

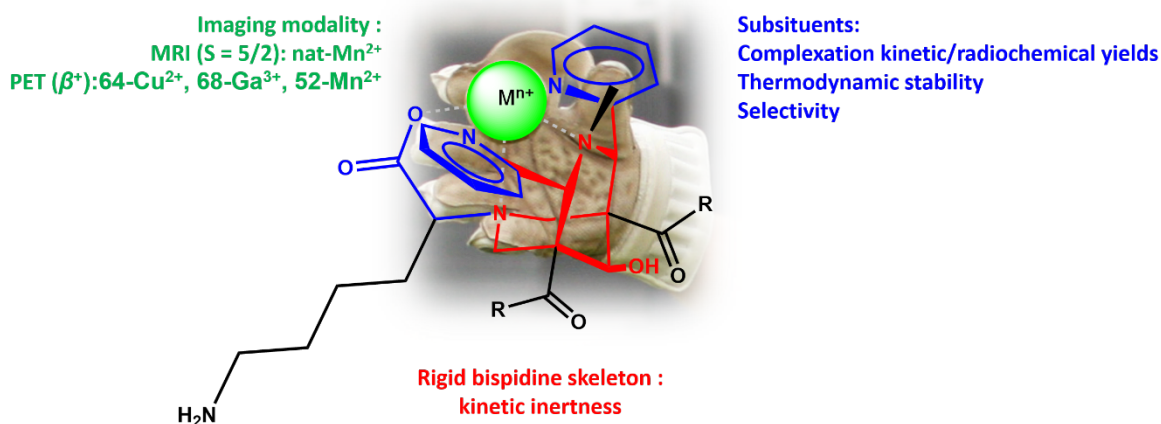
Bispidine : a privileged scaffold for metal-based imaging agents ?

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Recent achievements in the synthesis and coordination chemistry of bispidines (bispidine = 3,7-diazabicyclo[3.3.1]nonane) have paved the way to a new field of application of bispidine coordination complexes : medical imaging.

Examples of practical applications to magnetic resonance imaging (MRI) and positron emission tomography (PET) will be presented. For each of these two techniques, a metal ion (Gd, Mn for MRI or a radioisotope for PET) plays the main role of "reporter" and induces the signal. Nevertheless, in both cases, the ions must be chelated and form complexes resistant to *in vivo* dissociation. In addition, the formation kinetic of the complex should be fast enough to allow for a complete complexation in highly dilute conditions (pM to nM concentrations), at room temperature and at pHs close to physiological pH. These two criteria may seem contradictory and only a handful of complexes can meet them simultaneously.

Thanks to their rigid and pre-organized skeleton, it appears that bispidine ligand could perfectly match to the specifications required for molecular imaging probes. Examples with Cu(II),^[1] Mn(II)^[2] and Ga(III)^[3] complexes will be discussed.



[1] R. Gillet, A. Roux, J. Brandel, S. Huclier-Markai, F. Camerel, O. Jeannin, **A. M. Nonat***, L. J. Charbonnière*, A Bispidol Chelator with a Phosphonate Pendant Arm: Synthesis, Cu(II) Complexation, and ⁶⁴Cu Labeling, *Inorg. Chem.*, **2017**, *56*, 11738-11752.

[2] D. Ndiaye, M. Sy, A. Pallier, S. Mème, I. de Silva, S. Lacerda, **A. M. Nonat**, L. J. Charbonnière*, E. Tóth*, Unprecedented kinetic inertness for a Mn²⁺-bispidine chelate: a novel structural entry for Mn²⁺-based imaging agents, *Angew. Chem. Int. Ed.*, **2020**, *13*, 11958-11963 (cover article).

[3] T. W. Price, S. Yap, R. Gillet, H. Savoie, L. Charbonnière, R. Boyle*, **A. M. Nonat***, G. J. Stasiuk*, Evaluation of a bispidine-based chelator for gallium-68 and of the porphyrin conjugate as PET/PDT theranostic agent, *Chem. Eur. J.*, **2020**, *18*, 7602-7608 (hot paper).