Highly stable Ln^{3+} azamacrocyclic chelates tailored for diagnosis and therapy: full control of the ligand design makes the difference!

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Cyclen, tacn, cyclam and pyclen based ligands are the most widely studied polyazamacrocyclic platforms for metal complexation because, suitably *N*-functionalized, they form stable and inert chelates. Lanthanide(III) ions belong to the large panel of cations strongly complexed by these ligands presenting a high coordination sites. The obtained chelates are then widely used for several applications ranging from Magnetic Resonance to Optical Imaging, depending on the nature of the central metal ion. However, even if some lanthanides chelates are already well performant for such uses, the room for improvement is still great both to design specific agents for a specific media and to develop agents that allow the combination of different modalities.

In this area we recently progressively reported picolinate *N*-functionalized tetraazamacrocycles presenting astonishing coordination properties with Ln(III) cations leading to new potential chelates for both MRI and photophysical applications but also for therapeutic purposes. We especially highlighted that the full control of the regiospecific *N*-functionalization of the macrocycles governs the final kinetic and thermodynamic properties of the chelates but also their magnetic or photophysical ones. For the latter, monophotonic investigations have been firstly performed considering the nature of the coordination arms. Two-photon π-conjugated antennas have then been introduced on the ligands to extend our works on biphotonic microscopy.[1, 2]
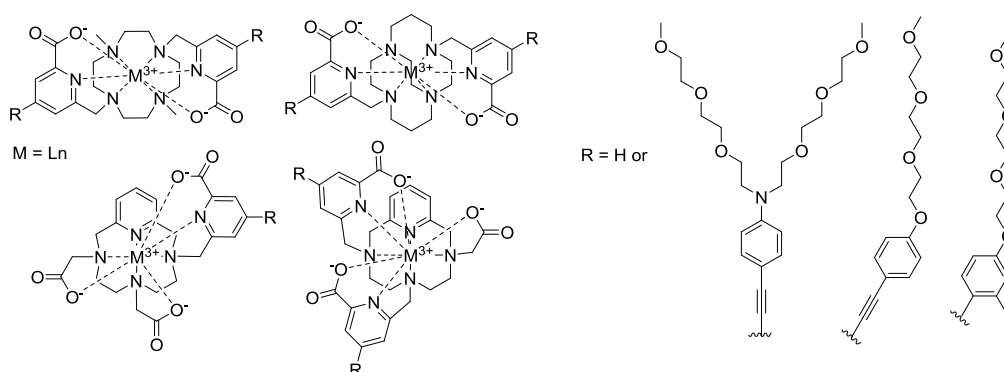

Figure 1 Ln^{3+} tetraazamacrocyclic complexes for MRI, optical and therapeutic applications

1 M. Le Fur, M. Beyler, E. Molnár, O. Fougère, D. Esteban-Gómez, G. Tircsó, C. Platas-Iglesias, N. Lepareur, O. Rousseaux, R.Tripier, *Chem. Commun.*, **2017**, 53, 9534; M. Le Fur, E. Molnár, M. Beyler, F. K. Kálmán, O. Fougère, D. Esteban-Gómez, O. Rousseaux, R. Tripier, G. Tircsó, C. Platas-Iglesias, *Chem. Eur. J.*, **2018**, 24, 13, 3127 ; M. Le Fur, M. Beyler, E. Molnár, O. Fougère, D. Esteban-Gómez, G. Tircso, C. Platas-Iglesias, N. Lepareur, O. Rousseaux, R. Tripier, *Inorg. Chem.*, **2018**, 57, 4, 205; N. Hamon, M. Galland, M. Le Fur, A. Roux, A. Duperray, A. Grichine, C. Andraud, B. Le Guennic, M. Beyler, O. Maury, R. Tripier, *Chem. Commun.* **2018**, *54*, 6173.
2 In collaboration with Guerbet group, France, University of Debrecen, Hungary, University of La Corunna, Spain, and University of Lyon – ENS, France.