Aureothin Antibiotic Analogues as New Antiparasitic Agents

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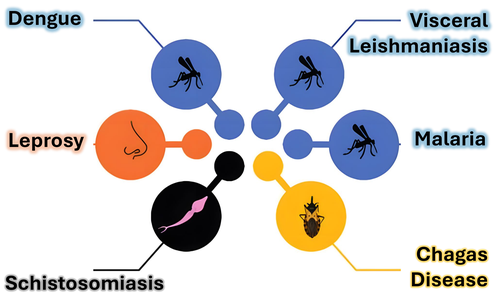
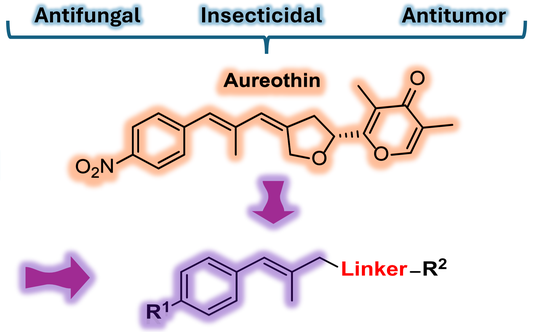
1 INTRODUCTION

Neglected diseases are a group of infectious, genetic, and nutritional conditions that disproportionately affect populations in remote areas of the world, often characterized by extreme poverty and limited access to healthcare services.



One such disease is **American trypanosomiasis**, also known as **Chagas disease**, which is caused by the parasite *Trypanosoma cruzi*. The primary mode of transmission occurs through the feces of infected triatomines.[1] However, alternative transmission routes have also been reported, including blood transfusions, organ transplantation, and vertical transmission from mother to fetus during pregnancy.

In the search for new therapeutic candidates, **Aureothin**, a polyketide antibiotic first isolated over 50 years ago from *Streptomyces thioluteus*,[2] has gained attention due to its versatile biological activities.[3]



More recently, in 2008, it was reported to exhibit antiparasitic activity against Trypanosoma brucei,[4] the causative agent of **human African trypanosomiasis (HAT).**

OBJECTIVES

Our research group has set out to synthesize various simplified analogs of Aureothin with the aim of developing new compounds as potential antiparasitic treatments for Neglected diseases mainly against Malaria and Chagas disease.

2.1 RESULTS

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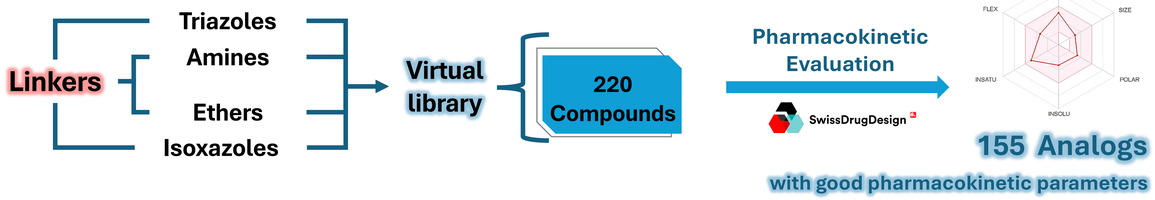
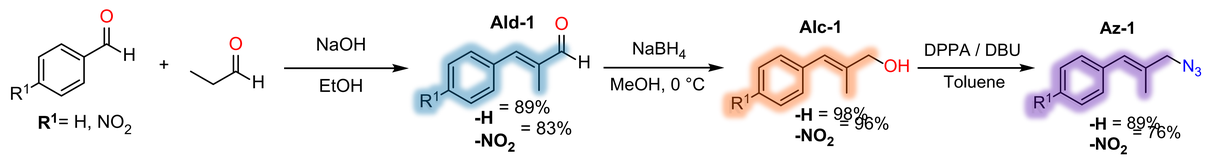


Intermediates Synthesis

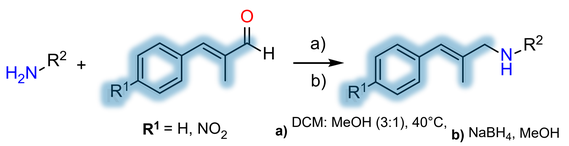


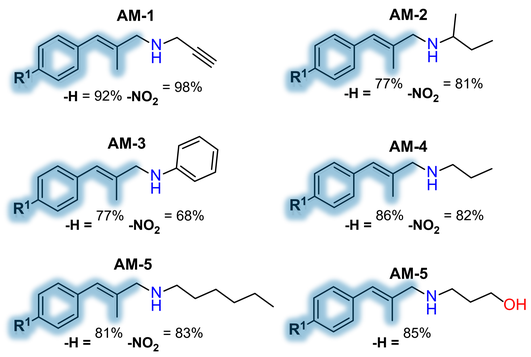
all percentages correspond to isolated yield

Once the analogs with the best pharmacokinetic properties were selected, an initial synthesis of intermediates or synthons was carried out.

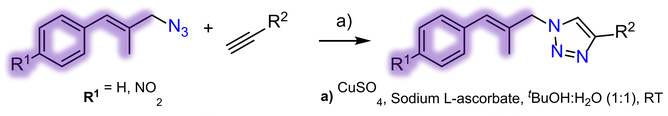
RESULTS 2.2

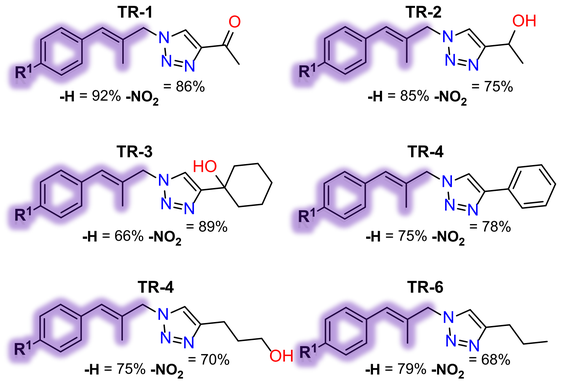
Amines Collection





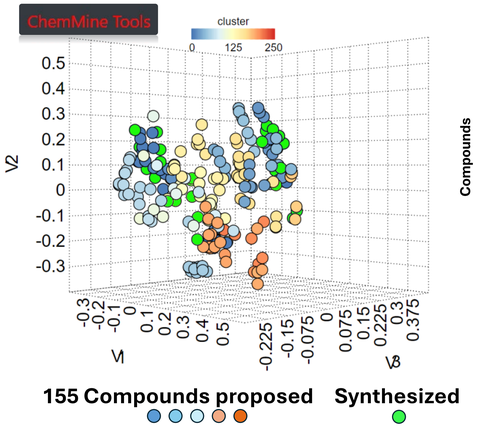
Triazoles Collection

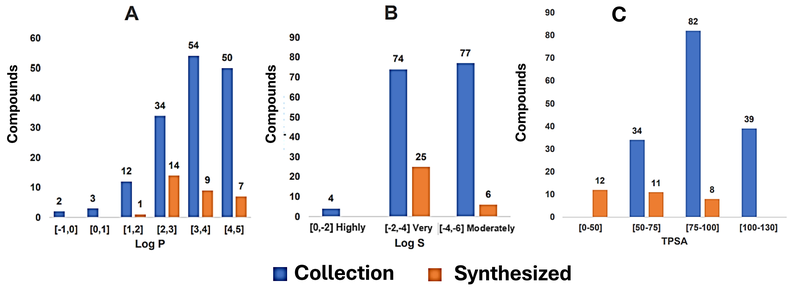




all percentages correspond to isolated yield

3D multidimensional scaling (MDS)





Currently, the collections of synthesized analogues are being tested against Malaria. We also aim to carry out biological assays against Trypanosoma cruzi soon.

CONCLUSIONS 3

We successfully obtained and characterized six key reaction intermediates essential for the synthesis of multiple proposed compound libraries. This effort resulted in the production of 12 final 1,2,3-triazole 1,4-disubstituted analogues with yields exceeding 66%, and 11 amine-type analogues with yields surpassing 77%.The spatial distribution of the synthesized analogues demonstrates excellent coverage of the chemical space, providing valuable insights into the applied substitutions and designed molecules. Additionally, the integration of computational chemistry and pharmacokinetic property screening has enabled significant reductions in experimental costs, facilitating the targeted synthesis of compounds with potential biological activity

Acknowledgments

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- Universidad Nacional de Rosario (UNR)

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