

# Bismuth-Catalyzed Synthesis of Macrocycle Bisguanidines

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## INTRODUCTION

The bisguanidines are a class of substances characterized by the presence of two guanidine groups separated by a carbon chain, **Figure 1**. The strong basicity of bisguanidines is due to stabilization of its conjugate acid by resonance effect, which occurs in each of the guanidine groups<sup>1</sup>. The bisguanidines have a broad pharmacological potential, with antiseptic, anti-hypertensive, anti-inflammatory, anti-trypanosomiasis, antidepressant, antitumor and antiviral activities.<sup>2</sup> The presence of nitrogen atoms and the planar geometry of guanidinium group allows for bisguanidines act as ligand for different metals, an important feature for the bioinorganic chemistry,<sup>3</sup> as well as for organocatalyses.<sup>4</sup> Due to large spectrum of activity of the bisguanidines, we developed a synthetic route to synthesize macrocycle bisguanidines through the reaction of bistiourea and amines, promoted by a mixture of NaBiO<sub>3</sub>/BiI<sub>3</sub>.

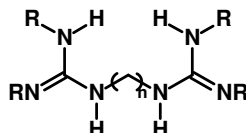


Figure 1. Bisguanidine general structure

## RESULTS AND DISCUSSION

To access the bisguanidines, we used the NaBiO<sub>3</sub> as oxidant agent and the BiI<sub>3</sub> 5 mol% as thiophile in the guanilation reaction. The reaction was performed in acetonitrile as solvent during 24 hours and reflux, Scheme 1. The Bi(III) should behave as thiophilic soft Lewis acid that coordinated to the thiourea followed by reaction with diamine and desulfurization after the Et<sub>3</sub>N to attack. It was seen that in the reaction of bistiourea with n<sub>1</sub>=2 and diamine, there was an intramolecular reaction producing the compound shown in Figure 2.

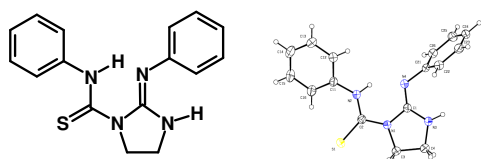
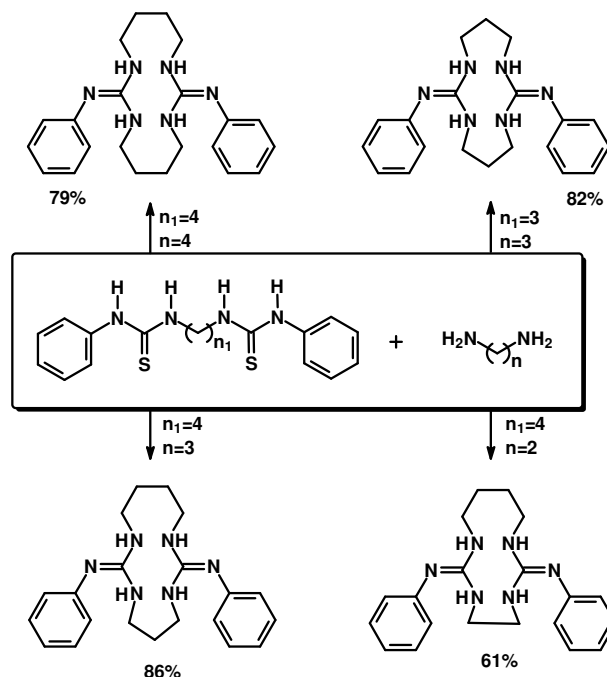


Figure 2. Product of the intramolecular reaction



Reactions Conditions: NaBiO<sub>3</sub>, BiI<sub>3</sub> (5 mol%), Et<sub>3</sub>N, CH<sub>3</sub>CN, reflux.

Scheme 1. Macrocylic Bisguanidines

## CONCLUSION

This methodology showed to be effective in the synthesis of macrocyclic bisguanidines with good yields, giving an alternative to synthesis of this class of compound.

## ACKNOWLEDGEMENTS

UFBA CNPQ CAPES

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