Heterocyclic Letters
Vol. 7| No.4|1061-1064|Aug-Oct|2017
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

FACILE AND GREEN ONE-POT SYNTHESIS OF 2-AMINOTHIAZOLES IN GLYCEROL-WATER

Mujahed H. shaikh,[a] Devendra S. Wagare,[a] Mazahar A. farooqui,[a] Ayesha N. Durrani*[a]

*[*c]Department of chemistry, Rafiq Zakaria College for Women, Aurangabad (M.S.), India*

Abstract: A facile, highly efficient and environmentally benign one-pot protocol has been developed for the synthesis of 2-aminothiazoles by stirring of acetophenone, N-bromosuccinimide and followed by thiourea at room temperature in glycerol-water as a greener reaction medium. NBS used as Brominating agent for monobromination of differently substituted acetophenones.

Keywords: One-pot; acetophenones; glycerol-Water; 2-amino thiazoles; Sonication; Green chemistry

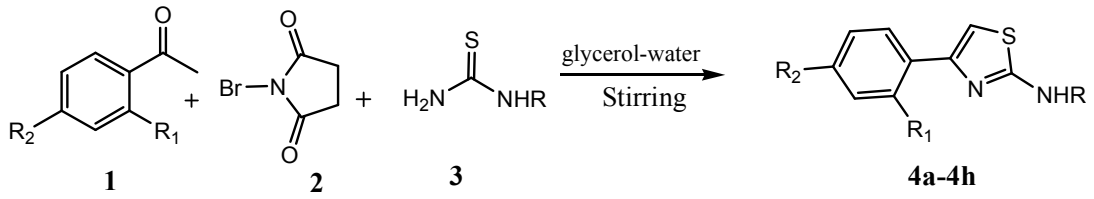
Introduction:

Glycerol known as a "organic water" since, like water, it is polar, easily available, biodegradable, cheap, non-toxic and easily form strong hydrogen-bond networks. Glycerol has a wide range of solubility for organic and inorganic compounds, including transition metal catalysts.[i] The peculiar physical and chemical properties of glycerol, such as low toxicity, non volatile solvent, easily removed from reaction matrix, high boiling point, and easily prepared from renewable feedstocks,[ii] widely use as a green medium in various organic transformation like, cross-coupling reactions[iii] include Pd-catalyzed Heck and Suzuki cross-couplings, base- and acid- promoted condensations, catalytic hydrogenation, and asymmetrical reduction.[iv] one-pot multicomponent reaction [v-vi]

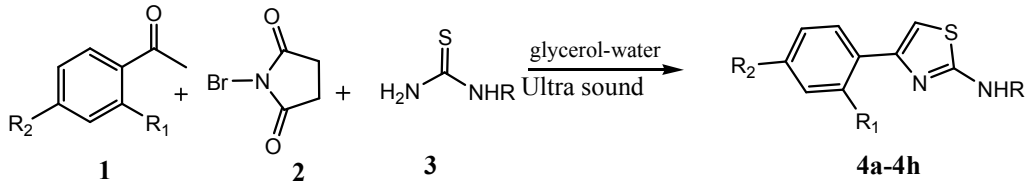
4-aryl-2-aminothiazole shows wide range of pharmacological, medicinal and biological applications like antiinflammation,[vii] antihelmintic, antihypertensive,[viii] antiHIV,[ix] and possesses immunosuppressant activity.[x] antifungal, antibiotic ,antibacterial activity.[xi]

According to Literature survey, different types of methods have been reported for the synthesis of 2-amino thiazoles from the reaction of thioureas and α-haloketones in various organic solvents at higher temperature but most of them have disadvantages like use of lachrymatric α-haloketones, severe heating condition, toxic solvents, toxic catalysts, etc. and recently, reusable reaction media and low waste route found to be significant place in organic synthesis, By considering this, we have designed green method for the one-pot synthesis of 2-aminothiazole in glycerol and water as recyclable and greener medium.

Scheme:-



One-pot synthesis of 2-aminothiazole



One-pot synthesis of 2-aminothiazole

Result and Discussion

In our continuation of study to synthesize heterocyclic compounds in greener medium like PEG, Glycerol, Water.[xii-xv] Initially we have carried out reaction of acetophenones and N-bromosuccinimides in glycerol to obtain phenacyl bromide in high yield, it was observed that Glycerol catalyzed the formation of the enolic form of acetophenones through hydrogen bonding interactions, which reacted with NBS resulted into α-bromoacetophenones followed by cyclization with thioureas to obtain 2-aminothiazoles. So we approached towards one-pot synthesis of 2-aminothiazoles from thiourea with in-situ generated α-bromoaromatic ketones by stirring in glycerol-water at room temperature (**scheme 1**) and same reaction is proceed in ultrasound (**scheme 2**), the result obtained with these reactions depicted in **table 1**. To generalised the scope of these reactions we have taken differently substituted acetophenones and treated with thioureas with both the type of reaction condition, we surprised that result obtained with high yield. (**table 1**) According to ^{1}H NMR spectra of compound **4d,** it gives **singlet, 2.46 ppm** for CH3 group **and 5.59 ppm** for 2 proton of amine group it confirmed the structure of compound **4d.**

Experimental :

Material and method :

M.P. are uncorrected taken microcontroller based melting point apparatus CL-726. NMR spectra recorded by Brucker300mHz spectrophotometer, IR Spectra recorded on Perkin Elmer, the product obtained monitor by thin layer chromatography.

General procedure for the synthesis of 4-phenyl-2-aminothiazoles[4a-4h]:- following two procedures

1) A mixture of acetophenone and N-bromonsuccinimide stirred for 4-6 hours at room temperature in glycerol and water to generate α-bromo acetophenones, and its formation monitored by thin layer chromatography. After completion of reaction thiourea was added

and stirred for 2 hours. After completion of reaction, reaction mixture was poured on crushed ice and basified with ammonium hydroxide to obtain solid, 2-amino thiazole (4a-4h).

2) A mixture of acetophenone and N-bromonsuccinimide sonicated for 1-1.20 hours in ultrasound at 80 ^{o}c temperature in glycerol and water to generate α-bromo acetophenones, and its formation monitored by thin layer chromatography. After completion of reaction thiourea was added and sonicated. After completion of reaction, reaction mixture was poured on crushed ice and basified with ammonium hydroxide to obtained solid, 2-amino thiazole (4a-4h).

Spectral data of some important compounds

4-Phenylthiazol-2-amine (4a). ^{1}HNMR: 5.12 ppm (br singlet, 2H, for NH2, D2O exchange), 6.89 ppm (s, 1H,thiazolyl proton) and 7.19–7.78 (m, 5H,for aromatic proton of benzene ring) .

4-(4-cholo-Phenyl)thiazol-2-amine (4b). 5.36 ppm (br singlet, 2H, for NH2 , D2O exchange), 6.73 (s, 1H, thiazolyl proton), 7.32 (d, 2H, J=8.63 Hz, aromatic proton of benzene ring) and 7.81 (d, 2H, J=8.58 Hz, aromatic proton of benzene ring).

4-(4-Bromo-Phenyl)thiazol-2-amine (4c): 5.24 ppm (br singlet, 2H, for NH2 , D2O exchange), 6.71 (s, 1H, thiazolyl proton), 7.45 (d, 2H, J=7.9 Hz aromatic proton of benzene ring) and 7.68 (d, 2H, J=8.1Hz, aromatic proton of benzene ring).

4-(4-methyl-Phenyl)thiazol-2-amine (4d): 2.46 ppm (s, 3H, for CH3 group), 5.59 (br singlet, 2H, for NH2, D2O exchange), 6.71(s, 1H, thiazolyl proton), 7.32 (d, 2H, d, 2H, J=7.8 Hz aromatic proton of benzene ring) and 7.59 (d, 2H, J=7.4 Hz d, aromatic proton of benzene ring).

Table 1 Evaluation of compounds [4a-4j]

Compound	R	R_1	Time		% Yield[a]		M.p (^{o}c)
			R. Temp.	ultrasound	R. Temp.	Ultrasound	
4a	H	H	6 hour.	2.00 hour.	92	95	146-148
4b	H	Cl	4.5 hour.	1.55 hour.	90	94	175-176
4c	H	Br	5 hour.	1.50 hour.	90	93	168-170
4d	H	CH_3	6 hour.	1.55 hour.	88	90	134-137
4e	H	OCH_3	5 hour.	1.50 hour.	87	90	206-209
4f	Cl	Cl	4 hour.	1.55 hour.	90	92	171-173
4g	H	F	4 hour.	1.50 hour.	92	95	102-105
4h	H	NO_2	4 hour.	1.50 hour.	90	96	287-289

Conclusion :

We have designed the new method for the synthesis of biologically important aminothiozoles by using green and recyclable glycerol and water as a solvent. The main advantage of this method is to avoid toxic organic solvents, high temperature, toxic catalyst and lachrymatric and unstable α-haloketones to obtained excellent yield.

Acknowledgement : We are thankful to principal, Dr. Rafiq Zakaria college for women for providing infrastructure facilities for this research work.

References

i. Alba E. Díaz-Álvarez, Javier Francos, Pascale Crochet and VictorioCadierno****Current Green Chemistry,*** **2014*****, 1,*** **51-65**

ii. Pagliaro, M.; Rossi, M. In The Future of Glycerol: New Usages for a Versatile Raw Material; Clark, J. H., Kraus, G. A., Eds.; RSC Green Chemistry Series: Cambridge, 2008.

iii. Loren C. Gonçalves, Gabriela F. Fiss, GelsonPerin, Diego Alves, Raquel G. Jacob, Eder J. Lenardão; Tetrahedron Letters 51 (2010) 6772–6775..

iv. AdiWolfson and Christina Dlugy; *Org. Commun*. 2:2 (2009) 34-41

v. Zheng-Jun Quan, Rong-GuoRen, Yu-Xia Da,Zhang Zhang, and Xi-Cun Wang; Synthetic Communications1, 41: 3106–3116, 2011

vi. V. RajeswarRao and P. Vijaya Kumar; Synthetic Communications, 36: 2157–2161, 2006

vii. F. Clemence, O.L. Marter, F. Delevalle, J. Benzoni, A. Joua-nen, S. Jouquey, M. Mouren, R. Deraedt, J. Med. Chem. 31 (1988)1453.

viii. W.C. Patt, H.W. Hamilton, M.D. Taylor, M.J. Ryan, D.J. Taylor Jr.,C.J.C. Connolly, A.M. Doharty, S.R. Flutchko, I. Sircar, B.A. Steinbaugh,B.L. Bately, C.A. Painchand, S.T. Rapundalo, B.M. Michniewicz, S.C.J.Olzon, J. Med. Chem. 35 (1992) 2562-2572.

ix. F.W. Bell, A.S. Cantrell, M. Hoberg, S.R. Jaskunas, N.G. Johansson,C.L. Jordon, M.D. Kinnick, P. Lind, J.M. Morin Jr., R. Noreen, B. Oberg,J.A. Palkowitz, C.A. Parrish, J. Pranc, H. Zhang, X.-X. Zhou, J. Med.Chem. 38 (1995) 4929.

x. K. Tsuji, H. Ishikawa, Biorg. Med. Chem. Lett. 4 (1944)1601.

xi. D. Lednicer, L. A. Mitscher, G. I. Georg,Organic Chemistry of Drug Synthesis, Wiley-Interscience Publication, John Wiley & Sons, Inc., New York,1990, Vol. 4, pp. 95–97.

xii. S. Giltaire, F. Herphelin, A. Frankart, M. Herin, P. Stoppie, Y. Poumay,Brit. J. of Dermatol.,2009, 160, 505-513.

xiii. D.V. Jawale et al. / Chinese Chemical Letters 21 (2010) 412–416.

xiv. Prashant D. Netankar , Syed Asif,, Shaikh Mujahed,, PathanMohd.Arif; Chemistry & Biology Interface, 2015, 5, 5, 296-300.

xv. Narsaiah et al., Org. Commun. (2011) 4:3 75-81.

xvi. Gu, Y.; Barrault, J.; Je´roˆme, F. Glycerol as an efficient promoting medium for organic reactions. Adv. Synth. Catal. 2008, 350, 2007–2012

Received on July 22, 2017.