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ENERGY TRANSFER IN A DISCRETE, SOLUBLE HETEROBIMETALLIC COMPLEX CONTAINING Tb^{3+} AND Eu^{3+}.

by

NIKHIL K. BARUA

THESIS

Submitted to the Graduate School

of Wayne State University,

Detroit, Michigan

in partial fulfillment of the requirements

for the degree of

MASTER OF SCIENCE

2014

MAJOR: CHEMISTRY

Approved by:

Advisor Date

DEDICATION

My thesis is dedicated to my lovingly and caring Mother Neetu Barua and my motivating Father Naresh Barua, who have made a lot of sacrifices in their life for me only to see me as an honest and successful person contributing something to this world.

ACKNOWLEDGEMENTS

I would like to thank my wonderful advisor, Dr. Matthew J. Allen, for helping me in every phase of the graduate school life. His promptness, patience to listen, never ending optimism and punctuality to guide and support me during every phase of my time in the Allen Research Group has given me enough boost to carry out any work in life independently. His commitment towards science by showing up to work at 5.00 a.m. in the morning has left a never ending motivation in me to move forward. I am thankful to my committee members Dr. Stanislav Groysman and Dr. Jennifer Stockdill for giving their precious time and efforts to review my project and thesis, and voice their opinions on it. I am thankful to Dr. Verani for his advices which will help me in the near future.

I thank the Allen Lab group members, Dr. Sashi Vithanarachchi who is one of the most enlightened person I have ever met, Dr. Jeremy Moore, Dr. Buddhima Mahanama, Dr. Joel Garcia, my best friend Akhila Kuda-Wedagedara, Lauren Hopper, Chamika Lenora, Zhijin Lin, Levi (also known as Dr. evil) the funniest person in my group, Lina Basal, Micheal Cross and Cheng Wang. I'm indeed lucky to have the best group I have ever met by far, who took good care of me when in need and most of the time made sure I had a smile on my face. I had a great time working with them, but find it very hard to leave them, that include my mentor Dr. Allen too.

I thank Melissa Barton who has been so kind to me and was always there willing to help me in any form when required. I thank the LIC and staff members Dr. Bashar Ksebati, Dr. Danyluk and Corey for their assistance in helping me to get data for my research.

No words in this world can or will be able to thank my parents Mrs. Neetu Barua, my dearly sweet beautiful mother and my awesome father Mr. Naresh Barua, without whom I wouldn’t have been able to appreciate the beauty of living life as a human being. I thank my brothers Anish and Jyothin to morally support me and guide me.

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I am grateful to Wayne State University for its amazing educational atmosphere where it creates a good learning environment for any form of education.

Finally I thank my failures rather than my success in the graduate school which has brought in the burning desire and motivation in my heart to chase my dreams and aim which will definitely lead me in becoming a successful scientist.

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Chapter 1: Energy transfer in multimetallic lanthanides

Multimetallic lanthanides are widely studied for their importance in contrast agents,[1] single molecule magnets,[2] as catalysts for specific cleavage of RNA,[3] and in luminescence imaging.[4] In luminescence imaging, several examples of multimetallic lanthanides have been shown to be useful in display devices,[5] telecom applications[6], and in imaging cells. In the last decade, there has been increased interest in the use of lanthanide probes for imaging cells because lanthanides exhibit long luminescence lifetimes that are on the order of milliseconds because their emissions are Laporte forbidden, in comparison to organic fluorophores that have emission lifetimes on the order of nanoseconds. Lanthanides show sharp emission bands which are narrow and do not overlap, in comparison with that of the broad emission bands of the organic fluorophores.[7] Thus, due to the advantages of lanthanide probes over organic fluorescent probes, lanthanide probes are used for the detection of several important biological species such as peptides, proteins, and DNA.[8] Based on the unique luminescence properties of lanthanides, energy transfer studies involving these rare earth metals have been attempted during the past few decades.

Lanthanide–lanthanide energy transfer has been studied in the solid state,[9] concentrated solutions,[10] and discrete homo- and hetero-bimetallic systems[11] for use in biological assays and display devices. Among the lanthanides, Eu^{3+} and Tb^{3+} are the most commonly used lanthanides for the study of energy transfer due to the long mean lifetimes of their excited states. Lanthanides such as Eu^{3+} and Tb^{3+} often are sensitized via chromophores connected to a ligand by an energy transfer process that involves the triplet state of the chromophore and an excited state of the lanthanide ion.[12] Although, numerous complexes have been reported involving the energy transfer to a monometallic lanthanide complex from an antenna,[13] energy transfers occurring in discrete multimetallic complexes containing lanthanides have been few (**Figure 1.1**).[14–17]

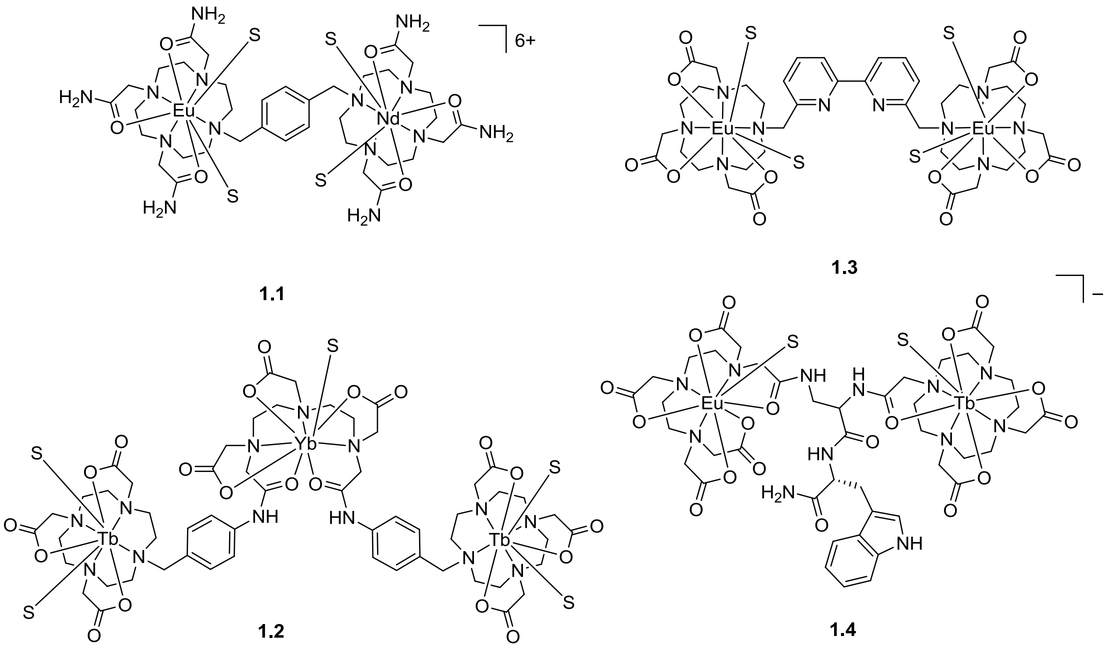


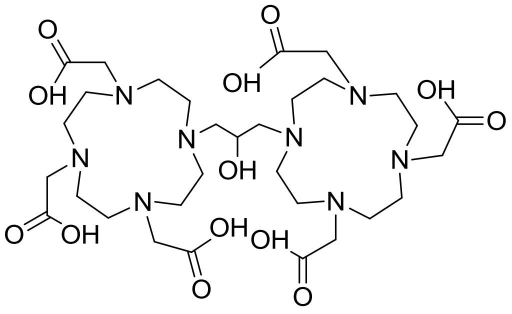
Figure 1.1 Chemical structures of reported complexes that show energy transfer using-ligand sensitzed excitation.[14–17] S stands for co-ordinated solvent molecules or anions.

The reported complexes include Eu^{3+}/Nd^{3+} heterobimetallic complex **1.1**,[14] Tb^{3+}/Yb^{3+} heterotrimetallic complex **1.2**,[15] and homobimetallic Eu^{3+}/Eu^{3+} complex **1.3**.[16] With these complexes, the presence of energy transfer was supported by decay data. Decay data provides information about the decay of an excited state of a lanthanide with respect to time. Apart from decay data, emission spectra have not been reported for these examples.[14–16] An emission spectra was reported for Tb^{3+}/Eu^{3+} heterobimetallic complex **1.4**,[17] but the excitation energy used to acquire that emission spectra was of the ligand-sensitized excitation that was of the correct energy to simultaneously excite both Tb^{3+} and Eu^{3+}; consequently, the complex does not show direct evidence of Eu^{3+} emission with direct Tb^{3+} excitation nor was Tb^{3+} luminescence-decay data was presented. While the reported systems mentioned above are discrete, soluble, and hold the metals close enough to detect interactions, they do not shield the metal ions from solvent.[14–17] The presence of solvent molecules co-ordinated to the complexes poses a problem because the vibrations of these molecules provide a route to quenching of excited states and consequently, to a decrease in luminescence intensity.

Dr. Moore, a former graduate student from Dr. Allen's Lab, published a paper on a di-Eu^{3+} complex that acted as a concentration-independent pH detection probe.[18] He observed an important feature on this complex that was the close proximity between the two metals and volunteered the possibility to make a heterobimetallic Tb^{3+}–Eu^{3+} complex using Tb^{3+} and Eu^{3+} ions. He carried out preliminary tests on the synthesis of the heterobimetallic complex and observed an energy transfer between the two metals in the discrete complex by the excitation of a lanthanide (Tb^{3+}), ruling out the need to excite the complex with an antenna.[19]

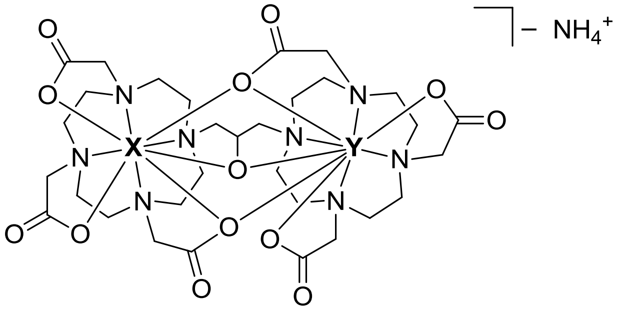
Based on the preliminary observations of Dr. Moore,[19] I began my thesis project by replicating his results and completing the control experiments necessary to publish the work. It is a difficult task to make a heterobimetallic or multimetallic complex containing lanthanides due to the small size differences in the co-ordination behavior across the lanthanides in the periodic table.[20] Considerable effort by Bünzli and co-workers has been shown earlier in making heterobimetallic complexes.[21] I synthesized heterobimetallic Tb^{3+}–Eu^{3+} complex **1.6** by controlled addition of Tb^{3+} and Eu^{3+} to the previously reported ligand system (**Figure 1.2**).[18]

Thus, taking the above stated points related to the complex **1.7**, I made complex **1.6** to observe energy transfer between Tb^{3+} and Eu^{3+}, using only Tb^{3+}-specific excitation. To the best of my knowledge, this complex is the first one to exhibit an energy transfer between lanthanides in a discrete heterobimetallic complex isolated from environment (solvent) without the use of an antenna. This novel finding for observing an energy transfer between lanthanides using a lanthanide excitation without the need of an antenna would be useful and interesting for fundamental studies of energy transfer.



1.5

Figure 1.2 Chemical structure of the ditopic ligand.



1.6, X = Tb, Y = Eu
1.7, X = Y = Eu
1.8, X = Tb, Y = Gd
1.9, X = Y = Tb
1.10, X = Y = Gd

Figure 1.3 Chemical structures of complexes **1.6–1.10**.

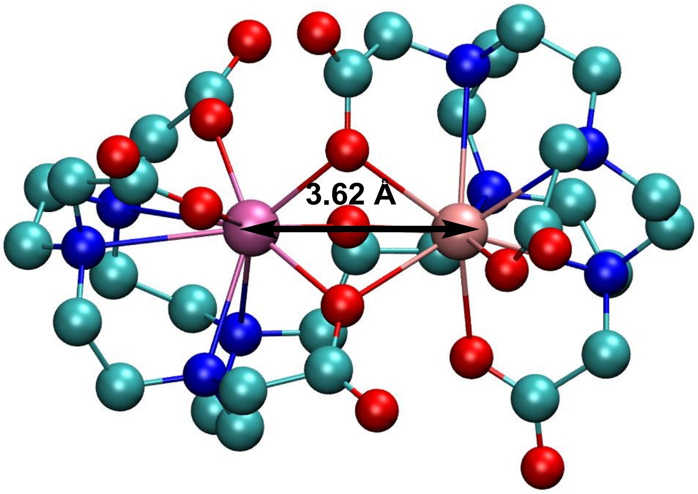


Figure 1.4 The optimized model of **1.6** was obtained using Gaussian-09 software and shows the Tb^{3+}–Eu^{3+} distance. Red, blue, cyan, magenta, and brown represent oxygen, nitrogen, carbon, terbium, and europium, respectively. Hydrogen atoms have been omitted for clarity. The computational data was performed by Dr. Cisneros.[22]

I confirmed what Dr. Moore proposed and observed in preliminary experiments,[20] that energy transfer occurs in the mixed metal Tb^{3+}–Eu^{3+} complex **1.6**, likely because of the short distance between the two luminescent centers at 3.62 Å (**Figure 1.4**)[9,23] and the optimal energy difference 3,100 cm^{-1} between the $^5D_0$ state of Eu^{3+} and the $^5D_4$ state of Tb^{3+} (**Figure 1.5**).[23] There are numerous reports that suggest that efficient energy transfer requires the distance between the donor and acceptor to be shorter than 10 Å and the difference between the excited states of the the donor and acceptor to be less than 5,000 cm^{-1}.[23] The structure of complex **1.6** was optimized with Gaussian 09 at the PBE0/SDDall level (small core for all atoms) using the default convergence criteria by Dr. Cisneros.[22] Even though I did not have crystallographic evidence for the distance between Tb^{3+} and Eu^{3+} ions, the computational data can be considered as support for the metal–metal distance of 3.62 Å.

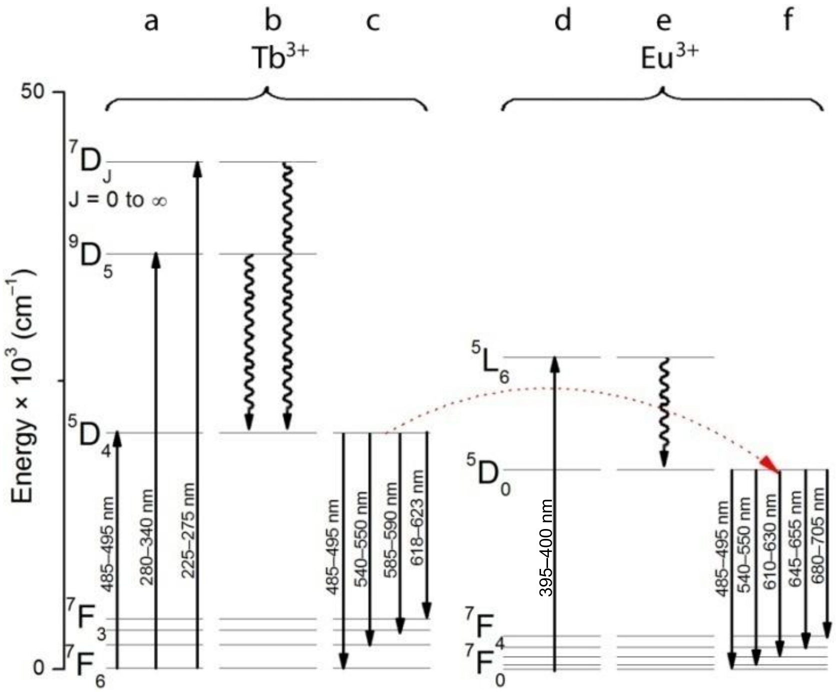


Figure 1.5 Simplified Jablonski diagram that shows **a**, excitation of Tb^{3+} ($^7F_6 \rightarrow {}^5D_4$, $^7F_6 \rightarrow {}^9D_2$, and $^7F_6 \rightarrow {}^7D_{J,\ J\ =\ 0\ \mathrm{to}\ \infty}$) with associated wavelengths; **b**, radiationless decay to the long-lived excited state of Tb^{3+} ($^5D_4$); **c**, radiative emission of Tb^{3+} ($^5D_4$ to $^7F_6$, $^7F_5$, $^7F_4$, and $^7F_3$) with associated wavelengths; **d**, Excitation of Eu^{3+} ($^7F_0 \rightarrow {}^5L_6$); **e**, radiationless decay to the long-lived excited state of Eu^{3+} ($^5D_0$); and **f**, emission of Eu^{3+} ($^5D_0$ to $^7F_0$, $^7F_1$, $^7F_2$, $^7F_3$, and $^7F_4$) with associated wavelengths. The red dashed line depicts energy transfer from the long-lived excited state of Tb^{3+} to the excited state of Eu^{3+} [$^5D_4(\mathrm{Tb}^{3+}) \rightarrow {}^5D_0(\mathrm{Eu}^{3+})$]. States that are irrelevant to this study have been omitted for clarity.

Because other reported bimetallic complexes show the energy transfer occurring via luminescence-decay studies, I thought of using luminescence-decay studies, to study complex **1.6**. I thought of measuring and comparing the decay rates of the donor Tb^{3+} ion in complexes **1.6** and **1.8**. Theoretically, the luminescence decay of Tb^{3+} should be faster in **1.6** (Tb^{3+} and Eu^{3+}) relative to **1.8** (Tb^{3+} and Gd^{3+}) due to the energy transfer from Tb^{3+} to Eu^{3+} and not from Tb^{3+} to Gd^{3+}. Thus, Dr. Moore's initial findings prompted me to synthesize complexes **1.6** and **1.8** and motivated me to further explore the energy transfer studies in **1.6**.

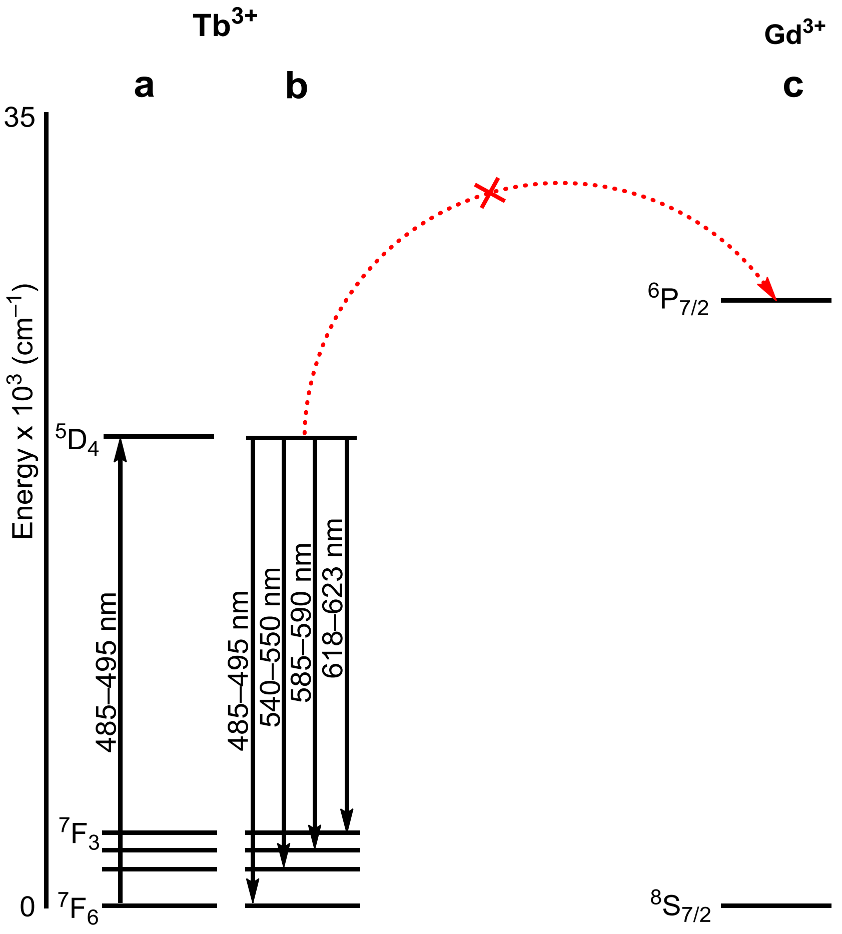
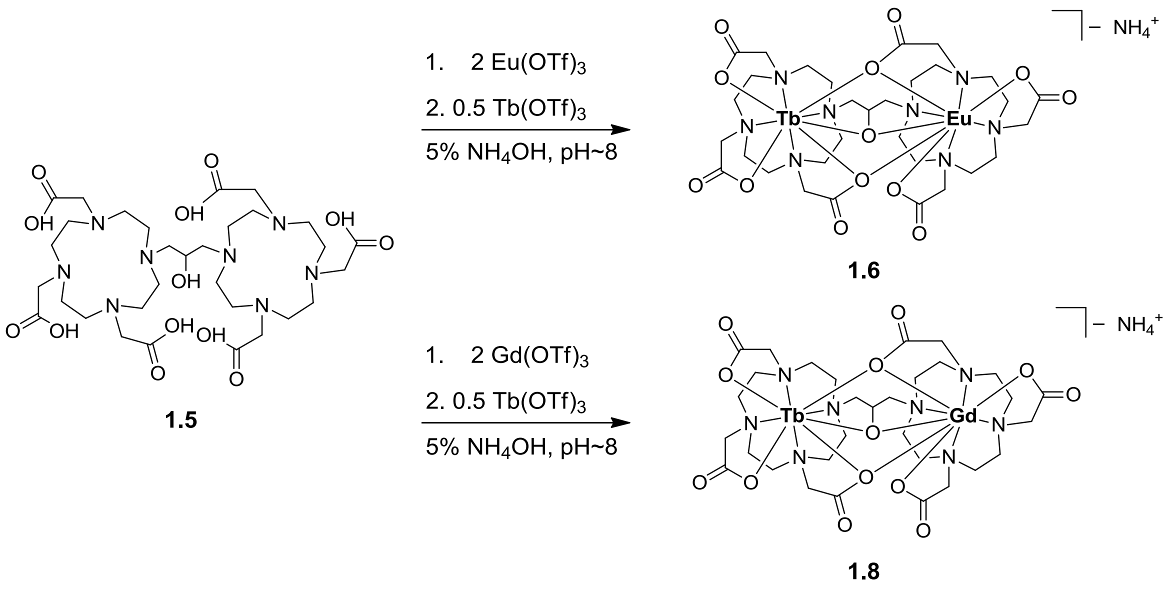


Figure 1.6 Simplified Jablonski diagram depicting lack of energy transfer between the excited states of Tb^{3+} and Gd^{3+}. **a,** Excitation of Tb^{3+} ($^7F_6 \rightarrow {}^5D_4$), with associated wavelengths. **b,** Radiative emission of Tb^{3+} ($^5D_4$ to $^7F_6$, $^7F_5$, $^7F_4$, and $^7F_3$) with associated wavelengths. The red crossed dashed line depicts the absence of energy transfer from the long-lived excited state of Tb^{3+} to the excited state of Gd^{3+} [$^5D_4(Tb^{3+}) \rightarrow {}^6P_{7/2}(Gd^{3+})$]. **c,** Depiction of Gd^{3+} states ($^8S_{7/2}$ and $^6P_{7/2}$). States that are irrelevant to this study have been omitted for clarity.

CHAPTER 2: Experimental Procedures for the Synthesis of Homo- and Hetero-bimetallic Complexes

Commercially available chemicals were used without purification. Water was purified using a PURELAB Ultra Mk2 water purification system (ELGA). After metallation, complexes were freeze dried to remove water. High performance liquid chromatography (HPLC) was performed using a 250 mm long Pinnacle PPFP column with 4 or 10 mm diameters for analytical and preparative HPLC, respectively. Detection of the complexes was achieved using a fluorescence detector. High resolution electrospray ionization mass spectra (HRESIMS) were obtained on an electrospray time-of-flight high-resolution Waters Micromass LCT Premier XE mass spectrometer and were acquired without the use of a column. Metal concentrations were determined using Horiba Ultima inductively coupled plasma optical emission spectroscopy (ICP-OES). Excitation and emission of complexes **1.6–1.10** were measured at ambient temperature using a Horiba Jobin Yvon Fluoromax-4 spectrofluorometer equipped with a 400 W xenon lamp in fluorescence mode (increment = 1 nm and the excitation and emission slit widths were 5 and 1 nm, respectively). Decay-rate measurements of complexes **1.6** and **1.8** were acquired on the same instrument with excitation and emission wavelengths of 487 and 545 nm, respectively. The pH for the samples was measured with pH paper. Settings for the decay-rate measurements included excitation and emission slit widths of 5 nm, an initial delay of 0.01 ms, a max delay of 3 ms, and a delay increment of 0.1 ms. Ligand **1.5** was synthesized following reported procedures.[18] The purity of complexes **1.6–1.10** was determined using a fluorescence detector in HPLC-MS. The method for analyzing the purity of complexes **1.6, 1.7,** and **1.9** by HPLC-MS was followed from Dr. Moore's procedure.[20] Whereas, the method for analyzing the purity of complexes **1.8** and **1.10** by HPLC-MS was my own procedure.

2.1 *Synthesis of Hetero-bimetallic complexes*



Scheme 2.1 Synthesis of hetero-bimetallic complexes using ligand **1.5** and lanthanide triflate salts under basic conditions.

The synthesis of heterobimetallic complex **1.6** was first carried out by Dr. Jeremy Moore by adding 2 equivalents of europium triflate and 1 equivalent of terbium triflate to 1 equivalent of ligand **1.5**.[20] But, this route led to a possibility for the formation of complex **1.9**, though **1.9** (di-Tb^{3+}) would not interfere in the emission spectra studies of **1.6**, it would certainly interfere in the luminescence-decay rate experiment performed with **1.6** because the decay experiment is performed with Tb^{3+}-specific excitation and emission wavelengths and complex **1.9** contains Tb^{3+} ions. To suppress the formation of complex **1.9**, I modified the synthetic route by adding 0.5 equivalents of terbium triflate instead of 1 equivalent. A similar strategy was adopted for the synthesis of the Tb^{3+}-Gd^{3+} complex **1.8**.

Synthesis of Ammonium{1-[europium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate)),3-[terbium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate))]propan-2-oxide} complex (**1.6)**:

To a solution of 1,3-di[1,4,7,10-tetraazacyclododecanyl(1,4,7-triacetate)]propan-2-ol[18] **1.5** (1.00 mL, 0.0710 mmol, 71.1 mM, 1 equiv) was added NH_4OH (1 mL, 5% aqueous solution) dropwise until the pH of the solution was 6.5. To the resulting solution was added an aqueous solution of europium triflate (1.57 mL, 0.0710 mmol, 45.6 mM, 2 equiv). The resulting solution was stirred at ambient temperature for 12 h, while the pH was maintained at 6.5 with the addition of NH_4OH (0.3 mL, 5% aqueous solution). To the resulting solution was added an aqueous solution of terbium triflate (2.51 mL, 0.0710 mmol, 28.2 mM, 0.5 equiv) (**Scheme 2.1**). The reaction was stirred for 12 h, then the pH was increased to 12 with the addition of NH_4OH (0.5 mL, 30% aqueous solution) to precipitate excess terbium and europium as hydroxides. After stirring for 6 h, the resulting suspension was filtered using a 0.2 µm syringe filter to remove terbium and europium hydroxides. The resulting solution was freeze dried and the solid was analysed using HPLC-MS. HRESIMS (*m/z*): $[M+H]^+$ calcd for $Eu_{Tb}C_{31}H_{51}N_8O_{13}$, 1053.2028; found, 1053.2015

Synthesis of Ammonium{1-[gadoliniumium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate)),3-[terbium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate))]propan-2-oxide} complex (**1.8)**:

To a solution of 1,3-di[1,4,7,10-tetraazacyclododecanyl(1,4,7-triacetate)]propan-2-ol[18] **1.5** (0.375 mL, 0.0710 mmol, 0.0267 mM, 1 equiv) was added NH_4OH (1 mL, 5% aqueous solution) dropwise until the pH of the solution was 6.5. To the resulting solution was added an aqueous solution of gadolinium triflate (1.77 mL, 0.0710 mmol, 30.1 mM, 2 equiv). The resulting solution was stirred at ambient temperature for 12 h while the pH was maintained at 6.5 with the addition of NH_4OH (0.1 mL, 5% aqueous solution). To the resulting solution was added an aqueous solution of terbium triflate (0.477 mL, 0.0710 mmol, 28.2 mM, 0.5 equiv) (**Scheme 2.1**). The reaction was stirred for another 12 h at which point the pH was increased to 12 with the addition of NH_4OH (0.3 mL, 30% aqueous solution) to precipitate excess of terbium and gadolinium as hydroxides. After stirring for 6 h, the resulting suspension was filtered using a 0.2 µm syringe filter to remove terbium and gadolinium hydroxides. The resulting solution was freeze dried and analyzed using HPLC-MS. HPLC-MS analysis indicated that complex **1.8** contained 6-arm and a small amount of 5-arm metal complexes, both of the species eluting under the same retention time at 6.91–9.01 min. It also showed the presence of **1.10**. Binary gradient method (pump A: water, pump B: acetonitrile; 0→9.8% B for 10 min, 9.8→10% B over 2 min, 10% over for 4 min, 10→5% B for 4 min, 5→0% for 4 min). HRESIMS (*m/z*): $[M]^-$ calcd for $GdTbC_{31}H_{51}N_8O_{13}$, 1055.1960; found, 1055.1945.

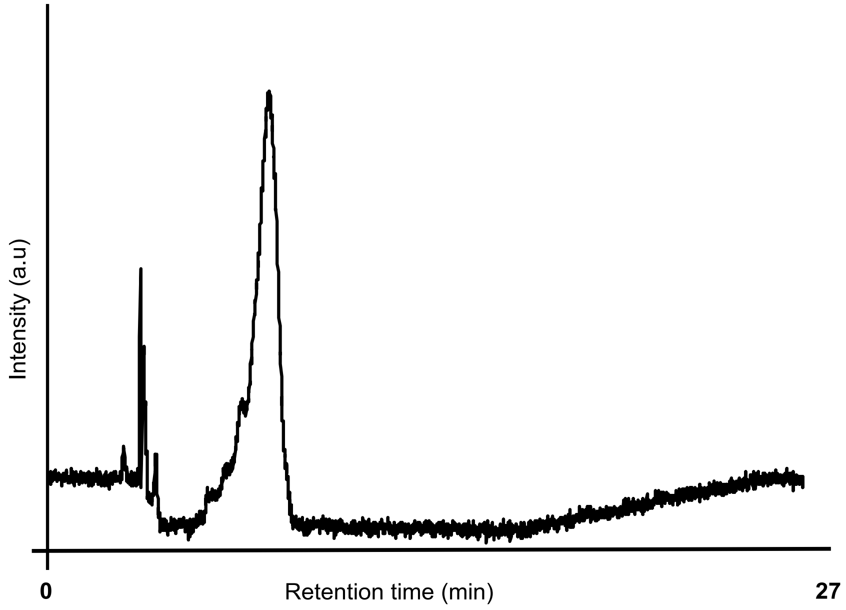


Figure 2.1 HPLC chromatogram of **1.8** detected using a fluorescence detector (λ_{ex} = 228 nm and λ_{em} = 545 nm). The identity of the complex eluted at 6.91–9.01 min was confirmed to be an inseparable mixture of **1.8** and **1.10** using mass spectrometry.

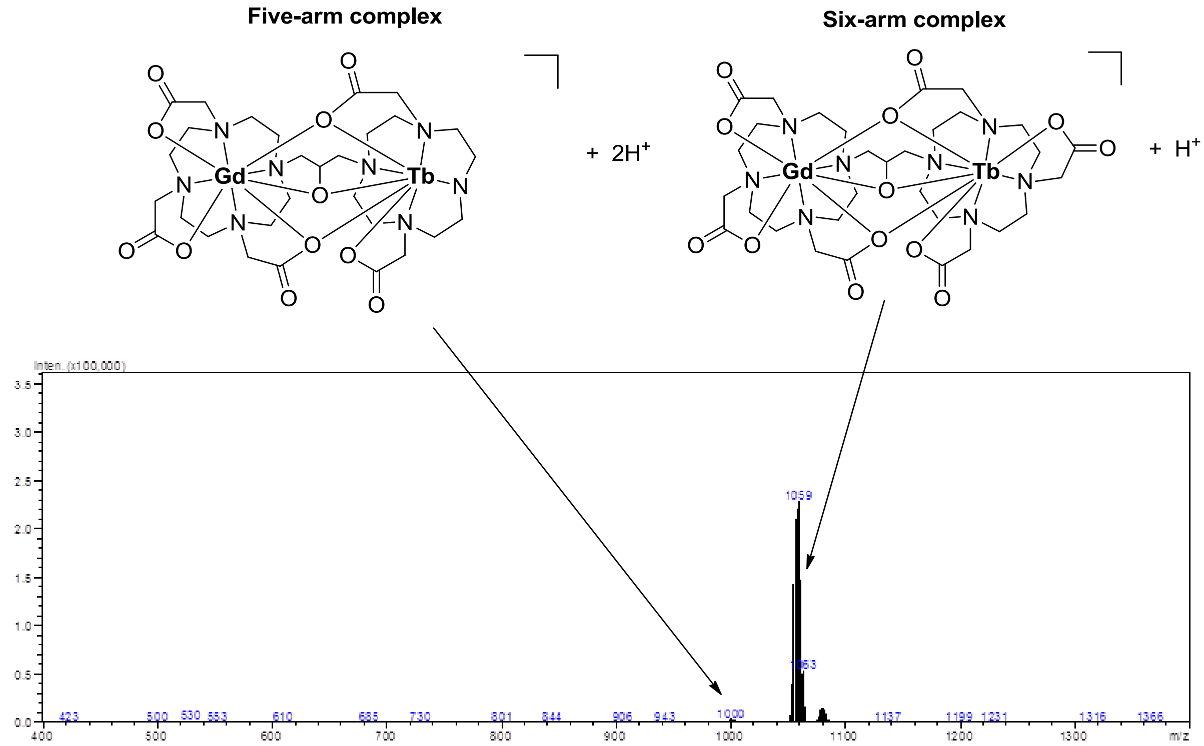


Figure 2.2 Extracted mass spectrum for metal complex **1.8** at 6.91–9.01 min retention time. The five-arm and six-arm complexes are pointed to in the spectrum.

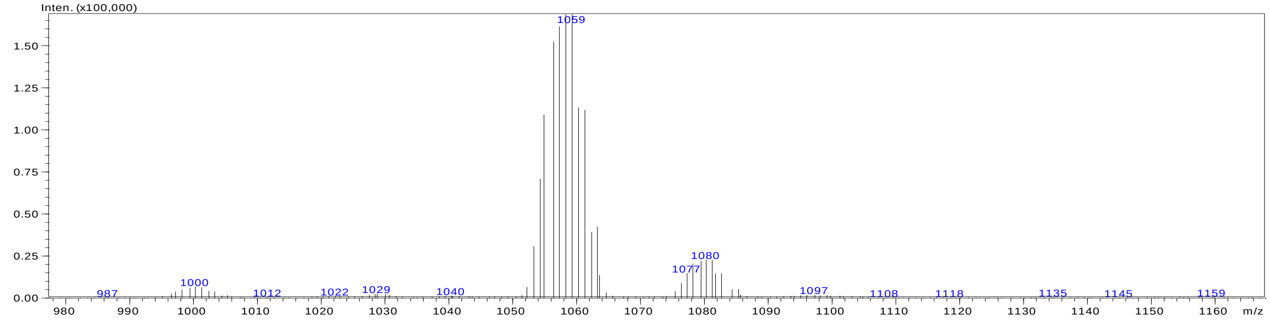
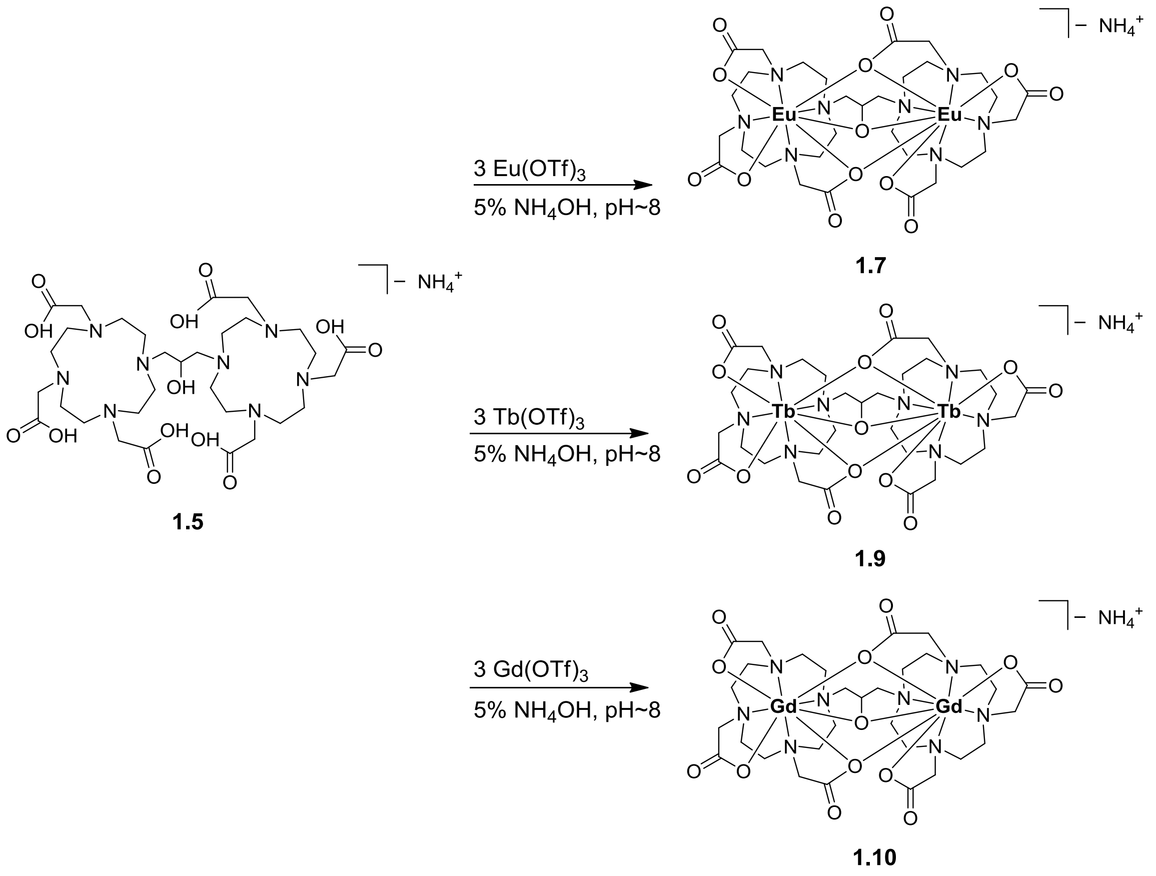


Figure 2.3 Isotopic distribution of the Gd^{3+}–Tb^{3+} complex **1.8** at 6.91–9.01 min retention time.

2.2 *Synthesis of homo-bimetallic complexes*



Scheme 2.2 Synthesis of homo-bimetallic complexes used for the study of energy transfer.

Synthesis of Ammonium{1,3-bis[europium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate))]propan-2-oxide} (NH$_4$) **(1.7)**:

To a solution of 1,3-di[1,4,7,10-tetraazacyclododecanyl(1,4,7-triacetate)]propan-2-ol[18] (4.73 mL, 0.0710 mmol, 71.1 mM, 1 equiv) was added NH_4OH (0.5 mL, 5% aqueous solution) dropwise until the pH of the solution was 6.5. To the resulting solution was added an aqueous solution of europium triflate (1.00 mL, 0.0710 mmol, 45.1 mM, 3 equiv). The resulting solution was stirred at ambient temperature for 12 h while the pH was maintained at 6.5 with the addition of NH_4OH

(1 mL, 5% aqueous solution) (**Scheme 2.2**). After the reaction was stirred for 12 h, the pH was increased to 12 by the addition of NH_4OH (0.8 mL, 30% aqueous solution) to precipitate excess europium as hydroxides. After stirring for 6 h, the resulting suspension was filtered using a 0.2 µm syringe filter to remove any europium hydroxides. The resulting solution was freeze dried and analyzed using HPLC-MS. HRESIMS (*m/z*): $[M]^-$ calcd for $Eu_2C_{31}H_{49}N_8O_{13}$, 1043.1816; found, 1043.1830.

Synthesis of Ammonium{1,3-bis[terbium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate))]propan-2-oxide} (NH_4) **(1.9)**:

To a solution of 1,3-di[1,4,7,10-tetraazacyclododecanyl(1,4,7-triacetate)]propan-2-ol[18] **(1.5)** (1.00 mL, 0.0710 mmol, 71.1 mM, 1 equiv) was added NH_4OH (0.5 mL, 5% aqueous solution) dropwise until the pH of the solution was 6.5. To the resulting solution was added an aqueous solution of terbium triflate (1.00 mL, 0.213 mmol, 28.2 mM, 3 equiv). The resulting solution was stirred at ambient temperature for 12 h while the pH was maintained at 6.5 with the addition of NH_4OH (1 mL, 5% aqueous solution) (**Scheme 2.2**). After the reaction was stirred for 12 h, the pH was increased to 12 by the addition of NH_4OH (1.4 mL, 30% aqueous solution) to precipitate excess terbium as hydroxides. After stirring for 6 h, the resulting suspension was filtered using a 0.2 µm syringe filter to remove any terbium hydroxides. The resulting solution was freeze dried and analyzed using HPLC-MS. HRESIMS (*m/z*): $[M]^-$ calcd for $Tb_2C_{31}H_{49}N_8O_{13}$, 1061.2083; found, 1061.2072.

Synthesis of Ammonium{1,3-bis[gadolinium-(1,4,7,10-tetraazacyclododecanyl-(1,4,7-triacetate))]propan-2-oxide} (NH_4) **(1.10):**

To a solution of 1,3-di[1,4,7,10-tetraazacyclododecanyl(1,4,7-triacetate)]propan-2-ol[18] (1.00 mL, 0.0710 mmol, 71.1 mM, 1 equiv) was added NH_4OH (0.5 mL, 5% aqueous solution) dropwise until the pH of the solution was 6.5. To the resulting solution was added an aqueous solution of terbium triflate (1.00 mL, 0.213 mmol, 28.2 mM, 3 equiv). The resulting solution was stirred at ambient temperature for 12 h while the pH was maintained at 6.5 with the addition of NH_4OH (1 mL, 5% aqueous solution) (**Scheme 2.2**). After the reaction was stirred for 12 h, the pH was increased to 12 by the addition of NH_4OH (1.4 mL, 30% aqueous solution) to precipitate excess of terbium as hydroxides. After stirring for 6 h, the resulting suspension was filtered using a 0.2 μm syringe filter to remove any terbium hydroxides. The resulting solution was freeze dried and analyzed using HPLC-MS. HPLC-MS analysis indicated that complex **1.10** contained 6-arm and a small amount of 5-arm metal complexes, both of the species eluting under the same retention time at 12.53 min. HPLC method: Binary gradient method (pump A: water, pump B: acetonitrile; 0→9.8% B for 10 min, 9.8→10% B over 2 min, 10% over for 4 min, 10→0% B for 4 min). HRESIMS (*m/z*): $[M]^-$ calcd for $Gd_2C_{31}H_{49}N_8O_{13}$, 1051.1872; found, 1051.1881.

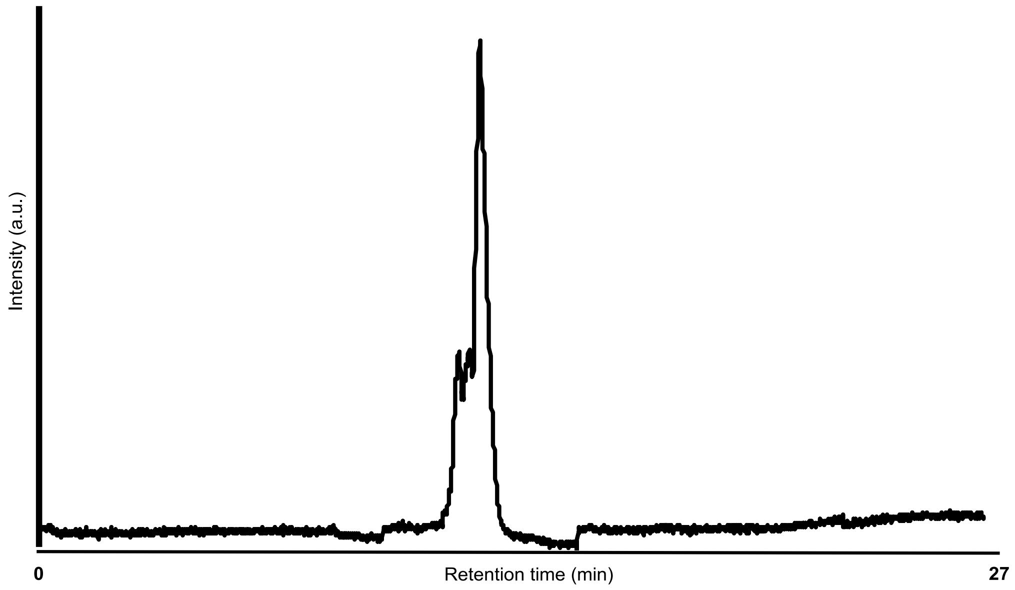


Figure 2.4 HPLC chromatogram of **1.10** detected using a fluorescence detector (λ_{ex} = 273 nm, and λ_{em} = 613 nm). The identity of the complex eluted at 12.53 min was confirmed to be **1.10** using mass spectrometry.

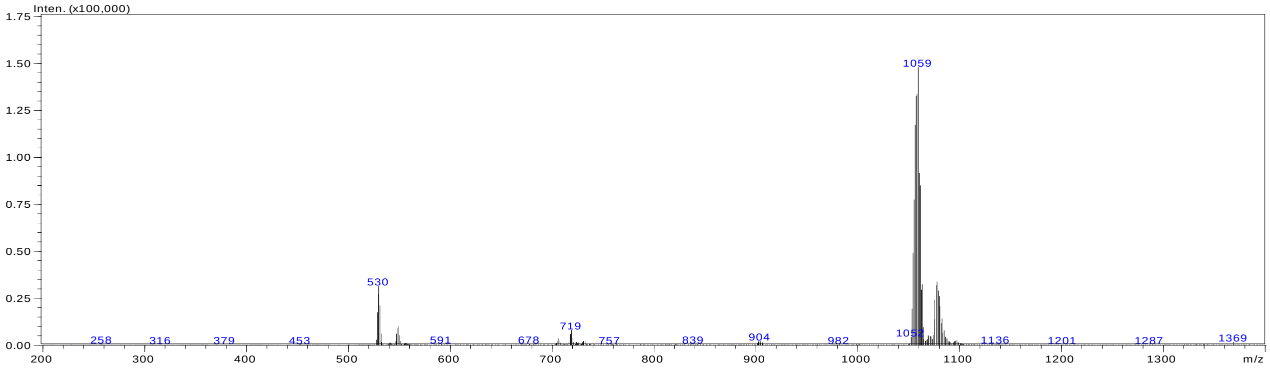


Figure 2.5 Extracted mass spectrum for metal complex **1.10** at 12.53 min retention time.

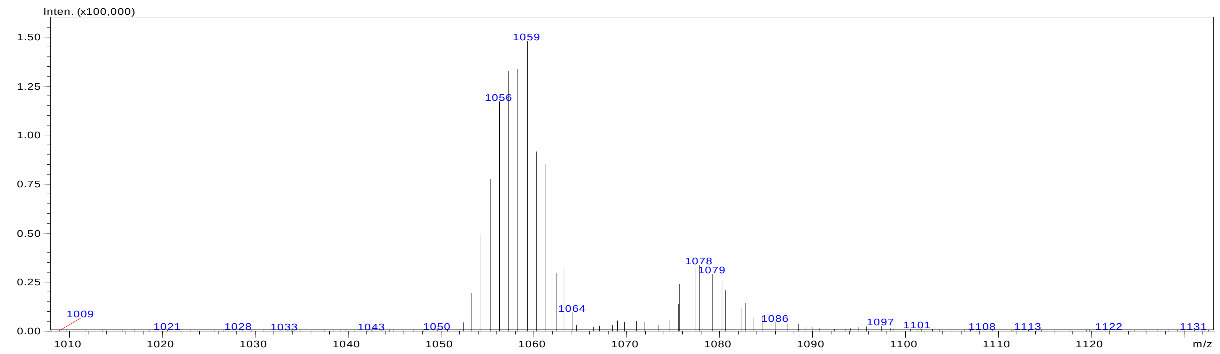
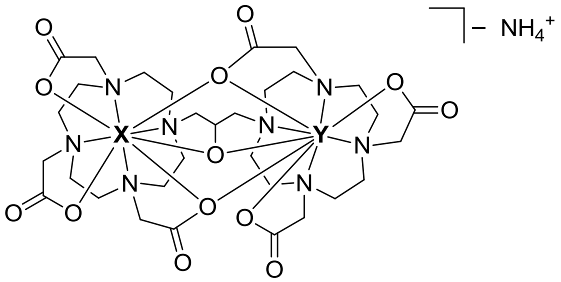


Figure 2.6 Isotopic distribution of the Gd^{3+} complex **1.10** at 12.53 min retention time.

CHAPTER 3: Energy Transfer Studies in a Eu^{3+}-Tb^{3+} Heterobimetallic Complex

Samples taken from complexes **1.6–1.10** (**Figure 3.1**) were prepared by dissolving solids (4 mg) in water (300 µL) and transferring an aliquot (250 µL) of the resulting solutions to a 2 × 2 × 32 mm^3 quartz cuvette.[19] The concentrations of all complexes used for measurements were 13.2 mM. The pH values for all samples measured were 8.0.



1.6, X = Tb, Y = Eu
1.8, X = Tb, Y = Gd

1.7, X = Y = Eu
1.9, X = Y = Tb
1.10, X = Y = Gd

Figure 3.1 Structure of homo-bimetallic complexes **1.6 and 1.8** and hetero-bimetallic complexes **1.7, 1.9,** and **1.10** used for the steady-state emission and luminescence-decay studies.

3.1 *Steady-state spectra*

Energy transfer between Tb^{3+} and Eu^{3+} was demonstrated with the emission spectrum of **1.6**, with a Tb^{3+}-specific excitation wavelength of 487 nm. The emission spectra for complex **1.6** displayed the expected Tb^{3+} transition at 545 nm ($^5D_4 \rightarrow {}^7F_6$) and a set of peaks at 579, 592, 612, 653, and 701 nm corresponding to $^5D_0 \rightarrow {}^7F_{0,1,2,3,4}$ that indicate Eu^{3+} emission (solid line in **Figure 3.2**). However, Tb^{3+}-specific emissions were not observed when Eu^{3+}-specific excitation wavelength 394 nm was used. These observations suggest that energy transfer occurs from Tb^{3+}

to Eu^{3+} and not from Eu^{3+} to Tb^{3+}. These observations are reasonable because the excited state of Eu^{3+} has a lower energy than that of the Tb^{3+} ion (**Figure 1.5**).

The HPLC data for Eu^{3+}-Tb^{3+} containing-complex **1.6** showed that it contained a mixture of **1.6** and di-Eu^{3+} containing complex **1.7**. To provide evidence that complex **1.7** does not interfere with the energy transfer occurring in **1.6**, I performed control experiments by exciting **1.7** with Eu^{3+}- and Tb^{3+}-specific wavelengths. For the excitation of complex **1.7** with Tb^{3+}-specific wavelength, no emission was observed, as was expected for a complex containing only Eu^{3+} (dotted line in **Figure 3.2**). But, when complex **1.7** was excited with Eu^{3+}–specific wavelength, a set of Eu^{3+} peaks were observed corresponds to transitions of $^5D_0 \rightarrow {}^7F_{0,1,2,3,\text{ and }4}$ at 579, 592, 612, 653, and 701 nm, respectively (**Figure 3.3**). Based on the observations of the excitation of di-Eu^{3+}-containing complex **1.7** with Eu^{3+}- and Tb^{3+}-specific wavelength indicated that the **1.7** was not playing a role in the energy transfer with complex **1.6** even though it was present as a mixture with **1.6**, as observed by HPLC-MS

Although, no evidence for di-Tb^{3+}-containing complex **1.9** was observed in the HRESIMS and HPLC-MS of **1.6**, complex **1.9** could be present in **1.6** because the absence of a peak in mass spectrometry does not mean the complex is not present. Thus, to confirm that complex **1.9** does not interfere with energy transfer in **1.6**, I ran a control experiment with **1.9** by exciting it using a Tb^{3+}-specific wavelength. The outcome of the control experiment was that when **1.9** was excited with Tb^{3+}-specific wavelength (487 nm), the emission spectra displayed a set of only Tb^{3+}-related peaks corresponding to transitions at $^5D_4 \rightarrow {}^7F_{6,\ 5,\text{ and }4}$ at 545, 586, and 622 nm, respectively. Thus, by interpreting the emission spectra (**Figure 3.4**) for complex **1.9** at 487 nm excitation, I infered that the presence of **1.9** in **1.6** would not interfere with the energy transfer from Tb^{3+} to Eu^{3+}.

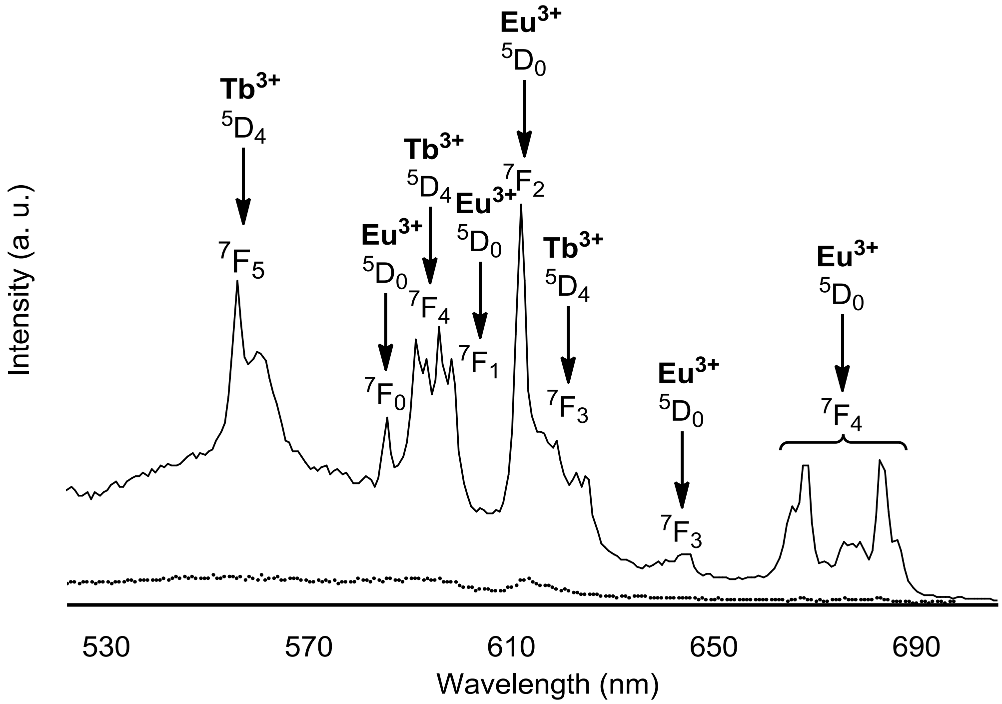


Figure 3.2 Emission spectra of complex **1.6** (——) and complex **1.7** (……). Excitation was performed at a wavelength specific to Tb^{3+} (487 nm), and assignments correspond to transitions listed in **Figure 1.5**. No emission was observed with di-Eu^{3+} complex **1.7**. Emissions specific to both Tb^{3+} and Eu^{3+} were observed for the mixed metal system **1.6** indicating energy transfer.

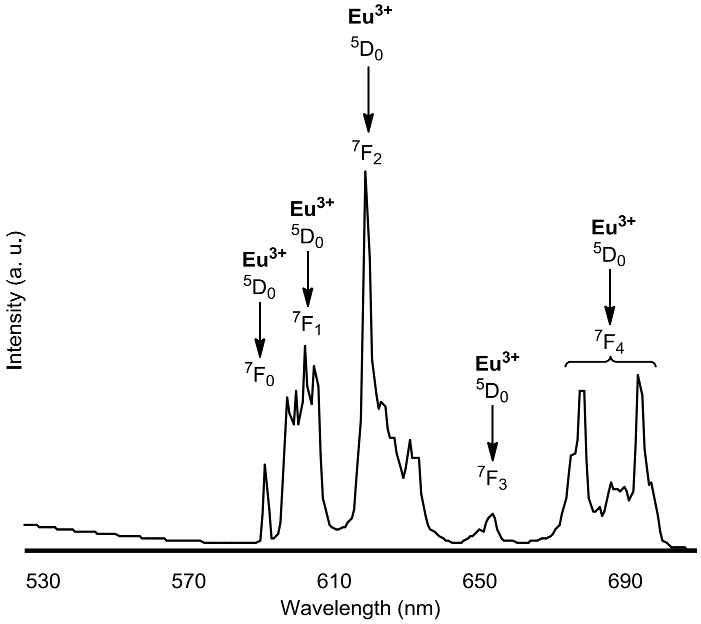


Figure 3.3 Complex **1.6** (——). Excitation was performed at a wavelength specific to Eu^{3+} (394 nm), and assignments correspond to transitions listed in **Figure 1.5** No emission was observed related to Tb^{3+}.

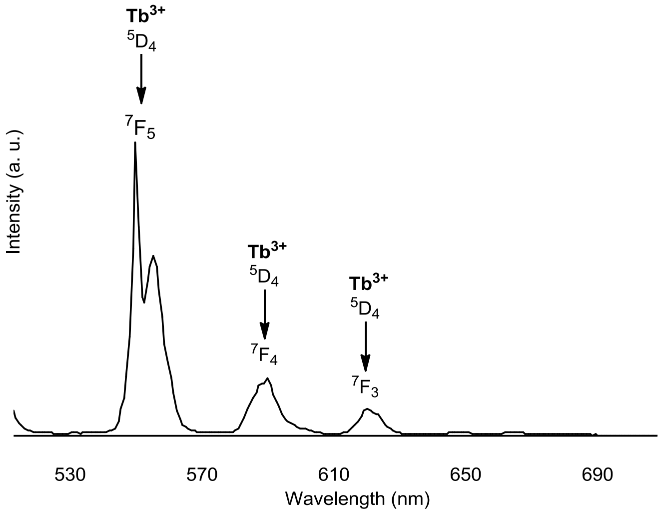


Figure 3.4 Emission spectra of the di-Tb^{3+} complex **1.9** that displayed only Tb^{3+} specific emissions when excited using a Tb^{3+} specific wavelength. No Eu^{3+} emissions were observed explaining the non-involvement of **1.9** in **1.6** for energy transfer studies.

3.2 *Luminescence-decay data*

Luminescence decay measures the mean lifetime of an excited state of a luminescent probe (which could be an ion or a fluorescent compound). Luminescence-decay data has been used to calculate the inner-sphere water co-ordination number (*q*) in MRI contrast agents or to show the existence of the energy transfer in a system by measuring the lifetime of the excited state of the donor ion or fluorescent compound for energy transfer. [24]

In the previously reported complexes,[14–17] energy transfer was demonstrated by luminescence-decay data. Based on this orthogonal way to demonstrate energy transfer, I designed an experiment (**Figure 3.5**) using luminescence-decay data to show that energy transfer is occurring in Eu^{3+}-Tb^{3+} containing-complex **1.6** and not in Gd^{3+}-Tb^{3+} containing-complex **1.8.** The luminescence decay-data was measured for both heterobimetallic complexes at Tb^{3+}-specific excitation and emission wavelength of 487 and 545 nm, respectively.

To support the observance of energy transfer in **1.6**, luminescence decay was measured for both **1.6** and **1.8**, and a comparison of their decay rates was done. The luminescence-decay measurements were taken 5–10 minutes after the preparation of the samples for complexes **1.6** and **1.8** in water. The luminescence-decay rate ($\tau_{H2O/ms}{}^{-1}$) of Tb^{3+} in complex **1.6** was measured to be 0.344 ms^{-1}, and in complex **1.8**, it was 0.296 ms^{-1} (**Figure 3.6**). This difference could be because the excited state of Gd^{3+} is higher than Tb^{3+} by 10,000 cm^{-1} based on the energy level diagram (**Figure 1.6**). The decrease of luminescence lifetime of Tb^{3+} ($^5D_4$) in complex **1.6** is likely due to quenching of the Tb^{3+} excited state by non-radiative transfer of energy (Decay pathway 1) from Tb^{3+} to Eu^{3+}, to the radiative emission of Tb^{3+} (Decay pathway 2), (**Figure 3.5**) and to other pathways of non-radiative decay including outer-sphere–OH vibronic coupling due to the solvent water.

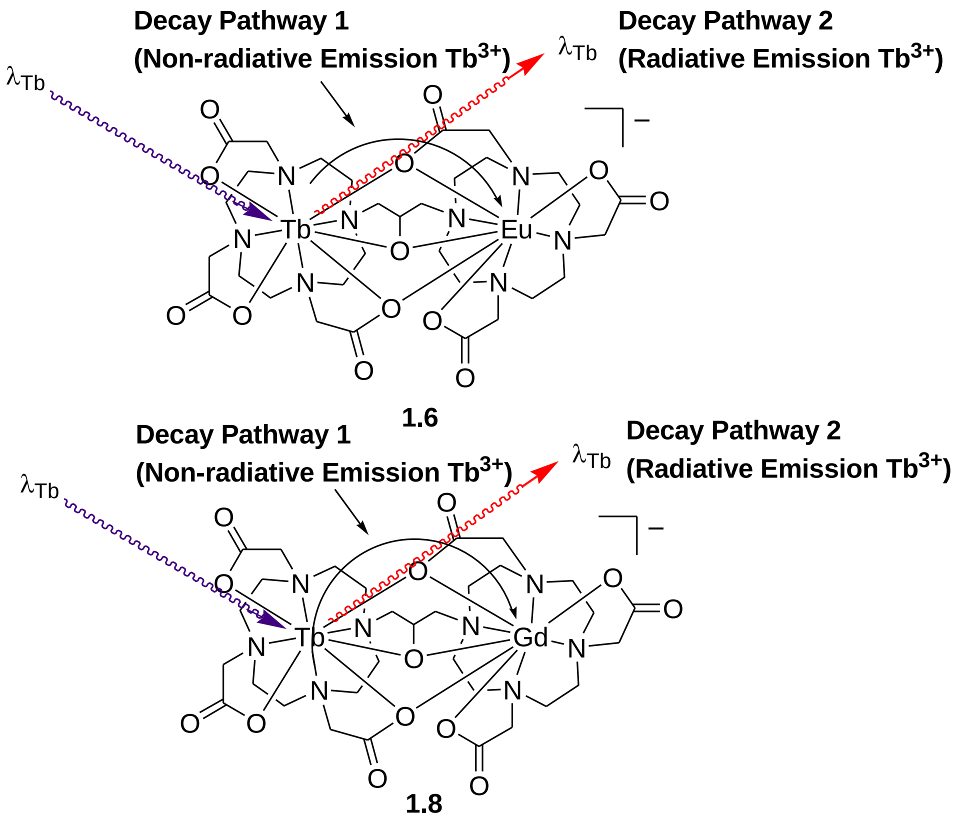


Figure 3.5 Proposed pathways for the decay of the Tb^{3+} excited state in complexes **1.6** and **1.8**.

In Tb^{3+}-Gd^{3+}-containing complex **1.8**, based on the luminescence decay plot (**Figure 3.6**), the luminescence lifetime of Tb^{3+} in **1.8** is shorter compared to **1.6** because of the non-occurrence of transfer energy from Tb^{3+} to Gd^{3+} (Decay pathway 1), even though the decay occurs by radiative emission of Tb^{3+} (Decay pathway 2) (**Figure 3.5**) and by other non-radiative pathways. When taking the luminescence-decay rate for complex **1.8** into consideration, complex **1.8** had a possibility to contain a mixture of **1.8**, **1.9,** and **1.10.** Through HPLC-MS, I found out that complex **1.8** was a mixture of **1.8** and **1.10**. But theoretically, di-Gd^{3+}-containing complex **1.10** should not interfere with **1.8** in the luminescence decay of **1.8** because the luminescence decay is carried out at Tb^{3+}-specific excitation and emission and complex **1.10** does not contain Tb^{3+} ions. So, I ran the luminescence-decay measurements for complex **1.10** at Tb^{3+}-specific excitation and emission (487 and 545 nm, respectively), and I observed that there was no exponential decay (**Figure 3.7**). This provided evidence that the presence of **1.10** in **1.8** doesn't interfere in the decay experiment performed on **1.8**. The presence of complex **1.9** in **1.8** would affect the decay-rate studies, because the decay studies are carried out with Tb^{3+}-specific excitation and emission wavelengths and because **1.9** contained Tb^{3+} ions that would interfere in the luminescence decay-rate carried on **1.10**. Thus, to prevent the formation of **1.9**, I added a small amount of terbium triflate (0.5 equivalents) during the metallation step for the synthesis of the heterobimetallic complex **1.8**. When taking the luminescence-decay rate for complex **1.8** into consideration, complex **1.6** had a possibility to contain a mixture of **1.6**, **1.7,** and **1.9**. It is fine to have complex **1.7** in the mixture because it contains only Eu^{3+} ions, but because complex **1.9** has Tb^{3+} ions, I suppressed its formation by adding a small amount of terbium triflate (0.5 equivalents) during the metallation of complex **1.6**.

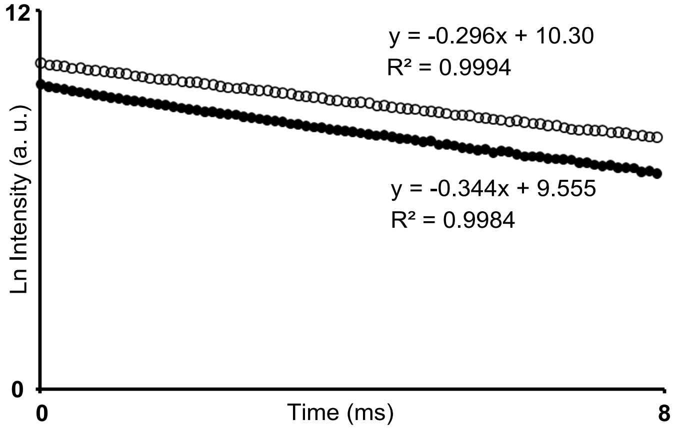


Figure 3.6 Natural log intensity plot of the decay curves for **1.6** (●) and **1.8** (○) in water, after excitation at a Tb^{3+}-specific wavelength (487 nm) with emission monitored at 545 nm.

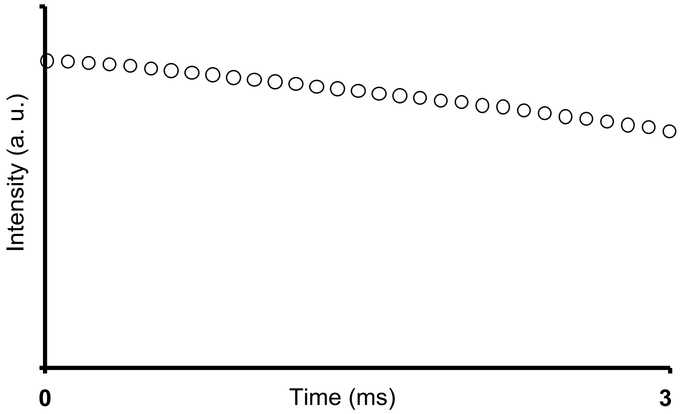
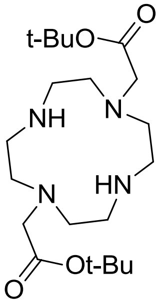


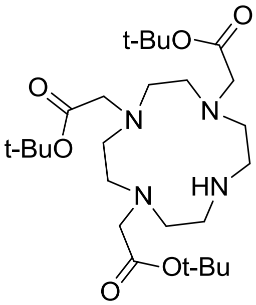
Figure 3.7 The absence of exponential decay curve for **1.10** (○) suggests the non-interference of **1.10** with **1.8** under an excitation at Tb^{3+}-specific wavelength 487 nm with corresponding emission at 545 nm.

Although, the decay rate values ($\tau_{H2O/ms}{}^{-1}$) of Tb^{3+} in the reported complexes **1.1, 1.3,** and **1.4** are 2.0, 1.8, and 1.4, the decay rate values of complexes **1.6** and **1.8** cannot be compared with those of the reported complexes.[14–16] The reason is due to the presence of five-arm complex along with the six-arm complexes as observed in the HPLC chromatogram (**Figure 2.2**). The presence of five-arm complexes as impurities in **1.6** and **1.8** will lead to inaccurate decay rate values because the five-arm complexes will contain inner-sphere water that will quench luminescence. The presence of five arm was likely due to the coupling of DO2A **1.11** and DO3A **1.12** during the route to synthesize the ligand **1.5**. This problem could be resolved by using an alternate synthetic route for **1.12**, to prevent the mixture of **1.11** and **1.12**.



1.11

DO2A



1.12

DO3A

Figure 3.8 Chemical structure of DO2A **1.11** (di-*tert*-butyl 1,4,7,10- tetraazacyclododecane-1,7-diacetate) and DO3A **1.12** (tri-*tert*-butyl 1,4,7,10- tetraazacyclododecane-1,4,7-triacetate).

Therefore the emission spectra (**Figure 3.2**), luminescence-decay plots (**Figure 3.5**), and the distance between the Tb^{3+} and Eu^{3+} in the computational optimized structure[22] (**Figure 1.4**) are the evidence indicative of energy transfer in **1.6**. The proposed Jablonski diagram and the computational optimized structure are in good agreement with experimental observations in emission spectra and luminescence-decay studies. The comparison of the luminescence-decay rates of the reported complexes with that of the hetero Tb^{3+}-Eu^{3+} and Tb^{3+}-Gd^{3+} complexes relate the importance of minimizing the inner-sphere co-ordination environment in a discrete complex for the energy transfer.

Hence, from the steady-state emission spectra, I report an interesting feature of complex **1.6** showing intra-molecular energy transfer from Tb^{3+} to Eu^{3+}, where Tb^{3+} can sensitize the luminescence of Eu^{3+} without the use of the excitation of antenna. Another noteworthy feature of the study is the luminescence-decay data of **1.6** that shows energy transfer by faster decay rate of the Tb^{3+} ion in the complex **1.6** than in complex **1.10**. The studies that remain include the quantum yield of the Eu^{3+} ion and measurement of the efficiency of the Tb^{3+} ion in complex **1.6**, and the preparation of prepare DO3A using a new synthetic route to avoid the formation of five-arm complexes. I expect the unique way of observing energy transfer in a discrete, soluble complex in this thesis to be useful for understanding fundamental concepts relevant to energy transfer in heterobimetallic complexes.

CHAPTER 4: Conclusions and Future Directions

I synthesized complexes **1.6–1.10** and have shown that energy transfer occurs in complex **1.6** using emission spectra and luminescence-decay studies. I expect my studies to be useful for the fundamental study of energy transfer. Therefore, after investigating the emission spectra and luminescence-decay data, I confirmed the occurrence of energy transfer in the heterobimetallic complex **1.6**.

For future plans, measuring the quantum efficiency for the Eu^{3+} emission in complex **1.6** is needed for publication. The quantum yield for complex **1.6** can be measured using cresyl violet as a reference.[25] The quantum yield for **1.6** can be calculated relative to the quantum yield of the fluorophor using the following formula:

$$\boxed{Q_x = Q_s \times \frac{Ex}{Es} \times \frac{As}{Ax} \times \left(\frac{\eta x}{\eta s}\right)^2}$$

In the formula, Q_x and Q_s are the quantum yield for the complex and the fluorophor, A_x and A_s are the absorbance for the complex and the fluorophor, and η_x and η_s are the refractive indices of the solvents used for complex and the fluorophor.

To confirm the structure of the homo-bimetallic complexes, crystallographic data should be obtained. But, the most interesting study, in my opinion, would be an order of addition study of the ligand (**Figure 1.2**) which would define the boundaries of selectivity of the ligand over the wide range of lanthanide ions.

References

(1) (a) Rudovsky, J.; Botta, M.; Hermann, P.; Koridze, A.; Aime, S.; *Dalton Trans.* **2006**, 2323–2326. (b) Powell, O. M.; Ni Dhubhghaill, Pubanz, D.; Helm, L.; Lebedev, Y. S.; Schlaepfer, W.; Merbach, A. E.; *J. Am. Chem. Soc.* **1996**, *118*, 9333–9335. (c) Andrews, M.; Amoroso, A. J.; Harding, L. P.; Pope, S. J. A. *Dalton Trans.* **2010**, *39*, 3407–3411.

(2) (a) Rinehart D. J.; Fang, M.; Evans, J. W. and Long, R. J. *Nature Chem.* **2011,** *3*, 538–542. (b) Habib, F.; Brunet, G.; Vieru, V.; Korobkov, I.; Chibotaru, F. L.; and Murugesu, M. *J. Am. Chem. Soc.* **2013,** *135*, 13242–13245. (c) Demir, S.; Zadrozny, J. M.; Nippe, M.; Long, J. R. *J. Am. Chem. Soc.* **2012,** *134*,18546–18549. (d) Anwar, U. M.; Thompson, K. L.; Dawe, N. L.; Habibb, F.; Murugesu, M. *Chem. Comm.* **2012,** *48*, 4576–4578.

(3) Nwe, K.; Andolina, C.M.; Morrow, J. R. *J. Am. Chem. Soc.* **2008**, *130*, 14861–14871.

(4) (a) You, Y.; Han, Y.; Lee, Y.-M.; Park, S. Y.; Nam, W.; Lippard, S. J. *J. Am. Chem. Soc.* **2011**, *133*, 11488–11491. (b) Beeby, A.; Botchway, S. W.; Clarkson, I. M.; Faulkner, S.; Parker, A. W.; Parker, D.; Williams, J. A. G. *J. Photochem. Photobiol. B* **2000**, *57*, 83–89. (c) Harte, A.J.; Jensen, P.; Plush, S. E.; Kruger, P. E.; Gunnlaugsson, T. *Inorg. Chem.* **2006**, *45*, 9465–9474.

(5) Wang, F.; Deng, R.; Wang, J.; Wang, Q.; Han, Y.; Zhu, H.; Chen, X.; Liu, X. *Nature Materials* **2011,** *10***,** 968–973.

(6) Mech Agnieszka.; Monguzzi .A.; Meinardi. F.; Mezyk. J.; Macchi. G.; Tubino .R. *J. Am. Chem. Soc.* **2010,** *132*, 4574–4576.

(7) Bünzli, J.-C.; Eliseeva, S.V. Basics of Lanthanide Photophysics. In Lanthanide Luminescence: Photophysical, Analytical, and Biological Aspects; Springer-Verlag: Berlin, 2010.

(8) (a) Yu, J.; Parker, D.; Pal, R.; Poole, R. A.; Cann, M. J. *J. Am. Chem. Soc.* **2006**, *128,* 2294–2299. (b) Halim, M.; Tremblay, M. S.; Jockusch, S.; Turro, N. J.; Sames, D. *J. Am. Chem. Soc.* **2007**, *129*, 7704–7705. (c) Kielar, F.; Congreve, A.; Law, G.-L.; New, E. J.; Parker, D.; Wong, K.-L.; Castreňo, P.; de Mendoza, J. *Chem. Commun.* **2008**, 2435–2437. Bobba, G.; Frias, J. C.; Parker, D. *Chem. Commun.* **2002**, 890–891.

(9) (a) Fang, Y.; Xu, A.-W.; You, L.-P.; Song, R.-Q.; Yu, J.C.; Zhang, H.-X.; Li, Q. and Liu, H.-Q. *Adv. Funct. Mater.* **2003,** *13*, 955–960 (b) Yang, J. Li. G.; Peng, C.; Li, C.; Zhang, C.; Fan, Y.; Xu, Z.; Cheng, Z.; Lin, J. *J. Solid State Chem.* **2010,** *183*, 451–457.

(10) Tanner, P. A.; Wang, J. *Chem. Phys. Lett.* **2008**, *455*, 335–338.

(11) Lee, M.; Tremblay, M. S.; Jockusch, S.; Turro, N. J.; Sames, D. *Org. Lett.* **2011**, *13*, 2802–2805.

(12) Thibon, A.; Pierre, V. C. *Anal. Bioanal. Chem.* **2009,** *394,* 107–120.

(13) Borgne. L. T.; Bénech. J.-M. Floquet, S.; Bernardinelli, G.; Aliprandini, C.; Bettens, P.; Piguet, C. *Dalton Trans.* **2006,** 3856–3868.

(14) Andolina, C. M.; Morrow, J. R. *Eur. J. Inorg. Chem.* **2011,** 154–164.

(15) Faulkner, S.; Pope, S. J. A. *J. Am. Chem. Soc.* **2003,** *125*, 10526–10527.

(16) Nonat, A.; Figueroa, R. M.; Gómez, D. E.; de Blas, A.; Blas, T. R.; Iglesias, C.P.; Charbonnière, L. J. *Chem. Eur. J.* **2012,** *18,* 8163–8173.

(17) Tremblay, M.S.; Sames, D. *Chem. Commun.* **2006,** 4116–4118.

(18) Moore, J. D.; Lord, R. L.; Cisneros, G. A.; Allen, M. J. *J. Am. Chem. Soc.* **2012,** *134*, 17372–17375.

(19) Moore, J. D. Design, Synthesis, and Luminescence Properties of Bridged Dimetallic Lanthanide Coordination Compounds. Ph.D. Thesis, Wayne State University, July **2013**.

(20) (a) Costes, J. P.; Dahan. F.; Dupuis. A.; Lagrave. S.; Laurent, J. P. *Inorg. Chem.* **1998,** *37*, 153–155. (b) Favera, N. D.; Borkovec, M.; Jeannerat, D.; Ercolani, G.; Piguet, C. *Inorg. Chem.* **2007,** *37*, 9312–9322. (c) Wu, S. L.; Horrocks, W. D., Jr. *Anal. Chem.* **1996,** *68*, 394–401.

(21) (a) Piguet, C.; Bünzli, J.-C.; Bernardinelli.; Hopfgartner, G.; Williams, F. A, *J. Am. Chem. Soc.* **1993,** *115*, 8197–8206. (b) André, N.; Jensen, T. B.; Scopelliti, R.; Imbert, D.; Elhabiri, M.; Hopfgartner, G.; Piguet, C.; Bünzli, J.-C. *Inorg. Chem.* **2004,** *43*, 515–529.

(22) (a) Gaussian 09, Revision A.1, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009. (b) Adamo, C.; Barone V. *J. Chem. Phys.* **1999**, *110*, 6158–6170.

(23) Stein, G.; Wurzberg, E. J. *Chem. Phys.* **1975,** *62*, 208–213.

(24) (a) Supkowski, R. M.; Horrocks, W. D., Jr. *Inorg. Chim. Acta* **2002**, *340*, 44–48. (b) Horrocks, W. D., Jr.; Sudnick, D. R. *J. Am. Chem. Soc.* **1979**, *101*, 334–340.

(25) Williams, A. T. R.; Winfield. S. A.; Miller. J. N, *Analyst* **1983,** 1067–1071.

Abstract

ENERGY TRANSFER IN A DISCRETE, SOLUBLE, HETEROBIMETALLIC COMPLEX CONTAINING Tb^{3+} AND Eu^{3+}.

by

Nikhil Kumar Barua

August 2014

Advisor: Dr. Matthew J. Allen

Major: Chemistry

Degree: Master of Science

A discrete, heterobimetallic Tb^{3+}–Eu^{3+} -containing complex has been synthesized, and energy transfer was observed in the complex without using an antenna. This result represents a new way of observing lanthanide emission using lanthanide excitation in discrete, soluble complex. The occurrence of energy transfer in the mixed heterobimetallic Tb^{3+}–Eu^{3+} complex was characterized using steady state luminescence spectroscopy and luminescence-decay studies. These findings are likely to be useful for fundamental mechanistic studies of energy transfer in lanthanide-containing systems.

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15th Annual Chemistry Graduate Research Symposium 2013 held at *Wayne State University, Detroit, MI.* September 28, 2013