



HAL
open science

Novel manganese complexes based on a pyclen derivative: synthesis and relaxometric characterization

Marie Devreux, Céline Henoumont, Fabienne Dioury, Marc Port, Olivier Sandre, Robert N. Muller, Sophie Laurent

► To cite this version:

Marie Devreux, Céline Henoumont, Fabienne Dioury, Marc Port, Olivier Sandre, et al.. Novel manganese complexes based on a pyclen derivative: synthesis and relaxometric characterization. The SFNano C'Nano joint meeting 2019, Dec 2019, Dijon, France. hal-04056417

HAL Id: hal-04056417

<https://hal.science/hal-04056417v1>

Submitted on 3 Apr 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Novel manganese complexes based on a pyclen derivative: synthesis and relaxometric characterization

•Devreux Marie ^[a,d], Henoumont Céline ^[a], Dioury Fabienne ^[b], Port Marc ^[b], Sandre Olivier ^[d] and Laurent Sophie ^{[a] [c]}

[a] University of Mons, UMONS, General, Organic and Biomedical Chemistry, NMR and Molecular Imaging Laboratory, 19 Avenue Maistriau, 7000 Mons (Belgium)

[b] Conservatoire national des arts et métiers, CMGPCE Laboratory, EA 7341, Paris (France)

[c] Center for microscopy and molecular imaging (CMMI), 8 rue Adrienne Bolland, 6041 Charleroi (Belgium)

[d] University of Bordeaux, UB, ENSCBP, Laboratory of organic polymer Chemistry, 16 Avenue Pey-Berland, 33607 Passac (France)

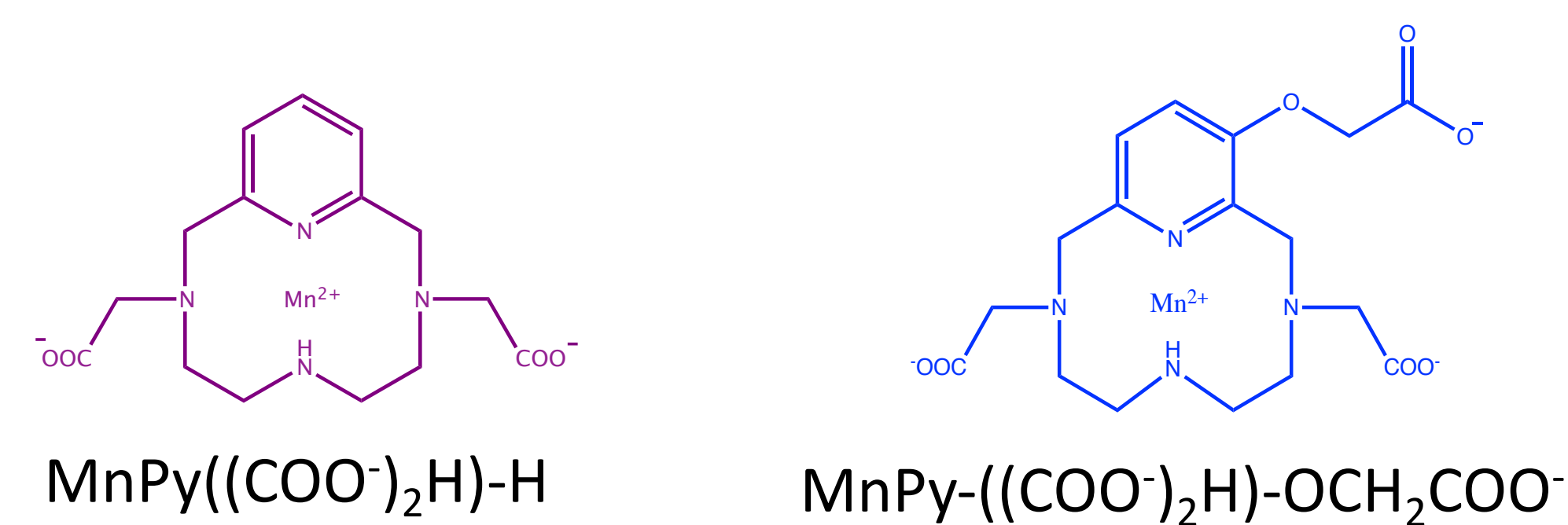
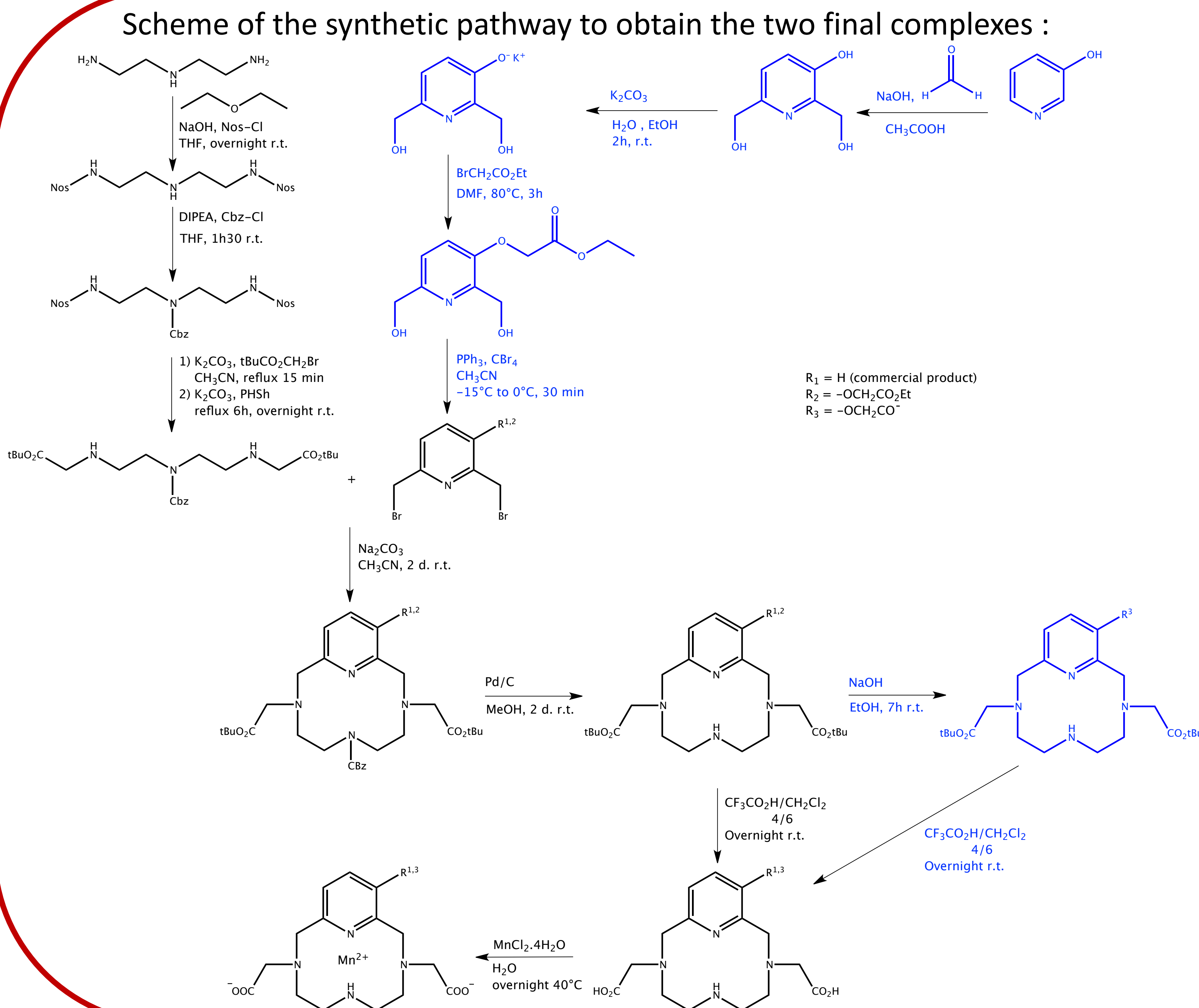


1. Introduction

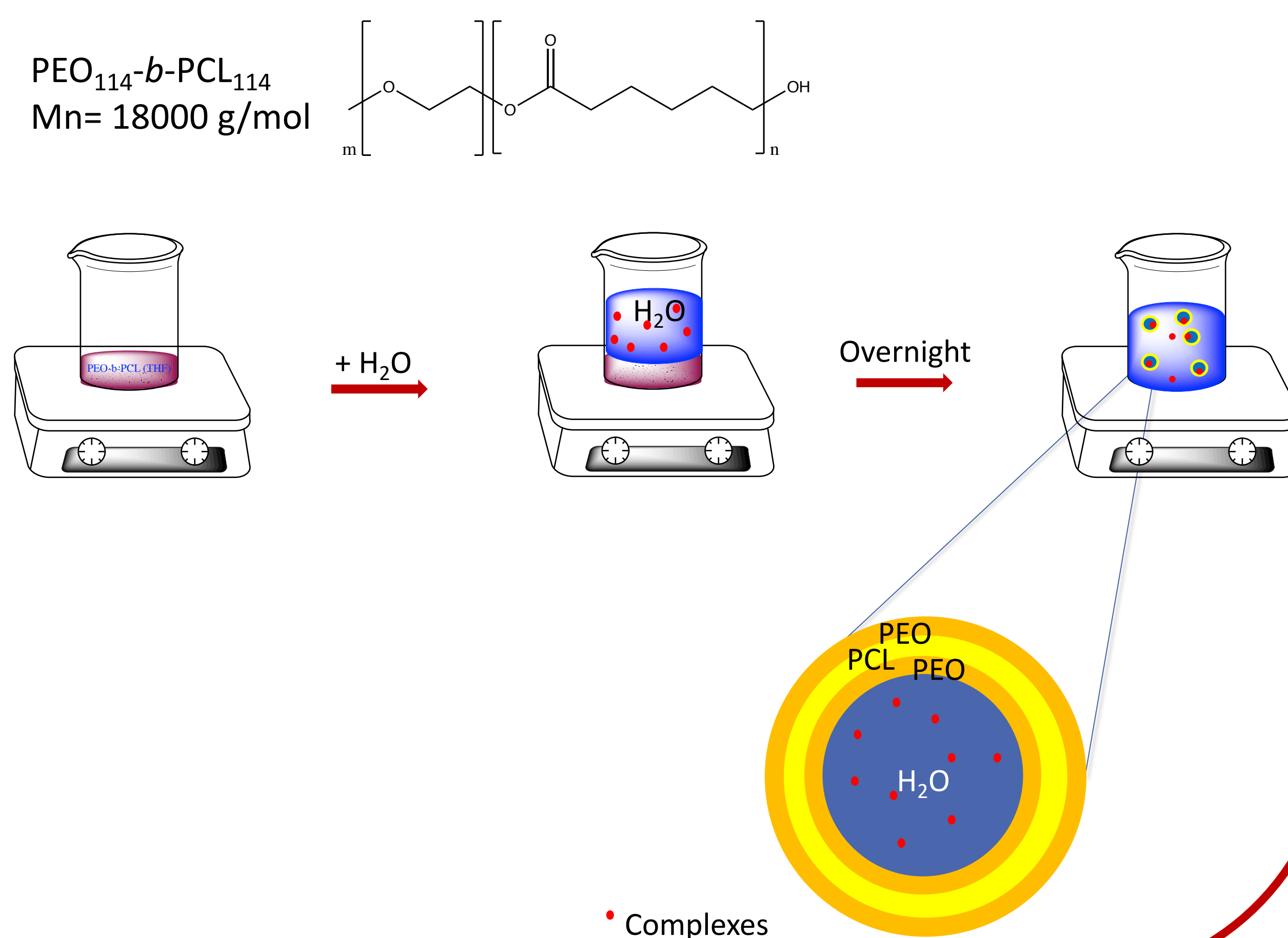
In medicine, medical imaging has a leading place in the diagnosis setting. This is why some researches are continually carried out to improve the available techniques. One of the most used techniques to obtain anatomical information is magnetic resonance imaging (MRI). Although it is a highly resolutive technique, it has a low sensitivity that can be relieved by a contrast agent. However, the commercially available contrast agents are based on gadolinium complexes which can lead to nephrogenic systemic fibrosis. That is why the synthesis of new complexes based on another cation, such as manganese (Mn^{2+}), is interesting. Manganese ions are indeed potentially less toxic since they are naturally present in the body. This study shows the synthetic way to obtain 2 different pyclen derivatives complexed with Mn^{2+} ions and their relaxometric studies to prove their efficiency. Further improvement will consist in the relaxometric study of the macrocyclic complexes encapsulated in polymer nano-vesicles also called "polymersomes" made of pH-sensitive polyester.

2. Methods

Scheme of the synthetic pathway to obtain the two final complexes :



Nanoprecipitation of copolymer to prepare polymersomes:



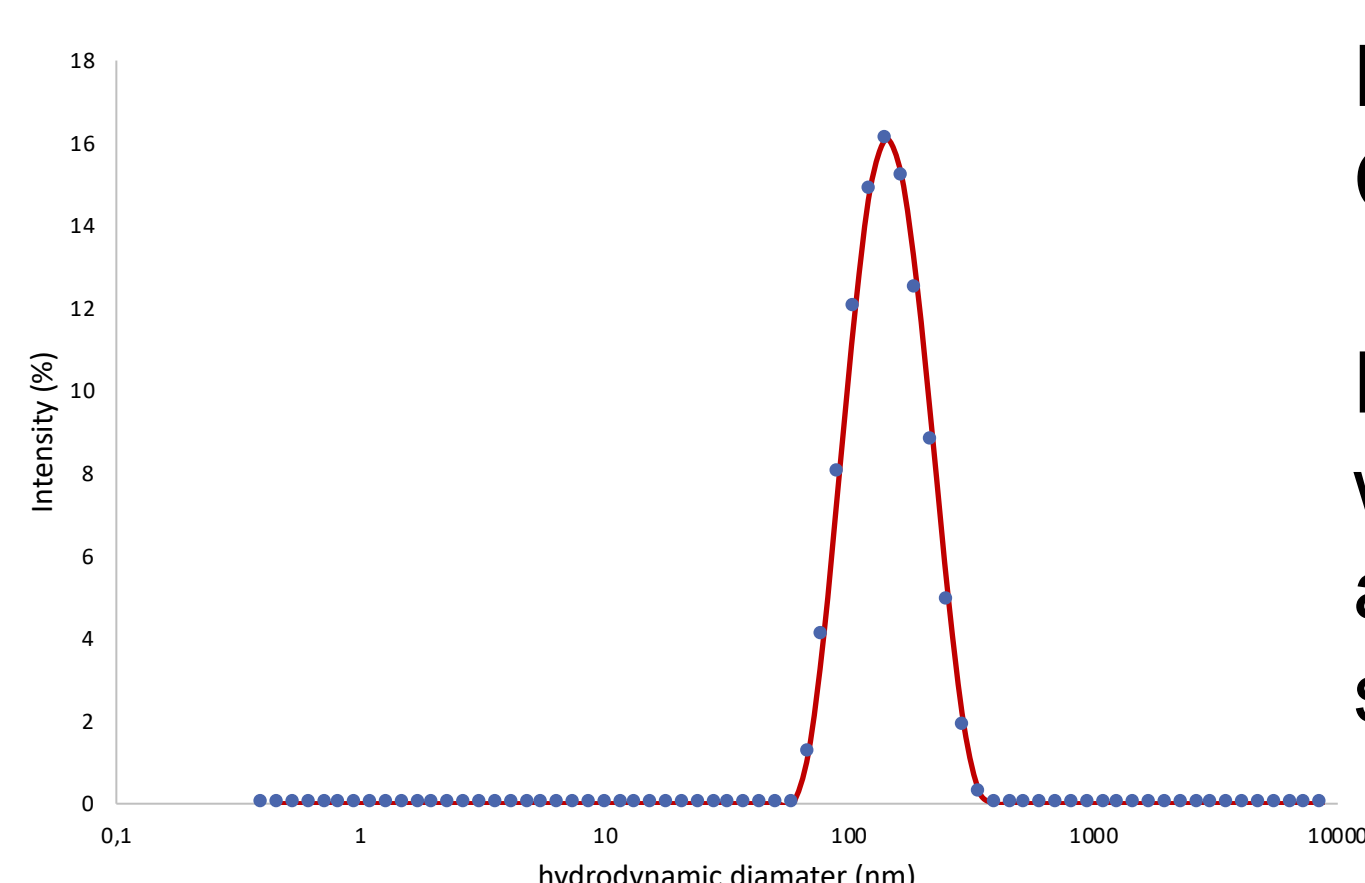
3. Results

To fit correctly the NMRD profiles, the number of inner-sphere coordinated water molecules (q) was evaluated by ^{17}O NMR ¹ and with NMRD profiles at 25°C ². A number of $q=1$ is obtained for both complexes. As shown by the NMRD profiles, the relaxivity of $MnPy((COO^-)_2H)-OCH_2COO^-$ is higher than that of $MnPy((COO^-)_2H)-H$, mainly due to an increase of τ_R .

Table 1: Determination of the number of coordinated water molecules in the metal inner-sphere (q) and characteristic relaxometric times of the two complexes extracted from the NMRD profiles

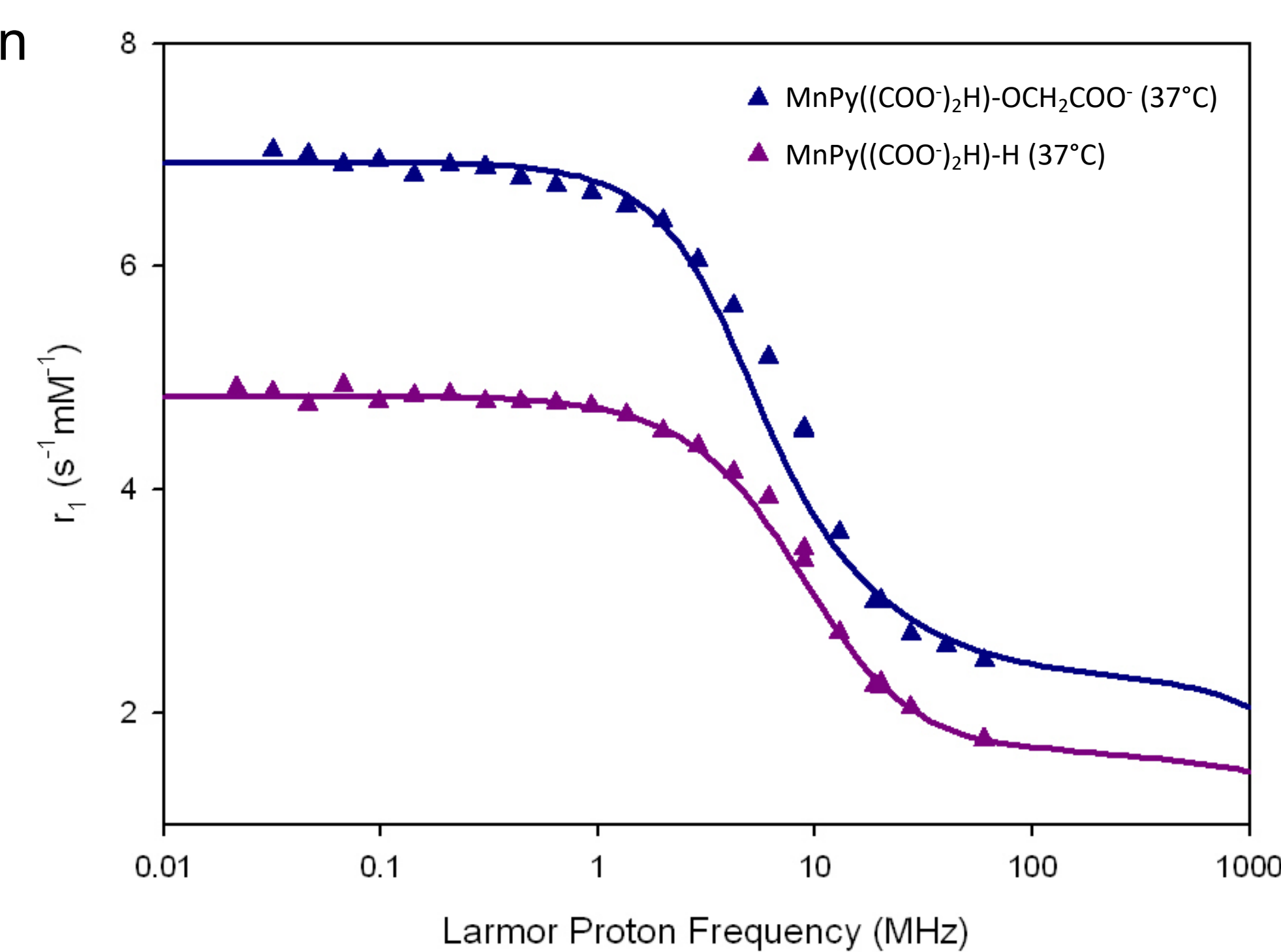
	q (by O^{17}) ¹	q (by NMRD profiles at 25°C) ²	τ_R (ps)	τ_M (μ s)	τ_V (ps)	τ_{50} (ps)
$MnPy((COO^-)_2H)-H$	0,72	1,02	31,30	0,10	3,13	340
$MnPy((COO^-)_2H)-OCH_2COO^-$	0,73	1,32	56,30	0,10	56	480

Dynamic light scattering (DLS):



$D_H = 136 \text{ nm}$, PDI = 0.1
 Concentration in copolymer = 0.08 mM (1.5 mg/mL)

Preliminary DLS analysis of the nano-precipitated samples without any Mn-complexes shows narrow size dispersity and average hydrodynamic size compatible with nanostructure structure obtained with similar PEO-*b*-PCL copolymer.³



NMRD profiles of the two molecules of interest at 37°C

4. Conclusion and perspective

This study shows that these manganese-pyclen derivatives are promising contrast agents to replace gadolinium complexes as T_1 MRI contrast agent. Moreover, different functions can be combined by conjugation with different other types of molecules to obtain a functionalized pyclen that can be encapsulated in polymersomes.

5. Acknowledgements

This work was performed with the financial support of SIRIC BRIO (COMMUNCAN), FNRS, ARC, the Walloon Region (Gadolymp, Holocancer and Interreg projects), the Interuniversity Attraction Poles of the Belgian Federal Science Policy Office and the COST actions. Authors thank the Center for Microscopy and Molecular Imaging (CMMI, supported by European Regional Development Fund and Wallonia)