

Organocatalytic Mannich reaction as key step for the synthesis of a series of L-pentofuranose-mimetic iminosugars with potential anti-trypanosomal activity

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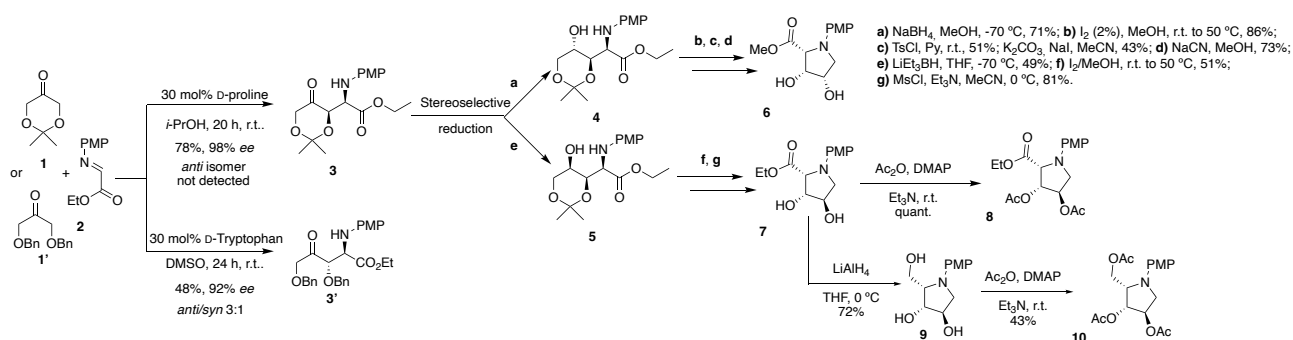
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ABSTRACT

Iminosugars are natural glycomimetics whose structural similarity to carbohydrates turns them into potential competitive inhibitors of enzymes acting on sugar substrates. Particularly, their antiparasitic activity has been studied, among others.¹ We are then focused on use of an organocatalyzed Mannich reaction as key step for the synthesis of a series of L-pentofuranose-mimetic iminosugars, with potential anti-trypanosomal activity.²



The *syn* Mannich reaction giving (2*R*,3*R*)-stereochemistry in compound **3** was performed using D-proline as catalyst, while the *anti* isomer (2*S*,3*R*, **3'**) was achieved using a primary aminoacid such as D-tryptophan as catalyst. A series of 5 L-pentofuranose-mimetic iminosugars was then prepared in a stereoselective manner from compound **3**.

As part of our search of novel antiparasitic agents, a preliminary characterization against bloodstream *T. brucei brucei* was investigated for compounds **3-10**.³ The screening was performed at 10 μM, and compound **6** showed an EC₅₀ = 3.8 μM, emerging as new head-of-series, to be optimized.

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