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## A mild and efficient synthesis of Benzimidazole by using lead peroxide under solvent free condition

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### ABSTRACT

*Benzimidazoles derivatives have been synthesized using a catalytic amount of Zinc acetate at room temperature with excellent yields. The remarkable selectivity under mild, neutral and solvent free conditions, commercially available inexpensive catalyst is an attractive feature of this method.*

**Key words:** benzimidazoles, Zinc acetate, solvent free

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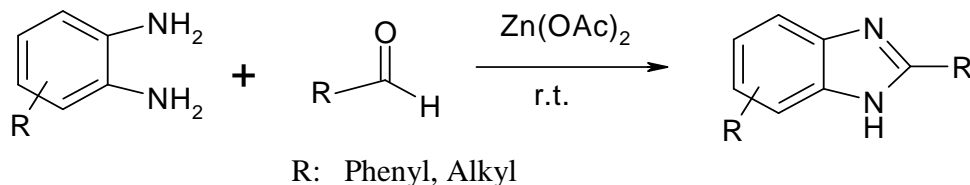
### INTRODUCTION

The development of simple, efficient, environmentally-benign and economically viable chemical processes or methodologies for widely used organic compounds is in great demand<sup>1</sup>. Benzimidazole are present in various bioactive compounds possessing antiviral, antihypertension and anticancer properties<sup>2,3</sup>. Compounds possessing the benzimidazole moiety express significant activity against several viruses such as HIV<sup>4</sup>, Herpes(HSV-1)<sup>5</sup> and influenza<sup>6</sup>. Bis-benzimidazole is DNA-minor groove binding agents possessing anti-tumour activity<sup>7</sup>.

The condensation of o-phenylenediamine with carbonyl compounds in the presence of strong acids such as polyphosphoric acid or mineral acids<sup>8</sup> and other reagents such as I<sub>2</sub>/KI/K<sub>2</sub>CO<sub>3</sub><sup>9</sup>, N-halosuccinamide (X=Cl, Br, I)<sup>10</sup>, Yb(OTf)<sub>3</sub><sup>11</sup>, PEG-100<sup>12</sup>, (NH<sub>4</sub>)H<sub>2</sub>PW<sub>12</sub>O<sub>40</sub><sup>13</sup> and palladium as well as microwave irradiation<sup>14</sup> and solid phase reactions<sup>15</sup> are reported in literature. However, many of the synthetic protocols reported so far suffer from disadvantages, such as a requirement for anhydrous conditions, use of organic solvents, harsh reaction conditions, prolonged reaction

times, expensive reagents and low to moderate yields. Almost all the reported methods make use of an acid catalyst, giving rise to tedious working procedures. Therefore, the development of a cost-effective, safe and environmentally friendly reagent is still needed.

Scheme – 1



In this communication, we report a simple and efficient method for synthesis of benzimidazole derivatives using zinc acetate as a catalyst under mild conditions.

### MATERIALS AND METHODS

All reagents and solvents for syntheses were commercially available and used without further purifications

#### General Procedure

A mixture of o-phenyldiamine (2 m mol), p-nitrobenzaldehyde (2 m mol) and Zinc acetate (0.1m mol) was stirred magnetically at room temperature and the progress of the reaction was monitored by thin-layer chromatography (TLC). The reaction mixture was filtered and extracted with ethyl acetates (3x30ml). The combined ethyl acetates extracts were dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. In all the cases, the product obtained after the usual work up gave satisfactory spectral data.

### RESULTS AND DISCUSSION

A wide variety of compounds were applied under optimal reaction conditions to prepare benzimidazoles. The results are summarized in Table-2. Variety of aldehydes, aliphatic, heterocyclic and aromatic having both electron- donating and electrone withdrawing groups were employed for benzimidazole formation. In all cases, the yields were excellent. (Table-2, entries 1-18). Four different types of o-phenylenediamines were employed and all of them reacted smoothly under the reaction conditions. The aliphatic aldehydes which were also reacted under similar conditions gave considerable yields (Table-2, entries 12-13). The spectral data of products were confirmed by IR and NMR.

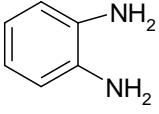
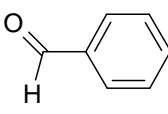
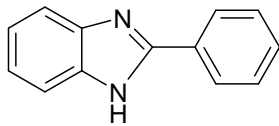
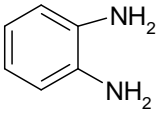
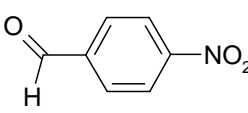
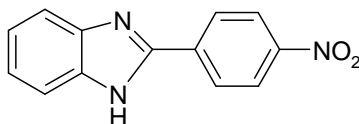
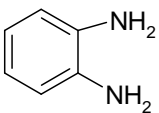
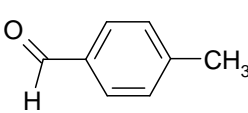
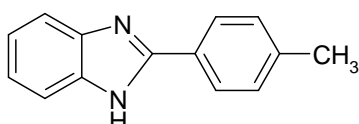
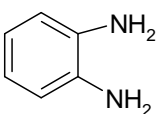
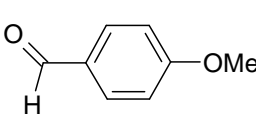
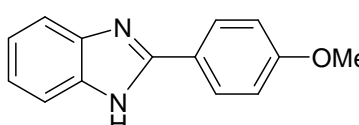
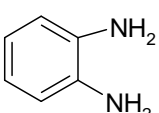
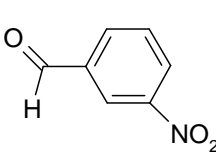
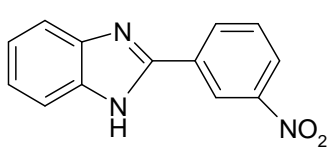
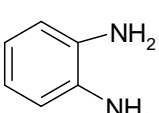
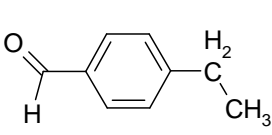
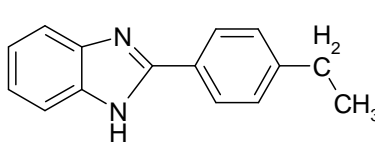
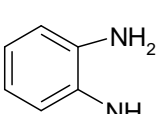
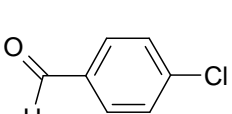
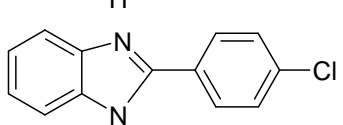
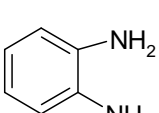
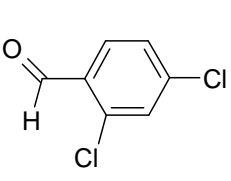
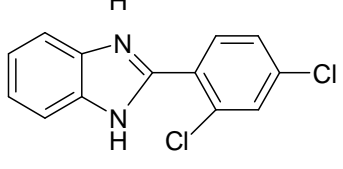
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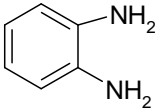
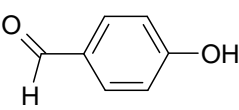
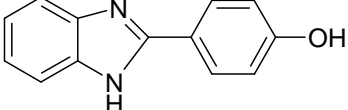
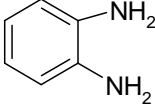
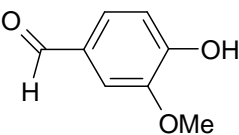
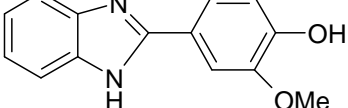
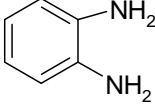
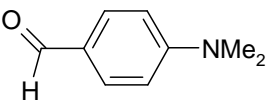
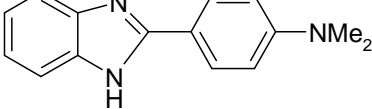
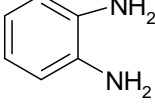
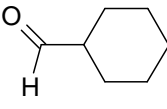
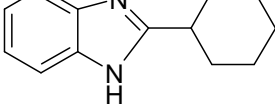
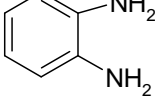
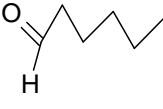
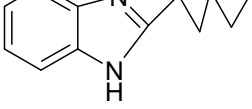
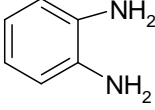
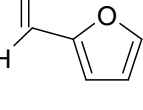
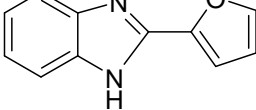
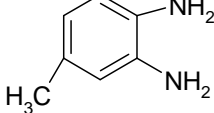
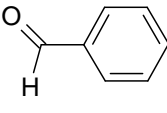
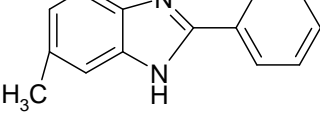
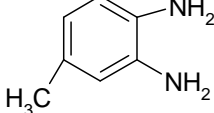
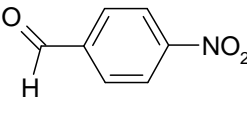
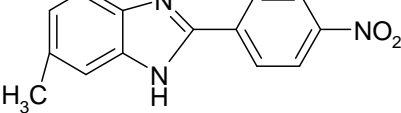
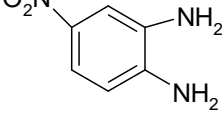
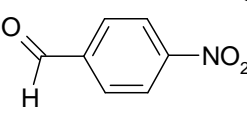
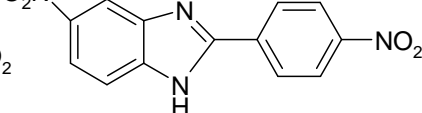
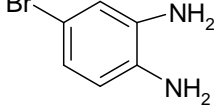
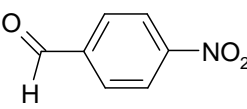
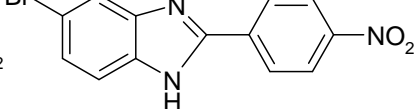
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**Entry 5:** IR (KBr): 837, 925, 1045, 1109, 1129, 1355, 1544, 1629, 2988, 3479  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (300MHz, DMSO):  $\delta$  = 7.2( m, 2H), 7.55 (d, broad,  $J=7.5\text{Hz}$ , 1H) ; 7.62 (d, broad,  $J= 7.5\text{Hz}$ , 1H); 8.21(d,  $J= 6.8\text{Hz}$ , 1H); 8.55(d,  $J= 7.8\text{Hz}$ , 1H); 9.12 (s, 1H), 12.5 (s, 1H)

**Entry 9:** IR (KBr): 732, 815, 1036, 1537, 1627, 2929, 3329, 3478  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (300MHz, DMSO):  $\delta$  = 5.2 (s, 1H), 7.3( s, broad, 2H), 7.5 (d, 2H,  $J=7.6\text{Hz}$ , 2H) ; 7.8 (m, 2H); 8.2(d,  $J=7.6\text{Hz}$ , 2H); 12.1 (s, 1H)

**Table- 2. Synthesis of benzimidazole in presence of  $\text{Zn}(\text{OAc})_2$  at room temperature**

Entry	1,2-Diamine <sup>a</sup>	Aldehyde	Product <sup>b</sup>	Time(min)	Yield <sup>c</sup> (%)
1.				10min	92
2.				10min	94
3.				10min	92
4.				15min	90
5.				20min	91
6.				15min	90
7.				10min	90
8.				20min	91

9.				25min	85
10.				40min	87
11.				40min	91
12.				40min	84
13.				50min	87
14.				50min	89
15.				10min	93
16.				10min	92
17.				10min	94
18.				20min	92

<sup>a</sup> The substrate was treated with benzaldehyde (2 mmol) by using 0.1 mmol of Zn(OAc)<sub>2</sub> in solvent free conditions and at room temperature.

<sup>b</sup> All products were identified by their IR and <sup>1</sup>H NMR spectra

<sup>c</sup> Isolated yields.

## CONCLUSIONS

In conclusion, this manuscript describes a method in which  $\text{Zn}(\text{OAc})_2$  is a highly efficient catalyst for the synthesis of benzimidazole derivatives. The advantages include low cost, ease of catalyst handling, mild reaction conditions and reactions carried out at room temperature with excellent yields.

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