Green Research Group

Department of Chemistry & Biochemistry

Manganese Complex of a Rigidified 15-Membered Macrocycle: A Comprehensive Study

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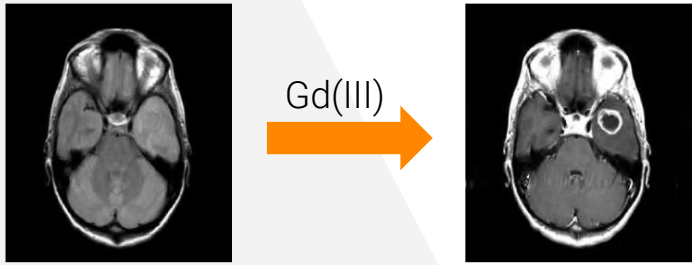
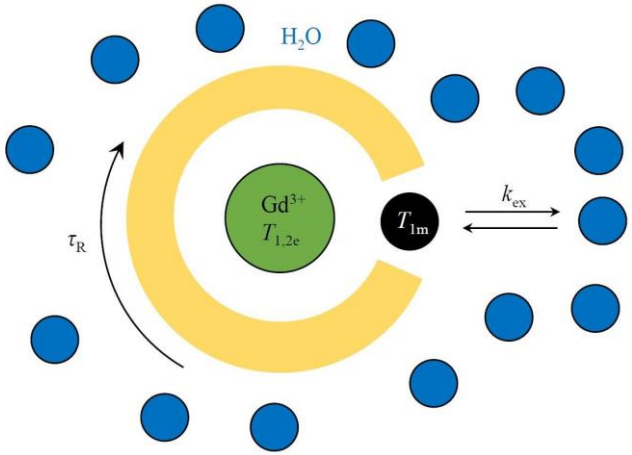
Introduction

Metal complexes in diagnostic imaging (Magnetic Resonance Imaging - MRI)

Gadolinium based complexes are used to enhance the contrast of the images generated based on the water content of soft tissues.





The problem - free Gd(III) ions are toxic

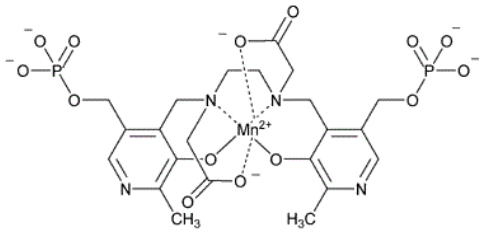
- Nephrogenic systemic fibrosis (NSF)
- Long term Gd(III) retention in the CNS

The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging. 2nd ed.; Wiley: 2013.

A possbile solution – replacement of the metal center

MEMRI (Manganese-Enhanced Magnetic Resonance Imaging)

Gd(III)		Mn(II)
✚ ✚	Contrast enhancing effect	✚
	Lack of toxicity at low concentrations	✚
	Miscellaneous	Ca(II) analogue



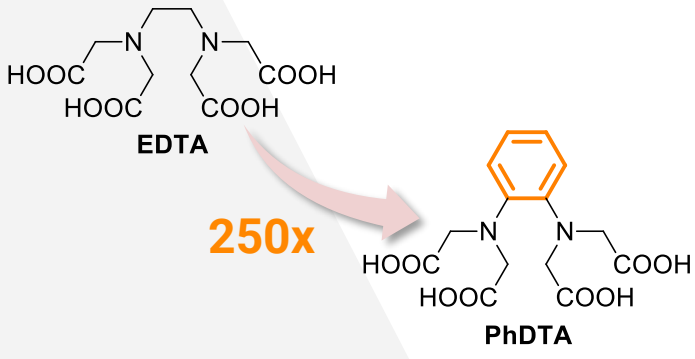
[Mn(DPDP)]$^{4-}$
Teslascan®

Issues to solve with Mn(II) based contrast agents

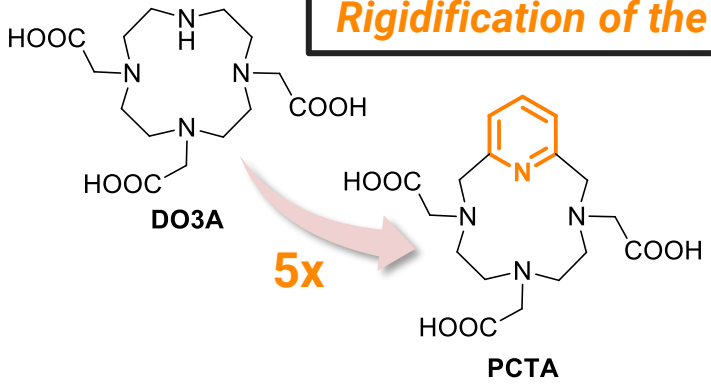
Main problem with Mn(II) complexes

- Dissociation ➡ metal ion release into the extracellular space

Proven strategies to overcome this adverse effect[1,2]



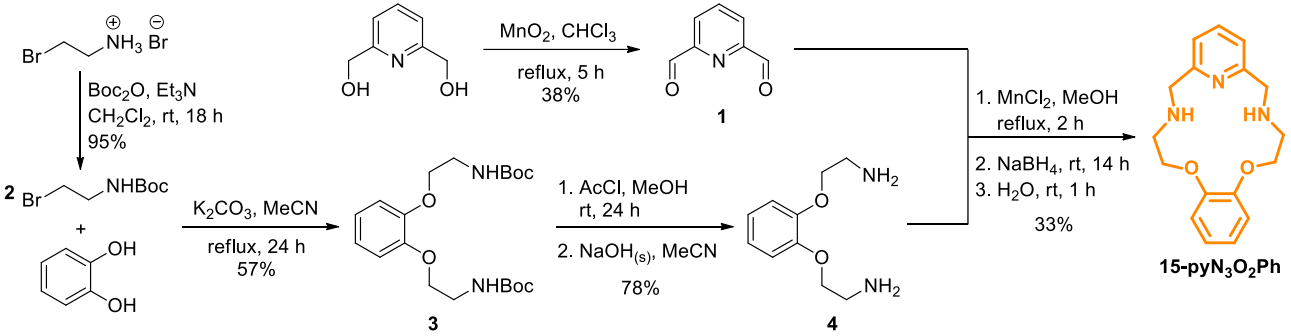
Rigidification of the backbone

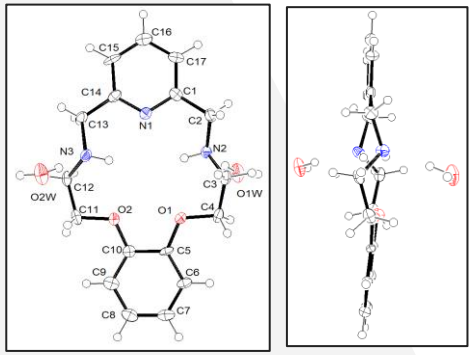


[1] Pota, K. *et al.; New J. Chem.* **2018**, *42* (10), 8001, [2] Garda, Z. *et al.; Front. Chem.* **2018**, *6*, 232/1-232/14.

Our goal – Synthesis of the target molecule

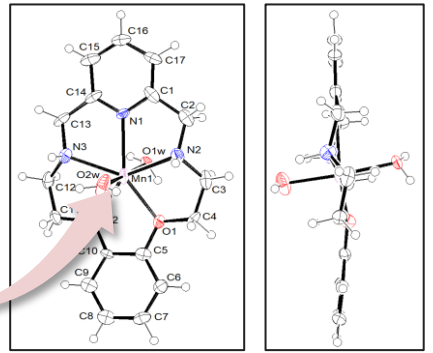
The organic synthetic route





Complex formation with Mn(II)

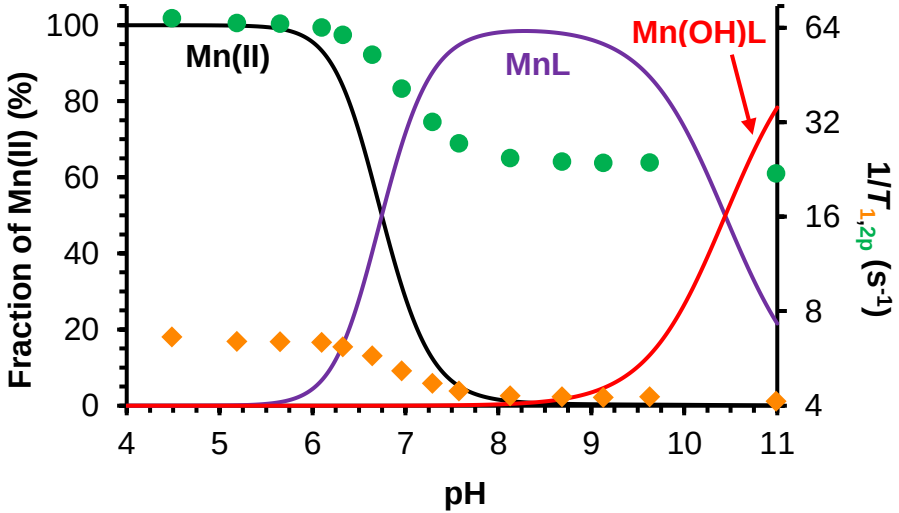
Mn(II) in the center of the cavity



Characterization of the Mn(II) complex

- Planar Mn(II) complex with ***two*** water molecules adjacent to the metal center.
- Due to the increased rigidity of the organic scaffold - ***slightly lower*** complex stability.
- ***Larger*** contrast enhancing potential compared to the FDA approved Gd(III) contrast agents.

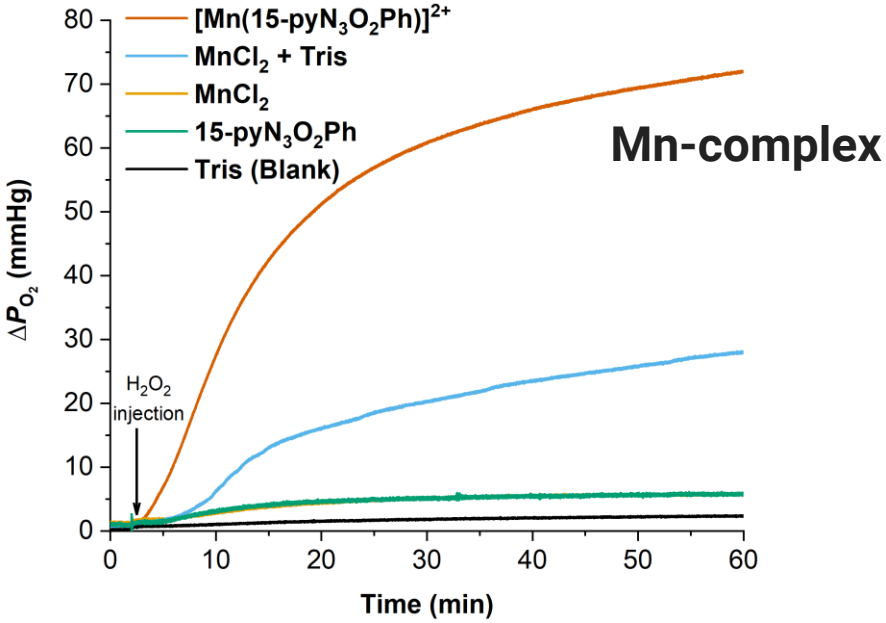
pH dependence of the relaxivity



An unexpected additional result

The Mn(II) complexes catalyzes the disproportionation of H_2O_2

Mimics the activity of the manganese catalase enzymes



THANK YOU!