New Versatile Chiral Platforms for Enantioselective Catalysis and Drug Delivery

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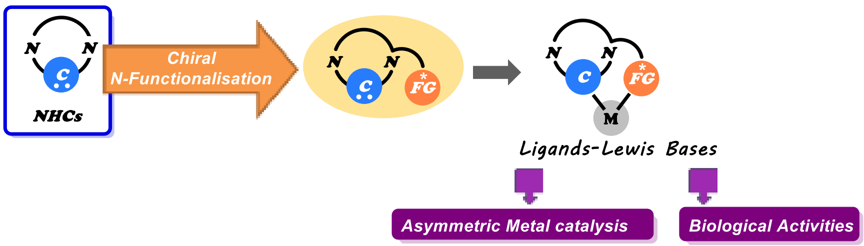
The need to create new chiral materials is constantly increasing to meet the major issues of our society that are health care and the environment. In this context the importance of designing new low-cost chiral tools with the most straightforward and atom-economical approaches is crucial. This will lead to the preparation of new organic/organometallic chiral pockets which would be capable of having a high specificity for their substrates.

Surprisingly, although chiral N-heterocyclic carbene (NHCs) are well established as enantioselective organocatalysts, their use as chiral ligands for transition metals is still marginal compared to well establish enantiopure phosphines.[1] Nonetheless, chiral NHCs are still attractive ligands considering their high synthetic modularity and the exceptional stability exhibited by the metal-NHC bond. On the other hand, the robustness of NHCs-metal complexes under physiological media and their tunability make them very attractive to provide a quick access to a large library of new metallo-drug candidates. Despite this fact, only few NHCs have been used in the therapeutic field and so far, they have been used only as an antimicrobial or anticancer agent.[2] Interestingly, the rules governing the elaboration of new ligands are suitable for both catalytic and medical applications and so will "kill two birds with one stone".[3]



In this thesis we plan to use a singular family of chiral NHC bidentate ligands with an ancillary arm with a chiral atom and attach them to transition metals such as ruthenium and less toxic and eco-friendly iron. This research project is based on synthetic innovation and meets the criterion of economy of steps to access molecular diversity. NHCs-metal complexes, and especially very challenging NHCs-Fe, will be evaluated in asymmetric catalysis. Additionally, this novel NHCs-metal family will be considered for the potential therapeutic applications of to deliver CO in the form of CORMs.[4]

To summarize, our goal for this interdisciplinary project is to synthesize new chiral objects based on NHC skeletons that will serve as a platform for different applications such as asymmetric metallo-catalysis but will also provide new drugs that will possess anti-inflammatory properties.

[1] (a) M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485.; (b) D. Janssen-Muller, C. Schlepphorst, F. Glorius, *Chem. Soc. Rev.* **2017**, *46*, 4845.
[2] W. Liu, R. Gust *Coord. Chem. Rev.* **2016**, *329*, 191.
[3] C. G. Hartinger, P. J. Dyson, *Chem. Soc. Rev.* **2009**, *38*, 391.
[4] (a) R. Motterlini, L. E. Otterbein *Nat. Rev. Drug Discov.* **2010**, *9*, 728.; (b) C. C. Romão, W. A. Blättler, J. D. Seixasab, G. J. L. Bernardes *Chem. Soc. Rev.* **2012**, *41*, 3571.