Efficient synthesis via molecular sieve of 3-(pyrimidin-2yl)-thiazolidinones

Ribeiro, C.S.[1]; Campos Jr, J.C.[1*]; Bierhals, M.P.[1]; Freitag, R.A.; Cunico, W.[1];Siqueira, G.M.[1]

[1]*Laboratório de Química Aplicada a Bioativos – LAQUIABIO, CCQFA, UFPel*

**coanjunior@gmail.com*

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INTRODUCTION

Several methods for the synthesis of thiazolidin-4-ones are described in the literature[1]. The most often used involves three components: a primary amine, a carbonyl compound and mercaptoacetic acid using azeotropic distillation with Dean-Stark trap, for the water removal, is the most common approach. Besides, other protocols were developed by using dehydrating agents among these Na_2SO_4, molecular sieves, DCC and others, with the purpose to improve the yield of the products.[2]

The aim of this study was explore the application of molecular sieves in compare with Dean-Satrk trap, as dehydrating agents in the synthesis of 3-(pyrimidin-2-yl)-thiazolidinones.

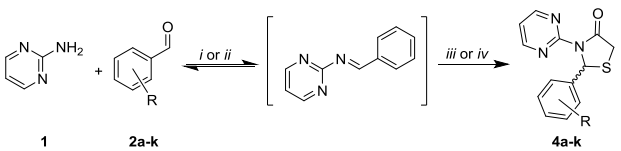
RESULTS AND DISCUSSION

In attempting to work with a less toxic solvents, some reactions with molecular sieve were tested with: ethanol, isopropanol, and tetrahydrofuran, however, toluene showed the best results. Moreover, high temperature (~80ºC) an BF_3 addition increased the efficiency of the reactions with molecular sieve, similar that reported by Gouvêa et al. under azeotropic distillation.[3]

The proposed compounds, **4a-k**, were obtained in two steps as show in **Scheme 1**. The progress of reactions was monitored by GC and TLC, and the compounds were confirmed by GC-MS and melting point determination. The novel compounds **4c**, **4e-g** and **4i** were also characterized by ^1H and ^{13}C NMR.

The synthesis using molecular sieve showed moderate yields when compared to use of azeotropic distillation **Table 1**.

Scheme 1.



I: toluene, BF_3:MeOH, reflux in Dean–Stark trap, 3 h; *ii*: toluene, BF_3:MeOH, molecular sieve, 80ºC, 3 h; *iii*: $HSCH_2COOH$ **3**, reflux in Dean–Stark trap, 16 h; *iv*: $HSCH_2COOH$ **3**, molecular sieve, 80ºC, 16 h.

Table 1. Yields of compounds **4a-k**.

Product	R	m.p.(ºC)[a]	Mol. S. Yield (%)[b]	Conv. Yield (%)[c]
4a	4-CH_3	147-150	35	53
4b	2-Cl	172-175	54	77
4c	3-F	166-168	30	45
4d	4-F	143-146	49	73
4e	3-OMe	144-147	37	60
4f	2-NO_2	174-177	56	98
4g	3-NO_2	175-178	52	76
4h	2,4-Cl	178-180	46	73
4i	2,3-OMe	131-135	52	82
4j	3,4-OMe	102-105	38	63
4k	2-Cl, 6-F	132-135	33	51

[a] Melting point are uncorrected. [b]Yields of pure compounds – Molecular sieve. [c]Yields of pure compounds – Conventional.

CONCLUSION

We report the efficient synthesis of eleven compounds of 2-(aryl)-3-(pyrimidin-2-yl)-1,3-thiazolidin-4-one using a molecular sieve that furnishes the desired products in a lower energy (~80ºC). Moreover, the procedure showed advantages like operational simplicity, moderate yields and overall lower cost.

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