

Rational design of new multifunctional compounds including an organometallic Mn(I) centre: a comparative study with the Re(I) analogues

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Chagas disease (American Trypanosomiasis), produced by the protozoan parasite *Trypanosoma cruzi*, constitutes an overwhelming health issue in Latin America. The lack of an adequate chemotherapy makes it urgent to develop new efficient and not toxic drugs. Our group has contributed to demonstrate that the strategy of hybridization of a metal or organometallic centre and a bioactive organic ligand leads, in many cases, to antiparasitic compounds bearing improved biological properties in respect to the free ligands and affecting multiple parasite targets. In particular, we have recently developed five new multifunctional Re(I) tricarbonyls, *fac*-[Re^I(CO)₃(NN)(CTZ)](PF₆), that include two different bioactive ligands with activity against *T. cruzi*: a bidentate 1,10-phenanthroline derivative NN and the monodentate azol Clotrimazole (CTZ). The compounds have been fully physicochemically and biologically characterized¹. They were more active than the reference antitrypanosomal drug Nifurtimox, showing IC₅₀ values in the low micromolar range. Stability in solution, lipophilicity, metallomics in *T. cruzi* (uptake and association to relevant biomolecules) and effect on molecular targets of the free ligands (DNA and CYP51 lanosterol 14- α -demethylase) were studied for the complexes. Based on these results, we recently expanded our research by exploring the potentiality against *T. cruzi* of Mn(I) tricarbonyl analogous compounds and performing a comparative study of both tricarbonyl families. The Mn(I) analogues were synthesized through a stepped procedure (Figure 1) and were fully characterized. Physicochemical (stability in solution, lipophilicity) and biological properties of both families of metal(I) tricarbonyls were compared and discussed to evaluate the potentiality of the new Mn(I) compounds as antitrypanosomal agents.

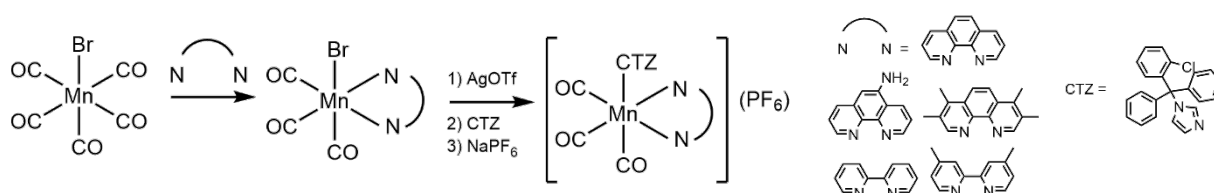


Figure 1: Synthesis scheme of $[\text{Mn}(\text{CO})_3(\text{NN})(\text{CTZ})](\text{PF}_6)$ compounds

Acknowledgments: Agencia Nacional de Investigación e Innovación (ANII, Uruguay), grants FCE_1_2019_155971 and FCE_1_2021_1_166665. CDM acknowledges ANII, grant POS_FCE_2021_1_1010807.

References

¹ M. Soba et al., *Dalton Trans.* **2023**, 52, 1623-1641.