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Convergent Synthesis of Proline-Functionalized Pyrazolopyrimidines as Anti-*T. cruzi* Bioactive Compounds

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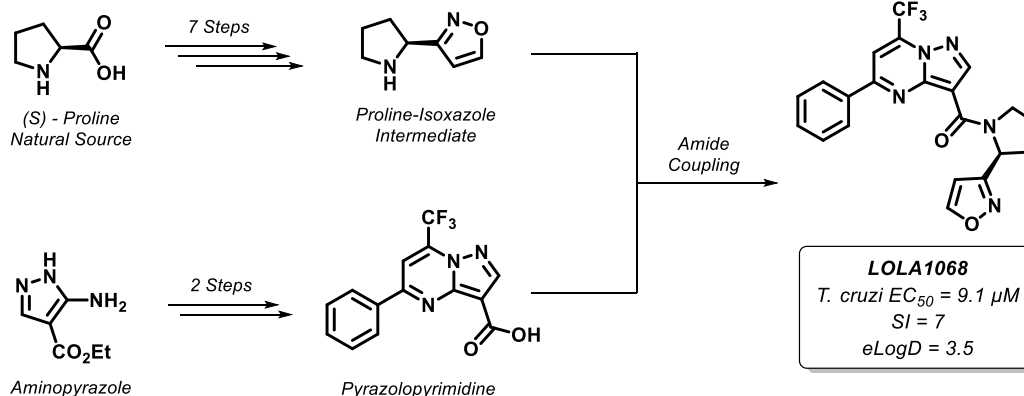
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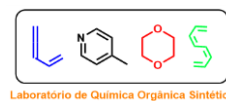
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ABSTRACT

Chagas disease is a chronic and parasitic malady, endemic to Latin-America, which affects around 7 million people worldwide. Caused by the protozoan *Trypanosoma cruzi*, this Neglected Tropical Disease (NTD) may lead to cardiac, digestive, and even neurological disorders, often associated with sudden death. Currently, only two drugs – effective exclusively in the initial stages of infection – are available for the treatment of Chagas disease, underscoring the need for new treatments. Herein, the LOLA consortium arises as a Drug Discovery project for NTDs devised by the Drugs for Neglected Diseases initiative (DNDi). This work consists of the obtention and biological evaluation of proline-functionalized pyrazolopyrimidines via convergent synthetic route starting from natural enantiopure proline and 3-amino-4-carbethoxypyrazole as a key step in the Hit Assessment phase of new anti-*T. cruzi* drugs. After 10 steps, the compound LOLA1068 was obtained in good purity, exhibiting a micromolar concentration activity against Tulahuen LacZ *T. cruzi* strains, and adequate lipophilicity.



ACKNOWLEDGEMENTS



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