Green Synthesis of Novel substituted 2-(1, 3-diphenyl-1H-pyrazol-3-yl) thiazole and using Ionic Liquid under Ultrasound and Microwave Condition

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ABSTRACT

A green protocol for the synthesis of series of novel substituted 2-(1, 3-diphenyl-1H-pyrazol-3-yl) thiazole is developed through the condensation of substituted 1, 3-diaryl pyrazole aldehyde and o-amino thiophenol in the presence of 1-butyl,3-methyl,1-imidazolium tetrafluoroborate [BMIM][BF4] as a catalyst under the conventional reflux condition, ultrasound and Microwave irradiation. The use of [BMIM][BF4] under USI and MWI conditions, and with easier isolation of the products in good yields makes this protocol eco-friendly and versatile compared to the conventional reflux conditions. The structures of the products were confirmed by IR, Mass, 1H-NMR, 13C-NMR spectral data.

Keywords: 1, 3-diaryl pyrazole aldehyde, Microwave, Ultrasound, Thiazole, [BMIM][BF4].

I. INTRODUCTION

Ionic liquids (ILs) offer an excellent and environmentally benign technique for the synthetic chemistry. The application of ionic liquids as reaction media and catalyst can offer a solution to solvent emission and catalyst recycle problems. Ionic liquids possess the important properties like negligible vapor pressure, thermal stability, recyclability, and higher solubility. Nowadays, ionic liquids have been successfully employed as solvents as well as catalyst for a variety of reactions [1-4]. ILs has been successfully used for various organic reactions like diels-alder reaction, electrochemical reaction, esterification, friedel-Craft reaction, hydrogenation, multicomponent reaction, coupling reaction [5-9].

The benzothiazole and their derivatives are an important class of heterocyclic compounds in medicinal, industrial, agricultural and synthetic organic chemistry. They are widely found in bioorganic and medicinal chemistry with applications in drug discovery such as antitumor, anticonvulsant, and antiviral applications [10–16]. They also found applications in industry as antioxidants, vulcanization accelerators, and as a dopant in a light-emitting organic electroluminescent device [17, 18]. Also the benzothiazole is an important nucleus in some rigid-rod polymer possessing high tensile strength, thermal stability and modulus [19, 20].

Many routes have been reported in the literature for the synthesis of benzothiazoles derivatives. However the most commonly used method involves the reaction of o-amino-thiophenols with substituted benzaldehydes in the presence of a catalyst such as animal bone meal, ZnBr2/ABM, ZnCl2/ABM, CuBr2/ABM [21], Pt/Al2O3 [22], SiO2 [23], vanadium...
(IV)-salen complexes [24], Fe(III)3/TEMPO [25], α-benzene disulfonylazide [26], sodium dodecyl sulfate [27], H2O2/CAN [28], cetyl trimethyl ammonium bromide (CTAB) [29], molecular iodine [30], p-TSA [31], diethyl bromophosphonate, tert-butyl hypochlorite [32], methanesulfonic acid/SiO2 [33], NaHSO4-SiO2 [34], H2O2/Fe(NO3)3 [35], silica, montmorillonite K-10 [36], PPA [37], etc.

The precursor substituted 1,3-diphenyl pyrazole aldehydes were synthesized by the Vielsmeier Haack formylation reaction. Firstly the phenyl hydrazone derivative was prepared from the reaction of differently substituted acetophenone with phenyl hydrazine in the presence of glacial AcOH in ethanol and then formylation of hydrazone in presence of N,N-dimethyl formamide and Phosphorous Oxichloride yield substituted 1,3-diphenyl pyrazole aldehyde [38]. These pyrazole aldehyde analogues have acknowledged significant attention because of their broad range of pharmacological and biological activities [39-41]. Thus the pyrazole aldehydes are used to gain more powerful biologically active heterocyclic systems.

II. METHODS AND MATERIAL

GENERAL PROCEDURE FOR THE SYNTHESIS OF BENZO[D]THIAZOLE DERIVATIVES

A) UNDER REFLUX CONDITION

A mixture of 3-aryl-1-phenyl-1H-pyrazole-4-carboxaldehyde 1 (1 mmol), α-aminothiophenol 2 (1 mmol) and a catalytic amount of [BMIM][BF4] (10 mmol %) was taken in a round bottom flask containing 10 mL of ethanol. The reaction mixture was refluxed for completion of the reaction. The course of the reaction was monitored by thin layer chromatography. After completion of the reaction the mixture was poured into crushed ice. Solid product was separated by filtration, dried well, and recrystallised by ethanol. The physical data of synthesized compounds are given in Table 2.

B) UNDER US IRRADIATION

A mixture of 3-aryl-1-phenyl-1H-pyrazole-4-carboxaldehyde 1 (1 mmol), α-aminothiophenol 2 (1 mmol) and catalytic amount of [BMIM][BF4] (10 mmol %) was taken in a round bottom flask containing 10 mL of ethanol. The round bottom flask was placed in an US bath for 7-9 min at room temperature. The course of the reaction was monitored by thin layer chromatography. After completion of the reaction the mixture was poured into crushed ice. Solid product derivative was separated by filtration, dried well, and recrystallised by ethanol. The same procedure was applied for the remaining substituents for confirming the consistency of the method. The physical data of synthesized compounds are given in Table 2.

C) UNDER MW IRRADIATION

A 10 mL round bottom flask was charged with 3-aryl-1-phenyl-1H-pyrazole-4-carboxaldehyde 1 (1 mmol), α-aminothiophenol 2 (1 mmol), catalytic amount of [BMIM][BF4] (10 mmol %), and placed under MW irradiation at 210 W for 3-5 min. The course of the reaction was monitored by thin layer chromatography. After completion of the reaction the mixture was poured into crushed ice. Solid product thus obtained was separated by filtration, dried well, and recrystallised by ethanol. The same procedure was applied for the remaining substituents for confirming the consistency of the method. The physical data of synthesized compounds are given in Table 2.
Scheme I: Synthesis of substituted 2-(1, 3-diphenyl-1H-pyrazol-3-yl)benzo[d]thiazole

III. RESULTS AND DISCUSSION

To achieve an optimum condition, o-aminothiophenol 2 (1 mmol) were treated with 1-phenyl-3- p-tolyl-1H-pyrazole-4-carbaldehyde 1a (1 mmol) in ethanol with catalyst [BMIM][BF₄] as a model reaction. It was observed that, the reaction did not proceed in the absence of [BMIM][BF₄] and the good results were obtained with 10 mmol % [BMIM][BF₄] under reflux condition; thus the catalyst is essential for the synthesis of benzthiazoles (Table 1, Entry 6).

Reaction Condition- benzil 1 (1eq), substituted 1, 3-diaryl pyrazole aldehyde 2 (1eq), ammonium acetate 3 (2eq) and Molar ratio [BMIM] [BF₄]/substrate

When the same reaction was carried out under ultrasound irradiation at room temperature, the desired product was obtained with high yield in few minutes (Table 1, Entry 7). Also under microwave irradiation, the model reaction at 140 W did not work, but it proceeds with the best results at 210 W (Table 1, Entry 9).

B) Table 2: Synthesis of 3(a-i) using [BMIM] [BF₄]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar – Group</th>
<th>Reaction in Min.</th>
<th>Time</th>
<th>Yield in %</th>
<th>MP in (°C)</th>
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<tr>
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<tr>
<td>3a</td>
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<td>240 9 4</td>
<td>80 86 90</td>
<td>144</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td></td>
<td>240 7 4</td>
<td>82 92 92</td>
<td>126</td>
<td></td>
</tr>
</tbody>
</table>
C) Spectral Data of Synthesized Compounds

3a: 2-(1-phenyl-3-p-tolyl-1H-pyrazol-4-yl)benzo[d]thiazole: Yellow Solid; M.P. 144°C; FT-IR (KBr) ν: 2917, 1593, 1554, 1505, 1407, 1217, 1044, 749; 1H NMR (DMSO-d6, 400 MHz) δ: 2.38 (s, 3H, Ar-CH3), 7.295 (d, 2H, Ar-H), 7.37-7.42 (m, 2H, Ar-H), 7.48-7.57 (m, 3H, Ar-H), 7.63 (d, 2H, Ar-H), 7.96 (d, 1H, J=7.6 Hz, Ar-H), 8.04 (t, 3H, J=7.6 Hz, Ar-H), 9.25 (s, 1H, Pyrazole ring-H); 13C NMR (DMSO-d6, 100 MHz) δ: 20.93, 116.40, 118.82, 122.01, 125.02, 126.35, 127.11, 128.88, 128.95, 129.11, 129.61, 129.90, 134.45, 138.44, 138.84, 150.97, 152.84, 159.56; MS: m/z=368.32 [M+1]+.

3b: 2-(1,3-diphenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Faint Yellow Solid; M.P. 126°C; FT-IR (KBr) ν: 1594, 1557, 1504, 1406, 1218, 1046, 759, 749; 1H NMR (DMSO-d6, 400 MHz) δ: 7.33-7.45 (m, 2H, Ar-H), 7.47-7.54 (m, 4H, Ar-H), 7.52 (t, 2H, Ar-H), 7.76-7.85 (m, 2H, Ar-H), 7.98 (d, 1H, Ar-H), 8.05-8.09 (m, 3H, Ar-H), 8.42 (s, 1H, Pyrazole ring-H); MS: m/z=354.28 [M+1]+.

3c: 2-3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Yellow Solid; M.P. 170°C; FT-IR (KBr) ν: 1595, 1556, 1472, 1312, 1218, 1158, 1046, 751; 1H NMR (DMSO-d6, 400 MHz) δ: 7.33-7.35 (m, 2H, Ar-H), 7.37-7.45 (m, 2H, Ar-H), 7.51-7.54 (m, 1H, Ar-H), 7.56-7.60 (m, 2H, Ar-H), 7.84-7.87 (m, 2H, Ar-H), 7.98 (d, 1H, Ar-H), 8.05 (dd, 2H, Ar-H), 8.09 (d, 1H, Ar-H), 9.31 (s, 1H, Pyrazole ring-H).

3d: 2-(3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Yellow Solid; M.P. 170°C; FT-IR (KBr) ν: 1598, 1559, 1505, 1447, 1394, 1209, 1061, 930, 755; 1H NMR (DMSO-d6, 400 MHz) δ: 7.44 (t, 2H, Ar-H), 7.53 (t, 1H, Ar-H), 7.58 (m, 4H, Ar-H), 7.85 (d, J=6.4 Hz, 2H, Ar-H), 7.98 (d, J=6.4 Hz, 1H, Ar-H), 8.05 (d, J=6.4 Hz, 2H, Ar-H), 8.10 (d, J=6.4 Hz, 1H, Ar-H), 9.32 (s, 1H, Pyrazole ring-H); 13C NMR (DMSO-d6, 100 MHz) δ: 116.87, 119.44, 122.58, 122.83, 125.68, 126.93, 127.81, 128.92, 130.15, 130.98, 131.22, 131.48, 13.24, 134.94, 139.25, 150.06, 153.43, 159.77; MS: m/z=388.26 [M+1]+.

3e: 2-(3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: White Solid; M.P. 190°C; FT-IR (KBr) ν: 1597, 1546, 1502, 1478, 1218, 1033, 1010, 751; 1H NMR (DMSO-d6, 400 MHz) δ: 7.43 (m, 2H, Ar-H), 7.49 (m, J=7.6 Hz, 1H, Ar-H), 7.58 (t, 2H, Ar-H), 7.71 (m, 2H, Ar-H), 7.77 (m, 2H, Ar-H), 7.98 (d, 2H, Ar-H).
1H, Ar-H), 8.05 (d, J=6.0 Hz, 2H, Ar-H), 8.10 (d, J=6.0 Hz, 1H, Ar-H), 9.31 (s, 1H, Pyrazole ring-H).

3f: 2-(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Brown Solid; M.P. 194˚C; FT-IR (KBr) v: 1597, 1563, 1506, 1394, 1340, 1314, 1033, 933, 852, 753; 1H NMR (DMSO-d₆, 400 MHz) δ: 7.10 (dd, 2H, Ar-H), 7.41-7.60 (m, 5H, Ar-H), 7.99-8.19 (m, 5H, Ar-H), 8.35 (d, J=5.6 Hz, 1H, Ar-H), 9.39 (s, 1H, Pyrazole ring-H).

3g: 2-(1-phenyl-3-(thiophen-2-yl)-1H-pyrazol-4-yl)benzo[d]thiazole: Yellow Solid; M.P. 92˚C; FT-IR (KBr) v: 1595, 1561, 1501, 1473, 1310, 1224, 1033, 751; 1H NMR (DMSO-d₆, 400 MHz) δ: 6.44 (t, 1H, Ar-H), 6.75 (dd, J=5.2 Hz, 1H, Ar-H), 7.02 (dd, 1H, Ar-H), 7.09 (t, 1H, Ar-H), 7.58 (m, 2H, Ar-H), 7.69 (dd, 1H, Ar-H), 8.02 (m, 2H, Ar-H), 8.08 (d, J=6.4 Hz, 1H, Ar-H), 8.14 (d, J=6.4 Hz, 1H, Ar-H), 8.19 (m, 1H, Ar-H), 9.31 (s, 1H, Pyrazole ring-H); 13C NMR (DMSO-d₆, 100 MHz) δ: 116.27, 119.38, 122.94, 125.85, 126.98, 127.83, 128.19, 129.29, 130.16, 131.61, 133.98, 134.91, 135.04, 139.04, 150.17, 153.54, 159.73; MS: m/z=360.26 [M+1]+.

3h: 2-(3-(3-bromo-4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Yellow Solid; M.P. 186˚C; FT-IR (KBr) v: 1598, 1558, 1506, 1447, 1405, 1234, 1048, 937, 747; 1H NMR (DMSO-d₆, 400 MHz) δ: 6.47 (m, 1H, Ar-H), 6.78 (dd, J=5.2 Hz, 1H, Ar-H), 7.07 (m, 1H, Ar-H), 7.19 (m, 1H, Ar-H), 7.31 (t, 1H, Ar-H), 7.49 (m, 3H, Ar-H), 7.83 (d, 2H, Ar-H), 7.90 (m, 1H, Ar-H), 8.05 (s, 1H, Pyrazole ring-H), 8.20 (m, 1H, Ar-H).

3i: 2-(3-(3,5-difluorophenyl)-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole: Faint Yellow Solid; M.P. 160˚C; FT-IR (KBr) v: 1628, 1594, 1562, 1432, 1396, 1202, 1114, 1033, 983, 748; 1H NMR (DMSO-d₆, 400 MHz) δ: 6.51 (m, 1H, Ar-H), 6.74 (dd, 1H, Ar-H), 7.10 (dd, 1H, Ar-H), 7.21 (m, 1H, Ar-H), 7.26-7.32 (m, 2H, Ar-H), 7.52 (t, 2H, Ar-H), 7.69 (d, 2H, Ar-H), 7.86 (d, 2H, Ar-H), 8.11 (s, 1H, Pyrazole ring-H).

IV. ABBREVIATIONS

MWI-Microwave Irradiation, USI-Ultrasound Irradiation, MCRs-Multicomponent Reactions, SF-Solvent Free, ILs-Ionic liquids, NR-No Reaction, RT-Room Temperature, [BMIM][BF₄]-1-butyl, 3-methyl, 1-imidazolium tetra floroborate.

V. CONCLUSION

In summary, we have described a novel simple, fast and environmentally benign protocol for the synthesis of 2-(3-aryl-1-phenyl-1H-pyrazol-4-yl)benzo[d]thiazole from 3-aryl-1-phenyl-1H-pyrazole-4-carbaldehyde and o-aminothiophenol in the presence of [BMIM][BF₄] under conventional reflux condition, US and MW irradiation. The present protocol avoids the use of less hazardous solvent, toxic catalysts, and long reaction times.

VI. REFERENCES


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