Title: **Bioconjugation of thiols and activated triple bonds**

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Date: January 2019

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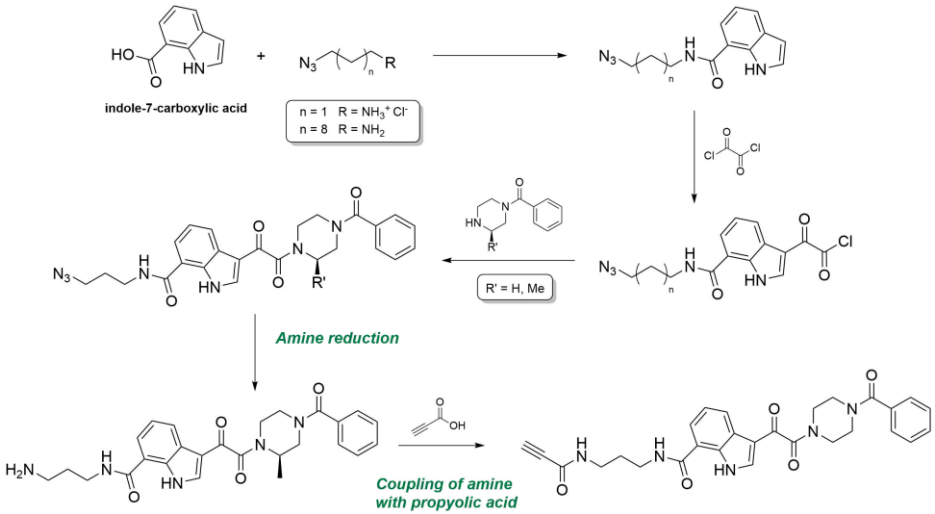
The preparation of bioconjugates provides new opportunities for the development of novel therapies and treatments for diseases such as AIDS or cancer. In this work we study a new method for the bioconjugation of aliphatic thiols with triple bonds linked to carboxamide groups.

First, the reaction of 3 different thiols or mercaptans (a protected cysteine, cysteine itself, and the reduced form of glutathione) with *N*-benzylpropynamide was examined. The reactions worked well under biologically relevant reaction conditions (37 °C, H_2O-^{t}BuOH 1:1 as the solvent). Next, an anti-HIV drug modified with a propynamide group was prepared, following the route shown below.



Scheme 1. Synthesis of BMS derivatives.

Finally, the reaction of thiols with our functionalized drug was studied, under the conditions determined before for *N*-benzylpropynamide. We could prepare and characterize the bioconjugate formed from reaction of a protected cysteine with our modified drug. However, the reactions of cysteine and reduced glutathione gave complex mixtures. All the products have been characterized by ^{1}H and ^{13}C NMR spectroscopy.

Keywords: bioconjugation, thiols, cysteines, activated alkynes, AIDS, BMS.