Microwave-assisted Synthesis of New Ethyl 2-amino-pyrimidine-4-carboxylates

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Keywords: microwave, pyrimidine, regioselectivity

INTRODUCTION

Pyrimidine are heterocyclic compounds which display a wide range of biological activities and thus have been a point of attraction in the eyes of synthetic organic chemists due to their us as potential pharmacophores.[1] As part of our growing interest in the synthesis of heterocyclic compounds and in conection with the reactivity of unsymmetrical enamino diketones in cyclocondensation reactions with different bisnucleophiles, we describe herein the synthesis of a new series of polyfunctionalized 2-amino-pyrimidines under thermal heating and microwave irradiation.

RESULTS AND DISCUSSION

Unsymmetrical enamino diketones[2] (Figure 1) are highly attractive and interesting building blocks for the preparation of new heterocyclic derivatives. These kinds of compounds show four electrophilic centers with different reactivity for nucleophilic attack.

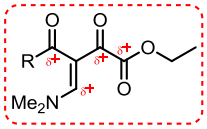
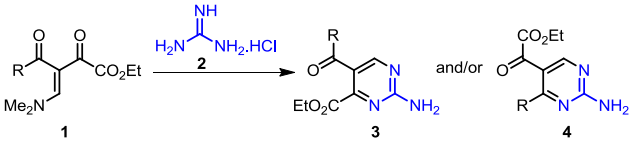


Figure 1. Electrophilic centers of enamino diketone.

The cyclocondensation reaction of unsymmetrical enamino diketones **1** with guanidine **2** was carried out in the presence of potassium carbonate in acetonitrile under reflux for 3 h, unfortunately under these conditions 2-amino-pyrimidines were obtained as a mixture of isomers **3** and **4**, in good yields (64-89 %). According Table 1, better regioselectivity was achieved when the substituents of enamino diketone were *4*-MeC_6H_4 and *4*-$MeOC_6H_4$. On the other hand, reaction of **1** (R = *4*-$NO_2C_6H_4$) did not give the expected product. In this case, it was observed that enamino diketone underwent cleavage, affording the enamino ketone in a classical retro-Claisen reaction. Microwave irradiation was used with aim to improve the regioselectivity of the 2-amino-pyrimidine. When, the reaction was performed in the presence of potassium carbonate in acetonitrile at 100 °C under microwave irradiation, the 2-amino-pyrimidine were obtained with high regioselectivity and with better yields when compared with the thermal heating (Table 1).

Table 1. Synthesis of 2-amino-pyrimidine under thermal and microwave heating.



R	Thermal Heating		Microwave Heating	
	Yield (%)	Ratio **3**:**4**	Yield (%)	Ratio **3**:**4**
Ph	64	71:29	89	100:0
4-MeC_6H_4	78	90:10	85	100:0
4-$MeOC_6H_4$	75	83:17	83	100:0
4-FC_6H_4	85	80:20	92	100:0
4-BrC_6H_4	89	60:40	92	90:10

*Conventional procedure: K_2CO_3, MeCN, 80 °C, 3 h;
Microwave procedure: K_2CO_3, MeCN, 100 °C, 10 min.

CONCLUSION

In summary, we described here an efficient microwave-assisted protocol for the synthesis of 2-amino-pyrimidines. Microwave irradiation proved to be more efficient protocol when compared to thermal heating allowing better yields, short reaction time and affording the 2-amino-pyrimidines with high regioselectivity.

ACKNOWLEDGEMENTS

UFSM, CAPES, CNPq and FAPERGS.

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