Heterocyclic Letters
Vol. 11| No.1|53-58| Nov-Jan |2021
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

SYNTHESIS OF 4-ARYL-2-AMINOTHIAZOLE USING ONION EXTRACT:A GREEN CHEMISTRY APPROACH

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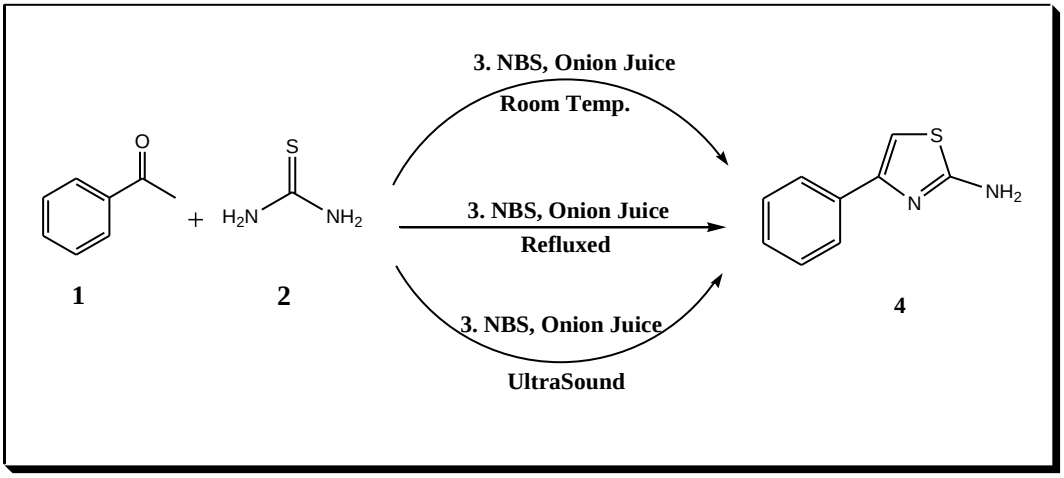
Abstract:
The development of greener synthetic strategies have attracted much attention of researchers for last 25 years. The thiazole having versatile applications in pharmaceutical, agriculture and industrial fields required easy and fruitful method. In this research paper, we have introduced the novel, green and cost effective protocol for the synthesis of most important thiazole moiety by using onion extract as efficient solvent. The synthesis has been performed by reaction between acetophenone and N-BromoSuccinamide in onion juice medium followed by addition of thiourea. The easy work up ,shorter reaction time , environmentally benign and good to excellent yield of product, are some specific features of this protocol. The results obtained are tabulated.

Keywords: Onion extract, Ultrasound, Green, Room temperature, N-bromosuccinamide.

Introduction: Thiazole is one of the most fruitful five membered nitrogen and sulphur containing Heterocycle. Although this heterocycle does not found as independent compound in nature but present in many naturally available compounds such as metabolites, alkaloids and peptides. [I] The pharmaceutical applications of this scaffold includes antihypertensive [II], anti-HIV [II-IV], anticancer [V], antifungal [VI], anti-inflammation [VII], antibacterial [VIII-X] and antibiotic [XI]. The versatile applications of thiazole and its derivatives attracted the researchers for its convenient synthesis, which resulted in introduction of several synthetic methodologies. The common method includes use of Bronsted acid or Lewis acid, inorganic salts as catalyst, PEG mediated synthesis, microwave assisted synthesis etc. [XII-XXIII] In spite of importance of these synthetic methodologies still these are suffering from limitations such as use of harsh chemicals as catalyst ,tedious work up, longer reaction time and low yield. The use of naturally available compounds such as fruit juice catalysed organic synthesis [XXIV-XXVI] and clay catalysed synthesis [XXVII] types of protocols are the need of time to implement the green chemistry protocols in organic transformations. In context to these approaches, we have selected the naturally available onion vegetable as source of efficient solvent (onion juice) for the organic transformation. The naturally available vegetable onion is used as preservative and flavour in food cooking [XXVIII]. Onion is naturally available, nontoxic, cost effective and eco-friendly

.[XXIX] The Allium Cepa species of onion is most cultivated vegetable worldwide.[30]. The vision for green chemistry protocols and inexpensive protocol for organic synthesis inspired us to select the onion juice as efficient solvent for synthesis of thiazole. In our recent work initially we have synthesised the 4–aryl,2-amino thiazole in onion juice medium at room temperature. Initially the reaction of acetophenone (1) and NBS (3) was performed in presence of onion juice which results in formation of phenacyl bromide within one hour, then thiourea (2) was added to this reaction mixture to get the desired product i.e. thiazole(4) (Scheme1) .Later on the same reaction had been performed in refluxed condition (Sceme2) and ultrasound irradiation. (Scheme3) The results obtained for these investigations has been tabulated. (Table1) The reaction optimisation has been carried out in different conditions to check the efficiency of onion juice as solvents.



Scheme 1: Onion Juice Mediated Synthesis of Thiazole

Result and Discussion

Green synthesis was very important using naturally occurring material hence we have designed and developed the method to synthesize heterocyclic compounds in one-pot and with greener medium like Onion Extraction. Here 4-Aryl-2-amino thiazole was synthesis at room temperature, in refluxed and with ultra sound wave all these three technique gives good yield but excellent yield (96-98) found in ultrasound wave with 70-75 ^{o}C.

The mixture of Acetophenone and N-bromosuccinimideswas taken in onion extract medium and reaction was initiated to produce in situ alpha-bromoacetophenones within 1 hour at room temperature. After generation of intermediate alpha-bromo ketone then thioure was added to get the 4-Aryl-2-aminothiazoles. The reaction took place at room temperature with good yield. The same reaction we have performed by reflux and under ultrasound irradiation and we have obtained surprising result by ultrasound method which indicates the completion of reaction within 30-40 minutes with yield upto 90-96 %. This typical method we have applied for the synthesis of substituted thiazole and results are tabulated. (Table1)

Experimental:

Onion Extraction

In the pressure cooker with stainless steel steamer, large glass bowl and small glass bowl were taken. The glass bowl with 100 ml water placed inside the pressure cooker, then the steamer was placed in the glass bowl, and small pieces of onion were placed which is covered by large glass bowl. After heating upto 30 minutes the exrtract of onion juice was obtained and used as solvent[28].

Material and method:

The melting point were determine with systonic digital melting point apparatus S-972 and were uncorrected. The product formation was monitor by thin layer chromatography. ^{1}H NMR spectra recorded by Brucker 400 MHz spectrometer and IR spectra with Bruker instruments.

Procedure for the synthesis of 4-Aryl-2-Aminothiazoles with stirring:-

Acetophenone (0.05mol) and N-bromonsuccinimide(0.055 mol) added in onion extract (5 ml) and was stirred up to 1.40-2.00 hour. Reaction was monitored by thin layer chromatography for formation of intermediate. Thiourea was added (0.06 **mol**) after formation of intermediate completely and again stirred for 1hour. Reaction mixture was poured on crushed ice and basified with ammonium hydroxide to obtain solid, 4-Aryl-2-amino thiazole.

Procedure for the synthesis of 4-Aryl-2-Aminothiazoles in Refluxed:-

Acetophenone (0.05 mol) and N-bromonsuccinimide (0.055 mol) added in onion extract (5 ml) and was refluxed (80-85 ^{o}C) for 30-40 minutes. The completion of reaction was monitored by thin layer chromatography. After formation of intermediate as indicated by TLC thiourea was added (0.06 **mol**) and refluxed again (80-85 ^{o}C) for 20-30 minutes. Reaction mixture was poured in crushed ice and basified with ammonium hydroxide to obtain solid, 4-Aryl-2-amino thiazole.

Procedure for the synthesis of 4-Aryl-2-Aminothiazoles inultrasound:-

The mixture of acetophenone (0.05 mol) and N-bromonsuccinimide(0.055 mol) was taken in onion extract (5 ml) and was sonicated under Ultrasounication at 70-75 ^{o}C up to 30-40 minutes. The progress of reaction was monitored by thin layer chromatography. Thiourea was added (0.06 **mol**) after formation of intermediate completely and again sonicated for 20-30 minutes at same temperature. Reaction mixture was poured in crushed ice and basified with ammonium hydroxide to obtain solid, 4-Aryl-2-amino thiazole.

Spectral data of some compounds

4-phenylthiazol-2-amine (3a).

^{1}HNMR (At 400 MHz):6.72 ppm (S, 2H, NH_2), 6.65ppm (S, 1H,thiazole proton) and 7.22–7.78 (5H, aromatic proton).

IR spectra in cm^{-1}: 3424-3306 (N-H), 3268 (C-H).

4-(4-chlorophenyl)thiazol-2-amine (3b).

^{1}HNMR (At 400 MHz):6.69 ppm (S, 2H, NH_2), 6.62 (S, 1H, thiazole proton), 7.28-7.82 (4H, aromatic proton).

IR spectra in cm^{-1}: 3420-3239 (N-H), 3204 (C-H), 721(C-Cl).

4-(4-BromoPhenyl)thiazol-2-amine (3c).

^{1}HNMR (At 400 MHz):6.71 ppm (S, 2H, NH_2), 6.64 (s, 1H, thiazole proton), 7.29-7.74 (4H, aromatic aryl proton).

IR spectra in cm^{-1}:3418-3224 (N-H), 3119 (C-H), 665 (C-Br).

Table 1 Evaluation of compounds [3a-3h]

Compounds	R1	Time in Hour			Yield %			M.P. (ºC)
		Reflux	Stirring	Ultrasound	Reflux	Stirring	Ultrasound	
3a	H	60 Minutes	3.0 Hours	35 Minutes	94	93	97	147 - 149
3b	Cl	50 Minutes	2.5 Hours	25 Minutes	95	94	98	176 - 178
3c	Br	50 Minutes	2.5 Hours	25 Minutes	95	94	98	166 - 168
3d	CH_3	60 Minutes	2.5 Hours	30 Minutes	95	94	98	135 - 137
3e	OCH_3	55Minutes	2.4 Hours	25 Minutes	95	94	98	206 - 208
3f	F	45Minutes	2.4 Hours	24 Minutes	96	95	98	101 - 103
3h	NO_2	60Minutes	3.0 Hours	35 Minutes	94	93	96	284 - 286

Conclusion:
The onion is easily available in nature and it enhances the rate of reaction to have 4-aryl-2-aminothiazole in just 2.5 to 3.0Hours at room temperature with good yield while in Ultrasounication reaction completed in minutes with excellent yield. The main advantage of this protocol is to use of onion extract, minimum time, avoid toxic organic solvents ,non-toxic catalyst,lachrymatory and unstable α-bromoketones is not separated.

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Received on December 14, 2020.