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Heteroelements and Polyazamacrocyclic Chelators : new properties for applications in medical imaging and therapy.

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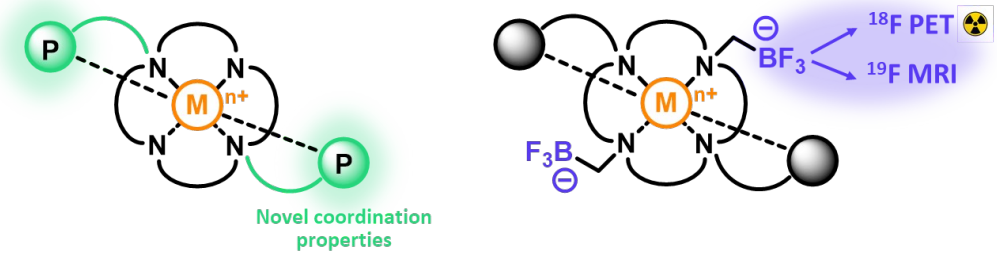
Polyazamacrocycles (such as cyclen and cyclam) are ubiquitous ligands that possess remarkable coordination properties towards a wide range of cations, from transition metals to lanthanides. In particular, they are cornerstone for the design of performant tracers in medical imaging and radiotherapy, where they chelate cations that would be toxic *in vivo* under their free form to allow their safe injection to patients. In particular, the well-known Dota ligand (cyclen-tetraacetate) and its derivatives are approved clinically for administration of MRI contrast agents (with Gd^{3+}, Dotarem®), PET probes ($^{68}Ga^{3+}$, Ga-Dotatate) or internal β radiotherapy ($^{177}Lu^{3+}$, Lutathera®).[1,2] However such ligands present limitations for the stabilization of complexes with some metals of interest (Copper, Bismuth…). In addition, the coordination chemistry of these chelators is almost exclusively based on C,N,O-based functional and coordinating groups (i.e. acetate, pyridyl, amide…). Therefore, our group is exploring the use of heteroelements (P, B, F) to bring novel properties to these chelating ligands, and potentially improve there behaviour towards certain metallic cations.



Recently, we have developed two novel families of cyclen- and cyclam-based chelators : i) using phosphorus-based coordinating units, we managed to improve the biodistribution of copper(II) chelates,[3] but also access specific coordination of Cu^{2+} vs. competing cations (Zn^{2+}, Co^{2+}, Ni^{2+}),[4] an extremely rare property for such ligands; ii) with trifluoroborate functional groups, we are also moving towards theranostic and smart contrast agents,[5,6] as they offer the unique possibility to easily combine the properties (magnetic, therapeutic) of the cations sequestered within the macrocyclic cavity with those of fluorine, which is pivotal in medical imaging thanks to two of its isotopes : radioactive ^{18}F used in PET imaging, and natural ^{19}F used in MRI.

References

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