Efficient multicomponent synthesis of thiazolidinones from 2-aminoethyl(propyl)morpholine

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INTRODUCTION

The small heterocyclic moieties with nitrogen, sulfur and oxygen atom has been an extensive interest in medicinal chemistry because considerable biological activities. Thiazolidinone is one of these types of molecules which exhibits important medicinal properties. These activities include antiinflammatory, antioxidant and antimicrobial.[1,2]

In the literature, methods and cleaner methodologies such as microwaves and sonochemistry are described for the synthesis of thiazolidin-4-ones.[3]

The ultrasound irradiation has generated beneficial effects in chemical processes, particularly in cases where traditional methods need prolonged reaction times. In continuation of our work [4], the aim of this paper is synthesis of five-membered heterocyclic thiazolidinones from the cyclocondensation reaction of 2-aminoethyl(propyl)morpholine, arenealdehydes and mercaptoacetic acid by conventional and sonochemistry methodologies.

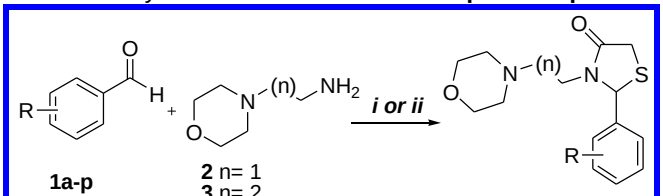
RESULTS AND DISCUSSION

First of all, we synthesized the desired heterocycles, using the conventional methodology. So, the reaction of 2-aminoethylmorpholine (**2**) or 2-aminopropylmorpholine (**3**), corresponding arenealdehyde (**1a-p**) and mercaptoacetic acid (**4**) were carried out in refluxing toluene for 16 hours (the acid was added 3 hours after beginning).

Such thiazolidinones were also obtained via ultrasound methodology. In this case, all reactants were added together in a one-step procedure. The solvent was toluene and the mixtures were sonicated for 25 minutes.

We obtained 32 thiazolidinones unpublished in the literature and the compounds were confirmed and characterized by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry.

Scheme 1. Synthesis of thiazolidinones **5a-p** and **6a-p.**



1a-p

2 n= 1
3 n= 2

5a-p n= 1
6a-p n= 2

R= **a**-2-NO_2, **b**-3-NO_2, **c**-4-NO_2, **d**-2-Cl, **e**-3-Cl, **f**-4-Cl, **g**-2-F, **h**-3-F,**i**-4-F, **j**-2-OCH_3, **k**-3-OCH_3, **l**-4-OCH_3, **m**-2-OH, **n**-3-OH **o**-4-OH, **p**-4-CH_3.

i. a) Toluene, 110ºC, 3h. b) $HSCH_2COOH$ **4**, 110ºC, 13h.

ii. $HSCH_2COOH$ **4**, toluene, ultrassonic irratiation 25 min.

The thiazolidinones were obtained by convention method with moderate to good yields for 16 hours [**5a-p** (45-97%) and **6a-p** (31-96%)]. However, by ultrasonic irradiation the reactions time was reduce to 25 minutes [**5a-p** (31-88%) and **6a-p** (33-93%)].

CONCLUSION

In summary, the sonochemistry can be used as an alternative method for conventional thermal synthetic methodology to promote the synthesis of thiazolidinones in good yields, high purities and short reaction times.

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