Synthesis of hybrids compounds by Click Chemistry and their bioactivities

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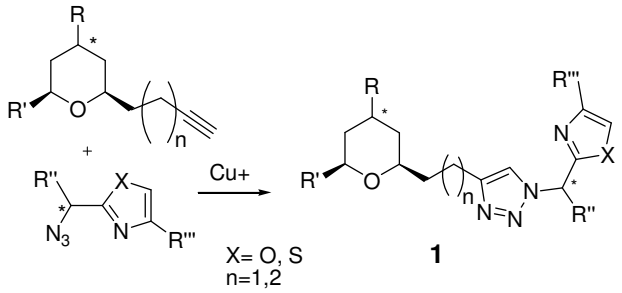
INTRODUCTION

In this work, a collection of hybrid compounds of type 1 (Scheme 1) were synthesized by a convergent route as potential anthelmintic drugs.
One fragment of the hybrids is an oxazole or thiazole prepared from a serine dipeptide.[1] The other domain, are a dihydropyran obtained by Prins's cyclization, functionally with ethynyl moiety by Corey-Fusch reaction.[2] Both heterocycles were coupled using the Huisgen´s reaction by a triazol.[3]
Cytotoxicity of hybrids were evaluated by seven cellular lines and anthelmintic activity by *Nippostrongilus brasiliensis* assay.

Scheme 1 Convergent synthesis of hybrids



RESULTS AND DISCUSSION

A collection of six hybrids and seventeen intermediates have been prepared, and their activities are being evaluated. Most of them not showed cytotoxicity against the lines assayed and only one hybrid showed a low cytotoxicity against four lines cells. Nevertheless some of the hybrids and the intermediates assayed until now against *N. brailiensis* showed an interesting activity (see table 1).

Table 1. Some of the hybrids synthesized

Comp	n, X	R	R'	R"	R"'	*N.brasiliensis* µM
2	1,O	Cl, 3,6dihydro 2H-pyran	H	CH_2Ph	CO_2CH_3	10
3	2,O	Cl, 3,6dihydro 2H-pyran	H	CH_2Ph	CO_2CH_3	**13**
4	1,O	OH	Pr	CH_2Ph	CO_2CH_3	

CONCLUSION

Through this convergent strategy and the different methodologies that were been explored, several hybrides compounds were obtained. Preliminarily anthelmintic activity was detected for some hybrids. The hybrids have a large number of groups that can be changed to modulate this activity to achieve a more potent anthelmintic.

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