IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A Solvent Free Approach Towards The Synthesis of Thiazolidine-4-one Over Metal Chloride Surfaces

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Abstract: A-few of thiazolidine-4-one derivatives were prepared via green route synthesis and using simple laboratory techniques and equipments. The synthesis involves new method for the synthesis of biologically/medicinally important thiazolidine-4-one compounds. In a one pot procedure carbonyl compound, amine and mercapto acetic acid were reacted together in the presence of different transition metal chlorides to furnish the desired products in good purity status under moderate yields. The protocol provides a new method for the synthesis of 4-thiazolidinones which gives fast delivery of reaction product compared to the existing synthetic methods.

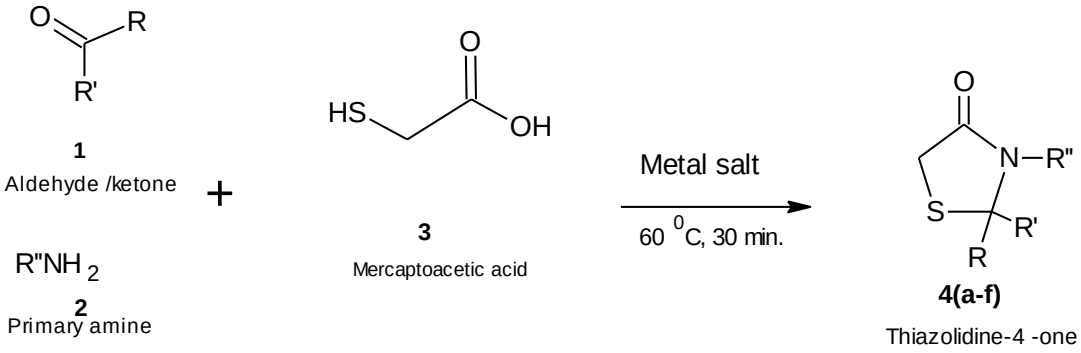
Keywords: thiazolidine-4-one, one pot synthesis, metal chloride, $FeCl_3$

Introduction

Thiazolidinones are five membered heterocyclic compounds with carbonyl group at the fourth position of the ring whereas thioether and amine groups present at first and third positions [1]. Thiazolidinones possess a wide range of pharmacological activity viz. anti-HIV[2], antiviral[3], anti-inflammatory[4], antimycobacterial[5], anticancer[5], analgesic[5], antitumor[6], antidiabetic[7], antioxidant[8], antimicrobial[9] etc. Therefore there have been several methods of the synthesis of thiazolidinones and their derivatives have been exercised in the past years.

In recent years, organic research is mainly focused on the development of green methods to synthesize various organic compounds. The role of transition metals and their compounds is already been recognized as effective catalyst[10]. The present work involves the synthesis of biologically and medicinally important

thiazolidinone molecule via a multi component one pot synthesis using basic equipment and simple techniques. The key molecule thiazolidine-4-one were synthesized from different aniline/substituted aniline, aldehyde/ketone and mercaptoacetic acid by reacting them over different metal chloride surfaces viz. Ferric chloride, Aluminum chloride, Cuprous chloride and Cobalt chloride to furnish the desired heterocyclic compound 4-thiazolidinone. All above mentioned metal chlorides have resulted in the successful generation of thiazolidinone-4-one in very less time (5-10 minute) as compared with other methods reported in the literature (3-10hr). Here the use of iron chloride and aluminum chloride gave best result for the generation of the desired heterocyclic compound thiazolidine-4-one.



Scheme 1: One pot synthesis of 4-thiazolidinone

Materials and methods:

The melting points were taken by using open capillary method. TLC were performed on silica gel G coated glass plates. ^{1}H NMR spectra was recorded on Brukar 200 MHz spectrophotometer.

General Synthetic Procedure:

To 1 g metal chloride ($FeCl_3$, $AlCl_3$, $CoCl_2$ and $CuCl_2$ taken separately in porcelain mortar) 0.5 ml (5 mmol) carbonyl compound (aldehyde or Ketone) was added and mixed with pestle. It was further added 0.6 ml (6.5 mmol) aniline and its 4-substituted derivatives and mixed followed by the addition of 0.35 ml (5 mmol) of mercapto acetic acid. The reaction mixture was mixed thoroughly. The mixture was kept in oven at 60°C for next 5 minute and then partitioned between 50 ml water and 20 ml ethyl acetate. The Ethyl acetate layer was further washed with saturated sodium bicarbonate solution (15 ml ×3 times) , water (15 ml×3 times) followed by 5% citric acid solution (15 ml ×3 times) and water (15 ml×3 times).

The ethyl acetate layer was dried over anhydrous sodium sulfate and evaporated. Furthered crystallized with chloroform-pet ether to impure the purity status i e. single spot over tlc with R_f 0.5 using 10% chloroform in benzene.

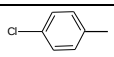
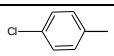
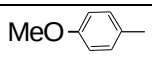
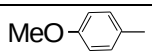
The synthesized compounds were characterized by using different analytical techniques like UV-Visible spectroscopy, IR-spectroscopy and ^{1}H-NMR spectroscopy. All the spectroscopic data indicated about the successful generation of the desired reaction product.

Table 1: Physical parameters of synthesized compounds

Compound	Mol. Formula	Mol. weight	Melting Point °C	Rf (10% $CHCl_3$ in benzene)	Elemental Analysis (calculated)		
					%C	%H	%N
4a	$C_{15}H_{13}NOS$	255.33	131-132	0.6	70.56	51.32	54.85
4b	$C_{16}H_{15}NOS$	269.36	153-154	0.61	71.34	56.13	52.00
4c	$C_{15}H_{12}ClNOS$	289.77	160-161	0.52	62.17	41.74	48.33
4d	$C_{16}H_{14}ClNOS$	303.80	165-166	0.45	63.25	46.45	46.10
4e	$C_{16}H_{15}NO_2S$	285.36	153-154	0.51	67.28	52.98	49.08
4f	$C_{17}H_{17}NO_2S$	299.38	155-156	0.53	68.20	57.23	46.78

.

Table 2: Yields of thiazolidine-4-one compounds

Compound	R	R'	R''	% Yield $FeCl_3$	% Yield $CuCl_2$	% Yield $AlCl_3$
4a	-H			68	21	59
4b	$-CH_3$			57	15	56
4c	-H			70	13	61
4d	$-CH_3$			64	17	52
4e	-H			58	25	60
4f	$-CH_3$			59	20	45

Result and Discussion:

By the present method different transition metal salts viz. $FeCl_3$, $AlCl_3$, $CoCl_2$, $CuCl_2$ are used in which

good results were obtained with the use of $AlCl_3$ and $FeCl_3$ whereas $CuCl_2$ gave poor results for the synthesis of 4-thiazolidinones whereas negative results are obtained for the use of $CoCl_2$.

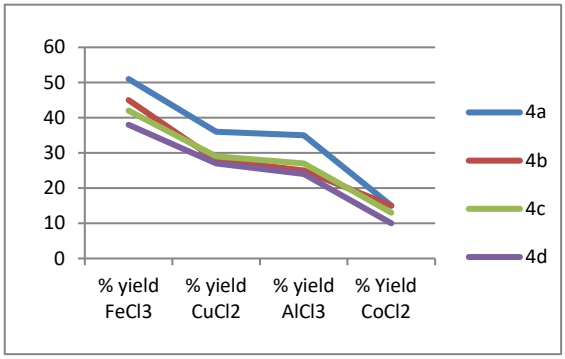


Figure 1: Presentation of relative yields of 4-thiazolidinonein over different metal chlorides

Using the above mentioned protocol a few compounds have been synthesized in moderate to good yield. The purity status of the compounds indicated about the importance of this method of synthesis over other existing method of synthesis of 4-ones. This protocol provides not only the one pot synthesis of the heterocyclic 4-ones, but also eliminates use of column chromatography for purification. Thus by exercising the present protocol the use of harmful solvents in the synthesis could be minimized because the purity status of the newly formed 4-ones is good and further purified by crystallization technique. This indicates about the increased efficacy of the synthetic technique over the already reported techniques in the literature.

Conclusion:

Present synthetic scheme provides new route for the preparation of biologically important 4-thiazolidinone derivatives by using simple chemicals and avoiding harmful solvents. The reaction completion time of the new method is less and status of purity is also good.

Acknowledgement : The author thanks Department of Engineering Sciences and Humanities (DESH) VIT, Pune for providing chemicals and equipment required for the synthesis. We also thank Central Instrumentation Facility (CIF), University of Pune for providing characterization facilities. The author thanks Govt. K. H. College Abhanpur, Raipur for their valuable support during the work.

References:

1. Mulay A, Mangesh G, Pratima N., (2009). Exploring potential of 4-thiazolidinone. International Journal of Pharmacy and Pharmaceutical Science**,** 1 **(**1): 47-64.

2. Bouzroura S, Bentarzi Y, Kaoua R, Nedjar K B, Poulain MS, Dunach E, (2010) A convenient one pot preparation of 4-thiazolodinone from enaminolactones. Org. commun., 8 (3): 8-14.

3. Navin B P, Sarvil D P, (2010) Synthesis and in vitro antimicrobial study of cshiff base and thiazolidinone of 1-cyclopropyl-6-fluoro-7-(4-(2,3-dichlorophenyl)piperazin-1-yl04-quinolone. Acta Poloniae Pharmaceutica-Drug Res. 67(1): 45-53

4. Dubey A, Srivastava SK, Srivastava SD, (2010) Synthesis of 2-substituted aryl-4-oxo-1,3-thiazolidine derivatives of indole: A new class of biologically active compound. Der Pharma chemica, 2 (5): 370-376.

5. Divyesh P, Premlata K, Navin P, (2010) Synthesis, characterization and biological evaluation of some thiazolidinone derivatives as antimicrobial agents.J. Chem. Pharm. Res., 2(5): 84-91.

6. Mosula L, Zimenkovsky B, Havrylyuk D, Vasile MA, Cornelia CI, Lesyk R, (2009) synthesis and antitumor activity of novel 2-thioxo-4-thiazolidinones with benzothiazole moieties. Farmacia., 57(3): 321-330.

7. Subudhi BB, Panda PK, Tosh BK, Sahu S, Majhi P, J. Pharm. Sci., **87**, 4, (2005).

8. P Shanmugapandiyan, KS Denshing, R Ilavarasan, N Anbalagan, R Nirmal, Int. J. Pharm. Sci. drug Res., **115**, 2 (2010).

9. GB Chandrakant, JG Naresh, Bioorg. Med. Chem., **2151**,12 (2004).