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# Tetra-*n*-butyl ammonium fluoride (TBAF) catalyzed convenient synthesis of 2-arylbenzothiazole in aqueous media

**Vishal U. Mane[a], B. R. Choudhari[b] and Dhananjay V. Mane*[a]**

[a]*Department of chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra, India-431004.*
[b]*Z. B. Patil College, Dhule (MS)- India*
**Email: dvmane11@gmail.com*
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**Abstract:** A new and efficient protocol is developed for the synthesis of benzothiazoles using TBAF as catalyst under environmentally friendly conditions. An attempt is made to develop synthetic protocol representing a novel and very simple route for the preparation of 2-substituted benzothiazole derivatives. In addition, a microwave irradiation technique is successfully implemented to carry out the reactions in short time period.

**Keywords:** Benzothiazoles, TBAF, Microwave irradiation, Greener protocol.

## Introduction

Benzothiazoles have been attracted much attention because of their wide range of biological properties, such as their anticancer [1], antimicrobial [2], anticonvulsant [3], antiviral [4], antihelmintic [5], analgesic [6], antinflammatory [7], antidiabetic [8], anti-HIV agents [9], PPAR agonists [10], H3-receptor ligands [11], nicotinic-acetylcholine-receptor ligands [12] and the structures are shown (**Figure 1)**. They also can be used as vulcanization accelerators in industry and as a dopant in light-emitting organic electroluminescent devices [13-14].

In addition, benzothiazole acts as core nucleus in various drugs due to their wide biological activities e.g. pramipexole, probenazole, lubeluzole, zopolrestat, ethoxazolamide and bentaluron etc. The high therapeutic properties of the heterocycles have been encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Benzothiazole derivatives catalyze the formation of sulfide linkages (reticulation) between unsaturated elastomeric polymers in order to obtain a flexible and elastic cross-

linked material. 2-Mercapto benzothiazole is mainly used for rubber accelerator in certain specialty products and tyre production.

Notably, among all these benzothiazole derivatives, 2-substituted benzothiazoles **(Figure**.**1)** are privileged heterocyclic systems due to their diverse biological activities and increasing applications in material fields [15]. The studies of structure activity relationship interestingly reveals that change of the structure of substituent group at C-2 position commonly results the change in its bioactivity. These structural frameworks have potent utility as imaging agents for antituberculotic [16] and antiparasitic [17]. Therefore, development of new methods for the synthesis of benzothiazoles and its analogues has drawn much attention.

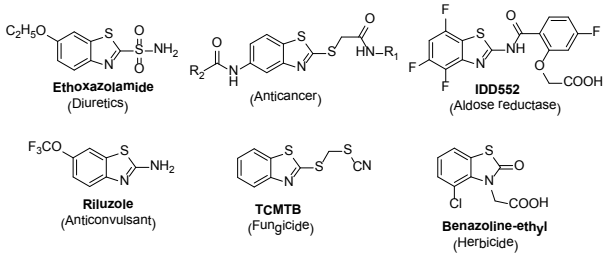



**Figure 1**. Representative compounds containing benzothiazole scaffold.

Over the past few decades, several methods have been developed for the synthesis of benzothiazole scaffolds. For instance, condensation reaction of 2-amino thiophenol with carboxylic acids [18], acid chloride [19], aldehydes [20] , nitriles [21], β-diketones [22], as well as the metal-free oxidative cyclisation /dehydrogenation of cyclohexanones and thioureas under aerobic condition [23] has been developed. The transition metal catalyzed intramolecular cyclization of 2-halo anilides [24] has also been reported. Additionally, iodine [25], p-TsOH [26] and CdSe/MMT nanocomposites [27] catalyzed benzothiazole synthesis. Nowadays, several novel approaches like metal free intramolecular cyclization of 2-halo-*N*-phenylthioacetamide [28] and visible-light driven photoredox catalytic formation of 2-substituted benzothiazoles through radical cyclization of thioanilides [29] has also been developed. Unfortunately, many of these processes endure limitations, such as extreme reaction conditions, low yields, dreary workup procedures, and co-occurrence of several side reactions. Thus, the introduction of green methods to overcome these limitations is still an important experimental challenge.

Quaternary ammonium fluorides, particularly tetra-alkyl ammonium fluorides, have been widely recognized as a convenient, organic-soluble source of naked fluoride ion. Their utility in modern organic synthesis has been well documented for a range of fluoride-assisted reactions [30], fluorination [31], deprotection of silyl groups [32] and desilylation [33] reactions. Moreover, it is evident from the literature that fluoride ions have invoked enormous interest as a green and potential catalyst [34-35] to construct carbon-carbon and carbon-heteroatom bonds in various organic transformations such as Knoevengel condensation, Michael addition and O, N, S-alkylation reactions. The potential ability of the fluoride ion to act as a base might be predicted on considering the strength of the H-F bond, solvent used for dissolution, amount of water that is present, and the counter cation. They react under essentially neutral conditions and are therefore often associated with clean reactions where side reactions are kept to a minimum [34].

Since, above heterocycles having tremendous significance in various areas, organic chemists have challenges to overwhelm them by searching a surrogate for the conventional bases which can work in water and to develop efficient methods for this nucleus using milder, non-hazardous and inexpensive reagents. Considering the properties of TBAF to act as base in aqueous medium [35]

and for exploitation of applications of TBAF in synthetic organic chemistry, efforts were directed for its use in benzothiazole synthesis. In this endeavor, it was thought worthwhile to study the task specific role of TBAF in water for the synthesis of 2-arylbenzothiazoles.

**Experimental Section:**

**2.1.1. Materials and methods**

$^1$H NMR spectra were taken on a Bruker 400 MHz DPX spectrometer with tetramethylsilane as internal standard and the chemical shifts are reported in δ ppm units. Analytical grade organic solvents such as hexane, methanol, ethyl acetate, diethyl ether etc were used for the chemical synthesis. Thin layer chromatography (TLC) was performed on pre-coated silica gel 60 $F_{254}$ aluminium sheets (E. Merck, Germany) using various solvent system and spots were identified by UV light.

**2.2. *General procedure for the synthesis 2-substituted benzothiazoles (*3a-r)**

**2.2.1. *Conventional method*:** *o*-Aminothiophenol **1** (1 mmol), aromatic aldehydes **2 a-r** (1 mmol) and TBAF (10 mol %) in water were added into a 50 mL round bottom flask and heated at 80 °C for the period of time as indicated in **Table 5**. The progress of the reaction were monitored by TLC. After completion of the reaction, the reaction mixture was poured into the ice cold water. The solid were filtered off and washed with water, dried and purified by crystallization from ethanol.

**2.2.2. *Microwave method*:** *o*-Aminothiophenol **1** (1.0 mmol), aromatic aldehydes **2a-r** (1.0 mmol), and TBAF (10 mol %) in water irradiated at 40 °C for the period of time as indicated in **Table 5**. The progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was poured onto crushed ice; the precipitate was filtered off and washed with water, dried and purified by crystallization from ethanol.

***2.2.3. 2-Phenylbenzothiazole [3a]***

The product was obtained as yellow needles (Yield = 95%); m.p. 115-117$^0$C (lit. m.p. 115-116 $^0$C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.03-8.16 (m, 3H), 7.91 (d, *J* = 8 Hz, 1H), 7.46-7.60 (m, 4H), 7.34-7.44 (m, 1H); ESI-MS (MeOH): m/z: 212 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{13}H_9NS+H]^+$: 212.0534 $[M+H]^+$; found: 212.0542.

***2.2.4. 2-(2-Chlorophenyl)-benzothiazole [3c]***
The product was obtained as an orange solid (Yield = 92%); mp 78-80$^o$C (lit. m.p. 76-78 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.18-8.29 (m, 1H), 8.14 (d, *J* = 8.16 Hz, 1H), 7.96 (d, *J* = 7.91 Hz, 1H), 7.49-7.59 (m, 2H), 7.37-7.48 (m, 3H); ESI-MS (MeOH): m/z: 246 $[M+H]^+$, 248 $[M+2+H]^+$; HRMS (ESI): m/z calculated for $[C_{13}H_8NSCl+H]^+$: 246.0144 $[M+H]^+$; found: 246.0148.

***2.2.5. 2-o-Tolyl-benzothiazole [3f]***

The product was obtained as yellow needles (Yield = 90%); mp 58-60$^o$C (lit. m.p. 52-54 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.06 (d, *J* = 8.03 Hz, 1H), 7.96-8.02 (m, *J* = 8.03 Hz, 2H), 7.90 (d, *J* = 8.03 Hz, 1H), 7.49 (t, *J* = 7.28 Hz, 1H), 7.37 (t, *J* = 7.28 Hz, 1H), 7.28-7.33 (m, *J* = 7.91 Hz, 2H), 2.43 (s, 3H); ESI-MS (MeOH): m/z: 226 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{14}H_{11}NS+H]^+$: 226.0690 $[M+H]^+$; found: 226.0695.

***2.2.6. 2-(4-Fluorophenyl)-benzothiazole [3g]***
The product was obtained as orange needles (Yield = 92%); mp 100-102$^o$C (lit. m.p. 98-100°C); ESI-MS (MeOH): m/z: 230 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{13}H_8FNS+H]^+$: 230.0440 $[M+H]^+$; found:

230.0444.

### *2.2.7. 2-(3-Bromophenyl)-benzothiazole [3h]*

The product was obtained as red needles (Yield = 90%); mp 88-90°C (lit. m.p. 84-86 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.28 (s, 1H), 8.08 (d, *J* = 8.16 Hz, 1H), 7.99 (d, *J* = 7.78 Hz, 1H), 7.92 (d, *J* = 8.03 Hz, 1H), 7.62 (d, *J* = 8.03 Hz, 1H), 7.51 (t, *J* = 7.72 Hz, 1H), 7.33-7.44 (m, 2H); ESI-MS (MeOH): m/z: 290 $[M+H]^+$, 292 $[M+2+H]^+$; HRMS (ESI): m/z calculated for $[C_{13}H_8NSBr+H]^+$: 289.9639$[M+H]^+$; found: 289.9645.

### *2.2.8. 2-Benzothiazol-2-yl-6-methoxy-phenol [3j]*

The product was obtained as a white solid (Yield = 95%); mp 108-110°C; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 12.73 (br. s., 1H), 8.01 (d, *J* = 8.16 Hz, 1H), 7.90 (d, *J* = 8.03 Hz, 1H), 7.51 (t, *J* = 7.65 Hz, 1H), 7.41 (t, *J* = 7.59 Hz, 1H), 7.32 (d, *J* = 7.91 Hz, 1H), 6.99 (d, *J* = 7.91 Hz, 1H), 6.90 (t, *J* = 7.91 Hz, 1H), 3.96 (s, 3H); ESI-MS (MeOH): m/z: 258 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{14}H_{11}NO_2S+H]^+$: 258.0589 $[M+H]^+$; found: 258.0585.

### *2.2.9. 2-Benzothiazol-2-yl-phenol [3n]*

The product was obtained as yellow needles (Yield = 95%); mp 130-132°C (lit. m.p. 127-128 °C); $^1$H NMR (400 MHz, $CDCl_3$) δ ppm 12.51 (s, 1H), 7.99 (d, *J* = 7.91 Hz, 1H), 7.88-7.92 (m, 1H), 7.69 (dd, *J* = 1.44, 7.84 Hz, 1H), 7.46-7.54 (m, 1H), 7.35 - 7.44 (m, 2H), 7.11 (dd, *J* = 0.82, 8.34 Hz, 1H), 6.92-6.99 (m, 1H); ESI-MS (MeOH): m/z: 228 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{13}H_9NOS+H]^+$: 228.0483 $[M+H]^+$; found: 228.0487.

### *2.2.10. 2-Furan-2-yl-benzothiazole [3p]*

The product was obtained as a yellowish orange needles (Yield = 90%); mp 100-102°C (lit. m.p. 103-104 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.05 (d, *J* = 8.16 Hz, 1H), 7.89 (d, *J* = 7.91 Hz, 1H), 7.61 (s, 1H), 7.48 (d, *J* = 7.40 Hz, 1H), 7.39 (d, *J* = 7.65 Hz, 1H), 7.20 (d, *J* = 3.39 Hz, 1H), 6.54-6.64 (m, 1H); ESI-MS (MeOH): m/z: 202 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{11}H_7NOS+H]^+$: 202.0327$[M+H]^+$; found: 202.0329.

### *2.2.11. 2-Thiophen-2-yl-benzothiazole [3q]*

The product was obtained as a red solid (Yield = 95%); mp 100-102°C (lit. m.p. 98-102 °C); $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (d, *J* = 8.28 Hz, 1H), 7.85 (d, *J* = 7.91 Hz, 1H), 7.62-7.70 (m, 1H), 7.43-7.53 (m, 2H), 7.34-7.40 (m, 1H), 7.14 (dd, *J* = 3.76, 4.89 Hz, 1H). ESI-MS (MeOH): m/z: 218 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{11}H_7NS_2+H]^+$: 218.0098 $[M+H]^+$; found: 218.0094.

### *2.2.12. 2-(1H-Indole-2-yl)-benzothiazole [3r]*

The product was obtained as a yellow solid (Yield = 88%); mp 146-148°C (lit. m.p. 144-146 °C) $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 8.58 (s, 1H), 8.46 (d, *J* = 6.53 Hz, 1H), 8.05 (d, *J* = 7.91 Hz, 1H), 7.99 (d, *J* = 2.76 Hz, 1H), 7.89 (d, *J* = 7.78 Hz, 1H), 7.43 - 7.52 (m, 2H), 7.29-7.38 (m, 3H); ESI-MS (MeOH): m/z: 251 $[M+H]^+$; HRMS (ESI): m/z calculated for $[C_{15}H_{10}N_2S+H]^+$: 251.0643 $[M+H]^+$; found: 251.0647.

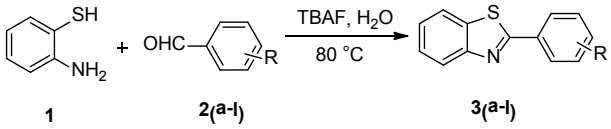
## Results and discussion:

### Chemistry :

An efficient and greener protocol for the synthesis of 2-arylbenzothiazoles (**3a-l**) using tetra-*n*-butyl ammonium fluoride (TBAF) in water is established. Comparative study for the synthesis of 2-arylbenzothiazoles using conventional as well as microwave method is discussed (**Scheme 1**). Remarkable advantages

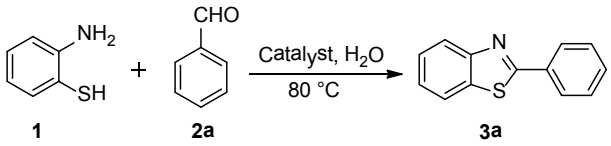
of the present synthetic strategy over the others are shorter reaction times, higher isolated yields, reuse of catalytic system and simple work-up procedure.

**Present Work :**




**Scheme 1**. TBAF catalyzed synthesis of 2-arylbenozthiazoles

In order to find the best experimental conditions, on preliminary basis, the condensation reaction of 2-aminobenzenethiol (**1**) and benzaldehyde (**2a**) at 80 ºC was considered as a standard model reaction for optimizing the reaction conditions (**Scheme 2**).




**Scheme 2**. Standard model reaction

Keeping in view the significance of above discussed aspects and in the context of green chemistry, it has been decided to prefer water as a solvent in our initial study for optimizing catalyst. For establishing the effectiveness of the catalysts, reaction was carried out using different fluorides as well as their halide analogs such as chloride and bromide. Fluoride ion was found to be more active among the used halides (**Table 1**, entries 4-6). The reactions carried out in the presence of tetra-*n*-butyl ammonium chloride (TBACl) and tetra-*n*-butyl ammonium bromide (TBAB) were sluggish and incomplete even after 5 h with 40 and 42 % yields respectively. KF and CsF afforded the desired products in 76 % and 85 % yields respectively, whereas in the presence of tetra-*n*-butyl ammonium fluoride (TBAF) the product was obtained in excellent yield (94 %). (**Table 1**, entry 6) and therefore, it was chosen as a catalyst of choice for further optimization studies.

**Table 1**. Screening of catalyst [a]

| Entry | Catalyst | Catalyst (mol%) | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| 1 | No catalyst | - | 5 | - |
| 2 | TBACl | 10 | 5 | 40 |
| 3 | TBAB | 10 | 5 | 42 |
| 4 | KF | 10 | 2 | 76 |
| 5 | CsF | 10 | 2 | 85 |
| 6 | **TBAF** | **10** | **1** | **94** |

[a]Reaction conditions: *o*-Aminothiophenol **1** (1 mmol) and benzaldehyde **2a** (1 mmol), catalyst (10 mol%), in water at reflux temperature; [b]Isolated yield.

Temperature of 80 ºC was intentionally chosen as most of the fluorides are thermally unstable [8] above 80 $^0$C. For evaluation of temperature effect, this reaction was performed at room temperature, 60 $^0$C, 80 $^0$C and reflux conditions (**Table 2**, entries 5-8). Reaction at room temperature and 60 $^0$C afforded product in good yields but it takes longer reaction period for completion, while at reflux condition the product was obtained in lower yield, since catalyst becomes unstable above 80 $^0$C. At 80$^0$C, reaction proceeds smoothly towards completion in excellent yield (94 %).

After finalizing the catalyst (TBAF) for this reaction, the next target was to choose suitable solvent, because of the variable basicity and solubility shown by ionic fluorides as well as the possibility of solvent participation in subsequent reactions. Various solvents like DMF, THF, acetonitrile, ethanol, methanol and toluene (**Table 2**, entries 6-11) have been tested and compared their results with water mediated reaction. Prior to using solvents, reaction was examined under neat conditions, but reaction failed to afford more than 55% yield in 1 hour.

**Table 2**. Screening of solvents at different temperatures [a]

| Entry | Catalyst | Solvent | Temp (°C) | Time | Yield[b] (%) |
|---|---|---|---|---|---|
| 1 | TBAF | Water | RT | 10 h | 87 |
| 2 | TBAF | Water | 60 | 5 h | 90 |
| 3 | TBAF | Water | 80 | 1 h | 94 |
| 4 | TBAF | Water | Reflux | 2 h | 78 |
| 5 | TBAF | - | 80 | 2 h | 55 |
| 6 | TBAF | DMF | 80 | 2 h | Trace |
| 7 | TBAF | THF | Reflux | 2 h | 30 |
| 8 | TBAF | MeCN | 80 | 2 h | 42 |
| 9 | TBAF | Ethanol | Reflux | 2 h | 63 |
| 10 | TBAF | Methanol | Reflux | 2 h | 65 |
| 11 | TBAF | Toluene | 80 | 2 h | 80 |

[a]Reaction conditions: **1** (1 mmol), **2a** (1 mmol) and Catalyst (10 mol %), in solvent (5 mL); [b]Isolated yields.

Subsequent reaction were carried out in the DMF, THF and acetonitrile, but afforded lower yields. Ethanol and methanol as a solvent were found to be compatible with the reaction conditions with moderate yields. Reaction in toluene proceeded smoothly in agreement with water. But its tedious work up procedure, toxicity and hazardous nature confined its use for this reaction.

We were pleased to find that among the conditions screened, the corresponding 2-arylbenzothiazole was obtained quantitatively with TBAF at $80^0$C in water. It is known that TBAF in water produces an equilibrium in which tetra-*n*-butyl ammonium hydroxide (TBAH) and $HF_2^-$ are present [34c], so one may speculate the possibility of catalysis of this reaction by TBAH. But, this possibility has been ruled out considering the following points: i) KF and CsF affords the products in good yields (76% and 84% respectively) and reaction in toluene also proceeds smoothly confirming the assistance of fluoride ion to catalyze the reaction, where chances of TBAH formation in reaction mixture are eliminated.

ii) Even it has been studied and proved that equilibrium generated due to addition of water to TBAF shifts towards the side of TBAF and not TBAH due to presence of $HF_2^-$[34c];

iii) Literature reveals that TBAF does not react with water in the presence of organic substrates, since organic molecules act as more powerful H-bond e-acceptors than water [35]. This dramatic influence of water over the other solvents could be attributed to H-bonding which must have played important role in the basic behavior of fluoride anion. In the presence of powerful H-bond e-acceptors (organic substrates), fluoride ion bonds with them and enhance their nucleophilicity, due to H-bonding between fluoride ion and organic molecule resulting in transfer of electron density from the anion to organic substrate. Water is only able to solvate and mask fluoride ion if more powerful H-bond e-acceptor than itself is absent. Increase in the thiols reactivity seems reasonable to assume the importance of H-bonding base like reactions of the anion [35]. One more aspect that could be helpful for bringing the reaction in favor of water is hydrophobic interactions which induce favorable aggregation of organic substrates in water.

In a simplified way, to understand the role of TBAF it should be noted that in water TBAF get dissociated to afford tetra-*n*-butyl ammonium cation and fluoride anion. Cationic species bind with the organic substrates (electrophiles) to increase their electrophilicity and fluoride ion (which plays major role) behave as a base in the presence of H-bond e-acceptors (organic substrates/nucleophiles), and enhance their nucleophilicity. In this manner, major role of fluoride ion as a base and assistance of tetra-n-butyl ammonium cation accelerate the rate of reaction. Plausible mechanism involved in the synthesis of 2-arylbenzthiazole is depicted with the help of **Figure 2**.

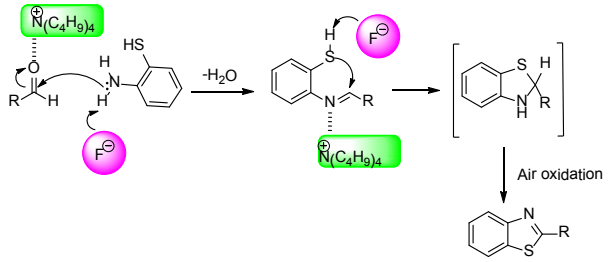



**Figure 2**. Plausible mechanism for the preparation of 2-arylbenzothiazole derivatives

To determine the appropriate concentration of the catalyst (TBAF), we have investigated the model reaction at the different concentrations of TBAF such as 0, 2.5, 5, 10 and 15 mol %. The product was formed in trace, 55 %, 75 %, 94 % and 94 % yield, respectively (**Table 3**). This indicates that 10 mol % of TBAF is sufficient to carry out the reaction smoothly.

**Table 3**. Concentration Effect of TBAF[a]

| **Entry** | **TBAF (mol %)** | **Yield[b] (%)** |
|---|---|---|
| 1 | 0 | Trace |
| 2 | 2.5 | 55 |
| 3 | 5 | 75 |
| 4[c] | 10 | 94 |
| 5 | 15 | 94 |

[a]*Reaction conditions*: *o*-Aminothiophenol **1** (1 mmol) and benzaldehyde **2a** (1 mmol) in water (5 mL) at 80 °C for 1 h; [b]Isolated yields.

It is worthy to note that, recently, recycling and reuse of TBAF in water [36] has been successfully achieved. Hence, we have carried out this experiment for the present reaction and it was observed that this catalytic system could be recovered and reused without any significant loss in its catalytic activity. Recovery process is very easy and convenient to carry out. On completion of reaction, filtrate is obtained after simple filtration can be reused directly for the same reaction (**Table 4**, entry 1-4).

**Table 4**. Reusability of catalyst for model reaction

| Entry | Run | Time[a] (h) | Yield[b] |
|---|---|---|---|
| **1** | 1 | **1 h** | **94** |
| **2** | 2 | 1 h | 92 |
| **3** | 3 | 1 h | 90 |
| **4** | 4 | 1 h | 88 |

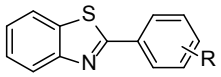
[a]Reaction progress monitored by TLC. [b] Isolated yield.

Considering the applications of microwave to promote various organic transformations, we next attempted to carry out the model reaction using optimized reaction conditions under microwave irradiation at 40°C with a view to explore whether, the reaction could be expedited and the product yield could be enhanced. It is observed that, microwave irradiation led to relatively higher yields and the reaction time reduced significantly as compared to conventional methods. Thus, microwave irradiation was found to have a beneficial effect on the synthesis of 2-arylbenzothiazole derivatives which was superior to the conventional method with respect to yield, reaction time, simplicity and safety.

To further establish the scope of optimized reaction conditions and in order to generalize the synthetic procedure, variety of electronically divergent aromatic aldehydes were treated with *o*-aminothiophenol under conventional and microwave method. The presence of electron-withdrawing and electron donating groups on the aromatic rings does not affect the yield of the product. More importantly, various hetero aryl aldehydes were observed to be well tolerated under optimized conditions furnishing the product in good yields. All the results are compiled in **Table 5**. The structures of synthesized compounds were confirmed by IR, $^{1}$H NMR, $^{13}$C NMR, Mass spectra and elemental

analysis.

**Table 5**. Synthesis of 2-aryl benzothiazole derivatives (**3a-r)**



**3(a-l)**

| Comp | Ar | Microwave method[a] | | Conventional method[c] | | MP (°C) |
|---|---|---|---|---|---|---|
| | | Time (min) | Yield[b] (%) | Time (h) | Yield[d] (%) | |
| **3a** | -$C_6H_5$ | 10 | 94 | 1 | 94 | 112-115 |
| **3b** | 4-Cl$C_6H_4$ | 12 | 94 | 2 | 92 | 115-117 |
| **3c** | 2-Cl$C_6H_4$ | 12 | 93 | 2 | 80 | 80-81 |
| **3d** | 4-$OCH_3C_6H_4$ | 15 | 89 | 2 | 84 | 121-123 |
| **3e** | 4-$CH_3C_6H_4$ | 15 | 93 | 2 | 83 | 82-84 |
| **3f** | 2-$CH_3C_6H_4$ | 12 | 90 | 2 | 88 | 58-60 |
| **3g** | 4-F$C_6H_4$ | 12 | 90 | 2 | 86 | 101-103 |
| **3h** | 3-Br$C_6H_4$ | 15 | 89 | 2 | 85 | 88-90 |
| **3i** | 4-HO-3-MeO$C_6H_3$ | 15 | 91 | 3 | 80 | 179-181 |
| **3j** | 2-HO-6-MeO$C_6H_3$ | 12 | 90 | 3 | 85 | 108-110 |
| **3k** | 4-$NO_2C_6H_4$ | 10 | 91 | 2 | 83 | 228-230 |
| **3l** | 3-$NO_2C_6H_4$ | 10 | 92 | 2 | 86 | 200-203 |
| **3m** | 4-HO$C_6H_4$ | 12 | 90 | 3 | 83 | 229-232 |
| **3n** | 2-HO$C_6H_4$ | 15 | 89 | 2 | 83 | 130-132 |
| **3o** | 4-N$(CH_3)_2C_6H_4$ | 15 | 89 | 3 | 82 | 181-183 |
| **3p** | 2-furyl | 15 | 87 | 2 | 79 | 108-111 |
| **3q** | 2-thiophenyl | 10 | 92 | 2 | 83 | 100-102 |
| **3r** | 2-indolyl | 12 | 90 | 2 | 86 | 146-148 |

[a] Reaction conditions: *o*-Aminothiophenol **1** (1 mmol), benzaldehyde **2a** (1 mmol), catalyst (10 mol %) in $H_2O$ at 40 °C. [b] Isolated yield.
[c] Reaction conditions: *o*-Aminothiophenol **1** (1 mmol), benzaldehyde **2a** (1 mmol), catalystm(10 mol %) in $H_2O$ at 80 °C. [d] Isolated yield.

## Conclusions

A facile, economic, and green protocol for cyclocondensation of o-aminothiophenol and aldehydes has been described. The reaction conditions are mild accepting several functional groups present in the molecules and reactions proceed under essentially neutral conditions, thus reducing the possibility of many unwanted side reactions. In addition, comparative study of the developed protocol with the known methods reveals the following advantages:

(i) This strategy is higher yielding under mild reaction conditions.

(ii) All the reported methods have been performed in either organic solvents or ethanol, in contrast, we have used greener aqueous medium, i.e. water.

(iii) In comparison to others, catalyst were used in this route can be reused up to four runs without loss of significant reactivity.

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