

Short communication

# Room-Temperature Synthesis of 2-Arylbenzothiazoles using Sulfuric Acid Immobilized on Silica as a Reusable Catalyst under Heterogeneous Condition

Behrooz Maleki,\* Hafezeh Salehabadi  
and Mona Khodaverdian Moghaddam

Department of Chemistry, Sabzevar Tarbiat Moallem University, Postal Code 397, Sabzevar, Khorasan, Iran

\* Corresponding author: E-mail: malekibehrooz@gmail.com

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## Abstract

Application of sulfuric acid immobilized on silica gel as an efficient and benign catalyst has been explored in the synthesis of 2-arylbenzothiazoles via condensation reaction of aldehydes with 2-aminothiophenol. The reactions proceed under heterogeneous and mild conditions in ethanol at room temperature to provide 2-arylbenzothiazoles in high yields.

**Keywords:** 2-Arylbenzothiazole, aldehyde, silica-supported sulfuric acid, heterogeneous catalyst

## 1. Introduction

Compounds containing benzothiazole nucleus belong to an important class of heterocycles which are known to possess important biological and pharmaceutical activities such as antitumors<sup>1</sup> and anticancers.<sup>2</sup> In addition, some of these compounds exhibit nonlinear optical,<sup>3</sup> and luminescent<sup>4</sup>/fluorescent<sup>5</sup> properties, and have therefore found applications in designing sensor molecules of specific interest. Consequently, preparation of benzothiazole derivatives with interesting biological activities has attracted particular attention, and a variety of methods for the synthesis of 2-arylbenzothiazoles have been developed.<sup>6–11</sup> The most common method for their synthesis involves direct condensation of aldehydes with 2-aminothiophenol in the presence of various catalysts such as MnO<sub>2</sub>/SiO<sub>2</sub>,<sup>12</sup> *p*-TsOH or graphite supported on solid minerals under microwave irradiation,<sup>13</sup> I<sub>2</sub>/DMF,<sup>14</sup> 1-phenyl-3-methylimidazolium bromide [pmIm]Br by microwave irradiation,<sup>15</sup> activated carbon (Shirasagi KL or Darco® KB) under oxygen atmosphere,<sup>16</sup> O<sub>2</sub> or H<sub>2</sub>O<sub>2</sub> in the presence of Sc(OTf)<sub>3</sub>,<sup>17</sup> cerium (IV) ammonium nitrate (CAN),<sup>18</sup> dowex 50W,<sup>19</sup> electrooxidation,<sup>20</sup> and direct condensation of 2-aminothiophenol with aromatic aldehydes under microwave irradiation.<sup>21</sup>

## 2. Experimental

IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr pellets). <sup>1</sup>H NMR spectra were obtained using Jeol FT NMR 90 MHz spectrometer in CDCl<sub>3</sub> as solvent and TMS as an internal reference. Melting points were determined in open capillary tubes in a Stuart BI Branstead Electrothermal apparatus and are uncorrected.

### 2.1. General Procedure for Synthesis of 2-Arylbenzothiazoles Catalyzed by H<sub>2</sub>SO<sub>4</sub>/SiO<sub>2</sub>

To a mixture of aldehyde **1a-m** (1 mmol) and 2-aminothiophenol (1.2 mmol) dissolved in ethanol (5 ml) was added H<sub>2</sub>SO<sub>4</sub>.SiO<sub>2</sub> (5 mg). The resulting mixture was stirred at room temperature for 15–40 min. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure. The residue was dissolved in diethyl ether (5 ml) and heated to 40 °C for 3–5 minutes. The mixture was then cooled to room temperature and filtered to remove the catalyst. The filtrate was evaporated under reduced pressure to isolate a solid residue which was recrystallized from ethanol (2 × 5 ml) to afford pure products (**2a-m**).

## 2. 1. 1. Spectral Data of the Selected Compounds

### 2-Phenyl-benzothiazole (2a)

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.41–8.08 (m, 9H, Ar-H).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 77.10 ( $\text{CDCl}_3$ ), 121.53, 123.23, 125.09, 126.22, 127.52, 128.91, 130.83, 133.64, 135.08, 154.19, 167.93. IR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) 3064, 1588, 1555, 1509, 1478, 1433, 1244, 962, 766.

### 2-(4-Methoxyphenyl)-benzothiazole (2c)

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 3.82 (s, 3H, OMe), 7.00–7.95 (m, 8H, Ar-H).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 77.10 ( $\text{CDCl}_3$ ), 55.45 ( $\text{OCH}_3$ ), 114.43, 121.53, 122.90, 124.81, 126.21, 129.16, 134.91, 154.38, 162.02, 167.85. IR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) 3023, 2996, 2900, 2836, 1605, 1521, 1485, 1260, 832.

### 2-(4-Methylphenyl)-benzothiazole (2e)

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 2.38 (s, 3H,  $\text{CH}_3$ ), 7.30–8.01 (m, 8H, Ar-H). IR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) 3024, 2905, 1609, 1521, 1484, 1456, 1434, 1384, 1312, 760.

### 2-(4-Cyanophenyl)-benzothiazole (2l)

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.37–7.96 (m, 8H, Ar-H).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 113.93, 118.08, 121.66, 123.68, 125.96, 126.69, 127.68, 132.50, 137.20, 153.88, 165.09. IR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) 3061, 2226, 1606, 1514, 1479, 1432, 1405, 764  $\text{cm}^{-1}$ .

### 2-(3-Nitrophenyl)-benzothiazoles (2m)

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.44–8.30 (m, 7H, Ar-H). 8.85 (s, 1H, Ar-H). IR (KBr):  $\nu$  ( $\text{cm}^{-1}$ ) 3058, 1611, 1576, 1529, 1459, 1433, 1347, 761.

## 2. 2. Preparation and Reusability of the $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ Catalyst

To a slurry of silica gel (10 g, 200–400 mesh) in dry diethyl ether (50 ml) was added concentrated  $\text{H}_2\text{SO}_4$  (3 ml) with shaking for 5 min. The solvent was evaporated under reduced pressure to obtain dry  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst which was then heated at 120 C for 3 hours.

In the next step, we investigated the reusability and recycling effect of  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst in these reactions. At the end of each reaction, the catalyst was filtered, washed with diethyl ether, dried at 120 C for 3 hours, and reused in a subsequent reaction cycle. The recycled catalyst was employed consecutively for three reactions and no significant loss in its efficiency was observed.

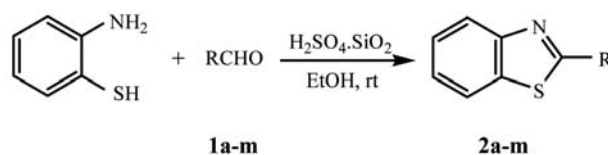
## 3. Results and Discussion

In recent years, many heterogeneous organic reactions have been performed using various reagents supported on solid materials.<sup>22–29</sup> Such procedures have many advantages over unsupported reagents such as cleaner

reactions, easier work up, reduced reaction times, high yields, and are environmentally benign.

$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst is an inexpensive, heterogeneous and stable catalyst possessing very high reactivity in comparison with unsupported  $\text{H}_2\text{SO}_4$ . This catalyst has been used in many different reactions including fisher type glycol silylation<sup>30</sup> and acetylation of sugar derivatives.<sup>31</sup>

In continuation of our research on synthetic applications of heterogeneous catalysts<sup>32–34</sup> and on synthesis of 2-arylbenzothiazoles,<sup>35</sup> we report here a very simple synthesis of 2-arylbenzothiazoles by condensation of 2-aminothiophenol with aromatic aldehydes under heterogeneous and mild reaction conditions, catalyzed by  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst at room temperature (Scheme 1).



Scheme 1

To achieve the best results in terms of yield and reaction time, we examined the efficiency of different reaction media and catalyst amounts in condensation reaction of benzaldehyde **1a** (1 mmol) with 2-aminothiophenol (1.2 mmol) as a model reaction. As shown in Table 1, a significant enhancement of the reaction rate and improvement of the yield of the reaction were observed when 5 mg of  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  in ethanol was used (entry 1). In the absence of  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst no formation of the expected product was detected even after 2 hours (entries 5 and 6). In order to evaluate the effect of the catalyst concentration, the reaction was also conducted in the presence of various amounts of the catalyst (3 and 8 mg) at room temperature (entries 7 and 8).

Table 1. Screening of the reaction conditions for the synthesis of 2-phenylbenzothiazoles (**2a**).

Entry	Catalyst	Solvent	Time (min)	Yield (%) <sup>a</sup>
1	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (5 mg)	EtOH	25	80
2	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (5 mg)	MeOH	35	60
3	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (5 mg)	$\text{CH}_3\text{CN}$	40	40
4	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (5 mg)	$\text{CHCl}_3$	45	20
5	$\text{SiO}_2$ (5 mg)	EtOH	120	–
6	–	EtOH	120	–
7	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (3 mg)	EtOH	35	60
8	$\text{H}_2\text{SO}_4\cdot\text{SiO}_2$ (8 mg)	EtOH	25	74

<sup>a</sup> Isolated yields.

The optimized reaction conditions were conveniently extended to a variety of aromatic aldehydes **1b-m**, and the results obtained are summarized in Table 2.

**Table 2.** Synthesis of 2-arylbenzothiazoles via condensation of 2-aminothiophenol with various aldehydes using  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  as a catalyst (5 mg) in EtOH at room temperature.

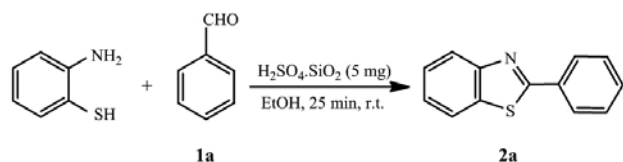
Entry	Aldehyde (1)	2-Arylbenzothiazole (2)	Time (min)	Yield <sup>a</sup> (%)	Observed mp (°C)	Literature <sup>b</sup>
a			25	80	111–112	112–113
b			30	70	226–227	225–227
c			20	94	120–122	120–121
d			40	70	126–128	125–126
e			35	78	83–85	84–86
f			40	64	54–56	53–54
g			20	84	130–131	130–131
h			25	80	84–86	84–86
i			20	88	160–162	160–161
j			20	60	115–117	115–117
k			30	80	102–104	101–103
l			15	94	161–162	162–164
m			35	92	180–183	181–182

<sup>a</sup> Isolated yields. <sup>b</sup> The yields refer to the isolated products characterized by spectroscopic (IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR) analysis and by comparison with the literature data.<sup>11–20,36</sup>

In order to examine the efficiency of the recycled catalyst in these reactions, the reaction of benzaldehyde **1a** (1 mmol) with 2-aminothiophenol (1.2 mmol) was performed in the presence of fresh  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst (5 mg) at room temperature (Table 3). The recovered catalyst in this reaction work up was reused in subsequent reactions and found to be almost as reactive as the fresh catalyst with no significant loss of efficiency.

In these reactions,  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst can possibly act as a convenient proton source. The proposed mecha-

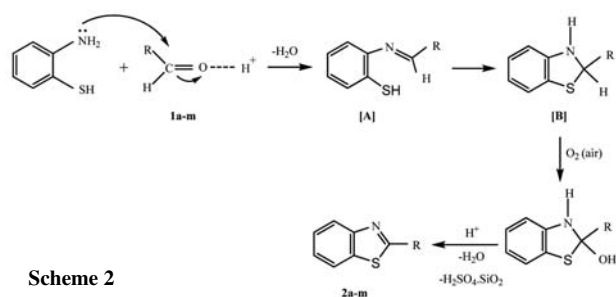
nism for this reaction is presented in Scheme 2 and involves (i) initial nucleophilic attack of  $\text{NH}_2$  group on aldehyde C=O group, activated by  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst, (ii) formation of an alkylidene intermediate [A], followed by cyclization to yield the adduct [B], and (iii) subsequent oxidation of [B] with  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2/\text{O}_2$  (from air), followed by dehydration to furnish the products (**2a-m**). It is important to note that, when these reactions were conducted under nitrogen atmosphere using similar reaction conditions, they stopped at the benzothiazoline [B] stage with no furt-

**Table 3.** The efficiency of recycled  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst.

Run	Time (min)	Yield (%) <sup>a</sup>
1	25	80
2	35	74
3	50	60

<sup>a</sup> Isolated yields.

her progress towards the expected benzothiazoles (**2a-m**). This implies that, the oxygen does not play any important role in the formation of benzothiazoline. However, the presence of air in the second, oxidation step of the reaction is essential to result in the formation of benzothiazoles.



## 4. Conclusion

We have demonstrated that  $\text{H}_2\text{SO}_4\cdot\text{SiO}_2$  catalyst is as a cheap, reusable and eco-friendly catalyst for the synthesis of 2-arylbenzothiazoles.

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## Povzetek

V prispevku je predstavljena uporaba žveplove (VI) kisline, imobilizirane na silikagelu kot učinkovitega in neškodljivega katalizatorja pri sintezi 2-arilbenzotiazolov v kondenzacijski reakciji aldehydov z 2-aminofenolom. Reakcije potekajo z visokimi izkoristki, pod milimi heterogenimi pogoji, pri sobni temperaturi in v etanolu kot topilu.