Synthesis of Ethyl 2-(methylthio)-6-substitutedpyrimidines-4-carboxylate of Promising Biological Potential

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Keywords: Pyrimidines, Cyclocondensation Reactions*, 3-methoxyvynil-2-oxo(ethoxy)-ketones*

INTRODUCTION

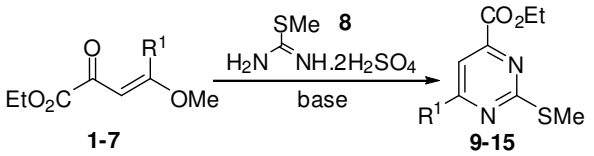
In recent years, the synthesis of many heterocycles has attracted the interest of the scientific community due to the wide applicability of these compounds in various fields of modern chemistry, and they have a huge variety and structural complexity. Among these systems stand out heterocyclic pyrimidines and their derivatives due to their biological importance and biological activities, such as antibiotics,[1] antiviral,[2] antitumor,[3] anti-inflammatory,[4] among others. This is because the pyrimidines are present in living organisms and many of them are part of nucleic acids (DNA and RNA), and therefore, are essential in protein biosynthesis. Moreover, it is observed that the bioactivity of these molecules can be changed or disabled by simply changing the position or the type of substituent in the heterocycle.

In this context, the synthesis of pyrimidines with an unprecedented variety of substituents and positions emerges as an important tool for the production of promising drugs for various diseases.

RESULTS AND DISCUSSION

Scheme 1 outlines the reaction method used for the synthesis of compounds **9-15**. The synthesis of compounds described in Scheme 1 was based on cyclocondensation reactions [3+3] of enones **1-7** with pseudothiourea **8.** The reaction was carried out by mixing the dinucleophile **8** with a base in ethanol and water and this mixture was added to enones **1-7**. Then, the reaction system was heated to reflux under vigorously stirring for 4 hours, leading to formation of compounds **9-15** in good yields (Table 1). Solvent was removed and the reaction mixture was purified by acid extraction from EtOAc, obtaining the products **9-15** with excellent purity.

Figure 1. Synthesis of compounds **9-15**.



#	1	2	3	4	5	6	7
R^1	Me	Ph	4-F-Ph	4-Br-Ph	4-MeO-Ph	4-NO_2-Ph	2-furyl

Table 1. Reaction condition used for the synthesis of compounds **9-15** and yields.

#	Ketone	Reaction condition[a]	Yield (%)[b]
9	1	*i*	48
10	2	*i*	86
11	3	*i*	80
12	4	*i*	68
13	5	*i*	74
14	6	*i*	71
15	7	*i*	90

[a]Reaction condition: $HNC(SCH_3)NH_2.2H_2SO_4$, Na_2CO_3, EtOH/H_2O (7:3), reflux, 4h. [b]Yield of isolated products.

CONCLUSION

In resume, we reported a simple and convenient synthesis of important novel pyrimidines **7-15**, which will be screened for possible antiplatelet activities.

ACKNOWLEDGEMENTS

The authors acknowledge the financial support of CNPq, CAPES and FAPERGS.

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