 1σ, while the error was propagated for ΔS and is reported at ± 2σ.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH (kJ/mol)</th>
<th>K</th>
<th>ΔG (kJ/mol)</th>
<th>ΔS (J/mol-K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>101 ± 2.2</td>
<td>56 ± 1</td>
<td>-9.97 ± 0.18</td>
<td>373 ± 14</td>
</tr>
<tr>
<td>Ce</td>
<td>47.2 ± 0.2</td>
<td>180 ± 2</td>
<td>-12.80 ± 0.13</td>
<td>201 ± 4</td>
</tr>
<tr>
<td>Pr</td>
<td>43.3 ± 0.2</td>
<td>870 ± 15</td>
<td>-16.78 ± 0.14</td>
<td>202 ± 4</td>
</tr>
<tr>
<td>Nd</td>
<td>45.7 ± 0.4</td>
<td>1300 ± 30</td>
<td>-17.80 ± 0.43</td>
<td>213 ± 10</td>
</tr>
<tr>
<td>Sm</td>
<td>44.5 ± 0.4</td>
<td>2200 ± 70</td>
<td>-19.08 ± 0.61</td>
<td>213 ± 14</td>
</tr>
<tr>
<td>Eu</td>
<td>38.7 ± 0.4</td>
<td>3100 ± 50</td>
<td>-19.93 ± 0.32</td>
<td>197 ± 6</td>
</tr>
</tbody>
</table>

The large value for the enthalpy in lanthanum is most likely artificial, and is due to the small value of the equilibrium constant under the conditions of the titration. The fitting equation optimally generates the equilibrium data, and the corresponding enthalpy data, from a sigmoid-shape curve, which is not seen in the 2.00 ± 0.010 M lanthanum lactate data (Figure 2-12). The fitting for the europium metal in 2.00 ± 0.010 M total lactate is shown in Figure 2-13 for comparison, clearly showing the sigmoid shape of the curve. Comparing the equilibrium constant determined in the calorimetry to that measured in the luminescence for Eu above, 2.00 ± 0.010 M data shows a more substantial change. The two values are close to one another, but the equilibrium constant measured by calorimetry is slightly larger. The large uncertainty in the medium independent values reported above prevents comparison to the luminescence data. However, given the difference of techniques applied to these two systems, the luminescence data suggests that the calorimetric model is a reasonable approach to determining these stability constants in this unusual medium.
Figure 2-12 Fitting of the integrated heats for 5.2 mM La$^{3+}$, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$ titrated with 51.0 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections are 5 μL. The red line is the fit according to equation 10. The uncertainty is the average of three replicates.

Figure 2-13 Fitting of the integrated heats for 5.5 mM Eu$^{3+}$, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$ titrated with 51.0 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. The red line is the fit according to equation 10. The uncertainty is the average of three replicates.
Comparing the results of the 2.00 ± 0.010 M total lactate data to the 1.00 ± 0.010 M total lactate data, the 2.00 ± 0.010 M data show a much more orderly increase in the Gibbs energy for the complexation reaction. Excepting the unusually large value of the lanthanum, the values for the enthalpy are very similar to the values in the 1.00 ± 0.010 M total lactate data. This result suggests that the overall reaction is not changing significantly between the 1.00 ± 0.010 M total lactate system and the 2.00 ± 0.010 M total lactate system. If the reaction is remaining the same, the change in the equilibrium constant, and the Gibbs energy, must be a result of changes in the entropy term. The slight decrease in the entropy term between the 1.00 ± 0.010 M and 2.00 ± 0.010 M data could correlate to the increase in the relative concentration of the tris-lactate complex in 2.00 ± 0.010 M total lactate vs. 1.00 ± 0.010 M total lactate. At the higher concentration of lactate, the relative concentration of the tris-complex is higher, and consequently there are fewer water molecules to displace from the metal upon formation of the final metal-DTPA complex. This condition would result in a lower apparent entropy for the complex formation.39

Conclusions

The 4f elements generally show a very orderly trend in ionic radius from the lightest lanthanides to the heaviest, and a purely ionic character in the binding would suggest this gradual increase in the binding strength.40 This is consistent with the literature behavior of DTPA over the light lanthanides; where the coordination number is nine, the lanthanides show an increase in binding affinity to DTPA until Eu³⁺, where the coordination number changes.2 Modeling of the expected behavior of TALSPEAK suggests that there are additional effects associated with the medium, and the calorimetric investigations reported here suggest similar changes for at least the light lanthanides. The novel application of entropy titrations to such a complex medium allows
direct investigation of the system thermodynamics, and suggests that the influence of the lactate on the lanthanide binding may be correlated to the decrease in the hydration of the metal.

Future work could extend entropy titrations into the rest of the lanthanide series. Samarium and europium show large errors in the current series of experiments, partly as a consequence of sharp transitions in the titration curve. These errors could be reduced by changing the conditions slightly to a different pH, where there is more acid competition for the DTPA. The reverse is true for lanthanum in the 2.00 ± 0.010 M total lactate study, which showed no equilibrium. Altering the conditions requires the comparison of the condition-independent values for the stability constants, and using the more complex model. Extending the condition-independent model to incorporate the condition-independent enthalpy will also provide some useful comparisons to the literature, and allow calculation of the entropy term directly. The combination of these data may provide additional insight into the origin of the medium effects.
References


Chapter 3

Determination of the Enthalpy, Entropy and Gibbs Energy of Glycolate-Based TALSPEAK by Calorimetric Entropy Titrations

Abstract

To further assess the impact of the buffer medium on the thermodynamics of lanthanide interactions with DTPA (diethylenetriamine-N,N,N’,N”N”-pentaacetic acid), glycolic acid (CH₂(OH)CO₂H) was chosen as an alternate buffer to lactate in this study of TALSPEAK-relevant complexation thermodynamics. As the lactate investigation revealed evidence for an effect of the medium on the Ln-DTPA thermodynamic parameters, it appeared reasonable to examine the potential influence of the smaller glycolate. Calorimetry can be used to study complexation reactions that are inaccessible by other means; the complex and concentrated aqueous buffer media associated with this system negate potentiometry and optical spectroscopic methods are only useful for a select few members of the lanthanide series. Under suitable conditions, calorimetric titrations can be used to determine the values of ΔG and ΔH directly for the observed reaction in a single experiment. In such a so-called “entropy titration” first reported by Izatt and Christensen in 1966, ΔS of a system can be calculated from the derived values of ΔG and ΔH via the relationship ΔS = (ΔH-ΔG)/T = (ΔH+R∙T∙lnK_{eq})/T. Calorimetric entropy titrations have been successfully applied to the lactate containing TALSPEAK system, and have suggested a possible influence of the medium on the measured thermodynamic parameters. There are indications from previous calorimetric experiments that medium effects associated with the high concentrations of the buffer may have an influence on the overall complexation behavior of the metal to the holdback reagent, DTPA. Luminescence titrations were performed to
validate the complexation reaction occurs as a 1:1 complex at both 1.00 M total glycolate and 2.00 M total glycolate; calorimetric studies were done to illuminate the thermodynamics of the system.

**Introduction**

Nuclear power is a mature, well developed technology and a potential source of additional carbon-free electricity generation. Mitigating the effects of climate change will require reducing the rapid growth in the concentration of greenhouse gasses produced by burning fossil fuels. At present, nuclear power accounts for approximately 20% of the power, and nearly 65% of the carbon-free electricity generated in the United States; with recycling it has substantial potential to increase that contribution. Expanding the components of the energy sector that generate electricity via carbon-free sources may additionally reduce the United States’ dependence on fossil fuels, both ensuring energy independence and a cleaner environment. One of the major reasons renewables have not dominated the energy mix already is the reliability of fossil fuels; these can provide steady base-load power that other intermittent sources such as wind and solar have difficulty competing against. Moreover, intermittent power sources require a significant investment in energy storage, another emerging technology with significant research investment. However, one possible technology that can address this need for base-load power generation is nuclear power that uses a relatively small mass of fuel, and generates fossil carbon-free electricity. Because the technology is well developed, it can be implemented fairly rapidly. However, final disposal of the irradiated fuel is still an open challenge in the management of the nuclear fuel cycle.

In the light water moderated nuclear reactors in use in the United States, a 1 GW<sub>e</sub> power reactor will require approximately 4 tons of 2-4% enriched uranium every 18 months.¹ During
the fission process a range of fission products are generated, several of which significantly reduce the efficiency of the nuclear reactions occurring in the fuel. The fission products that can absorb additional neutrons are known as neutron poisons, and as the duration of fuel irradiation increases the increase in these neutron poison fission products decreases the amount of power produced by a given fuel load. Upon discharge, the heavy metal fraction of the fuel consists primarily of unused uranium (95%), plutonium (1%), and the rest fission products and other actinides (~4%). Once discharged from the reactor, there are several options for disposal or recycling of the spent fuel.²

The current policy in the majority of nations that employ nuclear power, including the United States, is a once-through fuel cycle, wherein the intact fuel unit is allowed to thermally and radiolytically cool and is then disposed of directly as waste in a geological repository.³ While this method can hinder tampering with the fuel rods, and in principle reduces the risk of diversion to other purposes, it is a relatively inefficient use of the fuel. In these spent fuel rods, the uranium constituent is still slightly enriched (0.8%) relative to natural uranium (0.71%), and the plutonium present in the fuel can also be used as fuel in a second cycle that both provides additional power and more efficient use of the initial uranium load. The products created by the fissioning of the uranium and plutonium represent approximately one third of the periodic table, and many of these components are economically valuable metals such as palladium and the rare earth elements.¹ Operating the nuclear fuel cycle with recycling of the fissionable components of the nuclear fuel (uranium and plutonium) and isolation of the dangerous high level waste from spent nuclear fuel is referred to as a closed fuel cycle.

Closing the nuclear fuel cycle requires separating the fuel into different fractions consisting of: the fissile/fissionable/fertile elements (e.g. uranium, plutonium), the medium- and
long-lived radioactive components (e.g. technetium, strontium, cesium, iodine, americium), and the stable species. This is generally done by selective solvent extraction in stages, where the fuel is dissolved and individual groups or elements are removed. The early stages in this process are represented by the Plutonium Uranium Redox EXtraction (PUREX) process, which has been used for isolation of plutonium and uranium in spent fuel since the 1950s. The most difficult stage is the separation of the lanthanide elements from the heavier actinides (Am, Cm) that are of similar ionic radius and preferentially maintain a trivalent oxidation state. The present work is focused on the final stage of this separation; the best developed process of which is known as the Trivalent Actinide Lanthanide Separations by Phosphorus reagent Extraction from Aqueous Komplexes (TALSPEAK) process. TALSPEAK was originally developed at Oak Ridge National Laboratory in the early 1960s by Weaver and Kappelmann for separations of the 4f lanthanides from the 5f actinides.4

TALSPEAK operates via the selective solvent extraction of the lanthanides into an organic phase from the aqueous phase containing both the lanthanides and the actinides. In its original form, the extractant is the acid cation exchanging ligand bis-2-ethylhexyl phosphoric acid (HDEHP).5 The prototypical form of TALSPEAK involves the use of high concentrations of lactic acid as the buffer in the system.4,6,7 This carboxylic acid influences in a favorable manner operation of the hydrometallurgical process, such as improvement in solubility of the holdback reagent, diethylenetriaminepentaacetic acid (DTPA), adjusting the order of extractability of the lanthanides, improving radiation stability of the chemical constituents, and enabling substantial improvement in the phase transfer kinetics in the solvent extraction reactions.6,8,9

The influence of the carboxylic acid has been studied extensively, but there are still significant uncertainties in the ultimate origin of the above effects.5,10,11 To study the impact of
the structure of the carboxylic acid buffer on the medium of TALSPEAK, the substitution of a simpler carboxylic acid and comparison of the thermodynamic characteristics of the two systems offers one possible approach. The simplest α-hydroxy acid, 2-hydroxyethanoic acid (glycolic acid) was one of a variety of carboxylic acids initially studied by Weaver and Kappelmann. Investigation of the aqueous thermochemistry of a glycolate-based TALSPEAK process may offer some insights into the origin of several of these effects. The studies conducted here focus on elucidating the details of the thermodynamics of the aqueous phase of the glycolic acid buffered TALSPEAK.

**Experimental**

**Reagents**

The lanthanide nitrate stocks used were prepared from 99.999% lanthanide oxides from Arris International Co. The oxides were mixed with HNO₃ (70%, Omnitrace nitric acid, Fisher Scientific) and gently heated to promote dissolution of the oxide. The pH of the stock solutions was adjusted to 2–3. The stocks were standardized to determine metal concentration, nitrate concentration, and acidity using ICP-MS, cation ion exchange chromatography (Dowex 50x beads, H⁺ form), and potentiometric titrations using a Mettler-Toledo DL-50 Graphix autotitrator and a Ross Semi-micro electrode with the internal reference solution switched to 3.0 M sodium chloride. The base was a solution of approximately 0.10 ± 0.01 M sodium hydroxide prepared by diluting a known amount of 50% NaOH (Sigma Aldrich, 50% used to minimize carbonate contamination) with degassed 18 MΩ-cm water, and standardized by titration against potassium hydrogen phthalate (KHP) that was dried in a 110°C oven overnight. The endpoint was determined by the color change in phenolphthalein, and a minimum of five replicates was performed to improve confidence.
Sodium nitrate (NaNO\textsubscript{3}, 95\%, Oakwood Chemical) crystals were dissolved in deionized water, passed through a fine frit filter, and recrystallized from hot water. The crystals were then dissolved in the minimum amount of DI water possible to create concentrated stock solutions of sodium nitrate. The concentration of the resulting NaNO\textsubscript{3} solution was then standardized by weighing a sample of the solution and using ion exchange chromatography (Dowex 50x beads, H\textsuperscript{+} form). The eluent was then titrated against standardized sodium hydroxide to a phenolphthalein endpoint. A minimum of three replicate standardization titrations were performed, and the NaNO\textsubscript{3} concentration was determined with high confidence in mol/kg solution. This stock solution could be added by mass, and was used to prepare the high ionic strength background for all solutions.

Diethylenetriaminepentaacetic acid, (DTPA 98\%, Sigma Aldrich), was purchased in the fully protonated form, and used as received with no further purification.

Glycolic acid, (98\%, Sigma Aldrich), was purchased in the protonated form and used without purification. Stock solutions of 1.00 ± 0.010 M and 2.00 ± 0.010 M total glycolic acid at a pH of 3.60 and ionic strength of 2.0 M in sodium nitrate were made for preparations of the lanthanide metal solutions and dilution heats in the calorimetry samples. High ionic strength solutions were used to minimize the influence of changes in activity of the reactive species.

Sodium hydroxide solutions used for pH control and potentiometric titrations were prepared from 50\% w/w (Sigma Aldrich) solutions to minimize the effect of carbonate uptake from the atmosphere. All solutions were prepared from 18 MΩ degassed, deionized water.
Methods

Luminescence

All luminescence spectroscopy titrations were performed at room temperature (20 ± 2°C). The metal solution in these titrations consisted of a 1.00 ± 0.1 mM Eu(NO$_3$)$_3$ in either 1.00 ± 0.010 M or 2.00 ± 0.010 M total glycolate, pH 3.60, ionic strength fixed at 2.0 M with sodium nitrate. Samples of 10.00 ± 0.10 mL of solution were prepared and pH controlled immediately before use. The titrant consisted of a 10.5 ± 0.2 mM solution of DTPA in the corresponding 1.00 ± 0.010 M or 2.0 ± 0.010 M total glycolate solution, also at pH 3.60, 2.0 M ionic strength. The titrand (1.000 ± 0.004 mL) was pipetted into an open top, 1.4 mL Spectrocell Semi-Micro Fluorimeter FUV cell (quartz). The titrant was added in 5.00 ± 0.06 μL aliquots using a 5-50 μL Finnpipette. The solution was thoroughly mixed using a transfer pipette prior to measurement.

Luminescence spectroscopy emission experiments were conducted using a HORIBA Jobin Yvon FluoroMax-4 spectrofluorometer. The excitation source for the emission experiments was an ozone-free, continuous output 150 W xenon lamp with an excitation wavelength range of 220-600 nm. An excitation wavelength of 393 nm (excitation slit width = 5 nm) was used to excite the 4$f$ electrons in the Eu$^{3+}$ cation. The excitation source was coupled to a Czerny-Turner monochromator with 1200 grooves/mm gratings. A second monochromator was set up at 90° angle relative to the excitation source. The emission slit width was set to 14 nm. The spectra were acquired using the FluorEssence software (HORIBA Scientific, version 3.5 for Windows). The emission spectra were recorded from 550-725 nm in increments of 0.25 nm and an integration time of 1 second.
Calorimetry

All calorimetry experiments were conducted using a Calorimetry Sciences Corporation ITC-4200 calorimeter. The temperature was maintained at 25.00 ± 0.01°C by a pulsed heater internal water bath. This model does not have a cooling bath, so an external circulating water bath (VWR) was set to 20.0 ± 0.1°C and used as an external heat sink. A stock solution of 50.00 ± 0.10 mL of 51.0 mM DTPA was prepared by adding the solid DTPA to enough solid glycolic acid to prepare a solution of either 1.00 ± 0.010 M or 2.00 ± 0.010 M total glycolic acid. The ionic strength for both solutions was fixed at 2.0 M by adding enough recrystallized sodium nitrate solution to ensure the final ionic strength was 2.0 M. In these systems, the glycolate anion significantly contributes to the total ionic strength so speciation calculations were conducted to determine this contribution. The final ionic strength was maintained using sodium nitrate. Prior to final dilution, the pH of the solution was set to pH 3.60 using concentrated sodium hydroxide, measured using a glass electrode (Ross Semi-micro), and finally diluted with 18 MΩ DI water. To minimize differences between lanthanide samples, stock solutions of 100.0 ± 0.10 mL of 1.00 ± 0.010 M total glycolate and 2.00 ± 0.010 M total glycolate, respectively, were prepared at a fixed pH of 3.60 and 2.0 M ionic strength. A sample of 1.000 ± 0.004 mL of the respective buffer solution was used in the reference cell for all experiments. The stock glycolate solutions were also used to prepare 10.0 ± 0.1 mL solutions of each of the lanthanides that were tested in this series. The concentrated lanthanide stocks were diluted to ca. 5.0 mM using the stock glycolate solution, and the density of the new lanthanide-glycolate solution was measured to minimize differences when dispensing volumes in the sample cell between replicate runs. Dilution heats were measured by titrating the DTPA into the buffer solution without metal present, and diluting the metal by titration with the buffer solution. These heats must be
subtracted prior to analysis, to minimize contributions of secondary heats. Triplicate samples were run for the purposes of statistical analysis. The experiment used the accompanying software ITCrun, and Bindworks 3.1 to correct for background drift and integrate the area of the peaks. The integrated areas were then dilution heat corrected, and the data were fit using a user defined 1:1 metal:ligand complex in OriginPro2015. The values were fit for enthalpy and equilibrium constant, and the resulting data were used to determine the Gibbs free energy and the entropy of the reaction.

**Results and Discussion**

*Modeling expected behavior*

The complexity of TALSPEAK medium may increase errors when extrapolating from the independently measured thermodynamics of the constituent components. These parameters are generally measured through techniques such as potentiometry or NMR which cannot be applied to the overall system due to signal interference from other species in the solution, particularly the high concentration buffer. Previous calorimetric studies into lactic acid based TALSPEAK have suggested an influence of this unusual ionic medium on the complexation thermodynamics of DTPA with the lanthanides. Therefore, to probe whether the structure of the buffer is a major contributor to the medium effects noted in lactate, a simpler carboxylic acid was substituted for the buffer in a TALSPEAK-like aqueous phase. In this study, to enable direct comparison between glycolate-based TALSPEAK and lactate-based TALSPEAK, all glycolate calorimetric and luminescence experiments were conducted with the same concentrations, pH, and ionic strength as previous lactate investigations.

The TALSPEAK aqueous phase has multiple competing equilibria that must be accounted for when modeling the system. These equilibria are based on the constituent species in
solution, and are governed in large measure by the protonation state of the ligands as seen in equations 1 and 2,

\[ H^+ + \text{Gly}^- \rightleftharpoons \text{HGly} \]  
\[ \text{DTPA}^{5-} + nH^+ \rightleftharpoons H_n\text{DTPA}^{n-5} \quad \text{(up to H}_3\text{DTPA)} \]  

the formation of 1:1, 1:2, 1:3, and 1:4 metal-buffer complexes,

\[ M^{3+} + n\text{Gly}^- \rightleftharpoons M(\text{Gly})^{3-n}_n \]  

the formation of 1:1 and 1:2 metal-nitrate complexes (much weaker than glycolate and DTPA complexes),

\[ M^{3+} + n\text{NO}_3^- \rightleftharpoons M(\text{NO}_3)_n^{3-n} \]  

and formation of the MDTPA\(^2^-\) and protonated M(HDTPA\(^-\)) complexes

\[ M^{3+} + \text{DTPA}^{5-} \rightleftharpoons \text{MDTPA}^{2-} \]  
\[ M^{3+} + H^+ + \text{DTPA}^{5-} \rightleftharpoons M\text{HDTPA}^- \]  

Considering the overall stability constants of the respective species at a pH of 3.60 which was selected for these studies, the strongest complex is generated by the formation of the MDTPA complex. At a pH of 3.60, the DTPA speciation is approximately 80\% H\(_3\)DTPA, 14\% H\(_2\)DTPA, and 6\% H\(_4\)DTPA. The predicted reaction that dominates these experiments is indicated in equation 7.

\[ M(\text{Gly})_3 + H_3\text{DTPA}^{2-} \rightleftharpoons \text{MDTPA}^{2-} + 3\text{HGly} \]  

While this is the expected dominant reaction, due to the high concentration of the buffer secondary metal-glycolate complexes may also contribute to the equilibrium. Previous work in
the literature suggests that the kinetics of exchange between multiple glycolate complexes is extremely rapid, and therefore the chemical equation is governed by the interaction of the DTPA with the metal.\textsuperscript{12} For the pH to remain constant as it does in this set of studies, the buffer must be consuming the protons released by the DTPA upon complexation to the metal, as is represented in equation 7. Based on the above equilibria, titration simulations were conducted to determine the expected conditions for the experiments.

A simulation of the expected titration using the same conditions as those in the luminescence experiments is shown in Figure 3-1. The speciation calculations were performed in the program HYSS, using data obtained from the NIST critically evaluated stability constants database, and stability constants and protonation constants for DTPA determined by Grimes at 2 M ionic strength.\textsuperscript{13–15} The majority of the lanthanides have reported stability constants for 1:1 through 1:4 metal-glycolate complexes at 2.0 M ionic strength. The europium data only listed the 1:1 through 1:3 species at 2.0 M ionic strength, and the 1:4 at 0.5 M ionic strength. Though these data are at different ionic strengths, the stability constant for the 1:4 species was included in the speciation and titration simulation calculations. The values of the stability constants in europium are generally consistent with those of samarium, which has the same value for the 1:4 species and is reported in the NIST database at 2.0 M ionic strength.\textsuperscript{13}
The simulation suggests that only a single species is formed in the course of the titration, and that the europium-glycolate complexes maintain a separate equilibrium until the reaction reaches completion after around 100 μL of titrant addition. The equilibria represented in equations 1, 2, 6, and 7 are strongly dependent on the concentration of free H⁺, which is not shown in Figure 3-1 but was also calculated in the simulation. The value remains very nearly constant, with a change of 0.005 pH units, as expected due to the high concentration of the buffer. Previous experiments in lactate were also conducted for both 1.00 ± 0.010 M and 2.00 ± 0.010 M buffer, so to maintain consistency a similar experiment was conducted in the present study. A simulation of the 2.00 ± 0.010 M total glycolate titration is shown in Figure 3-2.
Figure 3-2 Titration simulation of glycolate-based TALSPEAK. Conditions: titrand: 1.0 mM Eu$^{3+}$, 2.00 M Na$^+/H^+$ glycolate, pH 3.60, 1.3 M NO$_3$; titrant: 10.5 mM DTPA, 2.00 M Na$^+/H^+$ glycolate, pH 3.60 1.3 M NO$_3$.

Under these pH conditions, and the high concentration of the buffer, the reaction does not go to completion. At 1.00 M total glycolate, the concentration of the free buffer (Gly$^-$) remains reasonably constant over the course of the titration at 0.371 M. In the 2.00 M total glycolate, this concentration doubles to 0.737 M. Because the pH remains fixed at 3.60, and the amount of buffer available for complexation remains high, there is substantial competition with the DTPA for the metal; while this is a necessary condition for the entropy titration, the excess free glycolate present in the 2.00 M total glycolate prevents the reaction from going to completion. The effect is significantly reduced at higher pH, as seen in Figure 3-3. The strong pH dependence of this titration suggests that the major competition occurring is between the proton and the DTPA. The titration simulation at the higher concentration of glycolate and higher pH, Figure 3-3, replicates the behavior of the 1.00 M total glycolate titration at pH 3.60 despite the apparent increase in the amount of the initial EuGly$_4^-$ species relative to Figure 3-1.$^{16}$ To interrogate these
systems more closely, and to determine whether there are other species present that must be accounted for, luminescence titrations were performed.

Figure 3-3 Titration simulation of glycolate-based TALSPEAK. Conditions: titrand: 1.00 mM Eu$^{3+}$, 2.00 M Na$^+/H^+$ glycolate, pH 4.6, I = 2.0 M; titrant: 10.5 mM DTPA, 2.00 M Na$^+/H^+$ glycolate, pH 4.6, I = 2.0.

In a system as complex as this, secondary reactions that are not accounted for in the model may be present, and characterizing these is necessary to properly interpret the calorimetry results. While it is unlikely that ternary complexes could form in TALSPEAK due to the octadentate DTPA nearly saturating the coordination sphere of the lanthanide, ternary complexes have been proposed in TALSPEAK-like systems and investigations have not ruled out formation as a minor species.$^{17-20}$ Previous studies have used luminescence spectroscopy, absorption spectroscopy, and thermometric titrimetric titrations to specifically identify whether ternary complexes could form in lactate-buffered TALSPEAK.$^{19}$ The authors concluded that under the conditions of their experiments, no ternary complexes were measured by those techniques. A separate set of studies was conducted using NMR; the author suggested that the NMR data proved inconclusive.$^{20}$ While these studies focused on lactate, the structural similarities to
glycolate suggest that it is unlikely for a ternary complex to form in these studies. However, to investigate whether ternary complexes may form to an appreciable extent (and must therefore be accounted for in models describing the calorimetry) luminescence titrations were conducted to determine the speciation in the aqueous phase of this TALSPEAK-like system.

Luminescence Spectroscopy

Luminescence titrations were conducted under conditions similar to the calorimetric experiments, with adjustments for the concentrations of the metal and titrant to avoid overloading the photomultiplier tubes in the instrument. The data are acquired as intensities in counts/second, but the analysis in the protonic software package, HypSpec, requires that the data be normalized and represented as intensity.\textsuperscript{15} The solutions are background subtracted in OriginPro2015 prior to normalization and input into the program. Normalization is done by dividing the counts/second determined by the fluorimeter by 200,000 to reduce the maximum value of the intensity to near 1. The spectra shown below are background subtracted, normalized, and dilution corrected for presentation. Figure 3-4 shows a representative titration for the 1.0 M total glycolate system.
Figure 3-4 Hypersensitive peak of 1.00 mM Eu³⁺, 1.00 M Na⁺/H⁺ glycolate, pH 3.60, I = 2.0 M with NaNO₃, titrated with 10.5 mM DTPA, 1.00 M Na⁺/H⁺ glycolate, pH 3.60, I = 2.0 M with NaNO₃, initial volume = 1.000 mL, 5 μL injections. Spectrum shifts from black to red over the course of the titration.

The isosbestic points in the 1.00 ± 0.010 M data clearly indicate a change from the initial metal-glycolate species to the final DTPA complex. The presence of only a single peak associated with the mixture of glycolate complexes is due to the rapid exchange between glycolate species, as well as the insensitivity of the spectrum to coordination of glycolate. A similar effect is seen in lactate, where the largest influence on the spectrum is an increase in intensity upon complexation of lactate. The final spectrum is consistent with the EuDTPA complex determined in a separate experiment in the absence of the glycolate.

In luminescence spectrum of europium, the number of coordinated hydroxide oscillators alters the intensity of the peak. Accompanying the shift, the slight increase in maximum intensity of the peak in Figure 3-4 indicates exclusion of quenching OH oscillating groups. The fitting of the spectra includes the stability constants for all the metal-glycolate, metal-nitrate, and protonation constants for the known equilibria, and returns a log value for the MDTPA formation constant of 21.28 ± 0.01. While the protonated metal-DTPA stability constant was also included
in the model, refinement of this stability constant does not converge. Grimes determined the
value of the formation constant for the MDTPA\(^2\) complex in both 2.0 M sodium perchlorate and
2.0 M sodium triflate (which was chosen as an analog for lactate in these systems).\(^{16,21}\) Grimes
determined the log of the formation constant potentiometrically in sodium perchlorate,
21.03 ± 0.01, which is in good agreement with the value determined via luminescence titration,
given the differences in technique and solution conditions.\(^{16}\) For comparison to the conditional
constants determined in the calorimetric experiments, an analysis removing all competing
equilibria was also done. This is equivalent the considering all the metal and DTPA present in
the system as “free,” and is comparable to the calorimetric conditional constants determined in
the next section. The log value for the stability constant of the MDTPA complex returned by
HypSpec for this simplified model in 1.00 ± 0.010 M total glycolate is 4.97 ± 0.01, equivalent to
93000 ± 1000. An additional feature of the HypSpec program is the ability to perform factor
analysis. As performed by HypSpec, factor analysis decomposes the measured spectrum into
individual contributing species, with the assumption that the sum of all of the concentration of
the individual components times the absorbance yields the overall spectrum. The factor analysis
in the 1.00 ± 0.010 M data also suggests that there are only two absorbing species in the titration,
which further supports the conclusion that no appreciable amount of spectroscopically active
ternary complexes are forming.\(^{15,22}\)
Figure 3-5 Hypersensitive peak of 1.00 mM Eu\(^{3+}\), 2.00 M Na\(^+/H^+\) glycolate, pH 3.60, I = 2.0 M, titrated with 10.5 mM DTPA, 2.00 M Na\(^+/H^+\) glycolate, pH 3.60, I = 2.0 M, 5 μL injections. Spectrum shifts from black to red over the course of the titration.

To maintain consistency, 2.00 ± 0.010 M total glycolate experiments were also conducted at a pH of 3.60; this must be kept in mind when considering the results of the experiments.

Comparing Figure 3-4 and Figure 3-5, the terminal complexes are nearly the same; however, there is a slight change in the structure of the peak near 617 nm. Figures 3-1 and 3-2 suggest the reaction does not go to completion in these titrations, so the change in the structure of the peak is assigned to this suppression in the reaction. Fitting these data also does not indicate the presence of a ternary complex, and the factor analysis suggests only the presence of two absorbing species. This does not preclude the formation of a spectroscopically silent species which have been reported to form in actinides; however, if such a species was present, the mass balance in the fitting equations would likely not converge.\(^{23}\) These spectroscopically silent species are proposed to form in complexes that have centrosymmetry, which the DTPA complex as seen in the proposed structure in Figure 3-6 does not.
The log of the stability constant value measured in 2.00 ± 0.010 M total glycolate for the model incorporating all competing equilibria (20.75 ± 0.01) is identical to Grimes’ data in a medium that is thermochemically similar to lactate and glycolate (20.74 ± 0.01 in sodium triflate).\textsuperscript{16,24} As before, a simplified model is also calculated that ignores all competitive equilibria, and gives a log value of 3.29 ± 0.01, equivalent to 1950 ± 20. This internal consistency improves confidence in the model, but also indicates a possible influence of the medium. A change of 1.00 M total glycolate from the lower concentration to the higher concentration seems to have appreciably lowered the stability constant. The fitting used in HypSpec is the same as the model used to generate Figure 3-2, and incorporated all of the known equilibrium constants between the metal, glycolate, nitrate, and the protonation constants of the DTPA. Therefore, model used to determine the stability constant via luminescence includes the competition for the metal center by the glycolate in the reaction, and remains consistent with the value determined in sodium triflate. The combination of these data suggest an effect associated with the medium, beyond simple competition between the free glycolate and the DTPA for the metal center.

In these solutions, a luminescence lifetime measurement offers insight into the coordination geometry and the hydration of the europium metal ion. For both the 1.00 ± 0.010 M total glycolate and the 2.00 ± 0.010 M total glycolate solutions, a luminescence lifetime study was conducted to determine whether the terminal complex contains a significant number of coordinated hydroxide oscillators, which would indicate a species other than the predicted DTPA complex.\textsuperscript{25} The initial tetra-glycolate complex believed to be the dominant species at the beginning of the titration should coordinate four hydroxides (assuming that the α-hydroxyl is coordinating to the metal center and that it remains protonated during the lifetime of the
experiment). Because the lifetime is dependent on the number of hydroxyl groups coordinated to the Eu$^{3+}$ metal center, the measured values should coincide with the equivalent of two water molecules in the initial complex, plus the contribution from the tris-glycolate complex (and the associated two or three water molecules necessary to saturate the eight or nine coordination sites in the lanthanide). The terminal complex in both cases should consist of the DTPA coordinating to 8 sites, with a single remaining water molecule, and therefore two hydroxyl groups.$^{26}$

A time resolved laser fluorescence spectroscopy (TRLFS) was conducted to determine the lifetimes ($\tau$) of the species, and the number of water molecules, or other hydroxyl oscillators, coordinated to the europium metal center. The excitation was conducted using a pulsed diode light source (SpectraLED-390, peak wavelength = 394 nm) to excite the europium metal directly, and the emission at 615 nm was monitored for the lifetime of the species in solution. The resulting lifetime was fitted to one, two, and three exponentials, and the best fit must have a $\chi^2 \leq 1.2$. In addition to a low value of $\chi^2$, the lifetimes of the relative species are examined to ensure that the error in the lifetime of the associated species is less than the measured lifetime. The fit generally improves upon addition of more species, and therefore considering only $\chi^2$ does not accurately reflect the actual number of species present in the solution. The measured lifetime(s) (measured in $\mu$s) are inserted into equation 8 and then fit to equation 9.

$$k_{\text{obs}} = \frac{1}{\tau}$$  \hspace{1cm} (8)

$$n(\text{H}_2\text{O}) = 1.05 \times 10^3 \times k_{\text{obs}} - 0.7$$  \hspace{1cm} (9)
where n is the number of water molecules, and τ is the observed lifetime in μs.\textsuperscript{26–28} This is an empirical equation, and provides predictions to approximately ± 0.5 water molecules. The number of coordinated water molecules is determined because the energy of the excited europium ion is similar to the energy of the vibrations in O-H bonds. As water consists of 2 OH bonds, this is counted as 2 OH oscillators.

In 1.00 ± 0.010 M total glycolate, the lifetime of the initial complex has a measured lifetime of 300.44 ± 0.53 μs, which corresponds to an average of 5.8 ± 1 hydroxide oscillators. Figure 3-6 shows several proposed structures for the glycolate complexes, as well as the terminal DTPA complex. The coordination number for Eu\textsuperscript{3+} in aqueous solution is 8-9; if there are four bidentate glycolate molecules coordinating through the α-hydroxyl groups, this corresponds to a coordination number of eight, and an expectation of two coordinated water molecule equivalents.\textsuperscript{25} For a coordination number of nine, the remaining site would be taken by a water molecule, giving the total number of three water molecules. Considering the initial speciation seen in Figure 3-1, the mixture of approximately 37% consisting of the M(Gly)\textsubscript{3} and approximately 57% of the M(Gly)\textsubscript{4} species suggests that the overall lifetime is best fit with a mixture of these two species. If the M(Gly)\textsubscript{3} species has three water molecules coordinated to the metal center, and the three glycolate anions coordinate through both the carboxylate and the α-hydroxyl group, the average number of waters for the tris species is 4.5. Assuming these values and the percentages for the species above, a weighted average gives a value of 2.8 water molecule equivalents (5.6 hydroxide oscillators), very close to the measured value.
Experiments described in the literature conducted at higher pH have indicated similar results. One additional aspect of the measurement is an indication of the rate of exchange between the two complexes. The fitting for the initial mixture of glycolate species fits a single exponential decay, despite the mixture of several contributing species. If the rate of exchange is long on the timescale of the experiment, then at least two separate lifetimes corresponding to the dominant two species should be resolved by this technique. If the exchange is rapid on the timescale of the measurement, then the instrument is incapable of resolving the dominant species, and an average value (generally with considerable error) is determined. There is a caveat in this argument; the lifetime was measured by following a single peak at 615 nm. If one or more of the species in the solution do not contribute to the monitored wavelength, then they will also not be resolved. This is not likely under the conditions that these lifetimes were measured, based on the hypersensitivity of the observed peak, and the apparent increase in the intensity of the hypersensitive peak upon addition of the glycolate when compared to europium in water.
After the titration, the lifetime measurement of the terminal complex of europium in 1.00 ± 0.010 M total glycolate titrated with DTPA has a measured lifetime of 646.31 ± 0.89 μs, and the fitting indicates only a single species, as expected. The lifetime corresponds to a value of 1.0 water molecule equivalents (2 hydroxide oscillators). DTPA has been characterized thoroughly in both the solid state and the solution environment, and the measured lifetime/single coordinated water molecule model is consistent with literature values.30–32

The 2.00 ± 0.010 M total glycolate solutions show trends similar to those predicted in the speciation plots. The measured lifetime in the initial solution of 2.00 ± 0.010 M total glycolate with no DTPA is slightly longer than that measured in the 1.00 ± 0.010 M total glycolate solutions at 327.8 ± 0.56 μs. The calculated number of water molecules is 2.6 ± 0.5 (equivalent to 5.2 ± 1 hydroxyl). As indicated from the titration simulation in Figure 3-3, there is significantly more of the tetra-glycolate complex than is present in the 1.00 ± 0.010 M total glycolate solutions, and the amount of the bis-glycolate complex is almost zero. Conducting a similar analysis for the expected number of waters, using the structures proposed in Figure 3-6 and values of 75% M(Gly)₄ with 25% M(Gly)₃, the expected value of water is 2.6. The agreement between the predicted values and the experimentally verified values further supports the proposed structures of the metal-glycolate complexes, though with an error of 0.5 water molecules these data are not conclusive.

Following titration of the solution with DTPA, the best fitting for the data occurs with a bi-exponential indicating two species, consistent with the predictions of Figure 3-2. These species have lifetimes of 385 ± 0.95 μs (2.1 water molecules), and 674.42 ± 1.63 μs (0.9 water molecules). The considerable lengthening in the lifetime of the first species, and assigning this to the metal-glycolate complex, suggests significant exclusion of water from the primary
coordination sphere of the europium metal center. The lifetime indicates that the proposed structure for the tetra-glycolate complex coordinated through the α-hydroxyl group is particularly likely under these conditions. If these structures are in fact those present in solution, it is interesting to note that the coordination number of the metal center changes from nine to eight, when coordinating glycolate, and back to nine when complexed to DTPA. This is one possible influence of the carboxylic acid on the system, and may affect the reaction thermodynamics. To investigate these values, calorimetry experiments have been conducted that directly probe the thermodynamics of the reaction proposed above.

Calorimetric Titrations

Analysis of calorimetric data can apply either a condition-independent model, where the data are corrected for the “free” concentrations of the reacting species, or a condition-dependent model, where the model neglects competition from other species in solution. The condition independent model generates the same stability constant that is calculated in the HypSpec calculations. Unfortunately, for a complete analysis that includes the reaction-independent enthalpy, the analysis requires the values of the competing condition-independent equilibria and the enthalpy or entropy of these reactions. The literature data for the enthalpy of complexation between the early lanthanides and glycolate are incomplete, though based on the trends in the lanthanide elements, approximate values for the enthalpy can be estimated. The condition dependent model is necessary to analyze the data for the enthalpy and entropy in the titration experiments, and is ideal for comparison to previously conducted calorimetry experiments using lactate as the buffer. While the condition-independent enthalpy and entropy are not well characterized, the stability constants of the glycolate species are well known via other methods such as potentiometry, and therefore the condition-independent stability constant of the MDTPA
complex formation reaction can be determined by entropy titration. This value is discussed first, followed by discussion of the conditional enthalpy, Gibbs energy, and entropy.

**Condition Independent Stability Constant**

Determining the condition independent value of the equilibrium constant, and the derived Gibbs energy, is done by modifying the mass balance equations for the reaction to account for the amount of “free” reactants. There are five mass balance equations that could potentially contribute to the model, represented by equations 10-14.

\[
\text{[M]}_T = [M] + [ML] + [ML_2] + [ML_3] + [MR] \tag{10}
\]

\[
\text{[R]}_T = [R] + [HR] + [H_2R] + [H_3R] + [H_4R] + [H_5R] + [MR] \tag{11}
\]

\[
\text{[L]}_T = [L] + [HL] + [ML] + 2[ML_2] + 3[ML_3] + 4[ML_4] \tag{12}
\]

\[
\text{[H]}_T = [H] + [HL] + [HR] + 2[H_2R] + 3[H_3R] + 4[H_4R] + 5[H_5R] \tag{13}
\]

\[
\text{[NO}_3\text{]}_T = [NO_3] + [MNO_3] + 2[M(NO_3)_2] \tag{14}
\]

where M refers to the metal, L refers to glycolate, R refers to DTPA, H is the hydrogen ion, and NO$_3$ is nitrate; charges are omitted for clarity. When fitting these data, the following simplifying assumptions were made: the contribution of the nitrate complexes was negligible and could be completely ignored, the concentration of the free glycolate is large and reasonably constant over the titration, and the pH of the solution corresponding to the free concentration of H remained constant to within the ability to measure with a pH probe. Using these assumptions, the mass balance equations can be rearranged to the following pair of equations.
\[
\frac{[M]_T-[MR]}{(1+\beta_{110}[L]+\beta_{120}[L]^2+\beta_{130}[L]^3+\beta_{140}[L]^4)} = [M]
\]

(15)

\[
\frac{[R]_T-[MR]}{(1+\beta_{101}[H]+\beta_{102}[H]^2+\beta_{103}[H]^3+\beta_{104}[H]^4+\beta_{105}[H]^5)} = [R]
\]

(16)

where the values for the overall stability constants, \(\beta\), are taken from the literature.\textsuperscript{13,16} These two equations are substituted into the equation for the formation of the MR species, equation 17, and rearranged to give equation 18.

\[
K = \frac{[MR]}{[M][R]}
\]

(17)

\[
K([M]_T-[MR])([R]_T-[MR]) - [MR](1 + \beta_{101}[H] + \beta_{102}[H]^2 + \beta_{103}[H]^3 + \beta_{104}[H]^4 + \beta_{105}[H]^5)(1 + \beta_{110}[L] + \beta_{120}[L]^2 + \beta_{130}[L]^3 + \beta_{140}[L]^4) = 0
\]

(18)

With the assumptions made above concerning the concentration of the glycolate and the free concentration of H, the only unknown values in the above equation are [MR], and K. The equation is quadratic in [MR], with K as a fitting parameter. The equation can be substituted back into the fundamental calorimetry equation for a 1:1 metal:ligand complex, given by equation 19.

\[
q_i = \Delta H \ast V \ast \Delta [MR]_i
\]

(19)
where $q_i$ is the heat evolved or absorbed during the $i^{th}$ injection, $\Delta H$ is the enthalpy, $V$ is the volume of the solution, and $\Delta [\text{MR}]_i$ is the change in the concentration of the MR complex. It should be noted that, while the data can be analyzed in either an integrated heat or a differential heat method, the above equation describes the heat evolved at each injection. The preferred analysis in this case is the differential method, which allows individual data points to be removed in the case of an issue with that point (such as a bubble in the injection needle). The differential method determines the change in the formation of the metal ligand complex between individual data points, and is generated by equation 20.

$$\Delta [\text{MR}]_i = \left( \frac{b+K[M]_T+K[R]_T}{2K} \right)^2 - \left( \frac{b+K[M]_T+K[R]_T}{2K} \right)^2 - 4K^2[M]_T[R]_T$$ \hspace{1cm} (20)

where the value of the stability constant, $K$, is a fitting parameter, and all other values are known. The $b$ in equation 20 is held as a constant in the current series of experiments, and is given by equation 21.

$$b = (1 + \beta_{101}[H] + \beta_{102}[H]^2 + \beta_{103}[H]^3 + \beta_{104}[H]^4 + \beta_{105}[H]^5)(1 + \beta_{110}[L] + \beta_{120}[L]^2 + \beta_{130}[L]^3 + \beta_{140}[L]^4)$$ \hspace{1cm} (21)

The condition-independent equilibrium constants determined by calorimetry are directly comparable to those determined via other experimental methods from the literature.

The values for the condition-independent equilibrium constants determined in these experiments are presented in Table 3-1. The uncertainties reported in the table are percent uncertainties rather than calculated through the propagation of error. These uncertainties are
calculated as the % uncertainty in K multiplied by the value of the log in K. The values listed from literature were taken from Grimes at 2.0 M ionic strength maintained with sodium perchlorate.

Table 3-1 Values of the condition-independent equilibrium constant for the lanthanides with DTPA. The 1.00 M and 2.00 M refer to the total concentration of glycolate in the system. The uncertainties are reported at ±1σ. Literature values are at 2.0 M ionic strength from 16.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>Literature log K</th>
<th>1.00 M log K</th>
<th>2.00 M log K</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>18.02 ± 0.02</td>
<td>19.06 ± 0.23</td>
<td>18.93 ± 0.38</td>
</tr>
<tr>
<td>Ce</td>
<td>19.06 ± 0.02</td>
<td>20.00 ± 2.20</td>
<td>19.93 ± 0.40</td>
</tr>
<tr>
<td>Pr</td>
<td>19.64 ± 0.01</td>
<td>20.50 ± 0.67</td>
<td>20.73 ± 0.41</td>
</tr>
<tr>
<td>Nd</td>
<td>20.23 ± 0.01</td>
<td>20.78 ± 0.67</td>
<td>20.72 ± 0.41</td>
</tr>
<tr>
<td>Sm</td>
<td>20.79 ± 0.01</td>
<td>21.48 ± 4.71</td>
<td>22.26 ± 1.78</td>
</tr>
<tr>
<td>Eu</td>
<td>21.03 ± 0.01</td>
<td>21.71 ± 1.89</td>
<td>22.45 ± 1.80</td>
</tr>
</tbody>
</table>

The uncertainty in the 1.00 ± 0.010 M glycolate Ce data is due to a large difference in one of the samples used for the triplicate runs. In an entropy titration, the value for the equilibrium constant is particularly sensitive to the initial volume of the sample cell; if there is a large discrepancy in either the metal concentration or the starting volume for a single sample, then the corresponding error in the value of the equilibrium constant is also large. A similar effect occurs in the europium data and the samarium data, though this is more closely associated with the approach to an end point in the titration, and consequently fewer data points near the equivalence point (see below).

There are some interesting trends between the values for the formation of the M-DTPA complex seen in the sodium perchlorate literature values and the glycolate data. The early lanthanides show a larger value for the stability constant in the glycolate data than those in the literature. A similar trend was seen in the lactate data, suggesting a common influence of the
medium between the two buffers, though the effect in the glycolate is slightly larger. The proposed origin for this increase in stability constant from the lactate data is a decrease in the hydration of the metal in the buffered system relative to the sodium perchlorate system. Perchlorate generally does not form inner sphere complexes with the lanthanides, and therefore does not dehydrate the metal to the same extent as the complexing buffer. As glycolate apparently forms a tetra-glycolate complex while lactate is limited to a tris-complex, glycolate may more completely dehydrate the metal than the lactate, resulting in an apparent increase in the stability constant. The dehydration effect is reduced toward the heavier lanthanides, due to a change in the coordination number (and the number of associated water molecules). The condition-independent values for all the lanthanides are well within error between the 1.00 ± 0.010 M data and the 2.00 ± 0.010 M data, suggesting that the influence of the medium does not increase at the higher concentrations of the glycolate. Limitations in the accuracy of the data make determining the difference in the samarium and europium data more difficult. For a similar comparison to the lactate data, conditional constants for the reaction were also determined, which should indicate whether there are significant differences between the medium effects of the two buffers.

**Condition Dependent ΔH, ΔG, and ΔS**

The condition dependent values of the enthalpy, entropy, and Gibbs energy can be determined directly from equation 20, assuming the value of b is equal to one. This assumption ignores the contribution of the independent equilibria for the metal-glycolate complexes, as well as the protonation of the DTPA. The values then represent the reaction-dependent 1:1 binding of the metal to the DTPA. This is a useful representation to compare the values determined in the
reaction with the structurally similar lactate, particularly as the systems are run under the same pH and concentration conditions further indicating differences in the influence of the buffer.

The overall values determined for the enthalpy, equilibrium constant, Gibbs energy, and entropy for the reaction measured in 1.00 ± 0.010 M total glycolate are shown in Table 3-2. As with the condition-independent values, the uncertainties are reported as percent errors.

Table 3-2 Values of ΔH, K, ΔG, and ΔS for the reaction of 51 mM DTPA with 5 mM of the respective lanthanides in 1.00 M H⁺/Na⁺ glycolate at pH 3.60 in 2.0 M ionic strength. The uncertainties are reported at ± 1σ

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH (kJ/mol)</th>
<th>K</th>
<th>ΔG (kJ/mol)</th>
<th>ΔS (J/mol-K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>37.4 ± 0.4</td>
<td>5400 ± 70</td>
<td>-21.31 ± 0.26</td>
<td>197 ± 4</td>
</tr>
<tr>
<td>Ce</td>
<td>37.9 ± 0.4</td>
<td>11000 ± 900</td>
<td>-23.07 ± 1.89</td>
<td>202 ± 34</td>
</tr>
<tr>
<td>Pr</td>
<td>37.5 ± 0.2</td>
<td>32000 ± 1000</td>
<td>-25.71 ± 0.84</td>
<td>211 ± 14</td>
</tr>
<tr>
<td>Nd</td>
<td>37.5 ± 0.1</td>
<td>43000 ± 1400</td>
<td>-26.45 ± 0.86</td>
<td>214 ± 14</td>
</tr>
<tr>
<td>Sm</td>
<td>35.9 ± 0.5</td>
<td>100000 ± 24000</td>
<td>-28.54 ± 6.85</td>
<td>216 ± 52</td>
</tr>
<tr>
<td>Eu</td>
<td>34.7 ± 0.1</td>
<td>182000 ± 16000</td>
<td>-30.02 ± 2.64</td>
<td>217 ± 19</td>
</tr>
</tbody>
</table>

The very large error in the samarium data is a consequence of the steepness of the curve. A representative titration is shown in Figure 3-7, and clearly indicates the rapid change near the equivalence point. Titrations with this large change are particularly sensitive to slight differences in the volume of titrand dispensed into the sample cell, as well as any differences in the concentration of the metal. A consequence of this is large errors when the average of the three runs is calculated. As can be seen in Table 3-2, those data that have large values in the equilibrium constant generally also have large errors in the value of K which are related to the steepness of the curve. Unlike the lactate data, there is significant disagreement between the conditional equilibrium constant measured in the luminescence experiments and the calorimetric data. This disagreement could be a result of the uncertainty in the calorimetric results, due to the steepness of the curve similar to that seen in the samarium data in Figure 3-7. The marked
increase in the stability constant relative to the lactate data is, however, consistent with that measured in the luminescence spectroscopy.

The enthalpy values for the reaction remain effectively constant over the entire series of the lanthanides studied here. The data are also more exothermic by ~6-12 kJ/mol than the corresponding lactate data. This is further evidence suggesting the effect of hydration of the metal is altered in these high buffer concentration systems. The hydration effect can be correlated to the speciation of the initial complexes; even at the high concentrations of free lactate the lanthanides are limited to three lactates in the complex, which still allows for coordination of additional water molecules. The glycolate forms a complex that, based on the proposed structures in Figure 3-6, nearly saturates the coordination sphere, resulting in only the displacement of the glycolate. The entropy values are similar across the series as well, and suggest that there is not a change in the reaction between the early and late lanthanides. The constancy of the entropy suggests that the number of displaced molecules does not change across
the series; the entropy terms in the lanthanum complexing DTPA in aqueous systems, at 0.50 M ionic strength in sodium perchlorate, are larger than europium by approximately 25 J/mol·K.\textsuperscript{37} The entropy values are also larger (239-264 J/mol·K) in the aqueous perchlorate system, suggesting greater displacement of water molecules in the perchlorate system than in the glycolate or lactate systems.

The values for the 2.00 ± 0.010 M total glycolate data are shown in Table 3-3. There are several trends consistent with the lactate data described previously. The total heat signal in the titrations is suppressed in the 2.00 ± 0.010 M total glycolate buffer, which leads to increased error in several of the terms. The trends in the equilibrium constant are the same, with increasing stability across the lanthanide series, and a slight decrease from praseodymium to neodymium. As with the 1.00 ± 0.010 M luminescence experiments, there is a significant discrepancy in the 2.00 ± 0.010 M data. The uncertainty in the equilibrium constant for the 2.00 ± 0.010 M total glycolate is considerably smaller than that measured in the 1.00 ± 0.010 M total glycolate, suggesting a substantial effect. This may be correlated to the relative concentration difference in the two experiments, where the luminescence experiments are at a lower concentration of metal, but the equivalent concentration of glycolate. The additional competition may suppress the value of the equilibrium in the luminescence experiment relative to the calorimetric titrations. The other thermodynamic parameters show similar influences relative to the lactate, and the 1.00 ± 0.010 M total glycolate solutions. The enthalpy values are more exothermic in 2.00 ± 0.010 M total glycolate, suggesting that the binding becomes more favorable in the higher glycolate system. This is consistent with a decrease in the hydration of the metal center. The decrease in entropy between the 1.00 ± 0.010 M total glycolate and the 2.00 ± 0.010 M total
glycolate data also suggests a change in the number of displaced molecules upon complexation to the DTPA.

Table 3-3 Values of ΔH, K, ΔG, and ΔS for the reaction of 51 mM DTPA with 5 mM of the respective lanthanides in 2.0 M H⁺/Na⁺ glycolate at pH 3.60 in 2.0 M ionic strength. The errors are reported at ± 1σ.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH (kJ/mol)</th>
<th>K</th>
<th>ΔG (kJ/mol)</th>
<th>ΔS (J/mol·K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>37.1 ± 0.2</td>
<td>400 ± 10</td>
<td>-14.85 ± 0.22</td>
<td>174 ± 3</td>
</tr>
<tr>
<td>Ce</td>
<td>30.9 ± 1.0</td>
<td>1720 ± 110</td>
<td>-18.47 ± 1.16</td>
<td>166 ± 10</td>
</tr>
<tr>
<td>Pr</td>
<td>33.3 ± 0.6</td>
<td>4810 ± 160</td>
<td>-21.02 ± 0.70</td>
<td>182 ± 6</td>
</tr>
<tr>
<td>Nd</td>
<td>37.6 ± 0.2</td>
<td>3400 ± 100</td>
<td>-20.16 ± 0.57</td>
<td>194 ± 5</td>
</tr>
<tr>
<td>Sm</td>
<td>35.2 ± 0.4</td>
<td>10200 ± 710</td>
<td>-22.88 ± 1.59</td>
<td>195 ± 14</td>
</tr>
<tr>
<td>Eu</td>
<td>32.6 ± 0.8</td>
<td>13000 ± 2000</td>
<td>-23.48 ± 3.61</td>
<td>188 ± 29</td>
</tr>
</tbody>
</table>

The decrease in the value of the stability constant when comparing the values of the 1.00 ± 0.010 M total glycolate and the 2.00 ± 0.010 M total glycolate suggests the expected increase in competition for the metal between the DTPA and the glycolate. Interestingly, the value of the enthalpy does not change significantly, despite the much larger change in the Gibbs energy. The decrease in the Gibbs energy is apparently due to the changes in the entropy, which are attributed to changes in the initial complex (with the increase in the tetra-glycolate species compared to the 1.00 ± 0.010 M total glycolate data).

Similar trends are seen in the lactate data presented previously, though the changes in the entropy are smaller in that system than in the glycolate system. It should be noted that, upon increasing the concentration of lactate from 1.00 ± 0.010 M to 2.00 ± 0.010 M at a constant pH, the change in the initial concentration of M(lac)₃ changes from approximately 90% to 95%, while the corresponding glycolate system, as seen in Figures 3-1 and 3-2, changes from approximately 57% M(gly)₄⁻ to 75% M(gly)₄⁻. The combination of these data indicates that the
buffer significantly alters the thermodynamics of the complexation, with important consequences for the TALSPEAK process.

Conclusions

Luminescence titrations conducted on europium in the glycolate-based TALSPEAK system suggested the absence of any ternary complexes under the conditions of these investigations, though they do suggest a suppression in the equilibrium constant for the formation of the metal-DTPA complex relative to aqueous systems. The luminescence lifetime studies are consistent with the modeling studies conducted at the beginning of this work, and lead to several proposed structures for the metal complexes. These metal-glycolate complexes offer evidence for changes in the hydration of the lanthanides, though the luminescence technique is only applicable to a few of the lanthanides. The glycolate and lactate show similar trends in the luminescence with respect to the decrease in stability constant at higher concentrations of the buffer.

The novel application of calorimetric entropy titrations to the glycolate-based TALSPEAK system has offered insight into the thermodynamic influence of the medium in both the lactate system and the glycolate system. The combined data suggest that dehydration of the metal center in the glycolate medium leads to a slight increase in the stability constant for the complex, and as the reactions are all endothermic, the primary driver for these systems is the change in the entropy. At the high concentrations of the glycolate, there is a substantial decrease in the entropy term, suggesting that there are fewer molecules displaced upon complexation to the DTPA. Future work should extend these studies into the heavier lanthanides for comparison to the literature values. A model incorporating the condition-independent enthalpy can be developed by including the changes in each of the competing metal-glycolate equilibria. This
will allow direct comparison between literature values and those measured in these calorimetric experiments.
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Chapter 4

Preliminary Studies on the Application of Calorimetric Entropy Titrations to Malonate-Based TALSPEAK

Abstract

The challenge of developing predictive modelling for the TALSPEAK system has led to several modifications to the extractant and holdback reagent that have allowed more predictable behavior. In addition to modifying these aspects of Advanced TALSPEAK, several of the alternative approaches to the TALSPEAK system also switch to different buffers. One of the current forms of advanced TALSPEAK utilizes 2-ethylhexylphosphonic acid mono-2-ethylhexyl ester (HEH[EHP]) as the extractant, N-(hydroxyethyl)-ethylenediaminetriacetic acid (HEDTA) as the holdback reagent, and malonate as the buffer. Previous studies targeting investigation of medium effects that alter the stability constant for the metal-holdback reagent complex and the thermodynamics for the lactate- and glycolate-based forms of TALSPEAK have suggested there is an influence of the high concentration of the buffer. To maintain consistency with these previous studies, luminescence titrations with europium were conducted, as well as luminescence lifetime studies, followed by calorimetric entropy titrations, all focusing on the malonate-buffered option for conducting Advanced TALSPEAK separations. Calorimetric entropy titrations have been successfully applied to the thermodynamics in lactate and glycolate media, so similar experiments were conducted with the malonate system.

Introduction

Growing awareness of the potential impact of climate change has led to an increase in interest in nuclear power as a carbon-free source of energy. At present, nuclear power provides approximately 20% of the electrical power in the United States, and approximately 65% of the
carbon-free electricity. The majority of these are light-water reactors, that operate on fuel slightly enriched (2–4%) in fissile uranium-235.\textsuperscript{1} During operation, nuclear reactors generate a significant number of fission products and heavier actinides such as plutonium and americium, resulting in a final mixture that contains elements from approximately 1/3 of the periodic table representing every group. Separation of this mixture and disposal is a significant unsolved problem in implementation of nuclear power, though a variety of options have been proposed and investigated.\textsuperscript{2–4}

Current methods of operating the back end of the nuclear fuel cycle fall into two broad categories: an open fuel cycle and a closed fuel cycle. In an open fuel cycle, the intact fuel element is allowed to thermally and radiolytically cool in a storage pond, and is then directly disposed of in a geological repository.\textsuperscript{5} This is the practice of the majority of states currently employing nuclear power. In a closed nuclear fuel cycle, following removal from the reactor the fuel rods are allowed to radiolytically and thermally cool, followed by dissolution of the fuel and recovery of the active components (uranium, plutonium). The components that are the greatest contributors to the medium-term fuel radiotoxicity (e.g. cesium, strontium) are isolated separately and disposed of in a geological repository. In addition, this separation allows for isolation of those components that are contributors to the long-term fuel radiotoxicity (e.g. americium, curium), and transmutation of these in either a reactor or with an accelerator driven system.\textsuperscript{6}

Separation of the components of nuclear fuel is generally done using a selective solvent extraction system, where a particular group of elements is separated into an organic phase while the rest of the components in that stage are retained in the aqueous phase and directed to further processing. The final stage of the separation is the most difficult, and occurs between the
chemically similar lanthanides and trivalent heavy actinides (americum and curium). The lanthanides and heavier actinides are all considered hard cations, have similar ionic radii, and have a preferred trivalent oxidation state.\textsuperscript{7,8} This makes the separation of these two groups a particular challenge.\textsuperscript{9,10} The most well developed method for the separation of these two groups is the Trivalent Actinide-Lanthanide Separation by Phosphorous reagent Extraction from Aqueous Complexes (TALSPEAK) process.\textsuperscript{11} Because of the complexity of the biphasic chemistry of the system, the classic TALSPEAK process has proven difficult to accurately model using available thermodynamic data from the literature. Identifying ultimate origin of these deviations from the model has proven elusive.\textsuperscript{12} A variety of studies have looked into the possibility of either competing extraction processes such as extraction of water or the buffer, or the formation of ternary complexes that alter the extraction behavior. These studies have proved inconclusive.\textsuperscript{13–15} Therefore, alternative forms of the TALSPEAK process, employing an alternative extractant, holdback reagents, or buffers have been investigated.\textsuperscript{16–19}

The original selection of the lactic acid buffer for implementation of the TALSPEAK process was to maintain a pH that optimized the effect of the holdback reagent diethylenetriaminepentaacetic acid (DTPA).\textsuperscript{20} Additional benefits to the presence of the lactate were noted, particularly improvement in the solubility of DTPA, improved phase transfer kinetics upon solvent extraction, increased radiolytic stability of the critical reagents, and improved phase disengagement between the aqueous and organic phases.\textsuperscript{9} The high concentration of the buffer is necessary for operation of the process; however, the precise mechanisms by which it operates have proven difficult to determine.\textsuperscript{10} Earlier work based on calorimetric entropy titrations has suggested an effect associated with the medium in lactate and glycolate buffers. Lactic acid was studied as the prototypical form of TALSPEAK, while
glycolic acid was substituted as a simpler α-hydroxy acid. A newer implementation of TALSPEAK chemistry uses malonate as the buffer, which has some different properties, such as the absence of an α-hydroxyl group, and different pKₐ values (2.6 and 5.0 at 1.0 M ionic strength versus 3.61 for lactic acid and 3.75 for glycolic acid at 2.0 M ionic strength). To assess whether there are medium effects associated with malonate as there are with lactate and glycolate, calorimetric entropy titrations were performed under the same conditions to allow direct comparison.

Calorimetric entropy titrations are a technique that, under suitable conditions, allows direct determination of the enthalpy, entropy, stability constant, and Gibbs energy for a reaction. When sufficient data from other experiments is available, the calorimetric technique can provide condition-independent constants, which are directly comparable to experiments performed by other techniques. When there are insufficient data, or the contributing model is overly complex, a more limited set of the thermodynamic parameters for the reaction can be determined. These are only comparable to systems conducted using the same conditions. To enable the comparison between these malonate experiments and the previous glycolate and lactate experiments, the malonate titrations were performed at pH 3.60 and 2.0 M ionic strength. The primary motivation for maintaining the same conditions for the pH and ionic strength is to maintain the speciation of the complexant, DTPA. The results of this investigation are described in the following.

**Experimental**

**Reagents**

The lanthanide nitrate stocks used were prepared from 99.999% lanthanide oxides from Arris International Co. The oxides were mixed with HNO₃ (70%, Omnitrace nitric acid, Fisher
Scientific) and gently heated to promote dissolution of the oxide. The pH of the stock solutions was adjusted to 2-3. The stocks were standardized to determine metal concentration, nitrate concentration, and acidity using ICP-MS, cation ion exchange chromatography (Dowex 50x beads, H\(^+\) form), and potentiometric titrations using a Mettler-Toledo DL-50 Graphix autotitrator and a Ross Semi-micro electrode with the internal reference solution switched to 3.0 M sodium chloride. The base was a solution of approximately 0.10 ± 0.01 M sodium hydroxide prepared by diluting a known amount of 50% NaOH (Sigma Aldrich, 50% used to minimize carbonate contamination) with degassed 18 MΩ-cm water, and standardized by titration against potassium hydrogen phthalate (KHP) that was dried in a 110°C oven overnight. The endpoint was determined by the color change in phenolphthalein, and a minimum of five replicates was performed to improve confidence.

Sodium nitrate (NaNO\(_3\), 95+, Oakwood Chemical) crystals were dissolved in deionized water, passed through a fine frit filter, and recrystallized from hot water. The crystals were then dissolved in the minimum amount of DI water possible to create concentrated stock solutions of sodium nitrate. The concentration of the resulting NaNO\(_3\) solution was then standardized by weighing a sample of the solution and using ion exchange chromatography (Dowex 50x beads, H\(^+\) form). The eluent was then titrated against standardized sodium hydroxide to a phenolphthalein endpoint. A minimum of three replicate standardization titrations were performed, and the NaNO\(_3\) concentration was determined with high confidence in mol/kg solution. This stock solution could be added by mass, and was used to prepare the high ionic strength background for all solutions.

Diethylenetriaminepentaacetic acid, (DTPA 98%, Sigma Aldrich), was purchased in the fully protonated form, and used as received with no further purification.
Malonic acid (Sigma Aldrich, 99%) was purchased in the fully protonated form, and used as received. Standard solutions of $1.00 \pm 0.010$ M and $2.00 \pm 0.010$ M malonic acid at a pH of 3.60 and ionic strength of 2.0 M in sodium nitrate were made for preparations of the lanthanide metal solutions and dilution heats in the calorimetry samples. High ionic strength solutions were used to minimize the influence of changes in activity of the reactive species. At pH 3.60 where these experiments were conducted, approximately 90% of the malonate is the singly-protonated anion, HMal\(^{-}\), which contributes to the ionic strength. Speciation calculations using literature values for the pK\(_{a}\)s of malonate (at 1.0 M ionic strength) determined the contribution to the ionic strength of these anionic species. The final ionic strength was fixed by addition of the sodium nitrate stock.

Sodium hydroxide solutions for potentiometric titrations for standardizations and pH control were prepared from a 50% w/w stock (Sigma Aldrich) to minimize the effects of carbonate contamination. The stock was centrifuged to ensure no suspended sodium carbonate solids were pipetted. Gran titrations were performed to calibrate the electrode and establish whether there was significant carbonate contamination.\(^{26,27}\) If the carbonate concentration was higher than 1.5%, the solution was rejected and remade. The base standardizations were performed against oven-dried potassium hydrogen phthalate allowed to cool in a vacuum desiccator and dissolved in boiled 18 MΩ-cm DI water.

**Methods**

**Luminescence**

All luminescence spectroscopy titrations were performed at room temperature (20 ± 2°C). The metal solution in these titrations consisted of a $1.00 \pm 0.10$ mM Eu(NO\(_3\))\(_3\) in either $1.00 \pm 0.010$ M or $2.0 \pm 0.010$ M malonate, pH 3.60, ionic strength fixed at 2.0 M with sodium
nitrate. Samples of 10.00 ± 0.10 mL were prepared and pH controlled immediately before use. The titrant consisted of a 10.5 ± 0.2 mM solution of DTPA in the corresponding 1.00 ± 0.010 M or 2.00 ± 0.010 M malonate solution, also at a pH of 3.60, 2.0 M ionic strength. The titrand (1.000 ± 0.004 mL) was pipetted into an open top, 1.4 mL Spectrocell Semi-Micro Fluorimeter FUV cell (quartz). The titrant was added in 5.00 ± 0.04 μL aliquots using a 5-50 μL Finnpipette. The solution was mixed thoroughly using a transfer pipette prior to measurement.

Luminescence spectroscopy emission experiments were conducted using a HORIBA Jobin Yvon FluoroMax-4 spectrofluorometer. The excitation source for the emission experiments was an ozone-free, continuous output 150 W xenon lamp with an excitation wavelength range of 220-600 nm. An excitation wavelength of 393 nm (excitation slit width = 5 nm) was used to excite the 4f electrons in the Eu³⁺ cation. The excitation source was coupled to a Czerny-Turner monochromator with 1200 grooves/mm gratings. A second monochromator was set up at 90° angle relative to the excitation source. The emission slit width was set to 14 nm. The spectra were acquired using the FluorEssence software (HORIBA Scientific, version 3.5 for Windows). The emission spectra were recorded from 550-725 nm in increments of 0.25 nm and an integration time of 1 second.

Calorimetry

All calorimetry experiments were conducted using a Calorimetry Sciences Corporation ITC-4200 calorimeter. The temperature was maintained at 25.00 ± 0.01°C by a pulsed heater internal water bath. This model does not have a cooling bath, so an external circulating water bath (VWR) was set to 20.0 ± 0.1°C and used as an external heat sink. Both the sample cell and the reference cell were composed of Hastelloy C. A stock solution of 50.00 ± 0.10 mL of 51.0 ± 0.2 mM DTPA was prepared by adding the solid DTPA to enough solid malonic acid to
prepare a solution of either 1.00 ± 0.010 M or 2.00 ± 0.010 M malonic acid. The speciation for the malonate solutions is more complex than those of the glycolate and lactate, as there is contribution from two separate protonation states. Speciation calculations were performed to determine the contribution of each protonation state to the ionic strength.

The ionic strength for both solutions was fixed at 2.0 M by adding enough of the recrystallized sodium nitrate solution to ensure the final ionic strength was 2.0 M. Prior to final dilution, the pH of the solution was set to pH 3.60 by addition of sodium hydroxide, and measured using a glass electrode (Ross Semi-micro) and finally diluted. To minimize differences between lanthanide samples, stock solutions of 100.0 ± 0.10 mL of 1.00 ± 0.010 M malonate and 2.00 ± 0.010 M malonate, respectively, were prepared at a fixed pH of 3.60 and 2.0 M ionic strength. Due to the high concentration of the buffer, there was minimum deviation from the average pH = 3.60. A sample of 1.000 ± 0.004 mL of the respective buffer solution was used in the reference cell for all experiments. This stock malonate solutions were also used to prepare 10.00 ± 0.10 mL solutions of each of the lanthanides that were tested in this series.

The concentrated lanthanide stocks were diluted to ca. 5 mM using the stock malonate solution, and the density of the new lanthanide-malonate solution was measured to minimize differences when dispensing volumes in the sample cell between replicate runs. Dilution heats were measured by titrating the DTPA into the buffer solution without metal present, and the dilution heat of the metal was determined by titration with the buffer solution without the DTPA in solution. These heats must be subtracted prior to analysis, to minimize contributions of secondary heats. Triplicate samples were run for the purposes of statistical analysis. Analysis of the experiment used the accompanying software ITCrun, and Bindworks 3.1 to collect the data, and correct for background drift and integrate the area of the peaks, respectively. The integrated
areas were then dilution heat corrected, and the data were fit using a user defined 1:1 metal:ligand complex in OriginPro2015. The values were fit for enthalpy and equilibrium constant, and the resulting data were used to determine the Gibbs free energy and the entropy of the reaction, where possible.

**Results and Discussion**

Investigations of TALSPEAK-like systems using lactate and glycolate have offered insight into applying calorimetric entropy titrations to determine the influence of the buffer on the thermodynamics of the dominant aqueous phase reaction. Because classical TALSPEAK has proven difficult to accurately model, alternative forms of TALSPEAK have been developed that are more readily modeled using values for the thermodynamic parameters listed in the prior literature. These Advanced TALSPEAK systems have significantly changed the extractant, the holdback reagent, and the buffer. Because the calorimetric techniques employed here are only considering the aqueous phase, and to maintain consistency with previously measured parameters in lactate and glycolate media, the change in the buffer was the primary concern. The choice of malonic acid as the buffer in the Advanced TALSPEAK system offers the potential advantage of operating the Advanced TALSPEAK separation system at lower pH, where the behavior of classical TALSPEAK is well behaved.\textsuperscript{12,19} Switching to a system that operates at lower pH offers the potential to apply the classical TALSPEAK holdback reagent, diethylenetriaminepentaacetic acid (DTPA). The work presented here focuses on the application of calorimetric entropy titrations to the malonate-buffered system using DTPA as the holdback reagent, and pH 3.60, to maintain consistency with previous studies in lactate and glycolate media. The light lanthanides lanthanum through europium were the only metals investigated; these represent the largest portion of the lanthanides formed during the fission process.\textsuperscript{1}
The speciation of the lanthanides in a malonate buffer is slightly different from the lactate and glycolate systems. Literature data suggest that with the early lanthanides through europium, the malonate buffer will coordinate as a mono- or a bis-complex and that either of these complexes may be protonated. An additional limitation: the available literature data are limited to 1.0 M ionic strength. As the current series of experiments are conducted at 2.0 M ionic strength, this is a potential limitation for comparison. However, as these are the best data available, a titration simulation is shown in Figure 4-1 and indicates that, prior to the first injection in the titration, the predominant species is the protonated bis-malonate complex, with a significant contribution of deprotonated bis-malonate complex.

Figure 4-1 Titration simulation of 1.0 M malonate experiment. Conditions: titrand: 1.0 M total malonate, 1.00 mM Eu$^{3+}$, pH 3.60, I = 2.0 M in sodium nitrate; titrant: 1.0 M total malonate, 10.5 mM DTPA, pH 3.60, I = 2.0 M in sodium nitrate. Calculations are performed in HYSS2008.$^{28}$ Stability constants from.$^{21,29}$

The speciation of the DTPA titrant at pH 3.60, I = 2.0 M is well known from previous work, and corresponds to approximately 80% H$_3$DTPA$^{2-}$, 15% H$_2$DTPA$^{3-}$, and 5% H$_4$DTPA$^{-}$.$^{29}$ The relative speciation is important to determine approximate values for the enthalpy of reaction, which is measured by the calorimeter. To use calorimetric techniques, the reaction must either evolve or
absorb heat in the course of the reaction. The two chemical equations that are expected to govern the enthalpy and Gibbs energy for the titration correspond to equation 1 and equation 2.

\[
\text{M(Mal)_2H + H}_3\text{DTPA}^{2-} \rightleftharpoons \text{MDTPA}^{2-} + 2\text{H}_2\text{Mal}
\]  (1)

\[
\text{M(Mal)}_2^{2-} + \text{H}_3\text{DTPA}^{2-} \rightleftharpoons \text{MDTPA}^{2-} + \text{H}_2\text{Mal} + \text{HMal}^{2-}
\]  (2)

where \(M\) is the lanthanide, \(\text{Mal}\) is the malonate, and \(H\) is the proton. Based on these two equations, a first approximation for the enthalpy can be determined for each of the lanthanides by weighting the enthalpy values in the literature according to the speciation of the starting malonate complex, and assuming the reaction goes to completion. This value will only be approximate, as the literature values for the malonate complexes are at 1.0 M ionic strength, while the DTPA enthalpies are at 2.0 M ionic strength, and the reactions assume complete neutralization of the acid by the buffer. The enthalpies for the first, second, and third protonation of the DTPA molecule are -30.3 ± 0.1 kJ/mol, -24.6 ± 0.1 kJ/mol, and -9.8 ± 0.1 kJ/mol, respectively. The values for the enthalpy of complexation of free DTPA with the lanthanides are listed in Table 4-1. These enthalpies are measured for the chemical reaction depicted in equation 3.

\[
\text{M}^{3+} + \text{DTPA}^{5-} \rightleftharpoons \text{MDTPA}^{2-}
\]  (3)
Table 4-1 Enthalpy for the formation of MDTPA complex with the light lanthanides at 2.0 M ionic strength. Data from.\textsuperscript{31}

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>Enthalpy (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>-30.3 ± 0.2</td>
</tr>
<tr>
<td>Ce</td>
<td>-31.2 ± 0.2</td>
</tr>
<tr>
<td>Pr</td>
<td>-35.5 ± 0.5</td>
</tr>
<tr>
<td>Nd</td>
<td>-38 ± 2</td>
</tr>
<tr>
<td>Sm</td>
<td>-41 ± 1</td>
</tr>
<tr>
<td>Eu</td>
<td>-42.6 ± 0.5</td>
</tr>
</tbody>
</table>

The values for the enthalpy of formation for the malonate complexes with the lanthanides are listed in table 4-2, and correspond to the chemical equilibria represented by equations 4 through 7.

\[
M + \text{Mal} \rightleftharpoons M(\text{Mal}) \tag{4}
\]
\[
M + 2\text{Mal} \rightleftharpoons M(\text{Mal})_2 \tag{5}
\]
\[
M(\text{Mal}) + H \rightleftharpoons M(\text{HMal}) \tag{6}
\]
\[
M(\text{Mal})_2 + H \rightleftharpoons M(\text{HMal}_2) \tag{7}
\]

where M refers to the lanthanide, Mal refers to malonate, and H refers to the hydrogen ion; charges are omitted for clarity.
Table 4-2 Overall enthalpy of complexation for the formation of the lanthanide-malonate complexes and the protonated lanthanide-malonate complexes at 1.0 M ionic strength. Data from.²¹

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH ML (kJ/mol)</th>
<th>ΔH ML₂ (kJ/mol)</th>
<th>ΔH MHL (kJ/mol)</th>
<th>ΔH MHL₂ (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>12</td>
<td>20</td>
<td>3</td>
<td>-2</td>
</tr>
<tr>
<td>Ce</td>
<td>12</td>
<td>20</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Pr</td>
<td>12</td>
<td>21</td>
<td>3</td>
<td>-2</td>
</tr>
<tr>
<td>Nd</td>
<td>12</td>
<td>20</td>
<td>2</td>
<td>-1</td>
</tr>
<tr>
<td>Sm</td>
<td>12</td>
<td>21</td>
<td>3</td>
<td>-2</td>
</tr>
<tr>
<td>Eu</td>
<td>12</td>
<td>20</td>
<td>3</td>
<td>-3</td>
</tr>
</tbody>
</table>

Combining these data, the approximate values for the enthalpy of complexation are calculated using the weighted average of the initial malonate complexes for each metal, and the assumed chemical equations 1 and 2. The approximate enthalpy values for the metal-DTPA complexation reaction with each of the light lanthanides in both the 1.00 M malonate buffer and 2.00 M malonate buffer are listed in table 4-3.

Table 4-3 Predicted values for the enthalpy of complexation according to chemical equations 1 and 2 at 1.0 M total malonate and 2.0 M total malonate. Enthalpy values from.²¹

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>1.0 M ΔH (kJ/mol)</th>
<th>2.0 M ΔH (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>14.0</td>
<td>14.6</td>
</tr>
<tr>
<td>Ce</td>
<td>11.7</td>
<td>12.3</td>
</tr>
<tr>
<td>Pr</td>
<td>8.5</td>
<td>8.8</td>
</tr>
<tr>
<td>Nd</td>
<td>6.8</td>
<td>7.0</td>
</tr>
<tr>
<td>Sm</td>
<td>3.4</td>
<td>3.6</td>
</tr>
<tr>
<td>Eu</td>
<td>3.5</td>
<td>3.6</td>
</tr>
</tbody>
</table>

The slight increase in the enthalpy between the 2.00 M malonate and the 1.00 M malonate is associated with a slight increase in the proportion of the bis-malonate and protonated bis-malonate species in the 2.00 M experiment relative to the 1.00 M experiment. These values
suggest that a calorimetric experiment can be performed, though there may be large errors associated with the samarium and europium data, due to the small enthalpies of formation.

To increase confidence in the model used for the calorimetry experiments, several initial luminescence studies were performed, followed by the calorimetric entropy titrations. Luminescence experiments and luminescence lifetimes were conducted to determine likely speciation under conditions similar to the calorimetric entropy titrations, and to determine the stability constant of the metal-DTPA complex spectroscopically. This is limited to europium, as there are few lanthanides with hypersensitivity in the accessible UV-vis spectrum. These experiments were followed by the calorimetric titration experiments, and compared to the glycolate and lactate results.

*Luminescence Spectroscopy*

To maintain consistency with previous experiments in glycolate and lactate media, luminescence spectroscopy experiments were performed using 1.00 ± 0.10 mM europium at pH 3.60, and 2.0 M ionic strength in either 1.00 ± 0.010 M or 2.00 ± 0.010 M total malonate. The selection of pH 3.60 was to ensure the speciation of the DTPA titrant remains the same in the solutions, which better allows comparison between the malonate and glycolate or lactate results. Titration calculations that considered pH showed a change of less than 0.01 pH unit, despite the poor buffering capacity of malonate at pH 3.60. The measured pH value remained the same to within the error of the glass pH probe. Europium is the only metal used due to the accessibility of the $^5D_0 \rightarrow ^7F_2$ transition (the “hypersensitive peak”).$^{32,33}$ A sample 1.00 ± 0.010 M malonate titration is shown in Figure 4-2. The data are background subtracted, dilution corrected, and normalized by dividing the experimental data by 200,000 to shift the data from counts/second to intensity with a value near one. The data are subsequently fit to determine the stability constant
for the formation of the metal-DTPA complex in these media using the Protonic software, HypSpec.²⁸

![Graph showing spectral shifts.](image_url)

**Figure 4-2 Hypersensitive transition of Eu-DTPA titration; spectrum shifts from initial black toward red. Conditions:**

- **titrand:** 1.000 mL of 1.00 mM Eu³⁺, 1.00 M total malonate, pH 3.60, I = 2.0 M with NaNO₃; titterant: 10.5 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M in NaNO₃, 5.0 μL injections.

The spectra indicate the formation of only a single metal-DTPA complex, as is seen in both lactate and glycolate. The initial spectrum consists of a mixture of metal-malonate species, consistent with the initial speciation in Figure 4-1. The selection of which species are considered absorbing in the model to fit the data is discussed below. When fitting these data for the condition-independent equilibria, the HypSpec program takes into account all the known equilibria between the metal, malonate, and any protonated species. Analysis suggested only two absorbing species in these solutions: the metal-DTPA complex, and a single signal associated with the metal-malonate species. Previous studies have offered a potential explanation for why only a single signal is seen in these systems. The presence of the protonated species was determined potentiometrically, which does not take into account inner versus outer sphere complexes.³⁴,³⁵ Studies have suggested that stability constants for species determined via
spectroscopic techniques may only consider inner sphere coordination; therefore, spectrophotometrically determined stability constants that cannot account for the outer sphere protonated ligand will be lower than those determined by potentiometric titrations.\textsuperscript{36} Because the spectroscopic technique is relatively insensitive to the presence of the protonated ligand, the model used to determine the metal-DTPA formation constant excluded the protonated metal-malonate complexes. The value of the log formation constant for the metal-DTPA complex determined in the 1.00 ± 0.010 M malonate solution in these experiments, when considering the protonated metal-malonate complex to be spectroscopically silent, is 20.55 ± 0.03. This value is lower than either of the log values determined by Grimes at 2.0 M ionic strength in either sodium perchlorate (21.03 ± 0.01) or sodium triflate (20.74 ± 0.01), which is a result consistent with the predictions by Wang et. al. when a spectroscopically silent species is present.\textsuperscript{29,36} If the protonated malonate complex is included, the data converge to an even lower log value of 20.44 ± 0.01. Consideration of the reaction-specific equilibrium constant, which neglects the competition for the metal center by species such as the malonate, gives a value for the log of the stability constant of 5.48 ± 0.03, equivalent to 302000 ± 9000. This analysis was performed for comparison to the calorimetric reaction-specific data, though with the increased complexity associated with inclusion or exclusion of the spectroscopically silent species, the value may not be comparable.

An additional feature of HypSpec is the ability to perform factor analysis. The program decomposes the spectrum into the probable contribution from each species which then suggests the number of individual spectroscopically active components. When this analysis is performed, there appear to be only two contributing species, with very large error in the spectrum if a third species is included. This is consistent with the expectation that the protonated malonate complex
is a spectroscopically silent species, due to the outer-sphere nature of the protonation. Therefore, although the error in the value decreases with the inclusion of a third species, the small contribution of the protonated species can safely be neglected.

A sample $2.00 \pm 0.010$ M malonate luminescence titration is shown in Figure 4-3. In previous work with lactate and glycolate, at the higher concentration of the buffer, there was significant competition for the metal between the buffer and DTPA, indicated by changes in the spectrum, and the reaction did not go to completion, even at significant excesses of DTPA. This is not apparent in the $2.00 \pm 0.010$ M malonate data, where the final complex is consistent with the data from the $1.00 \pm 0.010$ M malonate, and the terminal species is exclusively the metal-DTPA complex (see below). Comparing the two spectra, there is clearly a larger peak at 611 nm in $2.00 \pm 0.010$ M malonate relative to the $1.00 \pm 0.010$ M malonate data. This peak is not an artifact of differences in concentrations of the metal, as the ratio between the 611 nm peak, and the 620 nm peak is also different. The change in the spectrum is most likely due to an increase in the amount of the bis-malonate complex at the higher concentration of buffer, and therefore greater exclusion of water from the inner coordination sphere. Water very efficiently quenches luminescence spectra from europium, and exclusion of these molecules leads to a higher intensity in the spectrum.\textsuperscript{32,37}
As with the $1.00 \pm 0.010$ M malonate data, the spectra were fit in HypSpec using the same model to determine the value of the metal-DTPA complex formation constant. As discussed above, the model can either include or exclude the protonated metal-bis-malonate complex. The log of the value for the formation of the metal-DTPA complex in the $2.00 \pm 0.010$ M malonate data when excluding the protonated metal-malonate complex is $21.18 \pm 0.01$. When including the protonated metal-malonate complex, the log $K$ value for the formation of the metal-DTPA complex converges to $21.13 \pm 0.01$; while the protonated bis-malonate complex should probably be excluded for the same reasons as above, it is interesting to note that the apparent effect from the protonated bis-malonate complex is smaller than that seen in the $1.00 \pm 0.010$ M malonate data. In addition, the value of the stability constant in the $2.00 \pm 0.010$ M malonate data is considerably closer to that determined by Grimes in sodium perchlorate. The condition-specific value for the formation of the metal-DTPA complex, using the same model as that for the $1.00 \pm 0.010$ M malonate data, indicates no change in the stability.
constant, with a log value of $5.48 \pm 0.01$ and equivalent to $302000 \pm 3000$. The similarity between the $1.00 \pm 0.010$ M and $2.00 \pm 0.010$ M malonate solutions assuming no competition is expected, as the model only considers the europium and europium-DTPA complex. In both glycolate and lactate, higher concentrations of the buffer suppress the formation of the metal-DTPA complex, which also changes the apparent value of the stability constant when neglecting these interactions. Malonate does not have an equivalent effect, so the apparent conditional stability constants are the same.

The increase in the condition-independent stability constant in $2.00 \pm 0.010$ M malonate compared to $1.00 \pm 0.010$ M malonate is the opposite of what was seen in the lactate and glycolate data, where the higher concentration of the buffer led to a decrease in the stability constant and a closer value to what was determined in sodium triflate. The effect of the medium in the previous work was attributed to changes in the energy of the hydration of the metal, upon complexation with the buffer. Each lactate anion and glycolate anion complexed to the metal most likely displaces two water molecules.\textsuperscript{37} While the malonate is expected to displace slightly more water molecules, as the structure itself is larger, the number only increases to approximately 2.8.\textsuperscript{36} Because malonate is only capable of forming a bis-complex with the light lanthanides, the overall influence of the high concentration of the buffer is greater in the glycolate and lactate data. The relative hydration of the metal can be inferred from luminescence lifetime measurements, which have been conducted for all of the respective buffers.

Luminescence lifetime measurements were performed in these solutions for the purposes of determining the number of hydroxyl groups directly coordinated to the europium ion. This offers insight into the possible changes in the hydration of the metal center, and is a useful comparison between the malonate data and the lactate/glycolate data. Luminescence lifetimes are
measured using a pulsed diode laser, and monitoring the decay of the 615 nm transition. These data are then fit using equations 8 and 9.\(^{39}\)

\[
k_{\text{obs}} = \frac{1}{\tau}
\]  

(8)

\[
n(\text{H}_2\text{O}) = (1.05 \times 10^3) \times k_{\text{obs}} - 0.7
\]  

(9)

where \(n(\text{H}_2\text{O})\) is the number of water molecules, \(\tau\) is the lifetime measured in \(\mu\text{s}\), and the \(k_{\text{obs}}\) is the decay constant. This is an empirical equation, and is therefore accurate to approximately 0.5 water molecules. The decay lifetime is sensitive to the number of hydroxyl groups coordinated to the metal center, as these offer a decay pathway that does not emit light.\(^{32,33,40}\) The lifetime measured in the 1.00 \(\pm\) 0.010 M malonate data with no DTPA added is 224.62 \(\pm\) 0.6 \(\mu\text{s}\), corresponding to 8.2 \(\pm\) 1 hydroxide oscillators. As noted above, the protonated metal-malonate is an outer-sphere effect and should not contribute significantly to the change in the lifetime, so the most likely coordination environment is with an average of 4 water molecules. When DTPA is added, the lifetime is fit with only a single species, and has a value of 2.0 \(\pm\) 1 hydroxide oscillators, consistent with a single water molecule coordinated to the metal-DTPA complex as is reported in the literature.\(^{41}\) Europium in aqueous solution has a coordination number of 8-9 indicating that the malonate displaces approximately 4-5 primary solvation sphere water molecules upon complexation.\(^{42}\) The glycolate and lactate complexes should displace 6-8 water molecules, depending on whether the metal speciation is dominated by the tris-complex or the tetra-complex, though lactate and glycolate contain a coordinating \(\alpha\)-hydroxyl group that is
absent in malonate. This is seen in the longer lifetimes of the glycolate and lactate data, which have lifetime measurements between 300 μs and 350 μs in 1.00 ± 0.010 M solution.

For comparison to the lactate and glycolate data, as well as the 1.00 ± 0.010 M malonate data, lifetime measurements were also conducted for the 2.00 ± 0.010 M malonate system. The lifetime measured in the 2.00 ± 0.010 M malonate in the absence of DTPA was 273.07 ± 0.75 μs, with 6.5 ± 1 coordinated hydroxide groups. The lengthening of the lifetime compared to the 1.00 ± 0.010 M malonate is consistent with removal of water molecules from the inner coordination sphere, and was seen in both the lactate and glycolate data. The most likely form is an average of three water molecules coordinated to the metal center. After addition of the DTPA, contrary to both the glycolate and lactate data, there was only a single species present with a lifetime of 628.06 ± 4.9 μs. This is the DTPA-only complex, and corresponds to 2.0 ± 1 hydroxide oscillators or a mono-hydrate. Interestingly, unlike the glycolate and lactate, the high concentration of the malonate buffer does not out-compete the DTPA under these conditions. This may be a useful feature of the buffer if applied to an advanced TALSPEAK process.

**Calorimetry**

**Model**

In this sequence of experiments, calorimetric entropy titrations were applied to determine the values for the thermodynamic parameters for the equilibrium constant, K, the enthalpy, ΔH, and from these the derived parameters of Gibbs energy, ΔG, and entropy, ΔS. There are two types of models that can be applied to these systems: conditional, in which the model does not account for any additional competing equilibria from species such as malonate, and condition independent, in which all competing equilibria are accounted for. Conditional constants can be useful for comparison between two sets of experiments conducted under identical conditions,
such as those between lactate, glycolate, and the current series in malonate. The condition independent models are useful for comparison to the literature values determined by other techniques such as potentiometry and van’t Hoff analysis.\textsuperscript{25,30} Determination of the conditional constants, for a 1:1 metal-DTPA complex formation, is a very straightforward analysis. Condition independent values are much more difficult, depending on the number of components in the model that is used, and what data are available for the model. Unfortunately, the fitting for the malonate data is poor, as is described below in the conditional constants. The more rigorous analysis including calculation of the condition independent constants was not performed for these data.

The model for the conditional constants ignores the contributions of the competing reaction equilibria, such as those from malonate or protonation. The conditional values of the equilibria are based on the mass balance equations 10 and 11.

\[
[M]_T = [M] + [MR] \tag{10}
\]

\[
[R]_T = [R] + [MR] \tag{11}
\]

where $[M]_T$ is the total metal concentration, $[M]$ is the free metal concentration, $[R]_T$ is the total DTPA concentration, $[R]$ is the free DTPA concentration and $[MR]$ is the concentration of the metal-DTPA complex. In these equations, $[M]$, $[R]$, and $[MR]$ are all unknowns. However, the concentration of the free species, $[M]$ and $[R]$, can be rearranged, and inserted into the equilibrium constant equation. The equilibrium constant for the formation of the complex is given by equation 12.
K = \frac{[\text{MR}]}{[\text{M}][\text{R}]} \quad (12)

Rearranging and inserting the mass balance equations 10 and 11, and substituting into equation 12 yields equation 13.

\[ K([M]_T - [\text{MR}])([R]_T - [\text{MR}]) = [\text{MR}] \quad (13) \]

This equation is quadratic in [\text{MR}], and can therefore be rewritten as equation 14 with the only unknown value being K, and therefore used as a fitting parameter.

\[ [\text{MR}] = \frac{(1 + K[M]_T + K[R]_T) \pm \sqrt{(1 + K[M]_T + K[R]_T)^2 - 4K^2[M]_T[R]_T}}{2K} \quad (14) \]

In addition to the model that is to be applied, there are two forms of analysis for titration data. These two methods are: the integral method, in which the heats from each injection are added and the cumulative heat is fit, and the differential method, which considers each injection individually. The differential method is preferable for the type of experiment conducted in the present work, as individual data points can be removed from the analysis should something cause a large deviation in that point, such as a bubble in the syringe. The fundamental equation describing a calorimetric titration is represented by equation 15

\[ q_i = \Delta H \ast V \ast \Delta [\text{MR}]_i \quad (15) \]
where $q_i$ represents the heat from the $i^{th}$ injection, $\Delta H$ is the enthalpy for the reaction, $V$ is the volume of solution in the reaction cell, and $\Delta[MR]_i$ is the change in the concentration of the metal-DTPA complex between injections. The measured value from the calorimeter is $q$, $\Delta H$ is a constant multiplier in the equation that is fitted in OriginPro2015, and $\Delta[MR]_i$ is determined by equation 16.

$$\Delta[MR]_i = \left(\frac{1 + K[M]_T + K[R]_T - \sqrt{(1 + K[M]_T + K[R]_T)^2 - 4K^2[M]_T[R]_T}}{2K}\right) - \left(\frac{1 + K[M]_T + K[R]_T - \sqrt{(1 + K[M]_T + K[R]_T)^2 - 4K^2[M]_T[R]_T}}{2K}\right)_{i-1} \quad (16)$$

The outcome of this analysis is the development of reaction-specific values for the enthalpy, $\Delta H$, and the equilibrium constant, $K$.

**Reaction $\Delta G$, $\Delta H$, and $\Delta S$**

A representative thermogram from the calorimeter is seen in Figure 4-4. Each peak corresponds to the injection of the DTPA-containing buffer solution into the metal-buffer solution. The negative power events indicate that the measured reaction is endothermic. Independent experiments are conducted to determine the dilution heats of each injection. The area for each of the peaks is integrated using the software that accompanies the instrument, Bindworks 3.1.
Figure 4-4 Representative power trace. Conditions: titrand: 5.6 mM Ce$^{3+}$, 1.00 M total malonate, pH 3.60, I = 2.0 M in NaNO$_3$, titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M in NaNO$_3$.

The integrated areas of these peaks are shown in Figure 4-5. The first two points of the titration are neglected, as the heats are clearly low. This is generally a result of either a lower concentration in the initial injection, due to diffusion of the complexant across the tip of the injection needle while the sample is equilibrating or a bubble in the tip of the needle. Figure 4-5 graphs the measured heat against the ligand/metal ratio, which is a useful check on the concentrations of the titrant and titrand. The lanthanide-DTPA titration forms a single 1:1 complex, as seen in the luminescence data and the literature. The inflection point in the titration should, therefore, occur at a ligand/metal ratio of 1.0 as occurs here.
Figure 4-5 Integrated heats for the thermogram in Figure 4-4. Conditions: titrand: 5.7 mM Ce³+, 1.00 M total malonate, pH 3.60, I = 2.0 M in NaNO₃; titrant: 51.0 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M in NaNO₃. Data are graphed according to the ratio of the final concentration of ligand to final concentration of metal.

A first derivative plot with respect to the change in heat vs. the change in volume, as seen in Figure 4-6, is also a useful to determine the location of the inflection point. If there are any side reactions that produce or absorb significant amounts of heat, and have alternate equilibria from the primary reaction, these may also be seen in the first derivative plot. There is only the single inflection point in this system, consistent with a 1:1 complex formation. Ensuring the formation of only a single complex is also important for application of the model; more complex models can be derived for systems with additional species, but was not done for the system studied in the present work.
The fitting of these data for the stability constant is not very good, as seen in Figure 4-7. This is may be a consequence of the fairly small heats from each injection. Relatively small errors in the triplicate runs may yield large errors in the central points of the titration curve. The fitting algorithm weights the error in the points during the minimization routine to determine the difference between the calculated and measured values for the heat, q. This iterative process means any errors in the points in the center of the curve lead to poor fitting of the equilibrium constant, though the fitting for the enthalpy is frequently reasonable. This is seen in Figure 4-7 by the good fit of the equation near the starting points, where the enthalpy is best evaluated, but the poor fits along the rest of the curve.

Figure 4-6 First derivative plot of the change in heat vs. change. Conditions: titrand: 5.6 mM Ce³⁺, 1.00 M total malonate, pH 3.60, I = 2.0 M in sodium nitrate; titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M in sodium nitrate.
Larger heats allow for improved signal-noise ratio, and generally have better fits. Similar issues were encountered in the $2.00 \pm 0.010$ M lactate data, where the change in the signal was too low for reasonable values of the equilibrium constant to be measured. For comparison, Figure 4-8 represents a titration performed in $1.00 \pm 0.010$ M lactate, where the much larger heats and the better fitting is apparent. The large error also limits the ability to conduct a more rigorous analysis that gives accurate condition-independent thermodynamic constants. Neglecting the weighting during the fitting of the data leads to a better apparent fit and a more reasonable value for the equilibrium constant. However, this is neglecting the measured uncertainties, reducing the soundness of the measured values. Despite the significant improvement in the apparent fit, the uncertainty measured in the fit is still approximately 10% for the cerium data presented in Figure 4-7.
Despite the poor fitting for the equilibrium constants in the malonate data, the enthalpy values can be determined with reasonable accuracy by this technique. As seen in Figure 4-7, the fit reasonably matches the initial points in the curve, where the enthalpy value is most accurately determined. This is generally true for the fitting in the lanthanide samples of the malonate, though the value of the enthalpy decreases over the range of lanthanides studied, as predicted with the approximate values in Table 4-3. This decreases the signal, making the samples successively more susceptible to small errors. The thermodynamic data from this suite of experiments are reported in Table 4-4. The large errors in the equilibrium constant result in large errors in both the Gibbs energy, and the entropy. The Gibbs energy is calculated from equation 17, while the entropy is calculated by equation 18.

$$\Delta G = -RT \ln K$$  \hspace{1cm} (17)
\[ \Delta S = \frac{\Delta H - \Delta G}{T} \]  

The uncertainty in the Gibbs energy is calculated by multiplying the percent uncertainty in \(K\) by the measured value of the Gibbs energy. Using the propagation of error equations yields unrealistic uncertainties in the Gibbs energy.\(^{46}\) Entropy uncertainties are calculated by taking the square root of the sum of squares of the uncertainties in \(\Delta H\) and \(\Delta G\). These are reported at 2\(\sigma\).

Table 4-4 Values of \(\Delta H\), \(K\), \(\Delta G\), and \(\Delta S\) for the reaction of 51 mM DTPA with 5 mM of the respective lanthanides in 1.0 M malonate at pH 3.60 in 2.0 M ionic strength. The errors are reported at ± 1\(\sigma\).

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>(\Delta H) (kJ/mol)</th>
<th>(K)</th>
<th>(\Delta G) (kJ/mol)</th>
<th>(\Delta S) (J/mol-K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>22.7 ± 0.2</td>
<td>4800 ± 400</td>
<td>-21.01 ± 1.75</td>
<td>147 ± 24</td>
</tr>
<tr>
<td>Ce</td>
<td>20.1 ± 0.4</td>
<td>7500 ± 800</td>
<td>-22.12 ± 2.36</td>
<td>142 ± 30</td>
</tr>
<tr>
<td>Pr</td>
<td>15.9 ± 0.4</td>
<td>10000 ± 1900</td>
<td>-22.83 ± 4.34</td>
<td>130 ± 50</td>
</tr>
<tr>
<td>Nd</td>
<td>5.7 ± 0.1</td>
<td>6.4E6 ± 4.6E6</td>
<td>-38.84 ± 27.66</td>
<td>149 ± 106</td>
</tr>
<tr>
<td>Sm</td>
<td>7.6 ± 0.2</td>
<td>120000 ± 34000</td>
<td>-28.99 ± 8.21</td>
<td>123 ± 70</td>
</tr>
<tr>
<td>Eu</td>
<td>6.2 ± 0.3</td>
<td>35000 ± 13000</td>
<td>-25.94 ± 9.63</td>
<td>108 ± 80</td>
</tr>
</tbody>
</table>

The trends in the lanthanides are distinct from those seen in the lactate and glycolate data. In the lactate and glycolate data, the enthalpy values remain relatively constant across the series. In the malonate, the enthalpy values decrease rapidly and then plateau around the middle lanthanides. These trends are consistent with what was seen in the predicted enthalpies seen in Table 4-1, though the measured data are clearly more endothermic than the predicted values. The calculations performed above combined data obtained at two separate ionic strengths, and do not account for contributions from different species than those predicted in chemical equations 1 and 2. While this reduces confidence in those values, there is a large difference seen in the measured values that may be attributed to the influence of the medium on the reaction enthalpies. The
2.00 ± 0.010 M malonate data were also analyzed for comparison to the predicted values, as well as the glycolate and lactate data.

The enthalpy, stability constant, Gibbs energy, and entropy calculated for the 2.00 ± 0.010 M malonate data are presented in Table 4-5. As occurred in both the glycolate and the lactate solutions, the total (endothermic) heat per each injection in the 2.00 ± 0.010 M malonate data was smaller than that in the 1.00 ± 0.010 M malonate data. The reduction in the heat makes the system somewhat more susceptible to small errors between titration runs. Interestingly, the decrease in the stability constant between the 1.00 ± 0.010 M data and the 2.00 ± 0.010 M data allowed for a better fitting of the data, though the analysis was still not extended to the reaction-independent thermodynamic constants. This analysis requires using the literature data, which were acquired at a different ionic strength, to fit the equilibrium constant. Comparing data at difference ionic strengths limits the confidence in the resulting constants, as the ionic strength can influence a number of parameters such as pKₐ values. If a new set of data for the malonate complexes is acquired at 2.0 M ionic strength, then this analysis may provide a useful comparison to literature for the metal-DTPA complex formation in malonate buffer.

Table 4-5 Values of ΔH, K, ΔG, and ΔS for the reaction of 51 mM DTPA with 5 mM of the respective lanthanides in 2.0 M malonate at pH 3.60 in 2.0 M ionic strength. The errors are reported at ± 1σ.

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>ΔH (kJ/mol)</th>
<th>K</th>
<th>ΔG (kJ/mol)</th>
<th>ΔS (J/mol·K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>La</td>
<td>20.6 ± 0.1</td>
<td>1700 ± 76</td>
<td>-18.44 ± 0.82</td>
<td>131 ± 6</td>
</tr>
<tr>
<td>Ce</td>
<td>19.4 ± 0.4</td>
<td>2800 ± 100</td>
<td>-19.68 ± 0.70</td>
<td>131 ± 5</td>
</tr>
<tr>
<td>Pr</td>
<td>14.2 ± 0.4</td>
<td>8800 ± 330</td>
<td>-22.51 ± 0.84</td>
<td>123 ± 5</td>
</tr>
<tr>
<td>Nd</td>
<td>2.7 ± 0.1</td>
<td>67000 ± 28000</td>
<td>-27.55 ± 11.51</td>
<td>101 ± 43</td>
</tr>
<tr>
<td>Sm</td>
<td>6.3 ± 0.1</td>
<td>4700 ± 610</td>
<td>-20.96 ± 2.72</td>
<td>91 ± 12</td>
</tr>
<tr>
<td>Eu</td>
<td>4.3 ± 0.1</td>
<td>53000 ± 9000</td>
<td>-26.96 ± 4.58</td>
<td>105 ± 18</td>
</tr>
</tbody>
</table>
Contrary to the predicted values in Table 4-1, the enthalpy terms in 2.0 M malonate are slightly less endothermic than the 1.00 ± 0.010 M malonate data. This effect is probably correlated to a reduction in the hydration of the metal center at the high concentrations of the buffer, removing the endothermic dehydration energy which was not accounted for in the predicted enthalpies above. Reactions with the lanthanides are frequently endothermic and complex formation reactions are generally entropy driven. The trends across the series remain the same as those in 1.00 ± 0.010 M malonate, with a decrease in the enthalpy from lanthanum through praseodymium with a larger drop near neodymium. The stability constant values show an inverse trend. This may offer a possible explanation for one of the effects reported in the original TALSPEAK papers, which noted a change in the order of extractability of the lanthanides when the buffer was added, relative to extraction from mineral acids. This change in extractability is one potentially significant effect from the high buffer concentration that can be further probed in calorimetric entropy titrations, but is difficult to determine by other chemical techniques.

Conclusions

The malonate buffer system was studied to investigate extensions of the calorimetric entropy titration technique beyond prior investigations of these reactions in concentrated lactate and glycolate buffers. Approximate values for the reaction enthalpy were calculated using data available in the literature, though the data in literature are at a lower ionic strength than the experiments conducted here. The data from the calorimetric entropy titrations indicate that the reactions in this series have much smaller heat per injection, causing larger uncertainties in the individual data points and a concurrent error in the fitting of these data.
There are several potential approaches to increasing the signal in a calorimetric experiment. Increasing the concentration of the titrant will improve the signal, though if the experiment is to match the conditions there also must be an equivalent increase in the metal concentration. Increasing the volume of the injections similarly improves the heat evolved or absorbed, but reduces the number of points in the overall curve, and may result in similarly poor fitting. Finally, changing the pH may provide changes in the signal, by having increased contributions from other protonation reactions. In the case of malonate, a change to a pH closer to the lower pKₐ of 2.6 or the higher pKₐ of 5.0 offers a potential way to increase the signal in the experiments. A lower pH will result in a more complex system including a protonated metal-DTPA complex making the modeling of the system more complex, though manageable. A higher pH will probably result in endpoints in the titration, rather than equilibrium curves, due to the absence of proton competition for the DTPA.

Some effects of the malonate buffer have been suggested. This system proved more difficult to analyze using the calorimetric technique, though the technique was not optimized for the system studied. Experiments to determine the thermodynamic values for complexation reactions and enthalpies in the malonate-lanthanide system at 2.0 M ionic strength would allow better comparison between the calorimetrically determined thermodynamics and those predicted based on chemical equations 1 and 2. These experiments may allow further characterization of medium effects in similarly complex systems as TALSPEAK with the entire lanthanide series. Further optimization of the entropy titration technique for the lanthanides offers an alternative method to determine stability constants and medium effects in this series of elements where chemical techniques such as spectroscopy or potentiometry have limited applicability.
References


(11) Weaver, B.; Kappelmann, F. A. TALSPEAK: A New Method of Separating Americium and Curium from the Lanthanides by Extraction from an Aqueous Solution of an Aminopolyacetic Acid Complex with a Monoacidic Organophosphate or Phosphonate; ORNL 3559; Oak Ridge National Laboratory: Oak Ridge, TN (United States), 1964.


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Chapter 5

Conclusions

Project Goals

The primary goal of the present work was applying a new technique to probe the thermodynamics of TALSPEAK-like systems directly. After verifying that the technique can provide thermodynamic data, this work was extended to examine the influence of the medium on the thermodynamics of complexation in concentrated buffer solutions: lactate, glycolate, and malonate. A calorimetric model was developed to determine condition-specific constants that can be compared between the different solutions under identical conditions. A separate model was developed for determining the stability constant for the metal-DTPA complex formation independent of experimental conditions. These experiments shed some light on possible origins of these medium effects, by comparing the influence of several structurally distinct background buffers. To complete the comparison between the systems, luminescence titrations and luminescence lifetime measurements were conducted to support the model applied in the calorimetric experiments, and to give some insight into the coordination modes of the buffers.

Lactate

The literature values reported in the Martell and Smith database for the formation constants between lactate and the lanthanides were incomplete, so a new set of these values was determined via potentiometric titrations in sodium nitrate. The values are in reasonable agreement with the literature, and were used for modeling titration experiments, as well as the analysis of the condition-independent stability constants in both luminescence titrations and calorimetry.
Luminescence titrations were conducted using europium, as this is the only lanthanide with a hypersensitive transition in the luminescence spectrum accessible to the instrument. These experiments confirmed the formation of a single metal-DTPA complex as expected from literature. At the 1.00 M lactate concentration, the DTPA completely displaced the metal-coordinated lactate molecules at the termination of the entropy titration, but this was not the case in the 2.00 M lactate data. The reaction does not go to completion in the high lactate concentration, instead reaching an equilibrium concentration of approximately 80% metal complexed to the DTPA, the rest in a tris-lactate complex. Luminescence lifetime measurements in the same solutions suggest the lactate coordinates through both the α-hydroxyl group and the deprotonated carboxyl group. Interestingly, the number of OH oscillators in the inner coordination sphere of the ion is between 5 and 6, suggesting that only a single water molecule is coordinated in the europium-lactate complex.

The calorimetric entropy titrations in both the 1.00 M lactate and 2.00 M lactate suggest a change in the stability constant for the metal-DTPA complex relative to 2.0 M sodium perchlorate. The condition-independent values for the equilibrium constant suggest that there is an effect associated with the medium, as when compared to the sodium perchlorate data at the same ionic strength, the stability constants for the metal-DTPA complex increase in the light lanthanides. The uncertainties in the heavier lanthanide experiments are too large to determine whether this effect continues. The enthalpy, stability constant, Gibbs energy, and entropy were determined for the reaction-dependent values from the calorimetric entropy titrations in the 1.00 M and 2.00 M lactate data. They indicate that, while enthalpy remains relatively constant, the equilibrium constant is significantly reduced at higher concentrations of the buffer suggesting a decrease in the favorable entropy for the reaction. An additional effect seen in the high
concentration buffer was a change in the thermodynamic trends in the series. In the 1.00 M lactate data, the values for the equilibrium constant increase, then decrease briefly before increasing again. The 2.00 M lactate data increase in an orderly fashion from La through Eu, though the equilibrium constant becomes so small for lanthanum that the fitting equation is no longer a sigmoid curve, and the resolved enthalpy values are unrealistically large.

**Glycolate**

Glycolate is a structurally analogous buffer to lactate, but is slightly smaller and was chosen to probe whether the structure of the buffer had a significant impact on the thermodynamics of the complex formation. The glycolate data available in the literature for 2.0 M ionic strength are complete for the 1:1 through 1:3 complexes. There is an additional 1:4 complex reported at 0.5 M ionic strength that was included in the modeling for the experiments conducted here. While the literature values are at different ionic strengths, including the tetra-glycolate complex simplifies the explanation for the luminescence titration data, and therefore the tetra-glycolate species is considered as the primary reactant species.

Luminescence titrations were performed with europium to determine whether there are differences in the metal-DTPA complex formation constant when the buffer is changed from lactate to glycolate. When the tetra-glycolate complex is included in the fitting, there is no difference in the value of the stability constant between the 1.00 M lactate and 1.00 M glycolate data. There is a difference of 0.1 in the values of the log K for the formation of the DTPA-metal complex in the 2.00 M glycolate and lactate, again when including the tetra-glycolate species. Excluding the tetra-glycolate complex lowers the stability constant by 0.5 in log K. In the 2.0 M glycolate, this is significantly lower than the stability constant determined in either sodium perchlorate or sodium triflate.
The luminescence lifetime measurements in glycolate gave longer lifetimes than those in the lactate solution, suggesting more water is excluded from the inner coordination sphere. Several possible structures for the glycolate complexes were proposed, and the approximate numbers of coordinated waters were calculated based on the speciation including the tetra-glycolate complex. The luminescence lifetimes are fit using an exponential decay, and the number of OH oscillators is calculated from an empirical equation from the literature. After addition of 2.63 equivalents of DTPA, the 1.00 M glycolate data show only the single DTPA species, while the 2.00 M glycolate data show the DTPA complex and a second species that has the equivalent of 4 OH oscillators coordinated. This was attributed to the tetra-glycolate species and offers further support for inclusion of this species in the calorimetric model.

Calorimetric entropy titrations were conducted using the same system as the lactate solutions for comparison. When comparing the reaction-independent stability constants to literature values, there is an apparent increase in the glycolate medium comparable to the increase in the lactate media. Though there are relatively large errors in the data, the effect appears to be significant. The alternative condition-specific model was used to determine the thermodynamic parameters for comparison to the lactate data. The values for the glycolate data follow similar trends from La to Eu, but are more exothermic. Greater exothermic character in the glycolate system was attributed to a decrease in the endothermic dehydration energy of the metal ion.

**Malonate**

Because malonate has been proposed as an alternative buffer for Advanced TALSPEAK, this system was also investigated in this work. There is increased uncertainty in modeling the malonate system, because most of the literature data for malonate was measured at 1.0 M ionic
strength, while the literature for DTPA and these experiments were conducted at 2.0 M ionic strength. Approximate values for the enthalpy were calculated from the literature values, and the trends were compared to the calorimetrically determined results. Luminescence spectroscopy and luminescence lifetime studies were conducted to compare to glycolate and lactate.

The stability constants determined via luminescence in the 1.00 M malonate data were low even when the protonated metal complex was included in the fitting. Protonated outer-sphere complexes have been suggested to artificially lower stability constants determined by spectrophotometric techniques relative to potentiometric determination, so this result is not surprising. At 2.00 M malonate, however, the stability constant for the DTPA complex is larger than that in literature, and the complex is insensitive to changing the model to include the protonated complex. This behavior is opposite that observed in the lactate and glycolate systems. This result was attributed to the differences in the hydration and complexation of the malonate relative to the lactate and glycolate.

Luminescence lifetime measurement suggest that the malonate removes less water from the inner coordination sphere of europium than either lactate or glycolate. The lifetimes suggest that either three or four water molecules remain coordinated to the europium metal center, even at the 2.00 M malonate concentration, in which the dominant species is Eu(mal)$_2^-$. Unlike both the lactate and the glycolate data, after the addition of 2.63 equivalents of DTPA only a single species was apparent in the lifetime measurement, indicating that DTPA completely displaces malonate by the end of the titration. This could have implications in the separations process, if an Advanced TALSPEAK system were to operate with these conditions.

The calorimetric titrations proved problematic with this buffer system. The enthalpy of complexation for each of the lanthanides studied in this system was small, resulting in relatively
little heat evolved at each injection. As a result, small errors in any of the triplicate runs resulted in large errors in the equilibrium constant, and consequently the more rigorous analysis to determine the condition-independent stability constants was not conducted. The reaction enthalpy values followed the trends calculated from literature, with a decrease from La through Eu, though they were more endothermic than predicted. Explicit comparison between measured and predicted values should be approached with caution, as the ionic strengths of the measurements from the literature were not the same as those of the experiments. There are several interesting characteristics of this system, however. The enthalpy for the reaction is considerably less endothermic than the lactate and glycolate data, the equilibrium constants even with large error are comparable, and the resulting entropy is smaller than that measured in glycolate or lactate. To confirm these results, several additional studies are necessary.

**Future Work**

Extending the application of calorimetric entropy titrations to the heavy lanthanides may offer additional insight into the influence of the medium. Optimizing the system for specific lanthanides also has the potential to address the challenges encountered in the analysis here. Changing the pH to a higher value would allow better assessment of the equilibrium constant for lanthanum and cerium, where the titration curve did not have a sigmoid shape. The opposite is the case for the europium and samarium samples, where the titration curve reaches an endpoint. When the titration curve is too steep, there are not enough points along the central curve and large uncertainties tend to appear. As a result of this lack of curvature, no equilibrium constant can be determined. A change to a lower pH in the heavy lanthanides offers a region in which more proton competition for the DTPA will shift the equilibrium, and allow for a significant number of points in the region of the curve where the equilibrium constant is measured. Further
development of the condition-independent model can also allow determination of the condition-independent enthalpy as well as the equilibrium constant. The combination of these data would allow comparison of enthalpy, entropy, and Gibbs energy in a wide variety of systems, potentially providing important insight into the effects of a range of different types of media.
APPENDIX A

Included in this appendix are representative thermograms for each metal and each buffer system. The captions for the figures indicate the conditions for each solution, and the conditions under which the titrations were conducted. All data were acquired at 25.00 ± 0.01°C.

Titrand: 5.2 mM La³⁺, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.0 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.2 mM La³⁺, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.0 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.9 mM La³⁺, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.9 mM La³⁺, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.4 mM DTPA, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.0 mM La$$^{3+}$$, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM La$$^{3+}$$, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Ce$$^{3+}$$, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Titrant: 51.0 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Ce$$^{3+}$$, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Titrant: 51.0 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$$\textsubscript{3}$$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.8 mM Ce³⁺, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.7 mM Ce³⁺, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.4 mM DTPA, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.6 mM Ce³⁺, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.7 mM Ce³⁺, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.2 mM DTPA, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
**Titrand:** 5.0 mM Pr³⁺, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.0 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

**Titrand:** 4.9 mM Pr³⁺, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.4 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

**Titrand:** 4.9 mM Pr³⁺, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

**Titrand:** 4.9 mM Pr³⁺, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.4 mM DTPA, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.0 mM Pr$^{3+}$, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Pr$^{3+}$, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 51.2 mM DTPA, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 6.4 mM Nd$^{3+}$, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 50.9 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.9 mM Nd$^{3+}$, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 51.4 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 4.6 mM Nd\(^{3+}\), 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Nd\(^{3+}\), 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Titrant: 51.4 mM DTPA, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.6 mM Nd\(^{3+}\), 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.6 mM Nd\(^{3+}\), 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Titrant: 51.2 mM DTPA, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO\(_3\). Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.4 mM Sm$^{3+}$, 1.00 M total lactate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Titrant: 51.0 mM DTPA, 1.00 M total lactate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.4 mM Sm$^{3+}$, 1.00 M total lactate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Titrant: 51.4 mM DTPA, 2.00 M total lactate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.9 mM Sm$^{3+}$, 1.00 M total glycolate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 4.7 mM Sm$^{3+}$, 2.00 M total glycolate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Titrant: 51.4 mM DTPA, 2.00 M total glycolate, pH 3.60, $I = 2.0$ M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.0 mM Sm$^{3+}$, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Sm$^{3+}$, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.2 mM DTPA, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.5 mM Eu$^{3+}$, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.0 mM DTPA, 1.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.2 mM Eu$^{3+}$, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Titrant: 51.4 mM DTPA, 2.00 M total lactate, pH 3.60, I = 2.0 M maintained with NaNO₃. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.
Titrand: 5.0 mM Eu$^{3+}$, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 50.9 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Eu$^{3+}$, 2.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 51.1 mM DTPA, 1.00 M total glycolate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.

Titrand: 5.0 mM Eu$^{3+}$, 2.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Titrant: 51.1 mM DTPA, 1.00 M total malonate, pH 3.60, I = 2.0 M maintained with NaNO$_3$. Injections 5 μL, initial volume 1.000 ± 0.017 mL, 300 rpm stirring speed, 5 min equilibration time.