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### Silica sulfuric acid: Recyclable and efficient catalyst for the 2-aryl benzothiazoles

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#### ABSTRACT

*The silica sulfuric acid (SSA) serves as mild, efficient and reusable catalyst for the synthesis of aryl benzothiazole in one pot conversion with excellent yield. The reusability, excellent yields with easy work up make it an interesting alternative for the synthesis of aryl benzothiazole.*

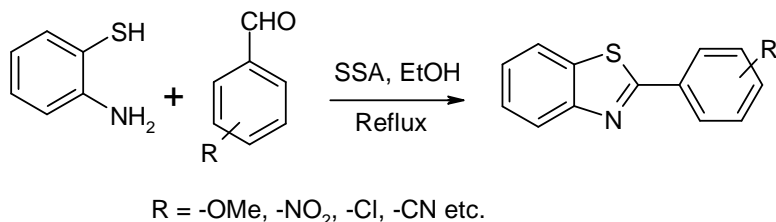
**Keywords:** Benzothiazole, Silica sulfuric acid, one pot reaction.

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#### INTRODUCTION

Benzothiazoles are found in a variety of natural products and are important targets in drug discovery (1-8). There are two commonly used approaches for the construction of the Benzothiazoles ring system, both of which employ 2-aminothiophenols as substrates (3). The first approach involves the coupling of the 2-aminothiophenols with carboxylic acid derivatives under strongly acidic conditions, such as in polyphosphoric acid (PPA)(9), a mixture of methanesulfonic acid and phosphorus pentoxide (10). The second approach uses the reaction of 2-aminophenols with an aldehyde via oxidative cyclization of imine intermediates (11,12). However, most of these methodologies suffer from one or more of the disadvantages such as use of costly, air sensitive, and toxic substances, the tedious work-up procedure, the necessity of neutralization of the strong acid media, producing undesired washes, requirement of excess of reagents/catalysts, special apparatus, and harsh reaction conditions(9-12). Thus, the need for the development of alternate synthetic route to construct the benzothiazolyl moiety is in high demand. The use of solid acid catalysts has received considerable attention in organic synthesis due to their environmental compatibility, ease of handling, non-toxic nature and above all their reusability. Silica-sulfuric acid has been used as a versatile and stable solid acid catalyst for various organic transformations (13). Knowing the utility of the solid acid catalyst and our previous success in the newer synthetic methodologies (14), we have developed the new facile

synthetic route for the benzothiazole using silica sulfuric acid as a recyclable catalyst from aminothiophenol and aromatic aldehydes. (Scheme-1).



Scheme-1

## MATERIALS AND METHODS

### Experimental

Melting points (uncorrected) were determined in open capillary tube. IR spectra were recorded on Shimadzu IR-470 spectrophotometer using KBr pellets. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra in CDCl<sub>3</sub> on Bruker (200 MHz) using TMS as an internal standard. The catalyst silica sulfuric acid was prepared by reported method (24).

### General Procedure

A mixture of o-aminothiophenol (2 mmol) and 4-methoxy benzaldehyde (2 mmol) and silica sulfuric acid (2.5 mmol) in ethanol was refluxed on boiling water bath. The progress of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was cooled and extracted with diethyl ether (10ml) and washed with sat. NaHCO<sub>3</sub>. The extract was dried over anhydrous sodium sulfate and residue was recrystallised from ethanol.

## RESULTS AND DISCUSSION

As mentioned in the literature<sup>24</sup>, silica sulfuric acid (SSA) was obtained from silica gel and chlorosulfonic acid. In a case study, mixtures of o-aminothiophenol (2 mmol) and 4-methoxy benzaldehyde (2 mmol) and catalytic amount of silica sulfuric acid in ethanol were refluxed on boiling water bath. The reaction mixture was cooled and extracted with diethyl ether. Evaporation of ether layer yielded crude product, which was recrystallised from ethanol. The crude product in most of the cases was completely pure and did not require to be purified or worked up anymore. The catalyst used was recovered from the reaction mixture. The separated product confirmed on the basis of IR, proton NMR and <sup>13</sup>C spectra and comparison with authentic sample. This primary success of the above results promoted us to find out the optimum quantity of silica sulfuric acid and percentage yield during recyclability of the catalyst. To find out the optimum quantity of the catalyst, the same reaction mentioned above has been carried out with variation in the percentage of catalyst. It was found that with 2.5% of catalyst the yield was maximum and thus, 2.5% of catalyst was used as optimized quantity for the reaction. The results are introduced in the table 1.

The recovered catalyst washed several times with chloroform, dried and reused three times successfully without any change in the activity concerning for the yield and reaction time. To prove the generality of the protocol, the reaction was then extended towards a variety of

aldehydes. It has been observed that all the substituted aromatic aldehydes containing either electron donating or electron withdrawing group giving the good to excellent yields. The results have been summarized in the table 2.

In conclusion, silica sulfuric acid was found to be a mild, efficient and reusable solid acid catalyst for the synthesis of 2-arylbenzothiazoles in almost quantitative yields. The main advantage of the present protocol is the recyclability and excellent yields of the products with simple work-up procedure.

#### Spectroscopic data of the representative compounds:

##### 2-(4-methoxyphenyl) benzothiazole (Table II, entry b)<sup>16</sup> M. P. 118°C,

IR (KBr): 2924, 1605, 1521, 1485, 1434, 1310, 1259, 1225 cm<sup>-1</sup> H<sup>1</sup>NMR (CDCl<sub>3</sub> 200MHz): δ 3.88(s, 3H, -OCH<sub>3</sub>), 6.97-7.02(dd, 2H, *J* = 8.0Hz), 7.34-7.85 (m, 4H, Ar-H), 8.01-8.06(dd, 2H, *J* = 8.0 Hz) <sup>13</sup>C NMR (CDCl<sub>3</sub> 200MHz): δ 55.40, 114.33, 121.46, 122.77, 124.75, 126.16, 126.80, 134.00, 154.17, 161.88 and 167.84.

**Table 1 Effect of the SSA on the yield of the benzothiazole:**

SSA (in mmol)	1.0	1.5	2.0	2.5
% Yield	40-50	58-60	72-80	80-90

**Table 2 Results of the 2-arylbenzothiazoles by using Silica sulfuric acid.**

Product	Ar-CHO	Time (h)	Yield(*) %	Mp(°C)
a	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	2	90	227(227-231°C)15
b	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	5	81	118(119-121°C)16
c	4-Cl C <sub>6</sub> H <sub>4</sub>	5	87	114(112-116°C)12
d	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3	88	183(185-186°C)19
e	2-OH C <sub>6</sub> H <sub>4</sub>	5	80	129(130-131°C)18
f	4-N(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4	86	173(175-178°C)20
g	Thiophene-2-yl	5	81	98(98-100°C)21
h	Furan-2-yl	4	82	103(105-108°C)21
i	4-CNC <sub>6</sub> H <sub>4</sub>	3	89	161(162°C)17
j	4-BrC <sub>6</sub> H <sub>4</sub>	5	85	129(130-131°C)16
k	C <sub>6</sub> H <sub>5</sub>	3	86	112 (113°C) 17
l	3-pyridine	3	80	134(137-138°C)22
m	3,4-(OCH <sub>3</sub> ) <sub>2</sub>	4	83	130(132-134°C)23

\* = Yield refers to the pure isolated products

##### 2-(4-cyanophenyl) benzothiazole (Table II, entry i)<sup>17</sup> M. P. 161°C,

IR (KBr): 3061, 2923, 2853, 2227, 1651, 1607, 1558, 1480, 1459, 1406, 1459 cm<sup>-1</sup> H<sup>1</sup> NMR (CDCl<sub>3</sub> 200MHz): δ 7.25-7.76 (m, 2H, Ar-H), 7.79-7.80(dd, 2H, *J* = 8.0), 7.92-8.08(m, 2H, Ar-H), 8.17-8.22(dd, 2H, *J* = 8.0). <sup>13</sup>C NMR (CDCl<sub>3</sub> 200MHz): δ 113.98, 118.20, 121.72, 123.71, 126.08, 126.75, 127.79, 132.65, 135.20, 137.33, 153.90 and 165.23

**2-(4-chlorophenyl) benzothiazole (Table II, entry c)<sup>12</sup> M. P. 114°C,**

IR (KBr):3055,2923,2853,1589,1556,1507,1474,1434,1399 cm<sup>-1</sup> H<sup>1</sup> NMR (CDCl<sub>3</sub> 200MHz): δ 7.36-7.39(m, 2H, Ar-H), 7.44-7.48(dd, 2H, J = 8.0 Hz), 7.88-7.92(m, 2H, Ar-H), 8.00-8.04(dd, 2H, J = 8.0 Hz). <sup>13</sup> C NMR (CDCl<sub>3</sub> 200MHz): δ 121.60, 123.26, 125.37, 126.43, 128.66, 129.22, 132.07, 135.01, 136.98, 154.03 and 166.56.

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