

Development of Mn²⁺-based MRI contrast agent candidates

Investigation of structure-activity relationships of new bispidine derivatives



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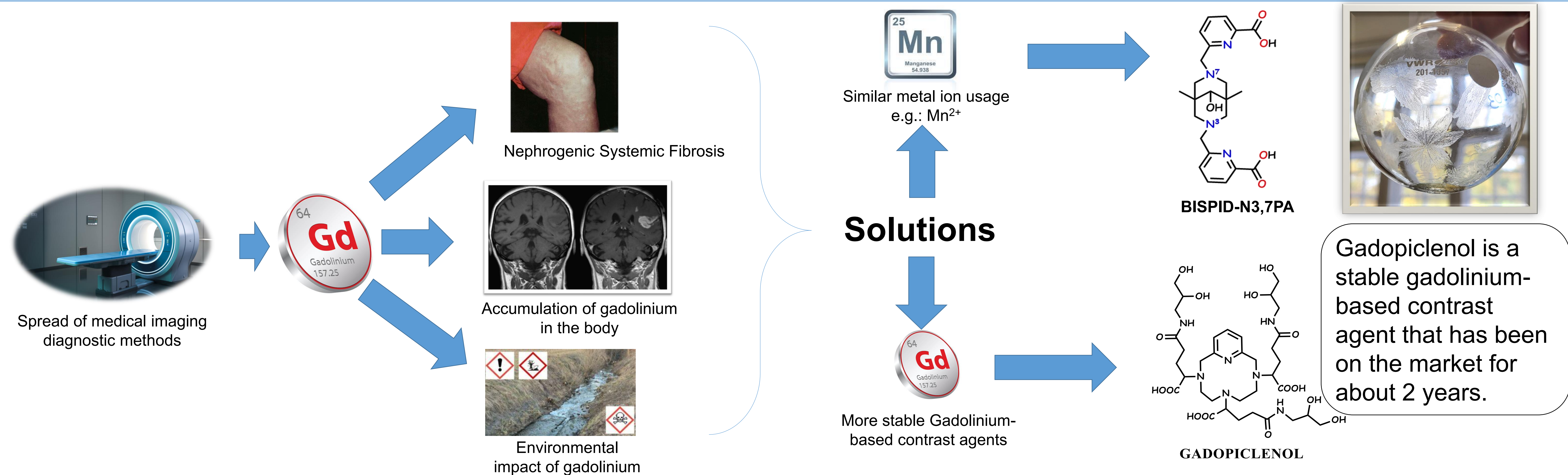
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Introduction



Economic importance

Compound	Prices
GdCl ₃	120-200 USD/100g
MnCl ₂	17.31 USD /100g

Table 1: laboratory price of some Gd,- Mn derivatives.

Methodology

Protonation and stability constant → pH potentiometry

Relaxivity → relaxometer

20MHz

r_{1p} (25 °C/ 37 °C)

2.36/ 1.75

r_{2p} (25 °C/ 37 °C)

2.65/ 1.94

Synthesis → HPLC, MS, NMR

60MHz

r_{1p} (25 °C/ 37 °C)

2.04/ 1.40

r_{2p} (25 °C/ 37 °C)

2.52/ 1.65



Results

- The protonation constants of the ligand and the thermodynamic stability constants of the complex were determined by pH-potentiometry (pMn = 6.84).
- The relaxivity value determined by relaxometry was >1.5 mM⁻¹s⁻¹, which assumes the presence of a coordinated water molecule, which is necessary for clinical application.

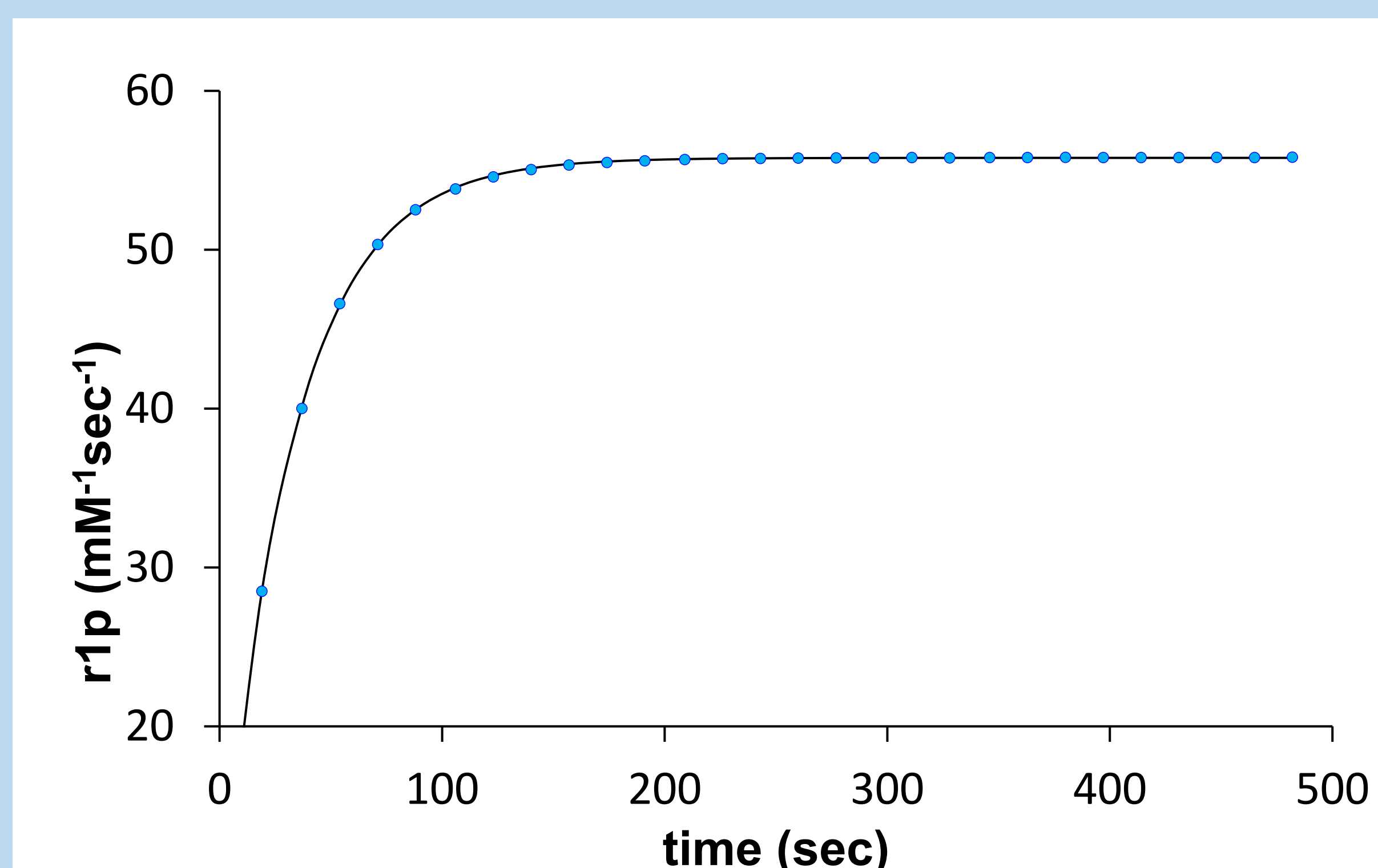


Figure 2: We chose Zn²⁺ as the exchange metal ion because it is also an essential metal ion, and in addition, based on the William-Irving series in the periodic table, it is expected to be more stable than the Mn²⁺ complex of the corresponding ligand. The half-life of my complex is 22.5 seconds

Objective

The aim of the project is to synthesize and physicochemically characterize a new type of Mn²⁺-ion complexing bispidine derivative, which has potential applications as an MRI contrast agent. The main scientific question of the project is whether the stability, inertness and relaxation effect of Mn²⁺ complexes can be increased by appropriate structural modifications. In addition, the aim is to preserve the biocompatibility of the complexes and reduce their potential toxicity.

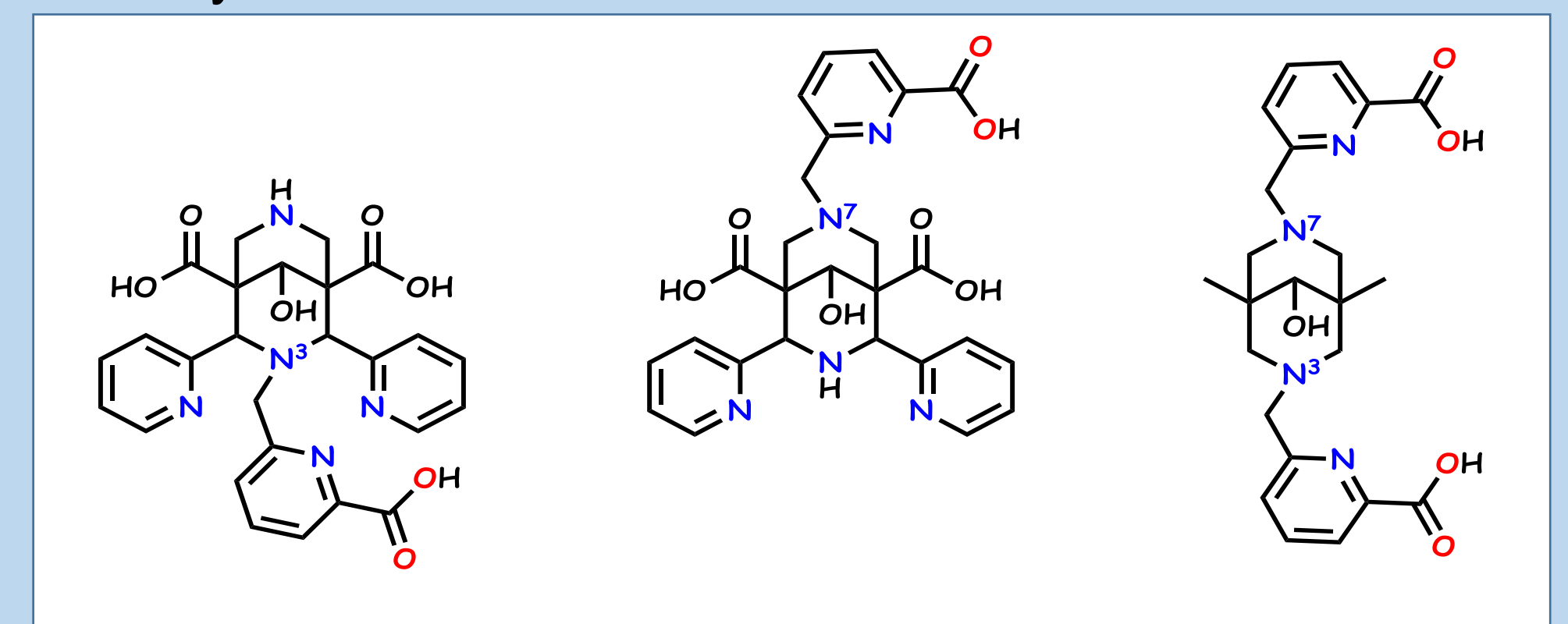
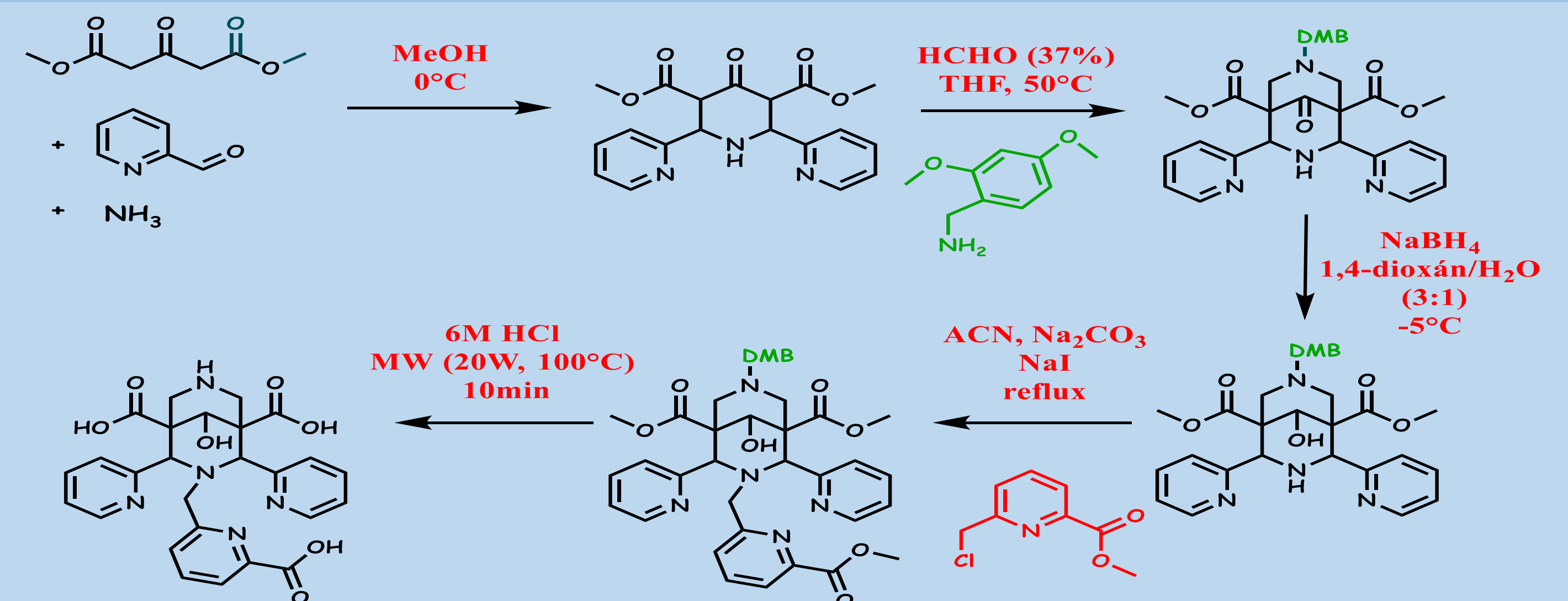


Figure 1: Structures of the ligands BISPIDIN-N3PA, BISPIDIN-N7PA and BISPIDIN-N3,7PA, indicating the donor atoms involved in the coordination of the Mn²⁺-ion.

Synthesis



References

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