

MILD AND EFFICIENT SYNTHESIS OF BENZOTHAIAZOLE USING $ZnFe_2O_4$ AS HETEROGENEOUS CATALYST IN WATER**Rupnar B. D.¹, Shirsat A. J.², Bhagat S. S.³ and Pawar R. P.⁴**^{1,2,3}Department of Chemistry, R. B. Attal College, Georai⁴Department of Chemistry, Deogiri College, Aurangabad**ABSTRACT**

A mild and efficient protocol has been developed for the synthesis of benzothiazole, from aldehyde and 2-aminothiophenol in presence of $ZnFe_2O_4$ as heterogeneous catalyst in water. High yield, simple workup procedure and mild reaction condition are main feature of this protocol.

Keywords: heterogeneous catalyst, benzothiazole, $ZnFe_2O_4$, efficient.

INTRODUCTION

Benzothiazole is a privileged bicyclic ring system, that possess unique pharmacophores and are well known in drug discovery due to their significant biological activities like antimalarials, antimicrobial, antitubercular, antitumour, anticonvulsant, anthelmintic, analgesic and anti-inflammatory activity.[1] Furthermore, benzothiazole highly found in numerous natural products, which have helpful biological activities. Due to their importance in pharmaceutical utilities, the synthesis of various benzothiazole derivatives is of considerable interests. Synthesis of privileged benzothiazoles through an economical and environment friendly method is always desirable because benzothiazole moieties are of paramount interest in medicinal chemistry due to their antitumor, anticancer, and antimicrobial activities.[2]

Green technology actively look for new, safer, alternative solvents as well as catalysts to replace common widely used organic solvents and catalyst that present inherent toxicity and high volatility, leading to evaporation of volatile organics to the atmosphere [3].

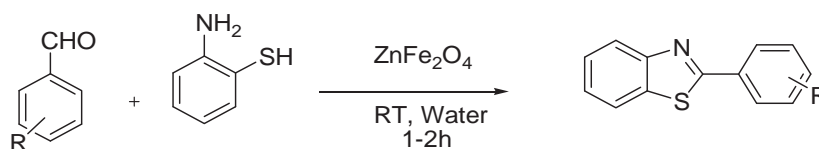
The reaction achieve in heterogeneous catalysts is another objective of green chemistry protocol in order to generate sustainable chemical transformations [4]. Heterogeneous catalysis is favored in industrial processes compared to homogeneous catalysis as the extraction of product and catalyst recovery is easier in heterogeneous catalysis [5]. Based on green chemistry desires, the development of new strategies for relatively nontoxic and recycling of this catalyst, which minimize the energy and time required in achieving separations, can result in significant economic and environmental benefits.[6]

Based on the importance of these compounds various catalysts have been described for the synthesis of benzothiazole. However some protocols suffer from one or more disadvantages like tedious work-up procedure, poor yield, prolonged reaction time, expensive and toxic catalysts and solvents. Therefore, development of new methods for synthesis of benzothiazole is important and much in demand.

$ZnFe_2O_4$ is highly stable bimetallic heterogeneous catalyst in which Fe^{3+} cation and counter anionic O^{2-} act as Lewis acid and base respectively [7]. Herein we report the application of $ZnFe_2O_4$ nanoparticles for the library synthesis of benzothiazole in water.

2. EXPERIMENTAL**2.1 General**

All chemical and reagents were purchased from Sigma Aldrich India and spectrochem Chemical companies in high purity which was used without further purification. Infrared (IR) spectra in KBr were recorded using a Perkin-Elmer FT-IR spectrometer 65. ¹H NMR spectra were recorded on Bruker Avance II 400 MHz FT-NMR spectrometer in DMSO-d₆ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me₄Si) as an internal standard. Abbreviations used for NMR signals are s = singlet, d = doublet, t = triplet, and m = multiplet. Melting points were determined in open capillaries using an electrothermal Mk3 apparatus. The progresses of the reactions were monitored by TLC (Thin Layer Chromatography).

**Scheme 1**

2.2 General Procedure for the synthesis of benzothiazole

A mixture of aromatic aldehyde (1 mmol), 2-aminothiophenol (1 mmol) and $ZnFe_2O_4$ in catalytic amount (30 mol%) was taken in 2 ml of water. Reaction mixture was stirred at room temperature for a period of 1-2 hours (Scheme 1). The progress of reaction was monitored by thin layer chromatography (ethyl acetate: hexane 4:2). After completion of reaction, the reaction mixture was cooled to room temperature, ethyl acetate (5 mL) was added to the reaction mixture and the solid catalyst was separated from the mixture by filtering through a sintered funnel. The recovered catalyst was washed with water and acetone, dried in desiccators and used for another consecutive reaction. Product was collected by evaporation of solvent in a rotary evaporator and the solid residue was finally recrystallized from ethanol. The products were confirmed by melting point, FTIR, 1H NMR with reported work.

RESULT AND DISCUSSION

In the current protocol, we have used 2-aminothiophenol and benzaldehyde as model substrates for the optimization of the reaction condition. The reaction conditions were optimized with respect to the quantity of catalyst (**Table 1**) and the solvent (**Table 2**) by studying the condensation of 2-aminothiophenol (1mmol) with benzaldehyde (1mmol). To determine the catalyst loading, a model reaction of 2-aminothiophenol and benzaldehyde with the different percentage of $ZnFe_2O_4$ in water was carried out. The reaction occurred smoothly in the presence of 30% $ZnFe_2O_4$ as a catalyst and water as a solvent at room temperature, affording product with 90% yield. Increasing the amount of catalyst, more than 30% showed no substantial improvement in the yield (**Table 1**). In the absence of $ZnFe_2O_4$, the reaction in water was incomplete even after an extended reaction time.

Table-1: optimization of catalyst loading

Entry	Amount of $ZnFe_2O_4$ (Mol %)	Time (h)	Yield %
1	----	3	Trace
2	10	3	50
3	20	3	70
4	30	1.5	90
5	40	3	80
6	50	3	80

In order to determine effect of solvent and solvent free reaction condition on the reaction conversion using 30 mol% of $ZnFe_2O_4$ as catalyst at room temperature. Various solvents like DMF, EtOH, CH_3CN , and water was examined. Among the various solvents (**Table 2, entries 1-4**) and solvent-free conditions (**Table 2, entry 5**), water was selected to be the best reaction media for its higher yield and shorter reaction time (**Table 2, entry 4**). The results of the optimization experiments are summarized in **Table 2**.

Table-2: Optimization of solvent

Entry	Solvent	Time (h)	Yield %
1	DMF	3	40
2	EtOH	3	70
3	CH_3CN	3	45
4	water	1.5	90
5	----	3	50

With the optimized parameters in hand we have also performed wide substrate study with different aromatic aldehydes for the synthesis of benzothiazole derivatives (**Table 3**). Good to excellent yields of the desired product were obtained with electron withdrawing and electron donating group on aromatic aldehydes.

Table-3: Synthesis of benzothiazole under optimized reaction conditions

Entry	R	Time (h)	Yield %	MP observed (°C)
1	H	1.5	90	220-221
2	4- NO_2	1	93	205-207
3	4-Cl	1.2	91	200-202
4	4-F	1.5	92	204-206
5	4-Br	1.3	88	201-202
7	4-OH	1.5	87	215-217
8	3-OH	2	85	185-187
9	4-Me	1.3	89	227-229
10	4-OMe	1.5	88	175-177

SOME SELECTED SPECTRAL DATA OF THE PRODUCTS**2-phenylbenzo[d]thiazole(1).**

White cream solid; Yield 90 %; mp 220-221 °C; FT-IR (KBr) ν_{\max} /cm⁻¹ 3066, 2919, 1599 (C=N), 1579, 1500, 1404, 1297, 1204, 1086, 1014, 834, 810, 747 ¹H NMR (400 MHz, CDCl₃, ppm) δ 7.27-8.03 (m, 9 H, Ar-H).

2-(4-chlorophenyl)benzo[d]thiazole(3)

White solid; Yield 91 %; mp 200-202 °C; FT-IR (KBr) ν_{\max} /cm⁻¹ 3066, 2919, 1599 (C=N), 1579, 1500, 1404, 1297, 1204, 1086, 1014, 834, 810, 747 ¹H NMR (400 MHz, CDCl₃, ppm) δ 7.27-8.09 (m, 8 H, Ar-H).

4. CONCLUSION

We have developed an environmentally benign protocol that is advantageous for the rapid and high yielding syntheses of benzothiazole by using ZnFe₂O₄ from 2-aminothiophenol and benzaldehyde in water medium. The advantages of this protocol are recyclability of catalyst, use of microwave and in water.

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