Synthesis of new heterocyclic compound, as analogue derivative of grandisin and veraguensin neolignans, with potential anti-trypanosomatid activity

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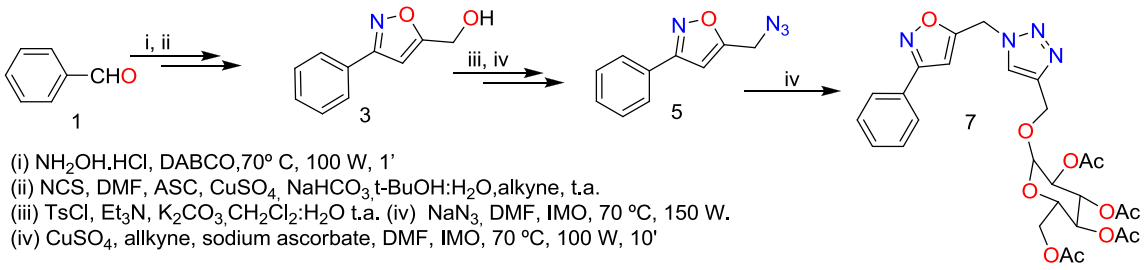
The currently available compounds for the treatment of Chagas disease (*Trypanosoma cruzi*) are not satisfactory, limited, and can have toxic side effects. There is the urgent need to develop new drugs and tools for the treatment of trypanosomatids. [1] Thus, we synthesized analogs of the anti-trypanosomatid lignans grandesin and veraguensin. The synthetic strategy involved the synthesis of the intermediate azide isoxazole, which is prepared in four steps, and it is used to make a cycloaddition reaction with an sugar alkyne, catalyze by copper (I), under heating by microwave irradiation, resulting the bisheterocyclic compound in good yield (17%). [2;3;4;5;6;7] Their antichagasic properties on trypomastigotes of *T. cruzi* and cellular toxicity activity has been evaluated. While the antichagasic effects of **7** were confirmed *in vivo*, there is currently no information on the actual drug target. Therefore, we will use publicly available virtual prediction tools to find the targets that this compound could act on in this parasite. The anti-trypanosoma targets suggested by the target fishing tools will be presented and discussed.

Figure1: Synthetic route to obtain the bisheterocyclic compound.



(i) $NH_2OH.HCl$, DABCO,70º C, 100 W, 1'
(ii) NCS, DMF, ASC, $CuSO_4$, $NaHCO_3$,t-BuOH:H_2O,alkyne, t.a.
(iii) TsCl, Et_3N, K_2CO_3,CH_2Cl_2:H_2O t.a. (iv) NaN_3, DMF, IMO, 70 ºC, 150 W.
(iv) $CuSO_4$, allkyne, sodium ascorbate, DMF, IMO, 70 ºC, 100 W, 10'

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