



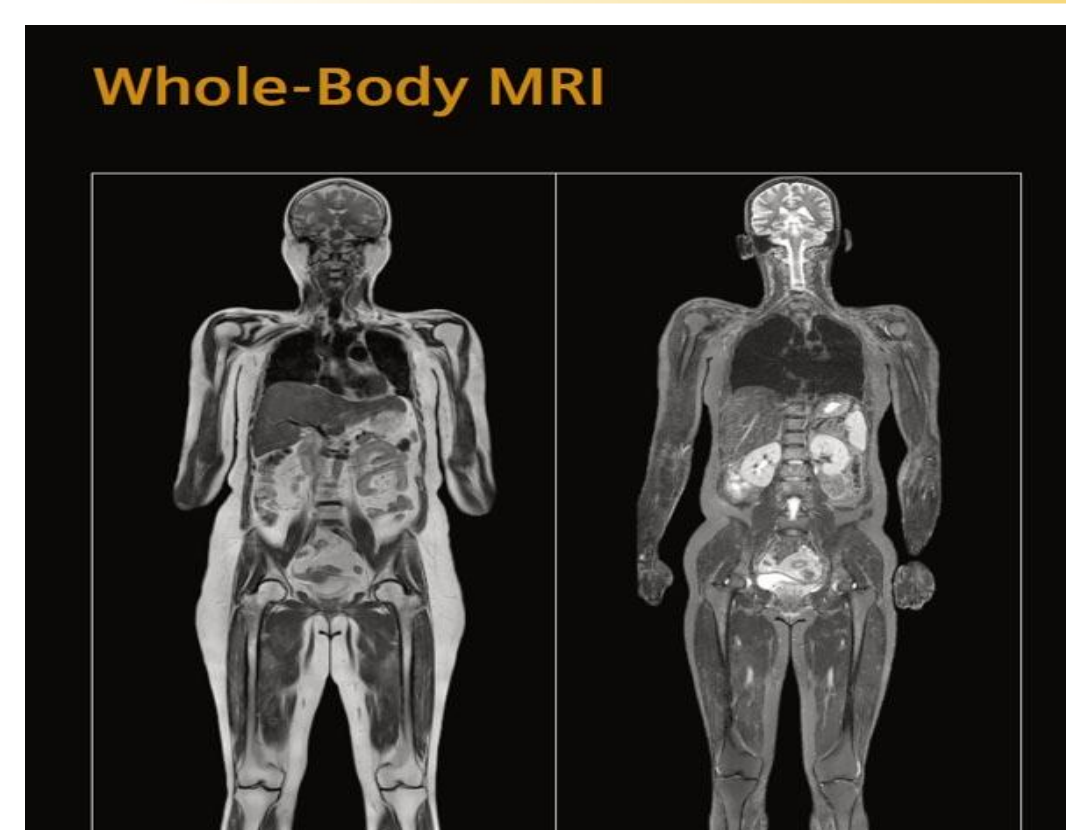
# Investigating the Impact of Bound-Water Exclusion on the PARACEST MRI and Optical Properties of Lanthanide (III) Complexes



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## Background and Introduction

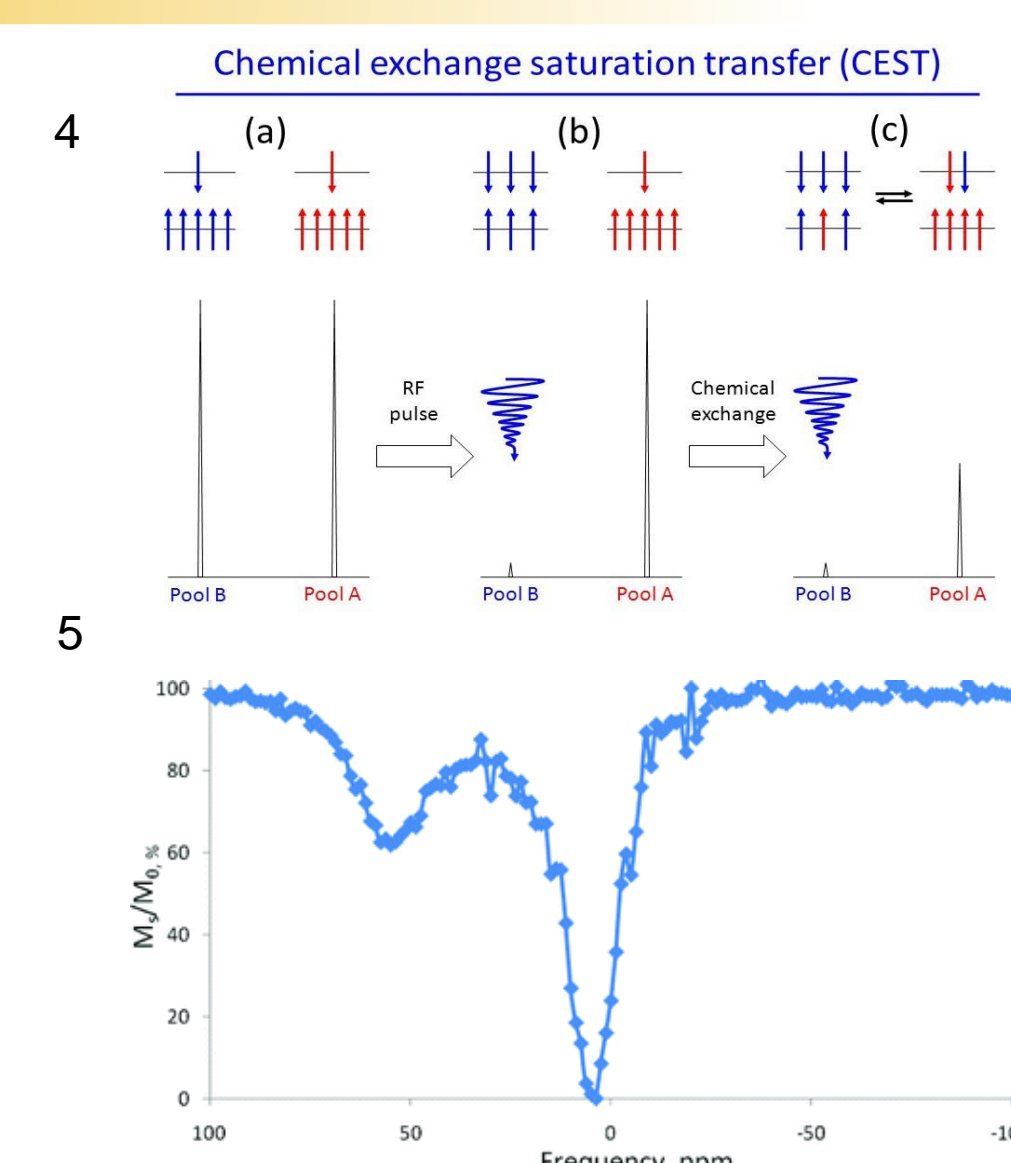
### Magnetic Resonance Imaging



- Non invasive imaging modality.<sup>1</sup>
- 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.<sup>1</sup>

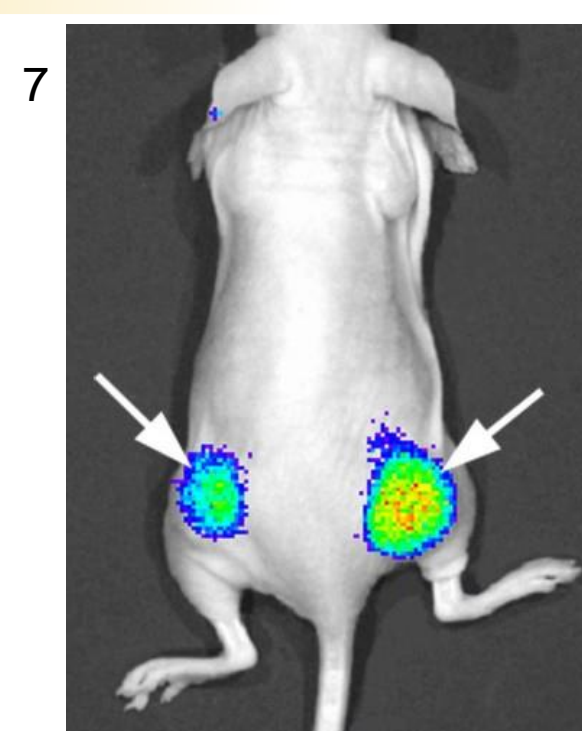
### Chemical Exchange Saturation Transfer (CEST)

- 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.<sup>3</sup>
- Transfer of the saturated protons decreases the intensity of bulk water and leads to a darkening of the MR image.<sup>3</sup>
- ParaCEST agents typically are comprised of a lanthanide ion chelated by a multidentate ligand.

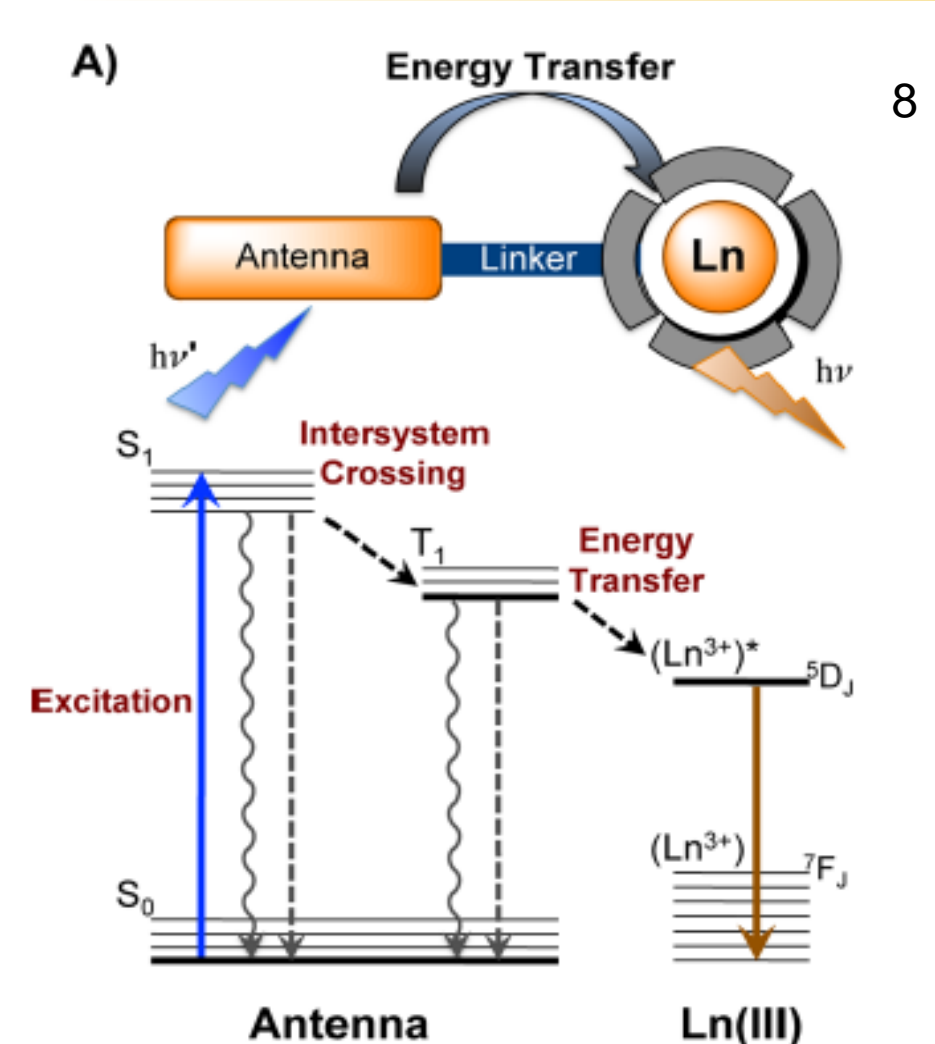


### Optical Imaging

- Optical imaging uses visible light for soft tissue visualization at the cellular and molecular level.<sup>6</sup>
- 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.<sup>6</sup>



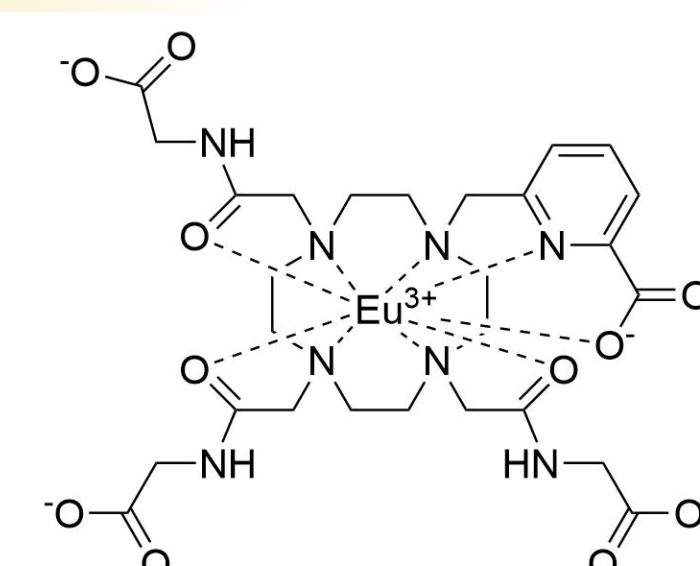
### Luminescence



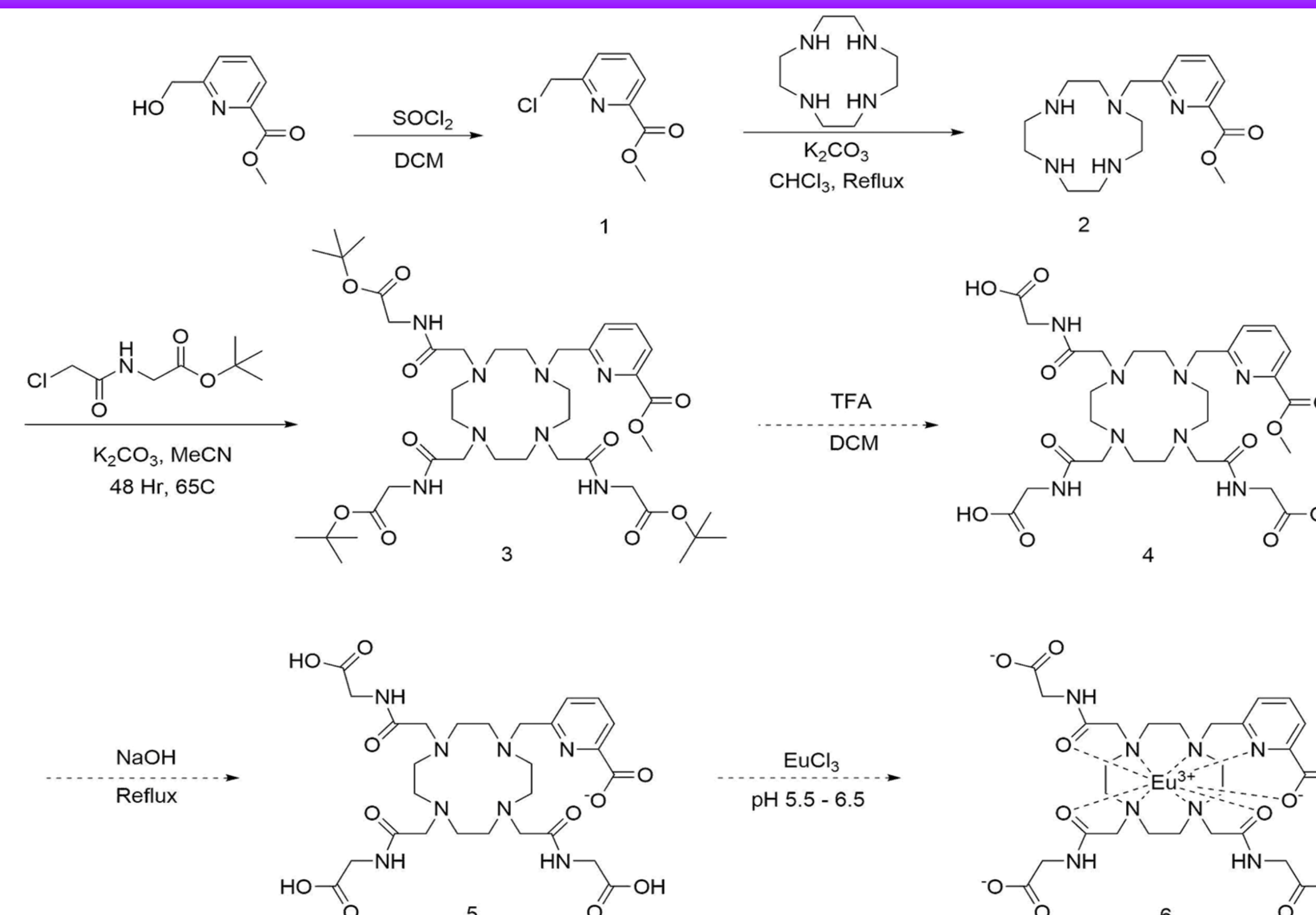
- Luminescence of a lanthanide ion is often induced through excitation by a high powered laser source.<sup>8</sup>
- The high energy of the laser could potentially damage biological tissue.
- To overcome this problem, an organic chromophore is attached to the complex to absorb energy of incident light.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

### 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.



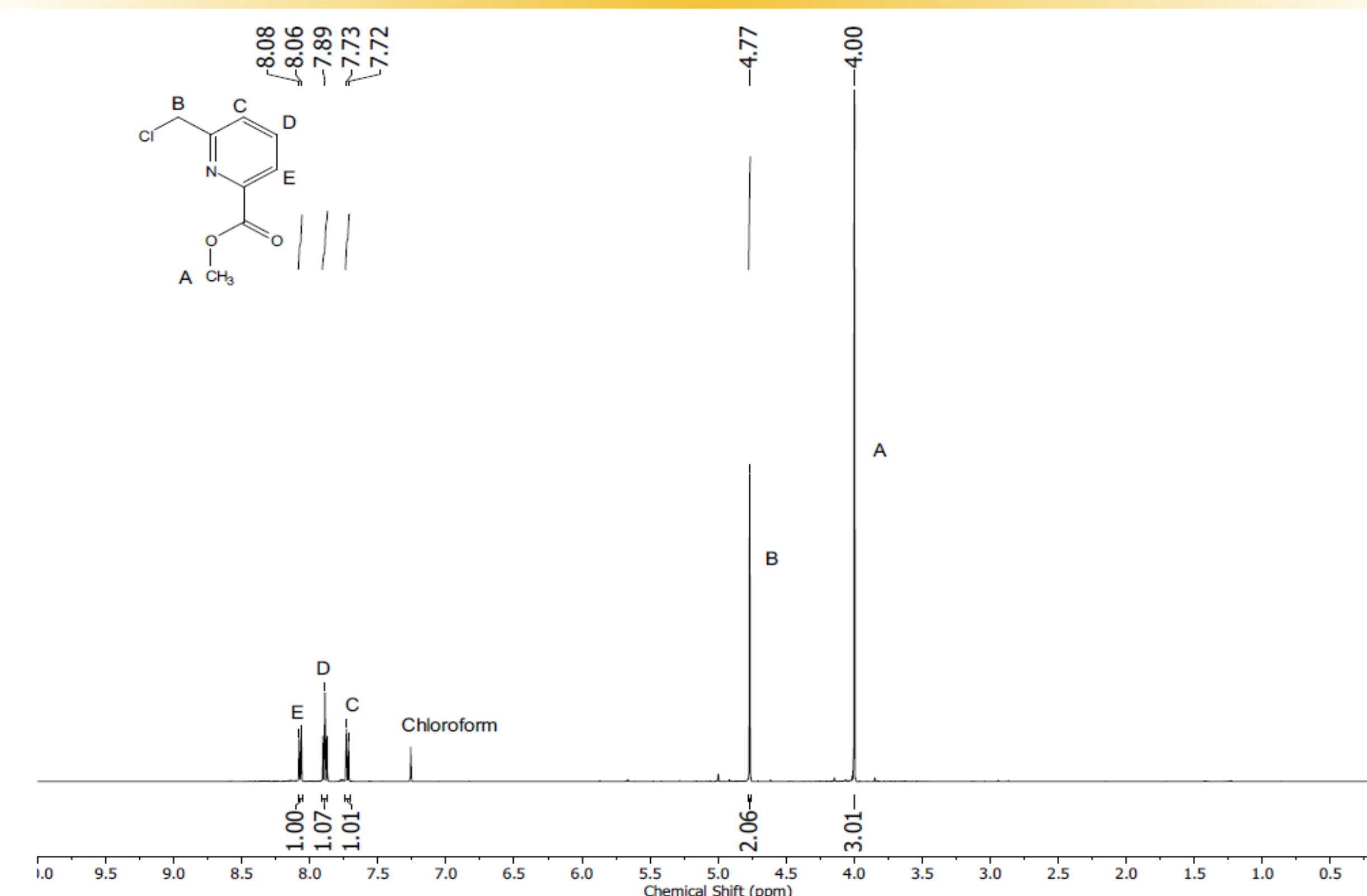
## Synthetic Scheme for Lanthanide Agent



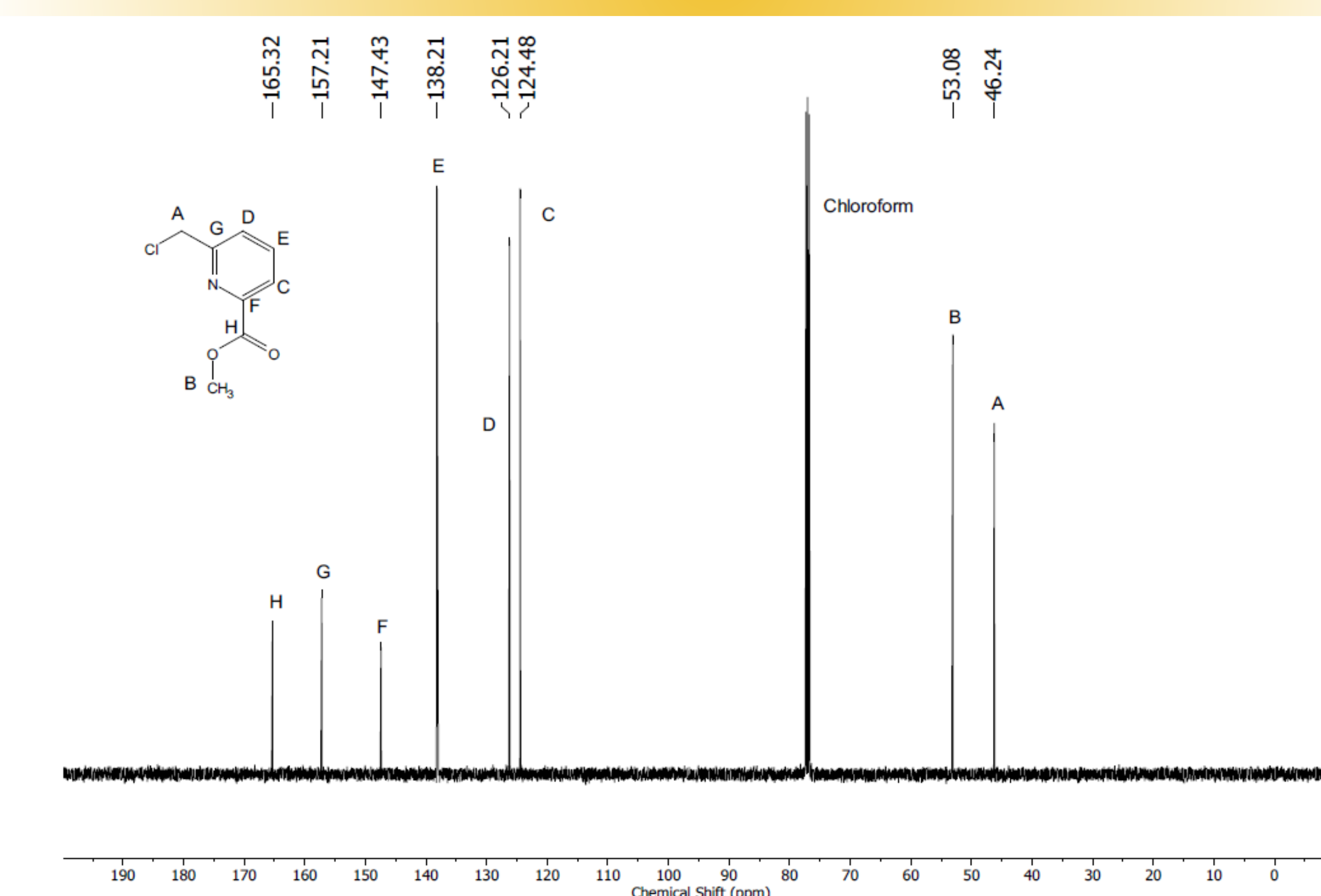
- Reagent-grade chemicals acquired from commercial sources were used as received.
- Compounds 1, 2, and 3 have been successfully synthesized and the identities were verified by <sup>1</sup>H and <sup>13</sup>C-NMR spectroscopy.

## Nuclear Magnetic Resonance Spectra (NMR)

### <sup>1</sup>H-NMR of Compound 1 in CDCl<sub>3</sub> at 500 MHz

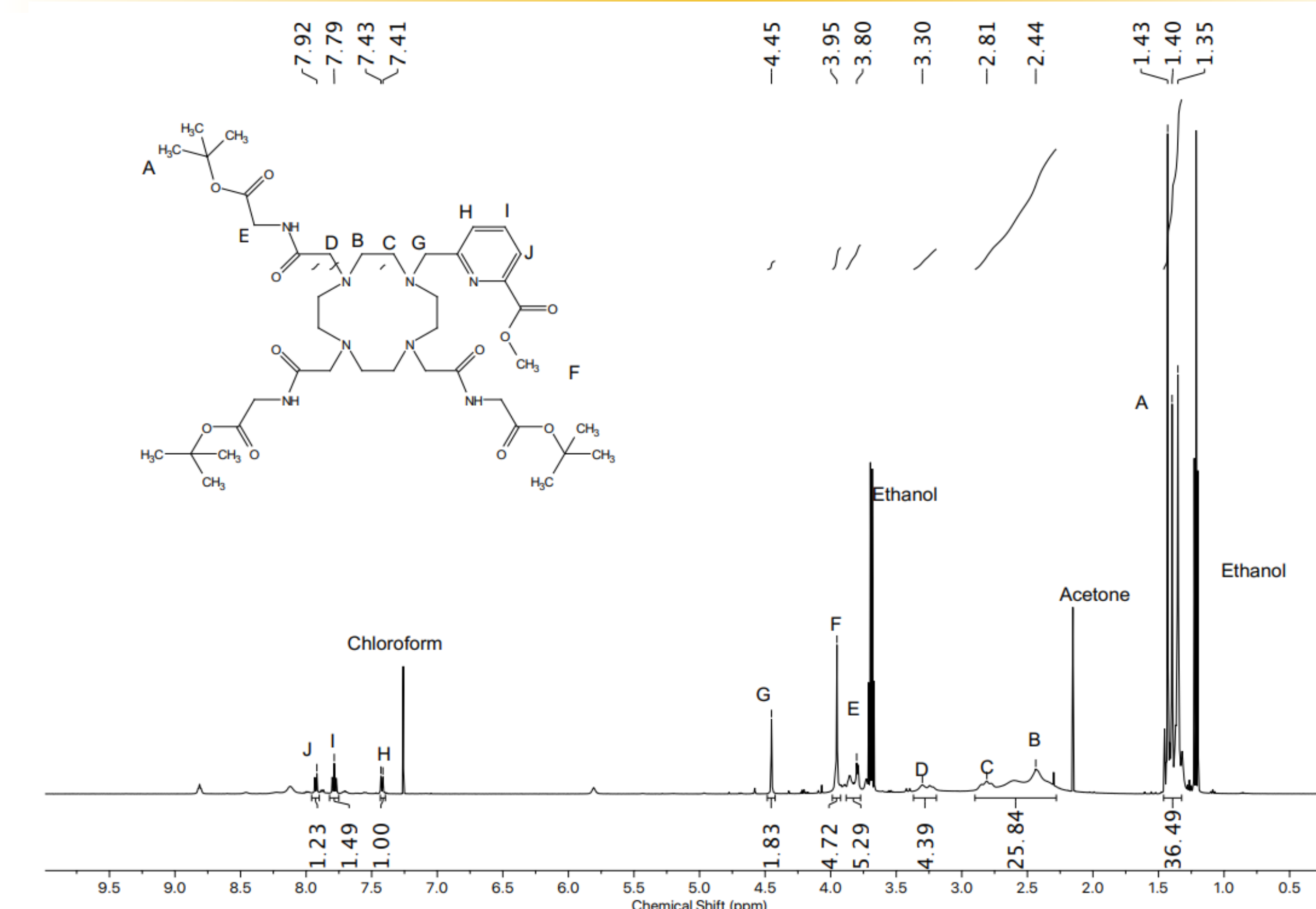


### <sup>13</sup>C-NMR of Compound 1 in CDCl<sub>3</sub> at 125 MHz

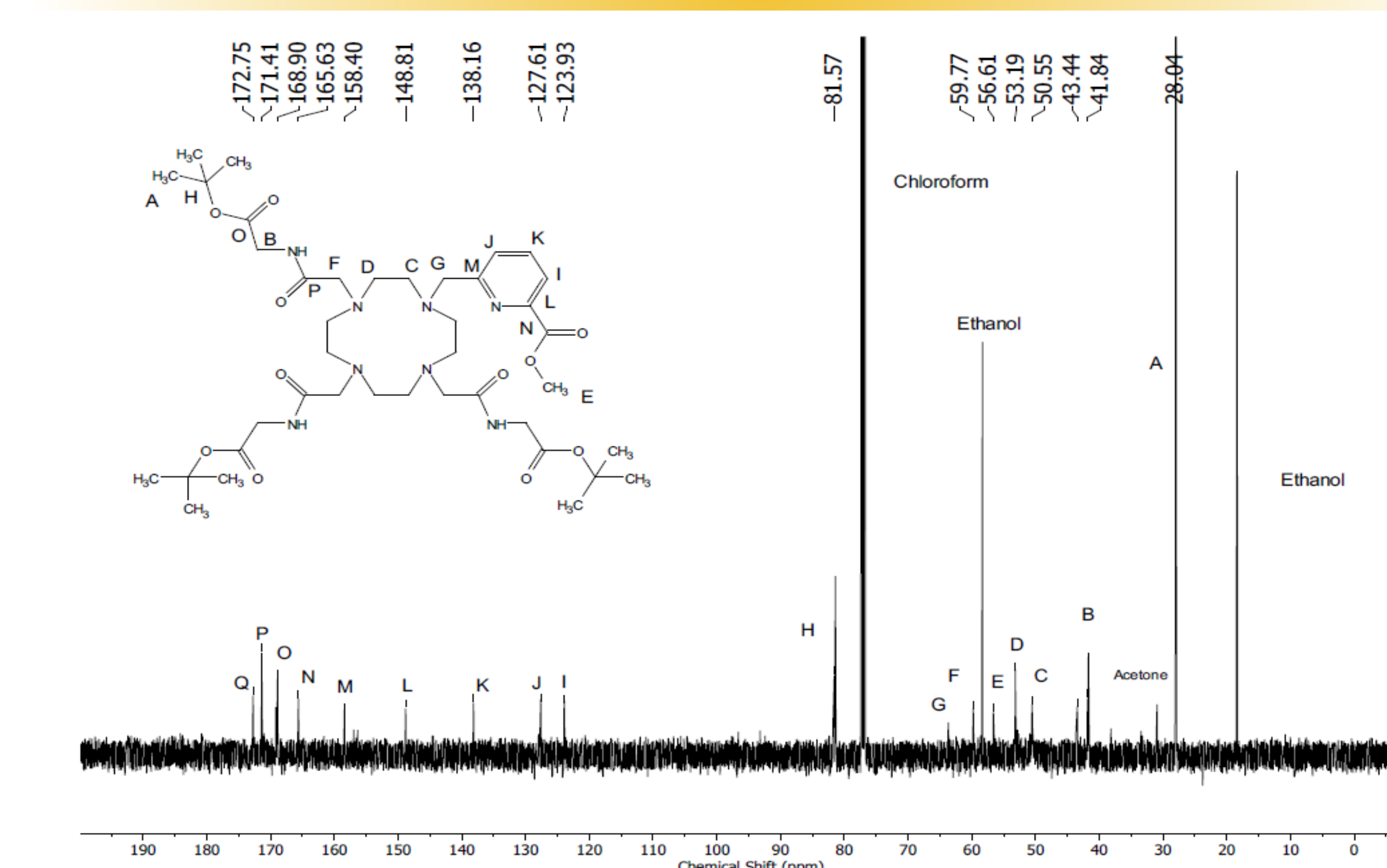


## Nuclear Magnetic Resonance Data (Contd.)

### <sup>1</sup>H-NMR of Compound 3 in CDCl<sub>3</sub> at 500 MHz



### <sup>13</sup>C-NMR of Compound 3 in CDCl<sub>3</sub> at 125 MHz



## Future Plans

- Completion of ligand synthesis
- Complexation of agent using the Ln<sup>3+</sup> ions: Tb<sup>3+</sup>, Eu<sup>3+</sup>, Dy<sup>3+</sup>, and Tm<sup>3+</sup>
- Evaluation of ParaCEST and luminescence properties of the various metal complexes

## Acknowledgements

- We would like to acknowledge funding from the USF Faculty Development Fund and the USF Startup Funds
- We would also like to acknowledge the USF Chemistry Department Faculty and Staff.

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