Ultrasonics promoted synthesis of thiazolidinones from 2-aminopyridine

Juliano Bosenbecker, Daniela P. Gouvêa, Geonir M. Siqueira, Wilson Cunico*

Núcleo de Química Aplicada (NuQuia), CCQFA, UFPel, Pelotas, RS, Brazil

wjcunico@yahoo.com.br

Keywords: thiazolidinones, 2-aminopyridine, sonochemistry

INTRODUCTION

Thiazolidinones are important five-membered heterocycles that have valuable biological activities in the medicine chemistry[1]. Our research group has been studied non-conventional methodologies for the synthesis of thiazolidinones.[2]

Ultrasound irradiation has been utilized to accelerate a number of synthetically useful reactions during the last few years[3]. In continuation of our studies, the aim of this paper is the sonocatalysis synthesis of thiazolidinones from the cyclocondensation reaction of 2-aminopyridine, arenealdehydes and mercaptoacetic acid.

RESULTS AND DISCUSSION

The conventional syntesis of thiazolidinones **5a-o** was carried out with 1:1:3 equivalents of 2-aminopyridine **2**, arenealdehyde **1a-o** and mercaptoacetic acid, respectly, for 16 h. The study of reaction conditions in ultrasound irradiation is summarized in Table 1 and the progress of reaction was monitored by GC analysis.

Table 1. Optimization of reaction medium for the synthesis of thiazolidinone **5k** under ultrasonic irradiation

Equimolar proportion amine:aldehyde:acid	Reaction time (min)	BF_3:MeOH (Drops)	GC (%)
1:1:3	25	No	46
1:1:3	5+20[a]	No	52
1:1:3	25	10	45
1:1:3	5+20[a]	10	67
1:1:3	10+25[a]	10	98
1:1:1	10+25[a]	10	94
1:2:3	10+25[a]	10	30

[a] Mercaptoacetic acid added after

So, the thiazolidinones **5a-o** were synthesized in good yields from the reaction 1 mmol of 2-aminopyridine **2**, 1 mmol of arenealdehyde **1a-o** using ultrasound irradiation for 10 minutes. After this time, the mercaptoacetic acid **4** (1 mmol) was added and the reactions were sonicated for more 25 minutes. For thiazolidinones 5a, 5b, 5c, 5e, 5g and 5h the pure product were obtained after washed with hot hexane / ethyl acetate 9:1 (3 x 10 mL). The structures were confirmed by ^1H, ^{13}C NMR and mass spectroscopy.

Scheme 1

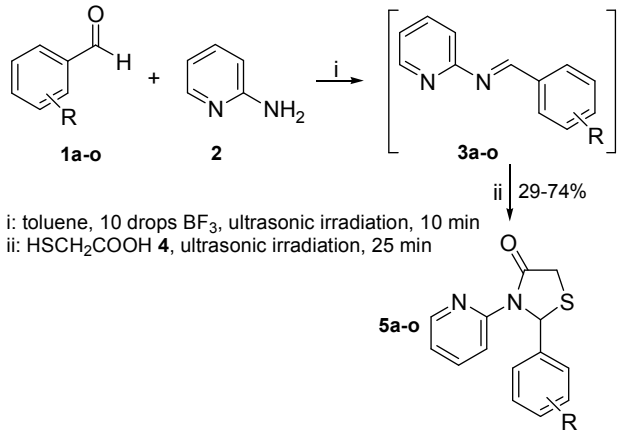

Table 2. Yields of thiazolidinones **5a-o**

Product	R	Ultrasound yield (%)	Conventional yield (%)
5a	2-NO_2	61	81
5b	3-NO_2	54	74
5c	4-NO_2	57	89
5d	2-F	59	75
5e	3-F	45	50
5f	4-F	62	59
5g	2-Cl	29	88
5h	3-Cl	30	83
5i	4-Cl	50	87
5j	2-OCH_3	55	64
5k	3-OCH_3	69	72
5l	4-OCH_3	74	64
5m	2-OH	57	59
5n	3-OH	53	50
5o	4-CH_3	73	62

CONCLUSION

The sonochemistry procedure can be used as a replacement for conventional thermal synthetic methodology, allowing rapid access to a wide range of thiazolidinones and reducing the reaction times.

ACKNOWLEDGEMENTS

The Authors thanks: UFPEL, CNPq, CAPES.

REFERENCES

[1] Jain, A.K.; Vaidya, A.; Ravichandran, V.; Kashaw, R.K.A.; Bioorg. Med. Chem. **2012**, 20, 3378.

[2] Gouvêa, D.P.; Bareño, V.D.O.; Bosenbecker, J.; Drawanz, B.B.; Neuenfeldt, P.D.; Siqueira, G.M.; Cunico, W.; *Ultrason. Sonochem.* **2012**, 19, 1127.

[3] Cravotto, G.; Cintas, P.; Chem. Soc. Ver. **2006**, 35, 180.