International Journal of Universal Science and Technology
ISSN: **ISSN: 2454-7263** Copyright © Universal Print
Volume No. 03, Issue No. 07, Page No. 348-351 Published: Jan. 2018
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Simple and Efficient one Pot Synthesis …

An Efficient One-Pot Synthesis of Thiazolidinone Derivatives using CAN as Catalyst

Prashant M. Kulkarni, Santosh V. Goswami, and Sudhakar R. Bhusare*

Department of Chemistry, Dnyanopasak College, Parbhani-431 401, MS, India
E-mail: bhusare71@yahoo.com

Abstract
A convenient catalyst ceric ammonium nitrate (CAN) was employed for the synthesis of thiazolidinone *via* a one-pot reaction of aromatic aldehydes, chloroacetic acid and thiourea in solvent ethanol under reflux condition. The present protocol offers some of the agreeable features such as environmentally benign, non-toxicity of reagent, easy experimental workup and excellent yields of desired products.

Keywords: One-pot synthesis, Ceric ammonium nitrate, Thiazolidinone, Chloroacetic acid, thiourea.

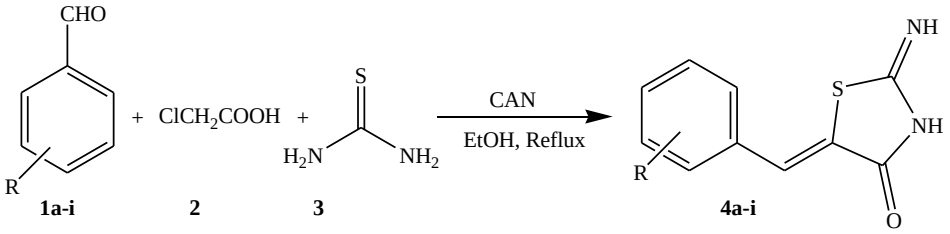
1. Introduction

4-Thiazolidinone derivatives are an important class of heterocyclic compounds known for their potential pharmaceutical applications. 4-Thiazolidinones are the structural units of biological and medicinal importance.[1] Some of the thiazolidiones are found to possess interesting biological activities, such as anticancer,[2] anti-HIV,[3] antimalarial,[4] tuberculostatic,[5] antihistaminic,[6] anticonvulsunt,[7] antibacterial[8] and antiarrythmic.[9] In view of the biological/pharmacological significance of 4-thiazolidinones considerable synthetic efforts have been made to construct this class of heterocycles.[10]

Several synthetic protocols for 4-thiazolidinones are reported in the literature. One-pot three component cyclocondensation of carbonyl compounds, amines, and mercaptoacetic acid or its derivatives has been widely used as a synthetic route for the 4-thiazolidinones. The above mentioned cyclocondensation can be either run in one-pot or in two steps with prolonged heating in toluene or benzene.[11] There are reports for accelerating the above cyclocondensation using catalysts like N,N-dicyclohexylcarbodiimide (DCC),[12] O-(benzotriazol-yl)-N,N,N,N-tetramethyluronium hexafluoro phosphate (HBTU),[13] ferrite,[14] $ZnCl_2$,[15] sodium sulfate,[16] [bmim][PF6][17] and activated fly ash.[18] However, the use of above mentioned protocols has certain limitations, such as harsh reaction conditions, prolonged heating and need of inert and dry atmosphere to accelerate the cyclocondensation.

As a continuation of our interest in the development of MCRs, here in we report first time the use of ceric ammoinium nitrate as catalyst for the synthesis of thiazolidinone derivatives by the condensation of thiourea with aromatic aldehyde and chloroacetic acid (**Scheme 1**).

International Journal of Universal Science and Technology
ISSN: **ISSN: 2454-7263** Copyright © Universal Print
Volume No. 03, Issue No. 07, Page No. 348-351 Published: Jan. 2018
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Simple and Efficient one Pot Synthesis …



Scheme 1

2. Experimental Section

All solvents were used as commercial anhydrous grade without further purification. Melting points were determined in open capillary tube and are uncorrected. ^{1}H spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ solvent and TMS as an internal standard. Mass spectra were taken on Polaris-Q Thermoscintific GC-MS.

Typical procedure for synthesis of thiazolidinone derivatives: Aromatic aldehyde (2 mmol), chloroacetic acid (2 mmol), thiourea (2 mmol) were mixed in ethyl alcohol (15 ml) and catalytic amount of ceric ammonium nitrate (20 mol %) was added and reaction mixture was refluxed for appropriate time (Table 2). After the completion of reaction indicated by thin layer chromatography (pet ether: ethylacetate; 8:2), reaction mixture was poured into crushed ice. Obtained precipitate was filtered and dried to give pure product. All of the compounds are identified from their spectral data.

5-(4-Hydroxybenzylidene)-2-iminothiazolidin-4-one (4d): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.68 (s, 1H), 6.12 (s, 1H), 6.95-7.30 (m, 4H, Ar-H), 8.90 (s, 1H), 9.12 (s, 1H); GC-MS (m/z): 221 [M+]; Anal for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72; Found: C, 54.56; H, 3.68; N, 12.76.

5-(4-Nitrobenzylidene)-2-iminothiazolidin-4-one (4i): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.87 (s, 1H), 7.10-7.38 (m, 4H, Ar-H), 8.68 (s, 1H), 9.42 (s, 1H); GC-MS (m/z): 250 [M+]; Elem. Anal for $C_{10}H_7N_3O_3S$: C, 48.19; H, 2.83; N, 16.86; Found: C, 48.15; H, 2.86; N, 16.87.

3. Results and Discussion

Here in, we report an efficient and environmentally benign protocol for the synthesis of thiazolidinone derivatives by the multicomponent condensation of aromatic aldehydes, chloroacetic acid and thiourea catalyzed by ceric ammonium nitrate in ethanol at reflux condition.

To find optimal conditions for the reaction, benzaldehyde (2 mmol), chloroacetic acid (2 mmol) and thiourea (2 mmol) was refluxed in the presence of ceric ammonium nitrate (20 mol %) employing various solvents such as water, acetonitrile, DMF, methanol and THF but these were found to be less effective. It is remarkable that the reaction is carried out in ethanol as a solvent in excellent yield (88%) (Table 1).

Table 1. Screening of the solvent on synthesis of thiazolidinones[a]

Entry	Solvent	Time(h)	Yield[b] (%)
1	H_2O	12.00	36
2	MeOH	7.00	68
3	CH_3CN	9.00	58
4	DMF	10.00	45
5	THF	10.00	40
6	EtOH	5.00	88

[a]Conditions: Benzaldehyde (2 mmol), Chloroacetic acid (2 mmol), thiourea (2 mmol), solvent (15 ml), ceric ammonium nitrate (20 mol %) at reflux condition. [b]Isolated yield.

The application of this protocol was extended to a variety of aromatic aldehydes. The reactions proceeded smoothly with different aldehydes substituted with electron-donating or electron withdrawing groups giving excellent yields (Table 2). It is observed that substituent in the aromatic ring of aldehydes shows a slight effect on the reaction

International Journal of Universal Science and Technology
ISSN: **ISSN: 2454-7263** Copyright © Universal Print
Volume No. 03, Issue No. 07, Page No. 348-351 Published: Jan. 2018
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: Simple and Efficient one Pot Synthesis …

process. Aromatic aldehydes with electron-withdrawing groups reacted faster than those with electron-donating groups.

Table 2: One-pot synthesis of thiazolidinone derivatives

Entry	R	Product	Reaction time (hrs)	M. P. (^oC)	Yield (%)[a]
1	3-NO_2	4a	4.00	113-115	87
2	3-OMe-4-OH	4b	3.30	154-156	86
3	3,4-OMe	4c	3.00	143-144	92
4	4-OH	4d	3.45	90-92	77
5	4-Cl	4e	3.30	165-167	84
6	-H	4f	5.00	172-173	88
7	4-Br	4g	4.00	189-191	89
8	3-Cl	4h	3.00	160-162	90
9	4-NO_2	4i	4.30	196-198	87
10	4-OCH_3	4j	4.00	120-122	88

[a]Isolated Yield

4. Conclusion

Our results demonstrate that ceric ammonium nitrate is very effective, environmentally friendly catalyst for the synthesis of thiazolidinone derivatives in excellent yield. The method offers several advantages such as mild reaction conditions, short reaction time, high yields, and a simple experimental operation leading to a useful and attractive process for the preparation of thiazolidinone derivatives.

5.Acknowledgement

We acknowledge Dr. S. S Kadam, Principal and Dr. B. C. Khade, Head, Department of Chemistry, Dnyanopasak College, Parbhani for providing necessary facilities for this work.

6.Reference

1. Verma, A.; Saraf, S. Eur. J. Med. Chem. **2008**, 43, 897.
2. Hongyu, Z.; Wu, S.; Zhai, S.; Liu, A.; Sun, Y.; Li, R.; Zhang, Y.; Ekins, S.; Swaan, P. W.; Fang, B.; Zhangand, B.; Yan, B. J. Med. Chem. **2008**, 51, 1242.
3. Barreca, M. L.; Balzsarini, J.; Chimirri, A.; De Clercq, E.; De Luca, L.; Höltje, H. D.; Höltje, M.; Monforte, A. M.; Monforte, P.; Pannecouque, C.; Rao, A.; Zapalla, M. J. Med. Chem. **2002**, 45, 5410.
4. Solomon, V. R.; Haq, W.; Srivastava, K.; Puri, S. K.; Katti, S. B. J. Med. Chem. **2007**, 50, 394.
5. Kucukguzel, G. C.; Shchullek, J. R.; Kaocatepe, A.; De Clercq, E.; Sahinv, F.; Gulluce, M. Eur. J. Med. Chem. **2006**, 41, 353.

6. Diurno, M. V.; Mazzoni, O.; Calignano, P. E.; Giorodano, F.; Bolognese, A. J. Med. Chem. **1992**, 35, 2910.
7. (a) Archana; Srivastava, V. K.; Kumar, A. Eur. J. Med. Chem. **2002**, 37, 873; (b) Dwivedi, C.; Gupta, S. S.; Parmar, S. S. J. Med. Chem. **1972**, 15, 553.
8. Desai, K. G.; Desai, K. R. J. Sulfur Chemistry **2006**, 27, 315.
9. Jackson, C. M.; Blass, B.; Coburn, K.; Djandjighian, L.; Fadayel, G.; Fluxe, A. J.; Hodson, S. J.; Janusz, J. M.; Murawsky, M.; Ridgeway, J. M.; White, R. E.; Wu, S. Bioorg. Med. Chem. Lett. **2007**, 17, 282.
10. Cunico, W.; Gomes, C. R. B.; Vellasco, W. T., Jr. Mini Rev. Org. Chem. **2008**, 5, 336.
11. (a) Belardi, P. G.; Simonoi, D.; Moroder, F.; Manferdini, S.; Muchhi, L.; Vecchia, F. D. J. Heterocyl. Chem. **1982**, 19, 557; (b) Holmes, C. P.; Chinn, J. P.; Look, C. G.; Gorden, E. M.; Gallop, M. A. J. Org. Chem. **1995**, 60, 7328.
12. Srivastava, T.; Haq, W.; Katti, S. B. Tetrahedron **2002**, 58, 7619.
13. Rawal, R. K.; Srivastava, T.; Haq, W.; Katti, S. B. J. Chem. Res. **2004**, 5, 368.
14. Sadashivaa, C. T.; Narendra, J. N.; Chandraa, S.; Kavithaa, C. V.; Thimmegowdab, A.; Subhashc, M. N.; Rangappaa, K. S. Eur. J. Med. Chem. **2009**, 44, 4848.
15. Srivastava, S. K.; Srivastava, S. L. J. Ind. Chem. Soc. **2002**, 77, 104.
16. Kumar, R. C.; Kumar, D. J. Ind. Chem. Soc. **2002**, 77, 492.
17. (a) Yadav, A. K.; Kumar, M.; Yadav, T.; Jain, R. Tetrahedron Lett. **2009**, 50, 5031.; (b) Zhang, X.; Li, X.; Li, D.; Qu, G.; Wang, J.; Loiseau, P. M.; Fan, X. Bioorg. Med. Chem. Lett. **2009**, 19, 6280.
18. Kanagarajana, V.; Thanusua, J.; Gopalakrishnana, M. Green Chem. Lett. Rev. **2009**, 2, 161.