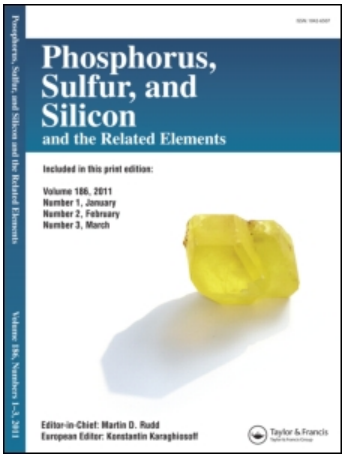

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Reactivity of Amidinium Salts' Access to Benzo[4,5]imidazo[2,1-b]Thiazoles

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We present the synthesis of benzimidazole substituted at the 1 and 2 positions. The appropriate 2-thioalkyl-substituted benzimidazoles undergo intramolecular cyclization for occuring [4,5] imidazo[2,1-b] thiazoles derivatives.

Keywords 1-thia-3-azabuta-1,3-diene; amidinium salts; anthelminthics; antiviral activity; benzimidazoles

INTRODUCTION

The various physiological actions of 2-substituted benzimidazoles have increased interest in their synthesis and chemical behavior. It is well known that a number of 1,2-substituted benzimidazoles possess some important biological properties and are potent anthelminthic and antiviral compounds.[1–3] The N-thioacylamidines **1**, which have been largely studied for their heterodienic behavior, are usually obtained by interaction between thioamides and orthoamides.[4–7]

By introducing an heteroatomic substituent linked to the thiocarbonyl function, we have replaced the phenyl group by a different thiolkyl and thiobenzyl group at the 2 position to obtain new dithiocarbamic analogs[8] **2**.

Dipole moment analysis revealed a strongly conjugated structure which can be trapped with methyliodine to provide expected amidinium salts.[9,10]

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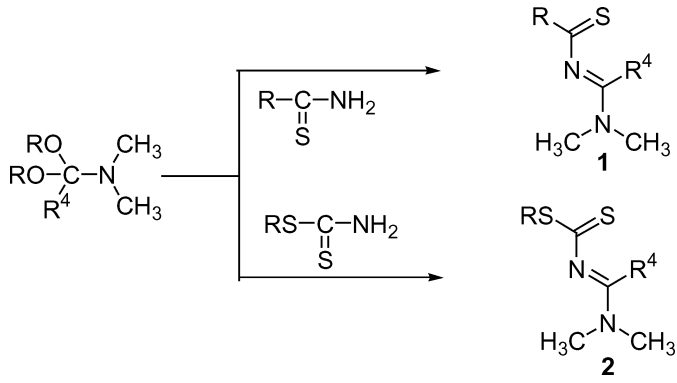


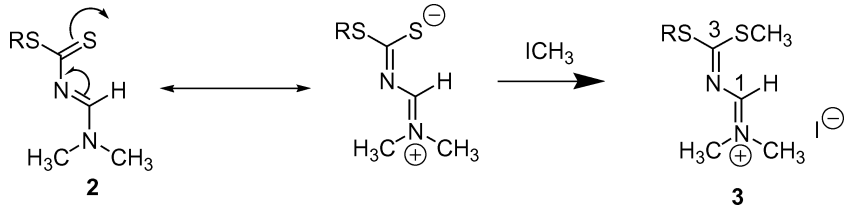
SCHEME 1

Semi-empirical calculations at the MNDO, AM1, and PM3 level suggested bis-electrophilic trends. In this work, we present some facets of the reactivity of the new amidinium salts that obtained, among others, the access to the 2-thioalkyl and thiobenzyl benzimidazoles and their intramolecular cyclization to deliver tricyclic derivatives. Moreover, we expand our research on the substitution at the 1 position to obtain N-alkylated derivatives. The substitution at the 1 and the 2 position on benzimidazoles are crucial for the versatylity of those compounds.[11,12]

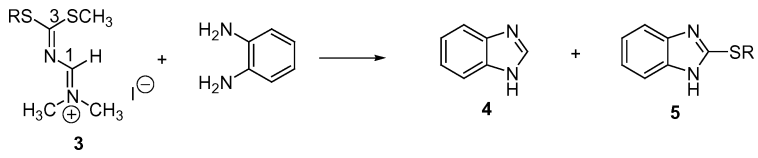
RESULTS AND DISCUSSION

The bis-electrophiles amidinium salts are prone to nucleophilic attack at C^1 and C^3; we tested their ability to react with bis-nucleophiles such as orthophenilenediamine to liberate 2-thio-substituted benzimidazole, considering the biological properties offered by these series.[13–15]

The interaction between orthophenilenediamine and amidinium salts results from a competitive process according to the reactivity of the carbons C^1 and C^3. The benzimidazole **4** would arise from a nucleophilic attack under charge control between the orthophenylenediamine and the carbon C^1.



SCHEME 2



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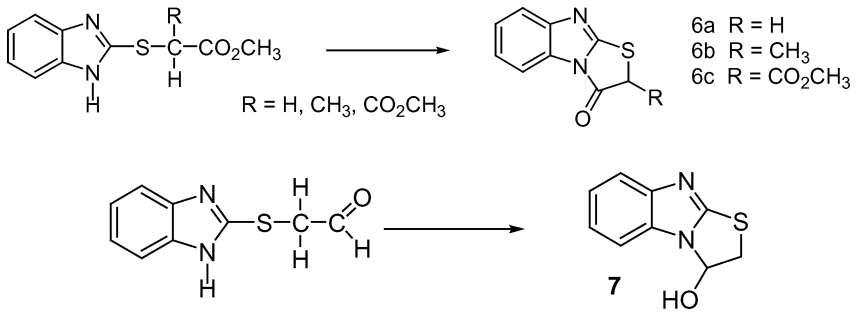
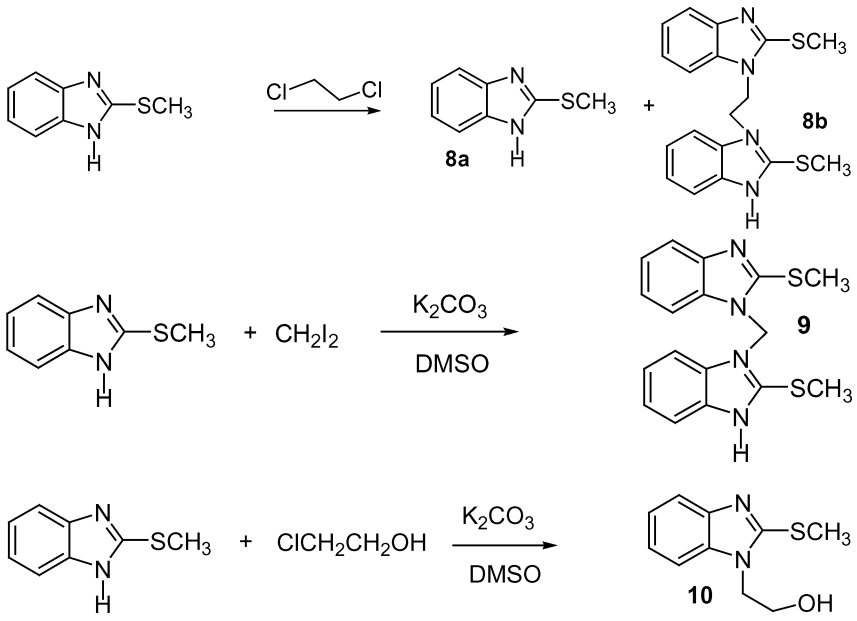


SCHEME 4



SCHEME 5

The thio-substituted derivatives **5** would result from a double nucleophilic attack on the carbon C^3 under orbital control.

The attempts to obtain each of the two compounds indicate that reaction leaded at high temperatures delivers benzimidazole, whereas the substituted compound is obtained in good yield when the reaction is produced at low tempreraturs.

A number of functionalized 2-substituted benzimidazoles have been synthesized to realize intramolecular cyclization for obtaining various benzo[4,5]imidazo[2,1-b]thiazoles.[16]

The obtained thio-substituted benzimidazoles give place to N-alkylation reactions in which we noted some dimerizations.

CONCLUSIONS

This study allowed us to make a contribution to the reactivity of amidinium salts and to explore a new access road to 2-substituted benzimidazole derivatives. These compounds are interesting intermediates for the elaboration of the mimes of new anthelmintis. Tricyclic derivatives are derived in the course of the elaboration of antiviral compounds.

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