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A Green Alternative Approach for Synthesis of 2-Substituted Benzothiazoles Catalysed by NBS in Ultra Sonication Method

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A B S T R A C T

NBS is an efficient, readily available and cheap catalyst for the synthesis of 2-substituted benzothiazole derivatives by condensation of 2-aminothiophenol and aldehydes under sonication conditions by application of green solvents. This protocol is very simple with easy workup and good to excellent yields of products. On completion of reaction the products were characterized by IR, NMR and Mass Spectra.

Keywords: Benzothiazoles, NBS, 2-Aminothiophenol, Sonication conditions

A R T I C L E I N F O

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1. Introduction

Benzothiazoles are fused membered rings, which contain the heterocycles bearing thiazole. Sulphur and nitrogen atoms constitute the core structure of thiazole and many pharmacologically and biologically active compounds. Thiazole is structurally related to thiophene and pyridine, but in most of its properties it resembles to the latter. The numbering in thiazole starts from the sulphur atom. The basic structure of benzothiazole consist of benzene ring fused with 4, 5 position of thiazole. The two rings together constitute the basic nucleus 1, 3-benzothiazole. Benzothiazole is a heterocyclic compound, weak base, found in bioorganic and medicinal chemistry with application in drug discovery. Benzothiazole moites are part of compounds showing numerous biological activities such

as antimicrobial [1-2] anticancer [3-4], anthelmintic [5], anti-diabetic [6] activities. They have also found application in industry as anti-oxidants, vulkanisation accelerators. Due to these biological activities, the synthesis of benzothiazole is a considerable area of current discussion. The classical method involves condensation of *o*-aminothiophenols with substituted aldehydes [7-13], acyl chlorides, carboxylic acids [14-15] or esters, nitriles [16]. Other most commonly used methods include Pd/Cu/Mn/ chloranil catalyzed cyclization of *o*-halothioformanilides [17-21]. The survey of literature related to benzothiazoles reveals the presence of this bicyclic ring system in various amine or terrestrial natural compounds, which have useful biological properties [22].

Among these methods are the condensation of 2-aminothiophenol with substituted nitriles, carboxylic acids, aldehydes, acyl chlorides or esters [23]. A number of catalysts namely, (PmIm)Br [24], TMSCl [25], I2 [26], $ZrOCl_2$•$8H_2O$ [27], PCC [28], H_2O_2, CAN [29], electro oxidation [30], Baker's yeast [31], PTSA [32], Dowex 50W reusable catalyst in water at 70°C [33], TCCA in 2-MeTHF at ambient temperature [34], PEG,200/400 under microwave heating [35], NIBTS at ambient temperature under solvent free conditions [36], H_2SO_4/SiO_2 as a reusable catalyst at room temperature [37], H_2O [38], animal bone meal [39]**,** $Na_2S_2O_5$ in refluxing DMF [40], $Cu(OAc)_2$/MCM41 supported catalyst under ultrasound irradiation [41], 2,4,6-trichloro-1,3,5-triazine under mild conditions [42], sulfamic acid [43], Glycerol as a solvent without catalyst [44], NH_4Cl [45], Silica sulfuric acid [46], $FeCl_3$/montmorillonite K-10 [47], Sm $(OTf)_3$ [48-49], Lithium bromide [50] and nano BF_3/SiO_2 [51]. However, many of these procedures suffer from one or more disadvantages such as harsh reaction conditions, prolonged reaction time period, poor yields with formation of many side products and use of large quantity of volatile organic solvents. So, the development of a clean, high yielding and ecofriendly approach is still desirable. In order to avoid the above disadvantages we used the aqueous medium under ultra sound irradiation in presence of NBS to accomplish good results. NBS is trouble-free for work up process which is simply soluble in water medium.

The toxic and volatile natures of many organic solvents have posed serious environmental problems. Due to this organic reaction in aqueous media have attracted much attention in synthetic organic chemistry because water is one of the most abundant, cheap and environmental friendly solvent however there are very few reports for synthesis of benzothiazoles in aqueous media. Ultrasound irradiation has been established as an important technique in synthetic organic chemistry. It has been used as an efficient energy source for the organic reactions. Simple experimental procedure, very high yields, increased selectivity and clean reaction of many ultrasound induced organic transformations offers additional convenience in the field of synthetic organic chemistry [52-55]. These finding promotes us to investigate the synthesis of benzothiazoles in aqueous media.

2. Materials and Methods

Melting points were determined in open-end capillaries and are uncorrected. Compounds were checked for their purity by TLC on silica gel G plates and spots were located by iodine vapors. The IR spectra were recorded on Perkin-Elmer spectrum RX IFT-IR System using KBr pellets. Ultra sonication was performed using BANDELIN SONOREX ® (Germany) 4D ultrasound cleaner with a frequency of 50 KHz and an output power of 480 W. The flask was located at the maximum energy area in the cleaner and addition or removal of water was used to control the temperature of the water bath. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400.1 and 100.6 MHz. Chemical shifts are given in ppm (δ) and are referenced to the residual proton resonances of the solvents. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$-*d* or DMSO-*d*6 as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm, DMSO at 2.50 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, DMSO at 40.00 ppm.

General Procedure for the Preparation of 3(a-j):

O-aminothiophenol (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask and irradiated by ultrasound for 15 min at room temparature. After formation of Schiff's base, NBS (0.266 g, 0.0015 mol) is added and raised the temperature to 70^{o}C and irradiated until the completion of starting compounds. The reaction progress was monitored by thin layer chromatography (TLC), ethyl acetate: hexane (3:2). After completion of the reaction, 20% NaOH solution was added and extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure; the crude material was purified by column chromatography over silica gel to afford products 3(a-j) with high purity. All the products were identified by spectral (IR, ^{1}H NMR, ^{13}C NMR) and analytical data.

Spectral data for selected compounds.

2-Phenyl-1,3-benzothiazole (3a):

IR (KBr): 3060, 3020, 1630, 1590, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 – 8.07 (m, 3H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.47 (m, 4H), 7.38 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 154.1, 135.1, 133.6, 130.9, 129.0, 127.6, 126.3, 125.2, 123.2, 121.6.

2-(4-Chlorophenyl) benzothiazole (3b):

IR (KBr): 3081, 3032, 1628, 1593, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.2 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.52–7.36 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 154.0, 137.0, 135.0, 132.1, 129.2, 128.7, 126.5, 125.4, 123.3, 121.6.

2-(4-Bromophenyl) benzothiazole (3c):

IR (KBr): 3000, 1400-1600, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8.0 Hz, 1H), 8.0 (d, *J* = 8.5 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.55 (t, *J* =8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ, 167.11, 154.52, 135.48, 133.00, 132.66, 129.34, 126.93, 125.87, 125.85, 123.76, 122.01.

2-(4-Nitrophenyl) benzothiazole (3d):

IR (KBr): 1605, 1518, 1341, 1311, 1250, 1107, 968, 851, 765,751, 729, 685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (brs, 4H), 8.19 (d, *J* = 7.2 Hz, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 7.64 (t, *J* = 7.1 Hz, 1H), 7.58 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 154.5, 146.8, 139.3, 134.9, 128.2, 127.0, 126.4, 124.1, 123.8, 121.6.

2-(4-Methylphenyl) benzothiazole (3e):

IR (KBr): 3026, 2811, 2343, 1606, 1581, 1520,760, 685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.00-8.06 (m, 3H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.4 Hz, 1H), 7.41 (t, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 154.2, 141.6, 135.0, 131.0, 129.7, 127.3, 126.2, 125.0, 122.9, 121.6, 21.2.

2-(4-N,N-Dimethylphenyl) benzothiazole (3f):

IR (KBr): 3355, 2358, 1598, 1478, 1210, 1017, 965, 743 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (t, *J* = 8.7 Hz, 3H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 8.9 Hz, 2H), 3.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 154.4, 152.2, 134.5, 128.9, 126.0, 124.2, 122.3, 121.4, 121.3, 111.7, 40.1

2-(3-Methoxyphenyl) benzothiazole (3g):

IR (KBr): 3544, 1754, 1630, 1450, 1100, 1200, 950, 650 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.67-7.52 (m, 2H), 7.48-7.30 (m, 3H), 7.18-7.00 (m, 1H), 3.87 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 158.4, 154.1, 135.1, 133.8, 129.9, 126.6, 125.8, 123.4, 121.3, 120.8, 117.9, 113.1, 55.2.

2-(2-Methoxyphenyl) benzothiazole (3h): IR (KBr): 3560, 1760, 1625, 1465, 1190, 1145, 950 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.6 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.47-6.99 (m, 5H), 4.00(3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 157.5, 154.8, 136.1, 129.9, 128.7, 126.0, 125.6, 122.4, 121.9, 121.8, 113.7, 55.8.

2-(Pyridin-2-yl) benzothiazole (3i):

IR (KBr): 3053, 1405-1600, 685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, *J* = 4.7 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.38-7.41 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.80, 154.73, 151.85, 150.08, 137.41, 136.58, 126.70, 126.07, 125.67, 124.02, 122.44, 121.19.

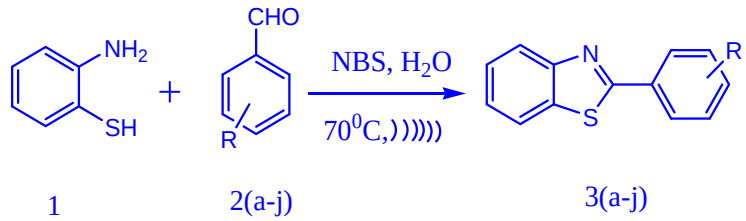
4-(benzothiazol-2-yl) benzenamine (3j):

IR: 3534, 3133, 1652, 1558, 1402, 1320,690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.5-8.2 (m, 4H), 6.5-7.2 (m, 4H), 4.0 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 226, 210, 149, 134, 76, 69, 57.

3. Results and discussion

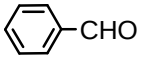
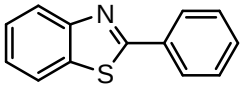
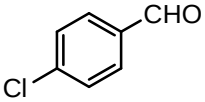
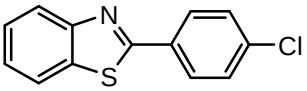
In the development of new and eco-friendly synthetic methodologies, we herein report an efficient, green and facile protocol for the synthesis of 2-substituted Benzothiazole (3a-j) catalyzed by NBS under ultrasound irradiation at 70°C in 13-25 min (Scheme 1). In this method Sonication was found to be better method giving high yields. The IR spectrum of the compound showed absorption peak at 3025 cm^{-1}, 1630 cm^{-1}, 690 cm^{-1} due to stretching of C-H, C=N, C-S. In sonication method, ultra sound will increase the collisions between the molecules and causes to form radicals very fast. So the rate of the reaction was increased. Here the solvent is water which is very effective solvent facilitate access to different reactivity and selectivity patterns and is also gracious to environment.

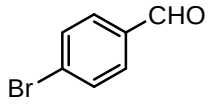
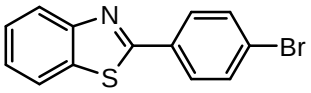
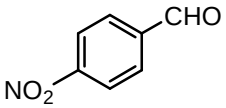
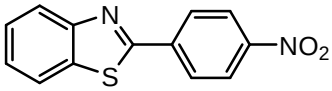
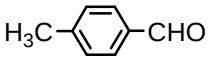
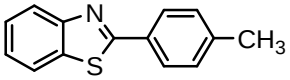
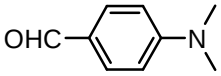
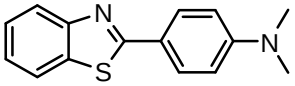
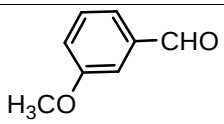
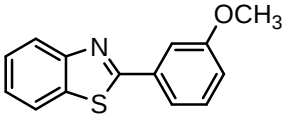
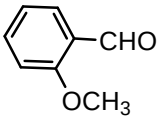
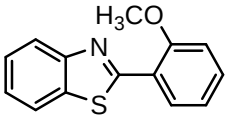
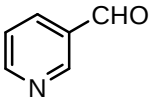
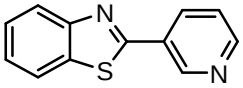
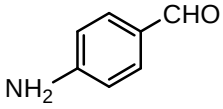
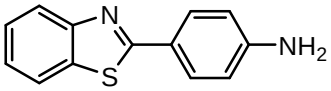
Scheme 1



Scheme I: The synthetic route was depicted in scheme I.

Table 1: Synthesis of 2-substituted Benzothiazole (3a-J)

Entry	Aldehyde	Product	Yield (%)
1			88
2			91

3			91
4			89
5			91
6			86
7			85
8			84
9			86
10			86

4. Conclusion

We have demonstrated a simple method for the synthesis of 2-substituted Benzothiazole using catalytic amount of NBS as ecofriendly and efficient catalyst under solvent free conditions in ultrasonication method. Short reaction times, high yields, a clean process, simple methodology, fast, easy work-up and green conditions are some advantages of this protocol. Performing organic reactions in water is safe, nontoxic, environmentally friendly, cheap, shorter reaction time and milder conditions, without generation of pollution.

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