



# Eco-Friendly Synthesis of 2-Arylbenzothiazole Using Lemon Juice Under Microwave Irradiation

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## Abstract

Eco-Friendly synthesis of 2-arylbenzothiazoles from 2-aminothiophenols and aromatic aldehydes using lemon juice as a green catalyst under microwave irradiation has been reported.

**Keywords:** 2-Arylbenzothiazoles, Aldehydes, 2-Aminothiophenol, Lemon juice, Microwave-irradiation.

## 1. Introduction

Benzothiazoles are bicyclic ring system with multiple applications. In the 1950s, a number of 2-aminobenzothiazoles were intensively studied as central muscle relaxants. Since then medicinal chemists have not taken active interest in this chemical family.

Benzothiazole and their derivatives are very important groups of heterocyclic compounds.<sup>1</sup> The small and simple benzothiazole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities, such as antimicrobial, anthelmintic, antileishmanial, anticonvulsant and antiinflammatory. The present review focuses on the benzothiazoles with potential activities that are now in development. Although they have been known from long ago to be biologically active,<sup>2-4</sup> their varied biological features are still of great scientific interest. Benzothiazoles show antitumor activity, especially the phenyl-substituted benzothiazoles,<sup>5-7</sup> while condensed pyrimido benzothiazoles and benzothiazolo quinazolines exert antiviral activity.<sup>8</sup> Recently, Racane *et al.*<sup>9</sup> have described the synthesis of bis-substituted amidino benzothiazoles as potential anti HIV agents.

Recently, some green approaches for the preparation of 2-arylbenzothiazoles based on the direct condensation of 2-aminothiophenols with aromatic aldehydes have been reported. They involve the use of PTSA or PEG, 200/400,<sup>11,12</sup> Cu(OAc)<sub>2</sub>/MCM<sub>41</sub>,<sup>13</sup> NIBTS,<sup>14</sup> Dowex 50W,<sup>15</sup> TCCA,<sup>16</sup> 2,4,6-trichloro-1,3,5-triazine,<sup>18</sup> H<sub>2</sub>SO<sub>4</sub>/SiO<sub>2</sub><sup>19</sup> or sulfamic acid.<sup>20</sup> However, most of these synthetic approaches suffer from drawbacks such as harsh reaction conditions, lengthy procedures, expensive catalysts which may be harmful to the environment. As a consequence, the introductions of new methods to overcome the limitations are still an important challenge.

The science of green chemistry is developed to meet the increasing demand of environmentally benign chemical processes. The application of microwaves (MWs), as an efficient heating source for organic reactions and it has been reported in the literature.<sup>21</sup> The main advantages of MW irradiation usage were: very short reaction time and the solvent less procedures which are eco-friendly.<sup>22,23</sup> To the best of our knowledge MW irradiation has been mostly reported as a heating technique particularly for low molecular weight compound chemical modifications.

Green chemistry approach as an eco-friendly approach has tremendous application for the synthesis of various organic compounds and key intermediates in recent past.<sup>24</sup> Recently fruit juice is known to be potential organic solvents for the synthesis of compounds of pharmaceutical interest.<sup>25</sup> The widespread applications of different fruit juices are due to their non toxic, safe, inexpensive and environmentally benign nature.<sup>26</sup> Fruit juice is being used on regular basis in various organic transformation reactions.<sup>27-30</sup> Among fruit juices, Lemon juice is the most familiar in different important organic reactions like Knoevenagel condensation reaction,<sup>31</sup> synthesis of triazoles<sup>32</sup> and synthesis of Dihydropyrimidinone<sup>33</sup> and many more. Herein, we would like to report the facile and ecofriendly methodology for the synthesis of 2-arylbenzothiazole.

## 2. Experimental Section:

Microwave oven (LG Smart Chef MS-255R operating at 2450 MHz having maximum output power of 960 W) was used for microwave irradiation. <sup>1</sup>H NMR spectra were recorded on Mercury plus Varian at 400 MHz in CDCl<sub>3</sub> as a solvent and TMS as an internal standard. IR spectra were recorded on a Perkin Elmer FTIR using KBr discs.

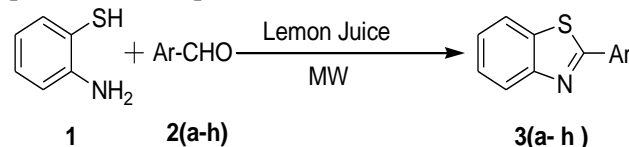
### 3. Typical experimental procedure

A mixture of 2 aminothiophenol (1 mmol), aldehyde (1 mmol) and lemon juice (1ml) were taken in a beaker. The reaction mixture was mixed properly with the help of glass rod and irradiated in a microwave oven at 45W, for the time indicated in **Table 2**. The progress of the reaction was monitored by TLC (ethyl acetate: hexane, 7:3). After completion of the reaction, the reaction mixture was cooled and dichloromethane (25 mL) was added, to obtain the product 3(a-h). All the products were characterized from their spectral data.

## 4. Results and Discussion:

In continuation of our research work on the development of novel synthetic methodologies, using microwave irradiation

techniques, herein, we have developed methodology for the synthesis of 2-arylbenzothiazole using lemon juice which makes use of mild catalyst over the reported procedure as depicted in (**Scheme 1**).



### Scheme 1:-Synthetic route for the synthesis of benzothiazoles

Here we have carried out the reaction of 2-aminothiophenol (1) and 4-methoxy benzaldehyde (2a) catalyzed by lemon juice under microwave irradiation, it has been considered as a standard model reaction.

We have screened a number of different catalysts on model reaction, herein, the result revealed that, when the reaction was carried out in the presence of KH<sub>2</sub>PO<sub>4</sub>, NH<sub>4</sub>VO<sub>3</sub>, acidic alumina, Amberlite-IR 120, sulphamic acid under microwave-irradiation it gave lower yield of product even after prolonged reaction time. However when the same reactions was conducted under microwave irradiation using lemon juice as a catalyst it gave excellent yields of product in short reaction time. (**Table 1**, entry 6).

After optimizing the catalyst, the generality of this method was examined by the reaction of 2-aminothiophenol and several substituted aldehydes using lemon juice as a catalyst under microwave-irradiation, the results are shown in **Table 2**. Here, we have found that both aldehydes bearing electron-donating substituents (**Table 2**, entries 1, 5) and electron-withdrawing (**Table 2**, entries 3, 4) substituents gave desired benzothiazoles in excellent yields. The synthesized compounds were compared (MS, NMR,

and IR) with compounds that were prepared by using the literature method.

### Conclusions:

In conclusion, lemon juice was found to be an efficient catalyst for the synthesis of arylbenzothiazole in good to excellent yields. The main advantages of the present

synthetic protocol are mild, ecofriendly catalyst and easy reaction work-up procedure. It is expected that the present methodology will find application in organic synthesis

**Table 1:-Screening of catalyst<sup>a</sup>**

Entry	Catalyst	Under MW	
		Time(min)	Yield <sup>b</sup> (%)
1	KH <sub>2</sub> PO <sub>4</sub>	10	40
2	NH <sub>4</sub> VO <sub>3</sub>	10	51
3	Acidic Al <sub>2</sub> O <sub>3</sub>	10	57
4	Amberlite-IR 120	10	65
5	Sulphamic acid	10	76
6	Lemon juice	10	90

<sup>a</sup>Reaction conditions:- **1** (1 mmol), **2a**(1 mmol), Catalyst (1 ml), <sup>b</sup>Isolated yield

**Table 2:-Synthesis of 2-arylbenzothiazole<sup>a</sup>**

Entry	Product	Ar	Time (min)	Yield (%) <sup>b</sup>	M.P(°C)
1	<b>3a</b>	4-OCH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	10	91	120-122
2	<b>3b</b>	C <sub>6</sub> H <sub>5</sub>	10	90	113-114
3	<b>3c</b>	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	10	92	181-182
4	<b>3d</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	10	94	226-228
5	<b>3e</b>	2-OCH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	10	89	103-105
6	<b>3f</b>	2-Cl-C <sub>6</sub> H <sub>4</sub>	10	87	72-74
7	<b>3g</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	10	91	133-134
8	<b>3h</b>	4-Cl-C <sub>6</sub> H <sub>4</sub>	10	90	116-118

<sup>a</sup>Reaction conditions:- **1** (1 mmol), **2 (a-h)**(1 mmol), catalyst (1 ml)

<sup>b</sup>Isolated yield. All the compounds characterised by their spectroscopy method <sup>1</sup>HNMR, Mass, IR and melting point and compare to their authentic sample

## 7. References

- Horton, D. A., Bourne, G. T., Smythe, M. L. *Chem. Rev.* 2003, 103, 893.
- Lacova, M., Chovancova, J., Hyblova, O. and Varkonda, S., *Chem. Pap.*, 1991, 45, 411.
- Chulak, I., Sutorius, V. and Sekerka, V., *Chem. Pap.*, 1990, 44, 131.
- Papenfuhs, T., *Ger. Offen. De.*, 1987, 3, 528.
- Bradshaw, T.D., Bibby, M. C., Double, J.A., Fichtner, I., Cooper, P.A., Alley, M.C., Donohue, S., Stinson, S.F., Tomaszewski, J.E., Sausville, E.A. and Stevens, M.F.G., *Mol. Cancer Therapeutics*, 2002, 1, 239.
- Bradshaw, T.D., Chua, M.S., Browne, H. L., Trapani, V., Sausville, E. A. and Stevens, M. F.G., *Brit. J. Cancer.*, 2002, 86, 1348.
- Hutchinson, I., Jennings, S.A., Vishnuvajjala, B. R., Westwell, A.D. and Stevens, M.F.G., *J. Med. Chem.*, 2002, 45, 744.
- El-Sherbeny, M.A., *Arzneim-Forsch.*, 2000, 50, 843.



9. Racane, L., Tralic-Kulenovic, V., Fiser-Jakic, L., Boykin, D.W. and Karminski-Zamola, G., *Heterocycles*, 2001, 55, 2085.
10. Mahmood-ul-Hasan, Chohan, Z.H. and Supuran, C.T., *Main Group Met. Chem.*, 2002, 25, 291.
11. Azizi, N., Amiri, A.K.; Baghi, R., Bolourtchian, M., Hashemi, M.M. *Monatsh. Chem.* 2009, 140, 1471.
12. Deligeorgiev, T.G. Kaloyanova, S., Vasilev, A., Vaquero, J. J. *Phosphorus Sulfur Silicon Relat. Elem.* 2010, 185, 2292.
13. Sadjadi, S., Sepeshrian, H. *Ultrason. Sonochem.* 2011, 18, 480.
14. Veisi, H., Ghorbani-Vaghei, R., Fraji, A., Ozturk, T. *Chin. J. Chem.* 2010, 28, 2249.
15. Mukhopadhyay, C., Datta, A. *J. Heterocycl. Chem.* 2009, 46, 91.
16. Xiao, H.-L., Chen, J.-X., Liu, M.-C., Zhu, D.-J., Ding, J.-C, Wu, H.-Y. *Chem. Lett.* 2009, 38, 170.
17. Chakraborti, A.K., Rudrawar, S., Jadhav, K.B.; Kaur, G., Chankeshwara, S.V., *Green Chem.* 2007, 9, 1335.
18. Maleki, B., Azarifar, D., Hojati, S.F., Gholizadeh, M., Veisi, H., Salehabadi, H., Khodaverdian Moghadam, M., *J. Heterocycl. Chem.* 2011, 48, 449.
19. Maleki, B., Salehabadi, H., Khodaverdian Moghaddam, M. *Acta Chim. Solv.* 2010, 57, 741.
20. Rostami, A., Yari, A. *J. Iran. Chem. Soc.* 2012, doi:10.1007/s13738-011-0059-y.
21. Kahveci, B., Ozil, M., Serdar, M. *Heteroatom Chem.* 2008, 19, 38.
22. Lange, J. H. M., Verveer, P. C., Osnabrug, S. J. M., Visser, G. M. *Tetrahedron Lett.* 2001, 42, 1367.
23. Çakmaka, O., Başturkmenb, M., Kisakurek, D., *Polymer* 2004, 45, 5421.
24. Patil, S., Jadhav, S.D. & Patil, U.P. *Arch. App. Sci. Res.*, 2012, 4, 1074.
25. Patil S., Jadhav, S.D., Mane, S.Y. *Int. J. Org. Chem.*, 2011, 1, 125.
26. Pal, R., Khannobis, S., Sarkar, T. *Chem. J.*, 2013, 3, 7.
27. 7. Pal, R. *Open J. Org. Chem.*, 2013, 1, 47.
28. Pramanik T., Pathan A.H. *Res. J. Pharm. Bio. Chem. Sci.*, 2014, 5, 444.
29. Pal, R. *Ind. J. Chem.* 2014, 53, 763.
30. Pal, R., Sarkar, T. *Int. J. Org. Chem*; 2014, 4, 106.
31. Bhuiyan, M.M.H., Hossain, M.I., Alam M.A., Mahmud M.M. *J. Chem.* 2012, 2, 30.
32. Sachdeva, H., Saroj, R. Khaturia, S., Dwivedi, D.. *Org. Chem. Int.*, 2013, 1.
33. Patil, S., Jadhava, S.D., Deshmukh, M.B. *App. Sci. Res.*, 2011, 3, 203.
34. **Spectral Data of Principal Compounds.** (3a) 2-(4-Methoxyphenyl)-1,3-benzothiazole : IR ( $\nu_{\max}$ , KBr,  $\text{cm}^{-1}$ ): 3105, 3060, 1604, 1585;  $^1\text{H-NMR}$ :  $\delta$  8.11 (d,  $J = 7.6$  Hz, 1H, Ar-H); 8.01-8.10 (m, 3H, Ar-H), 7.53 (t,  $J = 8.0$  Hz, 1H, Ar-H), 7.43 (t,  $J = 7.8$  Hz, 1H, Ar-H), 7.12 (d,  $J = 7.8$  Hz, 2H, Ar-H), 3.87 (s, 3H,  $\text{OCH}_3$ ), MS m/z 241 (M+1). (3b): 2-Phenyl-1,3-benzothiazole: IR ( $\nu_{\max}$ , KBr,  $\text{cm}^{-1}$ ): 3068, 3015, 1609, 1588;  $^1\text{H-NMR}$ :  $\delta$  8.16 (d,  $J = 7.8$  Hz, 1H, Ar-H); 8.07-8.12 (m, 3H, Ar-H), 7.54-7.60 (m, 4H, Ar-H), 7.48 (t,  $J = 7.8$  Hz, 1H, Ar-H), MS m/z 211 (M+1). (3d): 2-(4-Nitrophenyl)-1,3-benzothiazole: IR ( $\nu_{\max}$ , KBr,  $\text{cm}^{-1}$ ): 3088, 3032, 1618, 1582;  $^1\text{H-NMR}$ :  $\delta$  8.9 (d,  $J = 8.0$  Hz, 2H, Ar-H); 8.32 (d,  $J = 8.0$  Hz, 2H, Ar-H); 8.23 (d,  $J = 8.0$  Hz, 1H, Ar-H); 8.02 (d,  $J = 8.0$  Hz, 1H, Ar-H); 7.44-7.53 (m, 2H, Ar-H); MS m/z 256.(M+1). (3i): 2-Thienyl-1,3-benzothiazole: IR ( $\nu_{\max}$ , KBr,  $\text{cm}^{-1}$ ): 3082, 3043, 1623;  $^1\text{H-NMR}$ :  $\delta$  8.22 (d,  $J = 8.0$  Hz, 1H, Ar-H); 8.13 (d,  $J = 8.0$  Hz, 1H, Ar-H); 7.74 (d,  $J = 4.0$  Hz, 1H, thiophene CH); 7.69 (d,  $J = 4.0$  Hz, 1H, thiophene CH); 7.54-7.63 (m, 2H, Ar-H); 7.33 (t,  $J = 4.0$  Hz, 1H, thiophene CH); MS m/z 217.0 (M+1).