Synthesis and *in vitro* antimicrobial evaluation of new thiosemicarbazones hybrid 1,2,3-triazole/morpholine.

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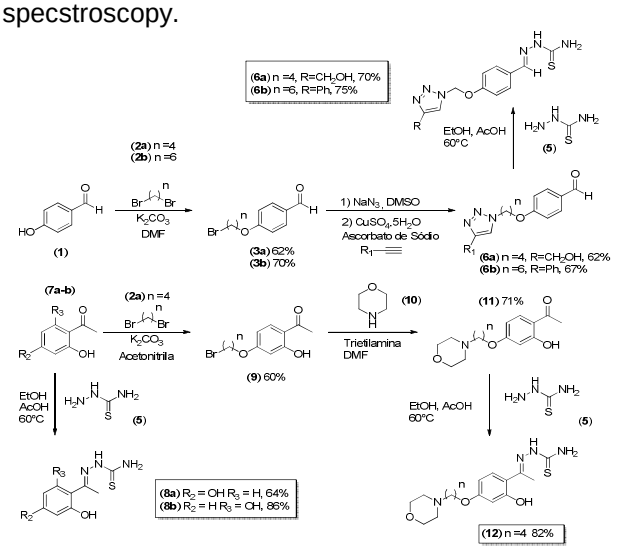
Introduction

The growing incidence of bacterial infections, together with the rise of resistance to conventionally-utilized antibiotics has added considerable urgency to the pursuit of safe and effective therapies. In this respect, the search for new compounds with effective antibacterial and antifungal activity for the control of these pathogens has become required[1]. Thiosemicarbazones, 1,2,3-triazoles and morpholines are an important class of antimicrobial compounds with easy preparation. The objective of this work was the synthesis, characterization and antimicrobial evaluation of thiosemicarbazones linked with 1,2,3-triazoles and morpholine group.

Results and Discussion

The compounds are synthesized according to the previously published procedure and their structures are presented in Scheme 1. All the compounds were characterized by NMR (^{1}H and ^{13}C) and Mass specstroscopy.



Scheme 1. Synthesis of thiosemicarbazones linked with 1,2,3-triazoles and morpholine group.

Monoalkylated aldehyde (**3**) and resacetophenone (**9**) were synthesized by selective *O*-alkylation of phenolic start materials[2]. Triazoles (**4a**) and (**4b**) were obtained from bromide (**3**) by reaction with sodium azide and followed by 1,3-dipolar cycloaddition catalyzed by Cu (I) in DMSO using propargyl alcohol or phenyl acetylene. In the next step, thiosemicarbazones (**6a**) and (**6b**) were synthesized by reaction with thiosemicarbazide in EtOH/AcOH in 70% yield. The same protocol was employed to the synthesis of thiosemicarbazones (**8a**) and (**8b**). Morpholine (**11**) was synthesized by alkylation of bromide (**9**) in 71% yield followed the reaction with thiosemicarbazide to afford compound (**12**). The antimicrobial activity of all the synthesized compounds were examined against different Gram-positive (*Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli*) and fugal strains *Candida albicans* and *Candida glabrata* organisms and only the most active (**8a**) and (**11**) were showed in table 1.

Tabela 1. MIC (µg/mL)

Compound	*Escherichia coli* ATCC 25922	*Staphylococcus epidermidis* ATCC 12228	*Candida albicans* ATCC 10231	*Candida glabrata* ATCC 2001
8a	65	260	525	1050
11	245	250	245	500
Ciprofloxacine	0,19	0,09	-	-
Cetoconazol	-	-	62,5	1,95

Conclusions

In summary, we have developed an efficient synthesis of biologically interesting thiosemicabazones linked with triazole or morpholine groups. These compounds were evaluated *in vitro* against antimicrobial organisms and two of them were active. This initial study is a promising work to the discovery of a series of compounds for further optimization aiming for more potent compounds.

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