3,4-(methylenodioxy)aniline as precursor to thiazolidinones

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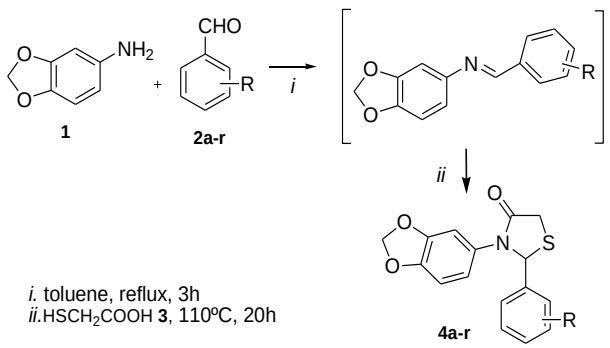
INTRODUCTION

The thiazolidinones are five-membered heterocyclic compounds that show a diverse range of biological activities[1], for example, as antitumor[2], antidiabetes[3], antitubercular[4] and anti-hepatitis C virus[5]. The main synthetic routes to thiazolidin-4-ones involves a three component reaction (an aldehyde or ketone, a primary amine or hydrazine and the mercaptoacetic acid) either in an one- or two-step process.[6] This work has as objective, report the synthesis of new thiazolidinones **4a-r** arising from the reaction of 3,4-(methylenedioxy)aniline **1** with substituted arenealdehydes **2a-r** and mercaptoacetic acid **3**.

RESULTS AND DISCUSSION

The synthesis of unpublished thiazolidinones **4a-r**, was carried out in a one-pot procedure (Scheme 1). First, the reaction of amine **1** (1 mmol) with arenealdehydes **2a-r** (1 mmol) in toluene reflux using a Dean–Stark trap for 3 h afforded the imine intermediate. Afterward, the mercaptoacetic acid **3** (3 mmol) was added and the reaction progress were monitored by thin layer chromatography (TLC) and/or Gas Chromatography (GC). The products were formed after overnight reflux and the pure thiazolidinones were obtained by washing with a hot solution of hexane/ethyl acetate 9:1 (compounds **4a-l**) and 8:2 (compounds **4m-r**) from good to excellent yields 47-90% (Table 1). All compound structures were confirmed by mass spectrometry (CG-MS), ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR)

Scheme 1. Synthesis thiazolidinones **4a-r**



i. toluene, reflux, 3h
ii. $HSCH_2COOH$ **3**, 110ºC, 20h

Table 1. Yields and melting points of thiazolidinones **4a-r.**

Product	R	yield (%)[a]	m.p. (ºC)[b]
4a	2-Cl	81	120-121
4b	3-Cl	75	131-134
4c	4-Cl	75	156-158
4d	2-F	73	120-122
4e	3-F	74	142-145
4f	4-F	76	153-155
4g	2-NO_2	76	158-163
4h	3-NO_2	85	147-150
4i	4-NO_2	90	99-101
4j	2-OCH_3	84	127-130
4k	3-OCH_3	81	118-120
4l	4-OCH_3	80	142-144
4m	3-OH	74	157-160
4n	4-OH	65	183-186
4o	2,4-OCH_3	47	oil
4p	3,4-OCH_3	74	72-75
4q	2,3-OCH_3	60	93-95
4r	2,5-OCH_3	58	oil

[a] – isolated product. [b] - melting points are uncorrected

CONCLUSION

In summary, this work showed the synthesis of eighteen new 3-(benzo[1,3]dioxol-5-yl)-2-phenylthiazolidin-4-ones from both electron-release and electron-withdraw substituted arenealdehydes. In the next step, these compounds will be submitted to biological studies.

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