

# Synthesis of Triazoles with Potential Antileishmanial Activity by Click Chemistry

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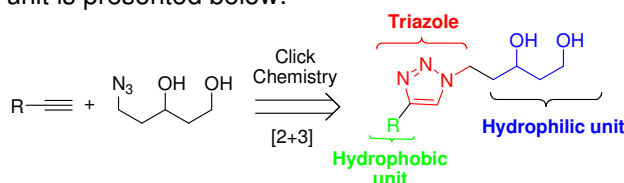
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## INTRODUCTION

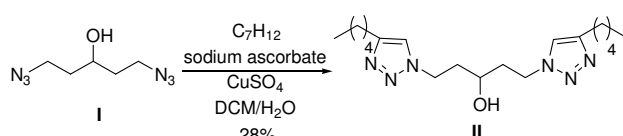
Click Chemistry is an organic synthesis procedure, which follows the principles of green chemistry, being introduced by Sharpless in 2001.<sup>1</sup> The most prominent chemical reaction using this procedure is the Cu(I)-catalyzed 1,3-dipolar azide-alkyne cycloaddition (CuAAC), leading to 1,2,3 triazoles.<sup>2</sup> From this context, our approach aims to synthesize substances with potential antileishmanial activity similar as presented by Silva,<sup>3</sup> using Click Chemistry but with innovation as the insertion of the triazole unit is presented below:



Scheme 1. General structure of bioactive triazoles.

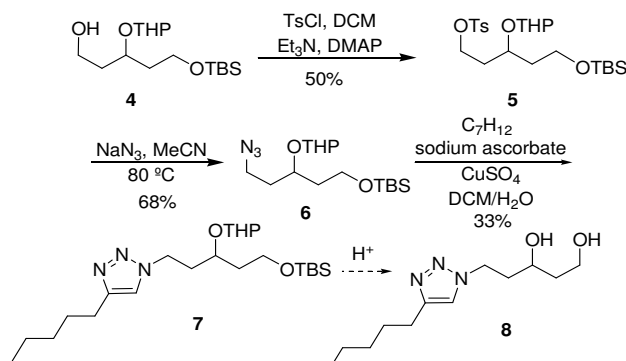
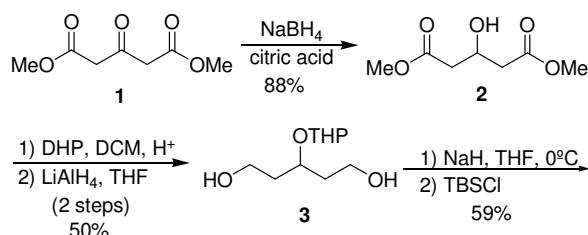
## RESULTS AND DISCUSSION

Primarily, we did a test reaction in order to ascertain the efficiency of the Click reaction with similar procedure described by Nierengarten<sup>4</sup> in 2008. The alcohol-bistriazole (II) was produced with 28% yield as a white solid.



Scheme 2. Synthesis of the alcohol-bistriazole II.

Our strategy to synthesize the alcohol-triazole is shown below:



Scheme 3. Synthetic route to hydroxyl-triazoles.

The synthesis began by chemoselective reduction of dimethyl 3-oxo-glutarate **1** using NaBH<sub>4</sub> and citric acid to afford dimethyl 3-hydroxy-glutarate **2**. The sequence of preparation required protection of secondary alcohol and reduction of esters moieties, performed with DHP on acid catalysis (PTSA) followed by treatment of crude with LiAlH<sub>4</sub> in THF, respectively. The symmetrical diol **3**, obtained in 50% for two steps, was monoprotected with TBSCl, leading to the alcohol **4**. The next stage was the hydroxyl protection with TsCl in the presence of DMAP and Et<sub>3</sub>N in DCM, leading to the formation of fully protected **5**. Azido treatment in hot acetonitrile yielded **6**. The cycloaddition of azide compound **6** with hept-1-yne in heterogeneous mixture of DCM and water with use of CuSO<sub>4</sub> as catalyst produced the alcohol-triazole **7** in 33%.

## CONCLUSION

We synthesized the alcohol-triazole **7** from dimethyl 3-oxo-glutarate in 8 steps, using Click Chemistry procedure as key step in cycloaddition between azide **6** and hept-1-yne.

## ACKNOWLEDGEMENTS

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