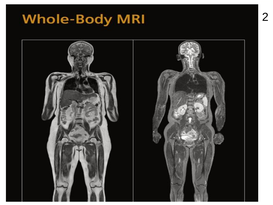
Investigating the Impact of Bound-Water Exclusion on the PARACEST MRI and Optical Properties of Lanthanide (III) Complexes

Adam Wedrychowski, Cyril Fong, and Dr. Osasere M. Evbuomwan

University of San Francisco, Department of Chemistry, San Francisco, CA 94117

Background and Introduction

Magnetic Resonance Imaging



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- Non invasive imaging modality.[1]
- Produces images of soft tissue with the aid of nonionizing radiation and an applied magnetic field.
- Contrast agents can be used to enhance the quality of an MR image.[1]

Chemical Exchange Saturation Transfer (CEST)

- The CEST signal acquired is a result of the exchange of saturated proton spins between the labile protons associated with the CEST agent and bulk water pool.[3]
- Transfer of the saturated protons decreases the intensity of bulk water and leads to a darkening of the MR image.[3]
- ParaCEST agents typically are comprised of a lanthanide ion chelated by a multidentate ligand.

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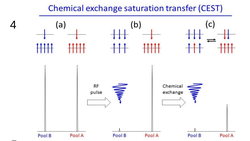

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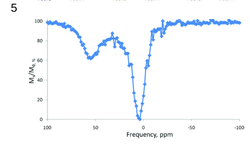

Optical Imaging

- Optical imaging uses visible light for soft tissue visualization at the cellular and molecular level.[6]
- Image contrast can be enhanced by the use of fluorescent dyes.
- The structure of fluorescent dyes can be modified to target biological regions of interest.[6]

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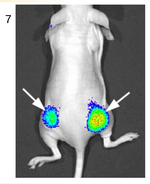

Luminescence

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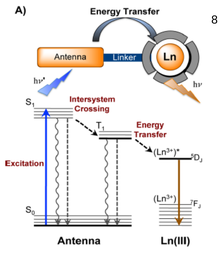
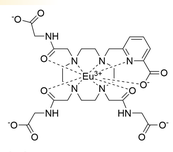


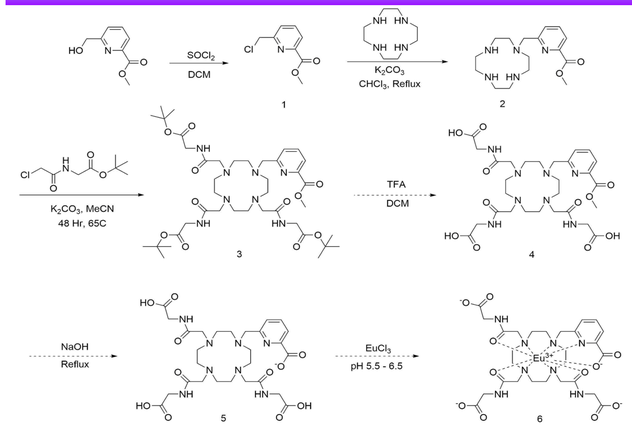
- Luminescence of a lanthanide ion is often induced through excitation by a high powered laser source.[8]
- The high energy of the laser could potentially damage biological tissue.
- To overcome this problem, an organic chromophore is attached to the complex to absorb energy of incident light.[8]
- The chromophore transfers the absorbed energy to the lanthanide, allowing for indirect excitation known as the antenna effect.[8]

Project Goal

- The paramagnetic and photophysical properties of Lanthanide ions make them attractive for bimodal imaging applications using a single agent.
- Although a lanthanide bound-water is essential for conventional MRI, it is detrimental to ParaCEST MRI and optical imaging.
- The goal of this project is to synthesize a bimodal imaging agent comprising a lanthanide ion, nonadentate ligand, and lacking a bound-water molecule
- We hypothesize that the exclusion of bound-water will enhance the resulting ParaCEST and luminescence signals.



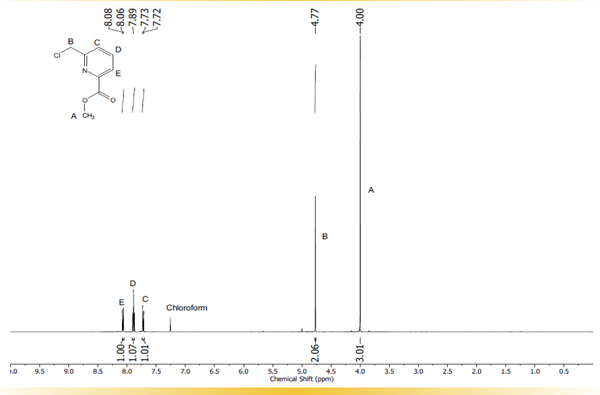
Synthetic Scheme for Lanthanide Agent



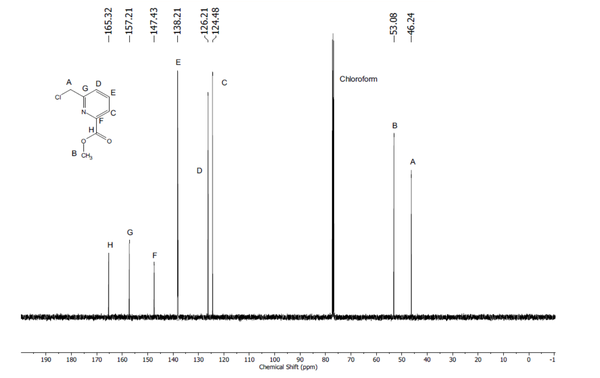
- Reagent-grade chemicals acquired from commercial sources were used as received.
- Compounds 1, 2, and 3 have been successfully synthesized and the identities were verified by ^{1}H and ^{13}C-NMR spectroscopy.

Nuclear Magnetic Resonance Spectra (NMR)

^{1}H-NMR of Compound 1 in $CDCl_3$ at 500 MHz

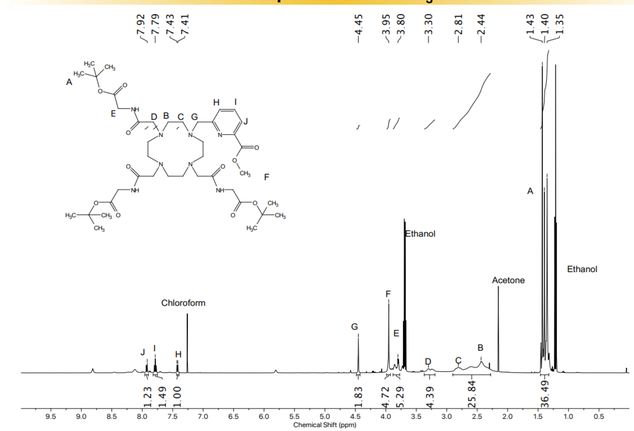


^{13}C-NMR of Compound 1 in $CDCl_3$ at 125 MHz

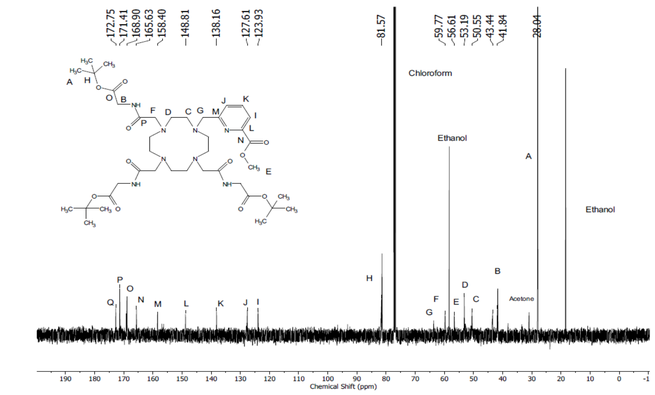


Nuclear Magnetic Resonance Data (Contd.)

^{1}H-NMR of Compound 3 in $CDCl_3$ at 500 MHz



^{13}C-NMR of Compound 3 in $CDCl_3$ at 125 MHz



Future Plans

- Completion of ligand synthesis
- Complexation of agent using the Ln^{3+} ions: Tb^{3+}, Eu^{3+}, Dy^{3+}, and Tm^{3+}
- Evaluation of ParaCEST and luminescence properties of the various metal complexes

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