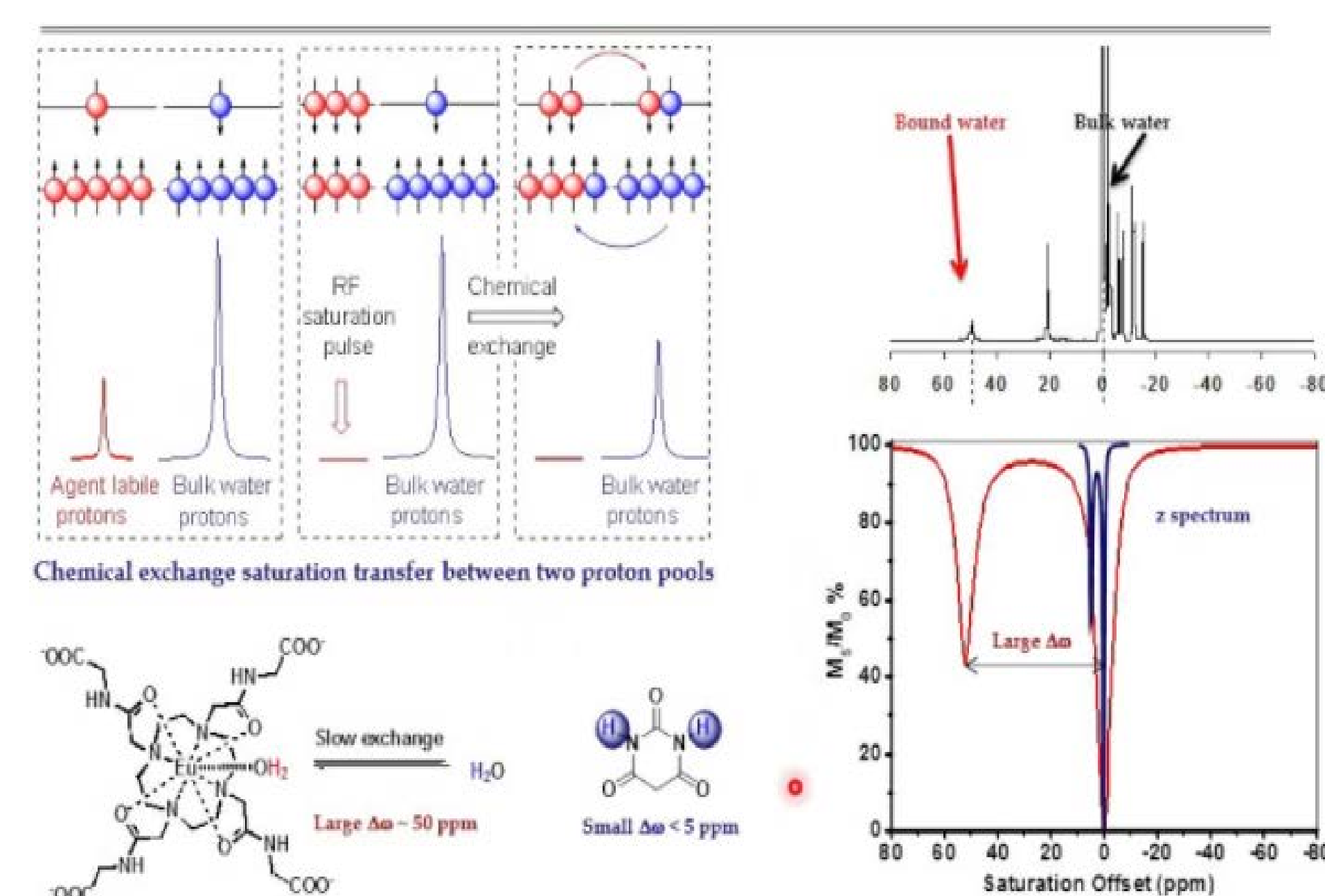


Potential paraCEST Contrast Agents for MRI Applications

Roy Cineus, Christopher J. Bond, Dr. Janet R. Morrow

Introduction

There's a new class of compounds being made for magnetic resonance imaging (MRI) contrast which are called paramagnetic chemical exchange saturation transfer (paraCEST) agents. The agents we study replace lanthanide metal ions used in earlier contrast agents with transition metal ions, which occur naturally in the body, and thus thought to be safer. These agents are also "smarter" than currently used agents, because they can respond to changes such as temperature and pH within the body.



Data

Table 1. Mass spectrum peaks of TPCZ ligand

Complex	Mass/Charge	Peak Assignment
TPCZ	521	[M+H]
	543	[M+Na]
dts-N ₂ O	439	[M+H]
	461	[M+Na]
N ₂ O	131	[M+H]

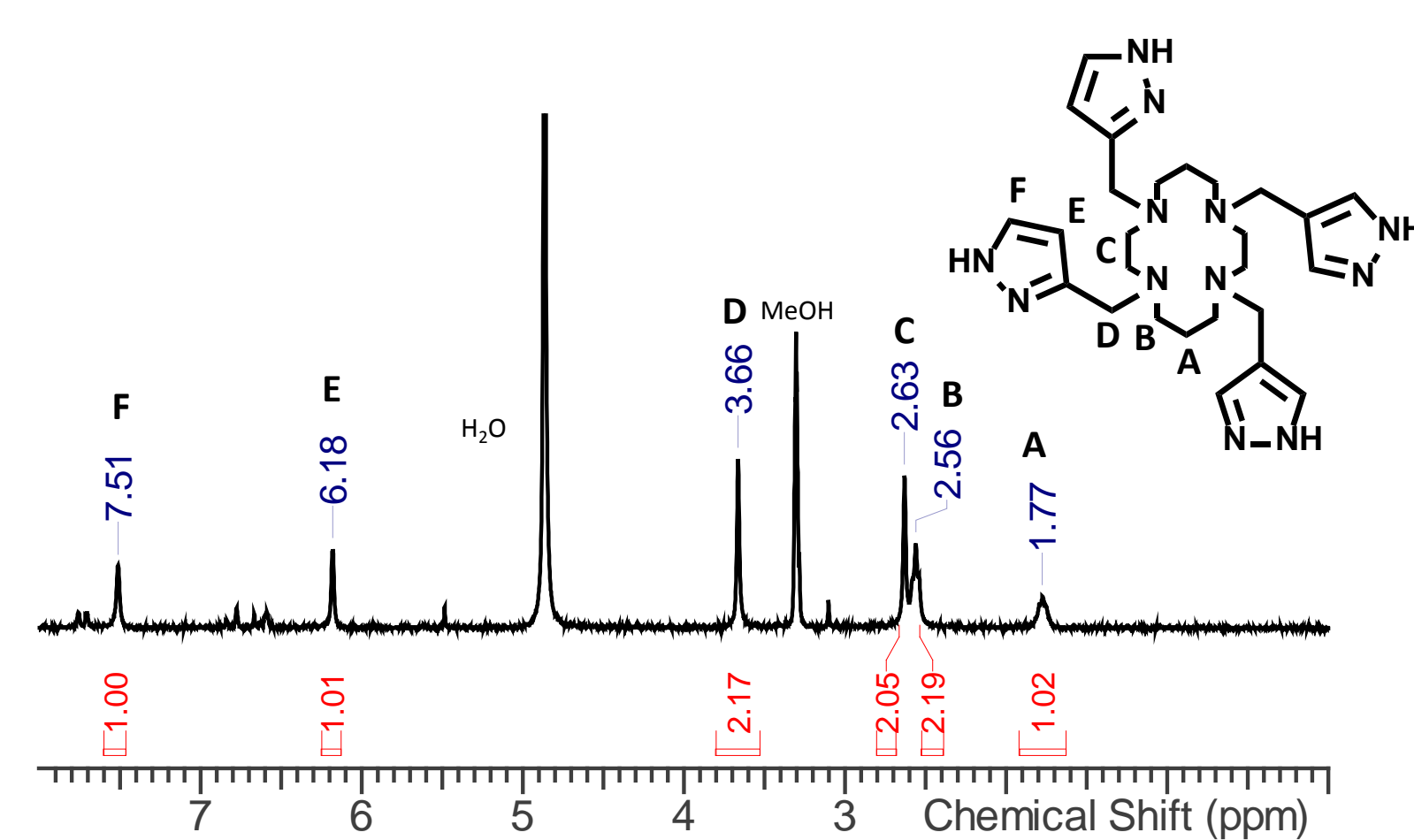


Figure 1. NMR spectrum of TPCZ ligand

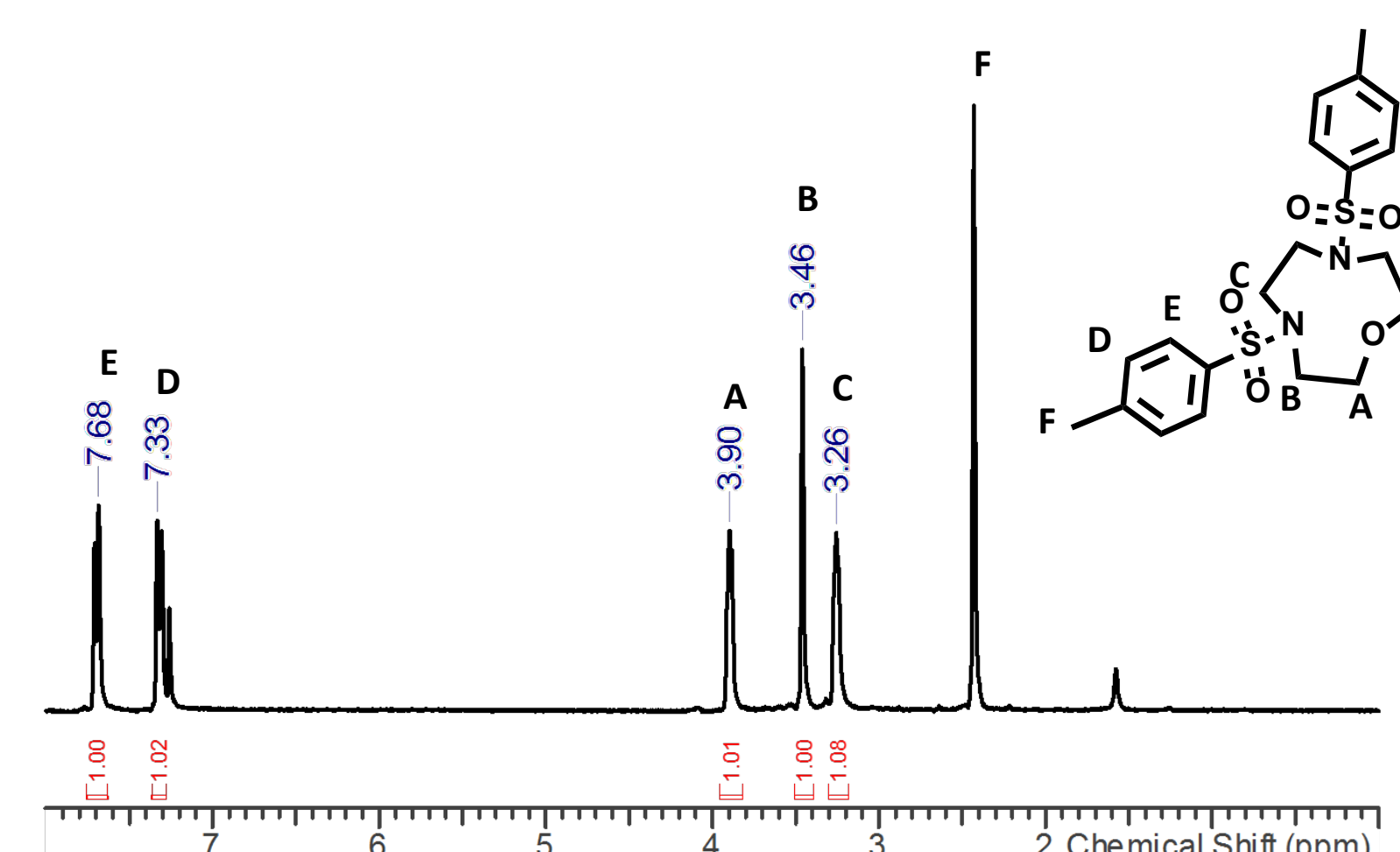


Figure 2. NMR spectrum of dts-N₂O

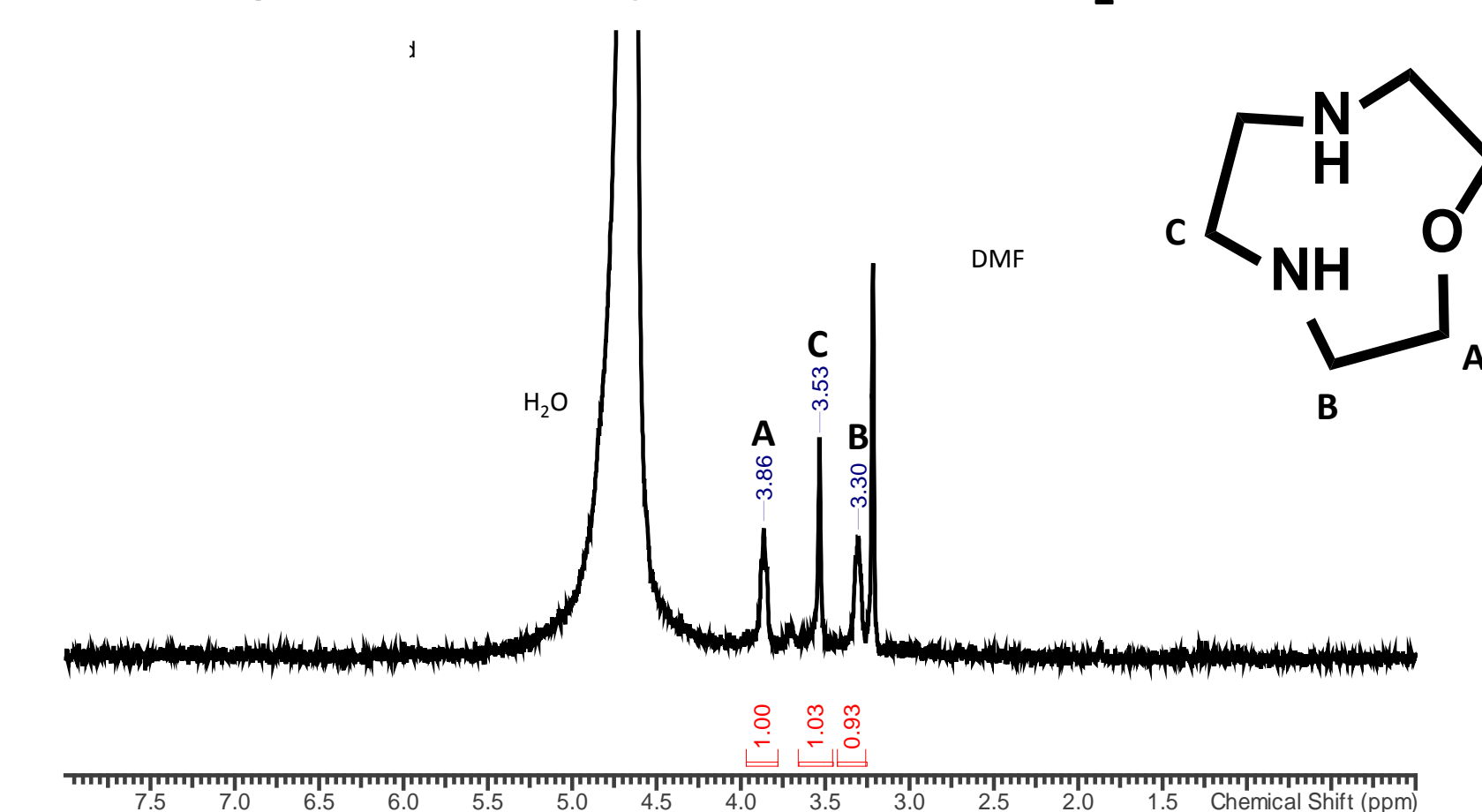


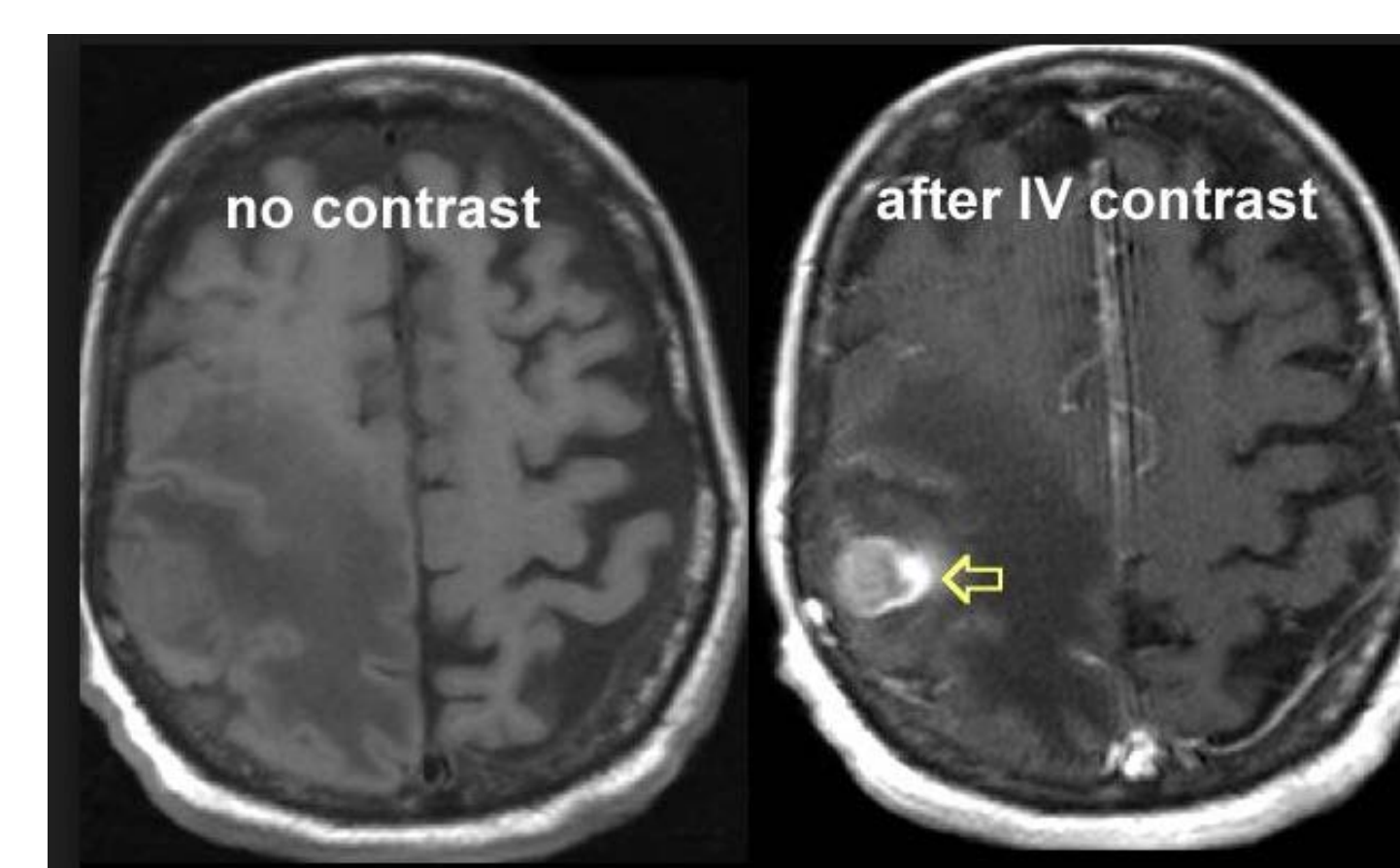
Figure 3. NMR spectrum of N₂O

Results

- The TPCZ ligand has been successfully synthesized. Purification is done on an alumina column. However, this results in a low yield.
- The metalation of the TPCZ ligand with Ni²⁺ and Fe²⁺ was attempted. However, the NMR spectrum of Ni(TPCZ)₂ and Fe(TPCZ)₂ shows that the metal hasn't bound to the cavity of the cyclam macrocycle.
- The deprotection step of the N₂O macrocycle synthesis results in a very low yield. However, a small quantity of N₂O has been isolated and was characterized by the NMR spectrum.
- The small amount of N₂O was used to successfully synthesize the DANNO ligand, which is characterized by NMR. However, metalation of the ligand bound with Co²⁺ was unsuccessful.

Conclusion

- The metalation reaction of TPCZ failed because of the small amount of starting material. Improving yields from purification to have larger quantities for the next reaction should allow for successful complexation of Fe²⁺ and Ni²⁺ complexes.
- A better solvent system is needed to precipitate N₂O out of solution after deprotection. The synthesis of more of DANNO ligand will improve the binding of Co²⁺ to the cavity of N₂O.



Future Work

- Successfully react the TPCZ ligand with Ni²⁺, Fe²⁺, and Co²⁺ for paraCEST studies.
- Find a better method of isolating the N₂O macrocycle to increase yield.
- Synthesize more of the DANNO ligand as well as the DONNO.
- Successfully react the DANNO and DONNO ligand with Fe²⁺ for paraCEST studies.

References

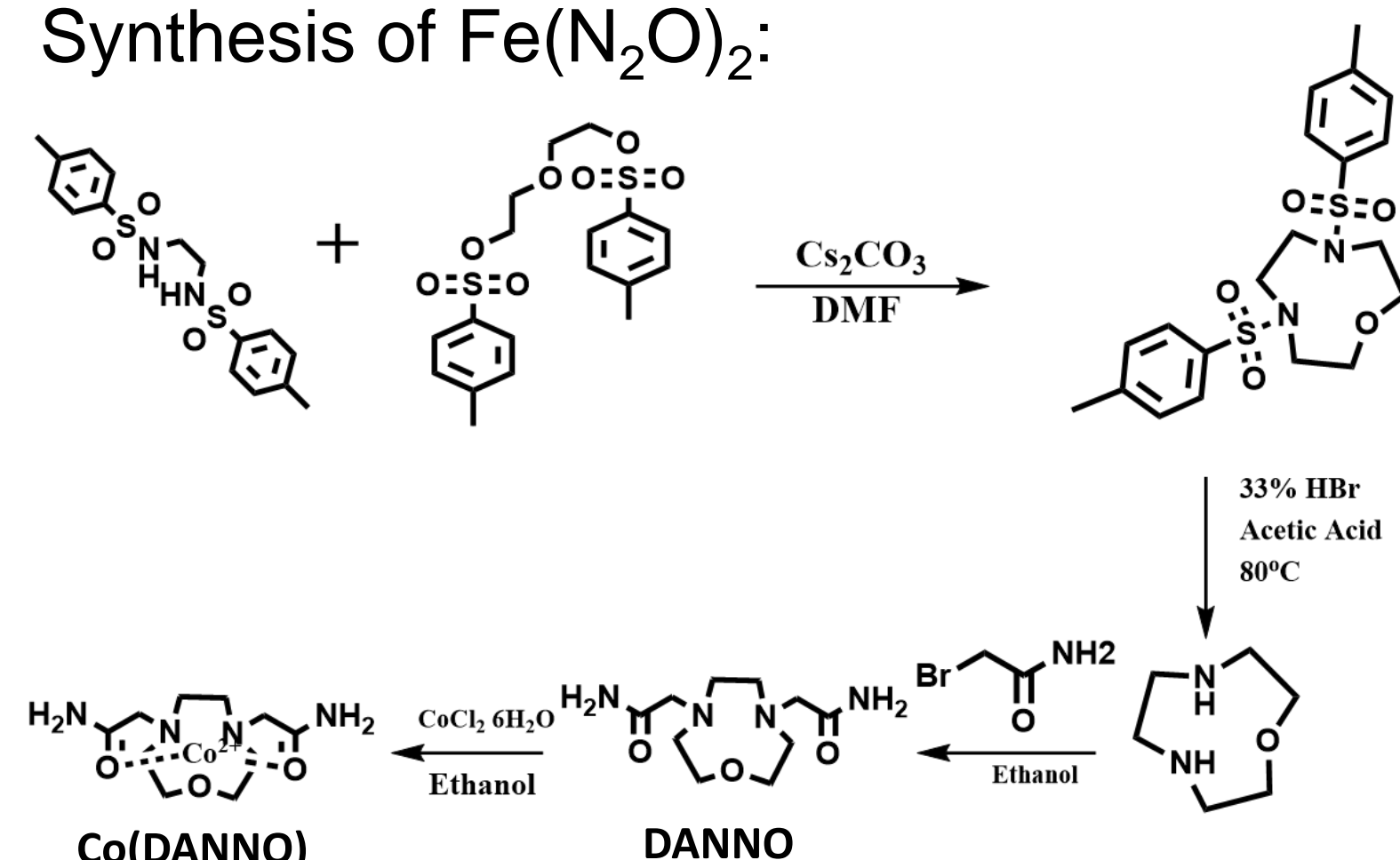
- Zhang, S.; Winter, P.; Wu, K.; Sherry, A. D., A novel europium(III)-based MRI contrast agent. *J Am Chem Soc* 2001, 123 (7), 1517-8.
- Dorazio, S.; Olatunde, A.; Tsitovich, P.; Morrow, J., *J. Biol. Inorg. Chem.* 2014, 19, 191.
- Dorazio, S. J.; Tsitovich, P. B.; Sifers, K. E.; Sperryak, J. A.; Morrow, J. R., *J. Am. Chem. Soc.* 2011, 133, 14154.

Acknowledgements

- Professor: Dr. Janet R. Morrow
- The Morrow Group:
 - Postdoctoral: Dr. Pavel Tsitovich
 - Current Grads: Timothy Tittiris, Patrick Burns, Christopher Bond, Eric Snyder, Naomi Bryner, Akanksha Patel, Didar Asik, Samira Mohammed, Raj
 - Current Undergrads: Greg Sokolow and Danny
- University at Buffalo – SUNY
www.buffalo.edu

Experimental

Synthesis of Fe(N₂O)₂:



Synthesis of M(TPCZ)₂:

