

## An efficient synthesis of 4-thiazolidinones derivatives

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(Received: October 03, 2008; Accepted: November 11, 2008)

### ABSTRACT

2-(Substitutedphenyl/ 2'-furanyl / 2"-thienyl)-3-(2'-ethylthiophene)-4-thiazolidinones (IIa-e) have been synthesized by cyclocondensation of thioglycolic acid with different Schiff-bases (Ia-e), which in turn were prepared by the action of different aromatic and heterocyclic aldehydes with thiophene-2-ethylamine. Cyclocondensation of Schiff-bases (Ia-e) with thiolactic acid resulted 2-(substitutedphenyl / 2'-furanyl / 2"-thienyl)-3-(2'-ethylthiophene)-5-methyl-4-thiazolidinones (IIa-e). The structure of newly synthesized compounds have been confirmed on the basis of IR, <sup>1</sup>H NMR spectral data and physical data.

**Key words:** Schiff-bases, thioglycolic acid, thiolactic acid, 4-thiazolidinones, spectral data.

### INTRODUCTION

4 -Thiazolidinone derivatives play a vital role owing to their wide range of biological activities<sup>1,2</sup>. The chemistry of 4-thiazolidinone ring system was reviewed in depth<sup>3</sup>. Compounds containing thiazolidine ring exhibit variety of biological activities such as anti-HIV<sup>4</sup>, antitubercular<sup>5</sup>, antioxidant<sup>6</sup> and antimicrobial<sup>7,8</sup>. 4 - Thiazolidinones are synthesized either by cyclisation of acyclic compounds or by interconversion among appropriately substituted thiazolidine derivatives. Different method for the preparation of 4 - thiazolidinones have been reported<sup>9-10</sup>. In continuation of our works on 4-thiazolidinone derivatives<sup>11-13</sup>, we have undertaken the synthesis of 4-thiazolidinones of type (IIa-e) by the condensation of Schiff-bases (Ia-e) with thioglycolic acid. Cyclocondensation of Schiff-bases (Ia-e) with thiolactic yielded 4 - thiazolidinones of type (IIIa-e). All the synthesized compounds were confirmed on the basis of their spectral data and physical data.

### EXPERIMENTAL

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer 237 spectrophotometer. <sup>1</sup>H NMR spectra on a Bruker Avance DPX 400 MHz spectrometer with CDCl<sub>3</sub> and DMSO as a solvent and tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as s (singlet), d (doublet) and m (multiplet). Thin Layer Chromatography (TLC) analytical separation was conducted with Silica Gel 60 F-254 (Merck) plates of 0.25mm thickness eluted with visualized with UV (254nm) or iodine to check the purity of the synthesized compounds.

#### Preparation of 2-(4'-methoxyphenyl)-3-(2'-ethylthiophene)-4-thiazolidinones (IIa)

Thiophene-2-ethylamine (0.01 mol) and 4-methoxy benzaldehyde (0.01mol) were refluxed in toluene (80 ml) using Dean-Stark water separator resulted in Schiff-base (Ia). Then the reaction was

cooled and thioglycolic acid (0.01 mol) was added in it and further refluxed till theoretical quantity of water separated from the reaction mixture. Excess of toluene was then distilled off and the resulting viscous liquid was treated with saturated  $\text{NaHCO}_3$  solution to remove unreacted thioglycolic acid. The resulting product separated was washed with water, dried and recrystallized from alcohol to give (IIa). IR (KBr); 1694 ( $>\text{C}=\text{O}$ , thiazolidine ring), 1262 (C-O-C), 854 (C-H bend, 1,4-disubstituted), 716 (C-S-C);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ );  $\delta$  2.8 (m, 2H,  $-\text{CH}_2-\text{CH}_2$ ), 3.0 (m, 2H,  $-\text{CH}_2-\text{CH}_2$ ), 3.7 (s, 3H,  $p\text{-OCH}_3$ ), 3.8 (m, 2H,  $-\text{CH}_2-\text{CH}_2$ ), 5.2 (s, 1H,  $-\text{CH}-\text{Ar}$ ), 6.6 - 7.2 (m, 4H,  $\text{Ar-H}$  and  $-\text{CH}$  of thiophene ring).

Similarly, other compounds of these series (IIb-e) were synthesized and their physical data are given in (Table-1).

#### Preparation of 2-(4'-methoxyphenyl)-3-(2'-ethylthiophene)-5-methyl-4-thiazolidinones (IIIa)

Thiophene-2-ethylamine (0.01 mol) and 4-methoxy benzaldehyde (0.01 mol) were refluxed in toluene (80 ml) using Dean-Stark water separator resulted in Schiff-base (Ia). Then the reaction was cooled and thiolactic acid (0.01 mol) was added in it and further refluxed till theoretical quantity of water separated from the reaction mixture. Excess of toluene was then distilled off and the resulting viscous liquid was treated with saturated  $\text{NaHCO}_3$

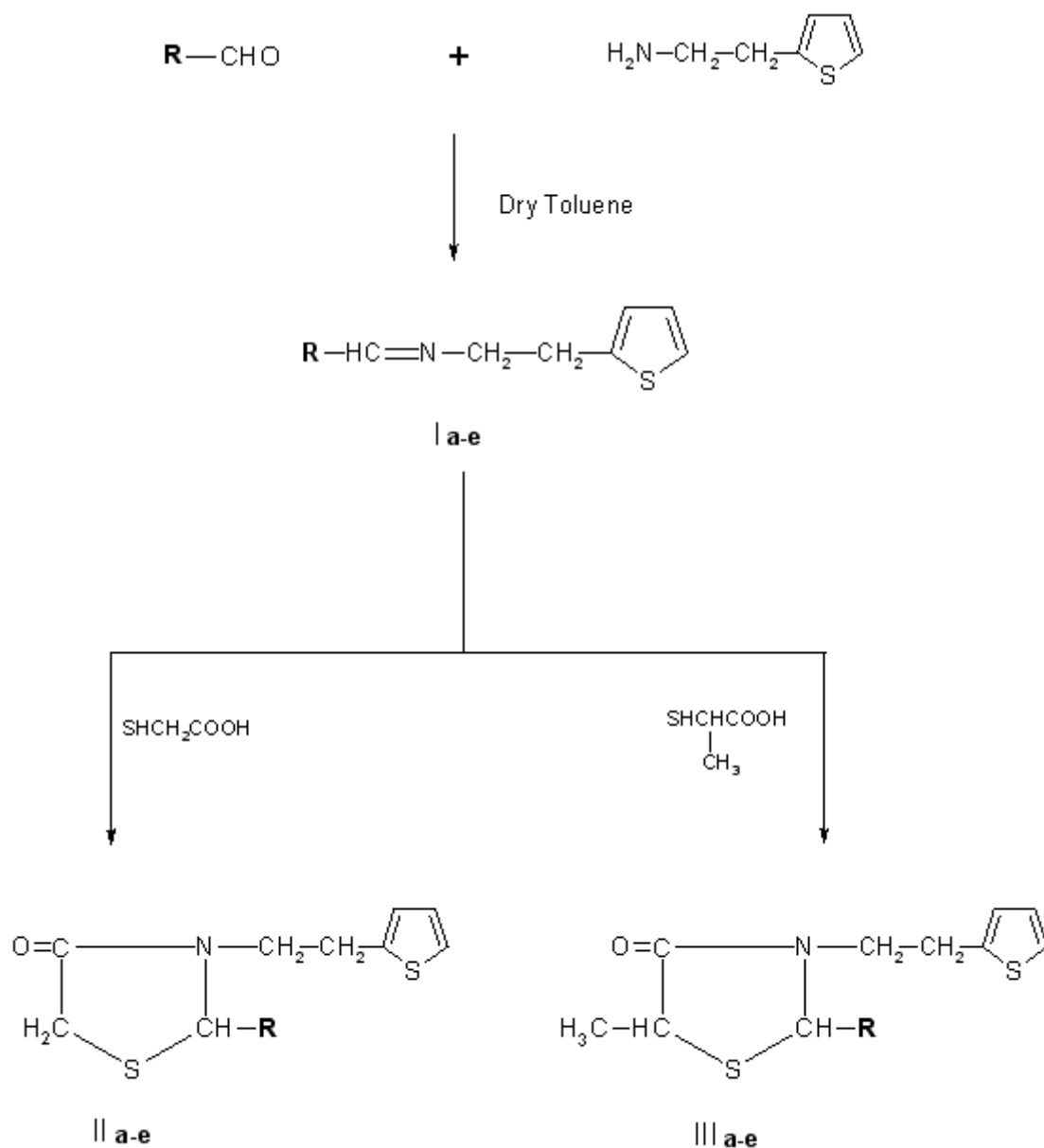
solution to remove unreacted thiolactic acid. The resulting product separated was washed with water, dried and recrystallized from alcohol to give (IIIa). IR (KBr); 2981 (C- $\text{CH}_3$ ), 1693 ( $>\text{C}=\text{O}$ , thiazolidine ring), 1262 (C-O-C), 857 (C-H bend, 1,4-disubstituted), 716 (C-S-C);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ );  $\delta$  1.5 (d, 3H,  $-\text{CH}_3-\text{CH}$ ), 2.7 (m, 2H,  $-\text{CH}_2-\text{CH}_2$ ), 3.0 (m, 2H,  $-\text{CH}_2-\text{CH}_2$ ), 3.8 (s, 3H,  $p\text{-OCH}_3$ ), 3.9 (q, 1H,  $-\text{CH}-\text{CH}_3$ ), 5.2 (s, 1H,  $-\text{CH}-\text{Ar}$ ), 6.6 - 7.2 (m, 4H,  $\text{Ar-H}$  and  $-\text{CH}$  of thiophene ring). Similarly, other compounds of these series (IIIb-e) were synthesized and their physical data are given in (Table 1).

## RESULTS AND DISCUSSION

The IR spectrum of compounds (IIa) and (IIIa) show the characteristic band near  $716\text{ cm}^{-1}$  due to  $-\text{C}-\text{S}-\text{C}$  linkage in 4-thiazolidine ring. The IR spectrum of compounds (IIa) and (IIIa) shows the characteristic band near  $1694\text{ cm}^{-1}$  which indicate the present of  $-\text{C}=\text{O}$  of 4-thiazolidinone derivatives.  $^1\text{H}$  NMR spectrum of compound (IIa) shows multiplet of  $-\text{CH}_2$  at  $\delta$  3.8. Compound (IIa) shows singlet at  $\delta$  5.2 due to ( $-\text{CH}-\text{Ar}$ ) which confirmed the cyclisation in 4-thiazolidinone derivative. The  $^1\text{H}$  NMR spectrum of compound (IIIa) shows doublet of  $-\text{CH}_3-\text{CH}$  at  $\delta$  1.5 and compound (IIa) shows singlet at  $\delta$  5.2 due to ( $-\text{CH}-\text{Ar}$ ) which confirmed the synthesis of 5-methyl-4-thiazolidinone derivative.

Table 1: Characterization data of compounds (IIa-e) and (IIIa-e)

Compd	R	M.P °C	% Yield
IIa	4-Methoxy phenyl	Limpid	69
IIb	2-Chlorophenyl	Limpid	70
IIc	3-Chloro phenyl	Limpid	68
IId	2-thienyl	90	63
IIE	2-furanyl	85	60
IIIa	4-Methoxy phenyl	Limpid	68
IIIb	2-Chloro phenyl	Limpid	65
IIIc	3-Chloro phenyl	Limpid	67
IIId	2-thienyl	Limpid	60
IIIe	2-furanyl	Limpid	61



Scheme 1

**ACKNOWLEDGEMENTS**

We are grateful to B. K. M. Science College, Valsad for providing research facilities.

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