# "GREEN SYNTHESIS OF BENZOXAZOLE DERIVATIES AND THEIR CHARACTERIZATION"

**P.R. Padole[1], H. G. Wankhade[1], B. N. Berad[1], P.P.Choudhari[2] and S. S. Ubarhande[2]**
1. Shri Shivaji Science College, Amravati (MS)
2 G.S. Tompe Arts, Commerce And Science College, Chandure Bazar (MS)

**ABSTRACT**
Synthesis of Benzoxazolederivatives by simple condensation of 2-aminophenol and different aromatic amd aliphatic acid in ethanol as solvent in presence of $NH_4Cl$ as catalyst at 80-90$^{o}$C. It give very good yield and the process was totally fallow green path and economically viable. Benzoxazolederivatives have many medicinal and other biological properties.. The characterization of newly synthesized compounds was made by chemical properties, elemental analysis and FT-IR,$^{1}$H-NMR and Mass Spectra. The advantage of this method is extremely mild reaction conditions, short reaction time, high yield, simple experimental technique and compliance with green chemistry protocols.
**KEYWORDS**- Green synthesis, benzaoxazole and their characterization.

## 1.INTRODUCTION

Molecules with benzoxazole, benzimidazole and benzothiazole moieties are attractive targets for synthesis since they often exhibit diverse and important biological properties. These heterocycles have shown different pharmacological activities such as antibiotic [1], antifungal [2], antiviral [3], anticancer[4], antimicrobial [5], and antiparkinson[6] properties. They have also been used as ligands for asymmetric transformations [7]. Benzimidazole derivatives are unique and broad spectrum classes of antirhino/enteroviral agents such as antiulcerative[8] and antiallergic[9] are effective against the human cytomegalovirus[10] and are also efficient selective neuropeptide Y Y1 receptor antagonist[11].Benzoxazoles are an important class of heterocyclic compounds that have many applications in medicinal chemistry. For example, benzoxazole derivatives have been characterized as melatonin receptor agonists,[12]amyloidogenesis inhibitors, Rho kinase inhibitors,[13] and antitumor agents.[14] In addition to their use in medicinal chemistry, benzoxazoles are recognized as an important scaffold in fluorescent probes such as anion and metal cation sensors.[15]
Benzoxazoles are an important class of heterocycles that are encountered in a number of natural products and are used in drug and agrochemical discovery programs, as well as for a variety of other purposes. For example, the benzoxazole core structure is found in a variety of cytotoxic natural products, such as the UK-1,[16] AJI9561,[17] and salvianen.[18] Recent medicinal chemistry applications of benzoxazoles include the cathepsin S inhibitor,[19] selective peroxisome proliferator-activated receptor $\gamma$ antagonist JTP-426467.[20]Other applications of benzoxazoles include their use as herbicides, such as Fenoxaprop, and as fluorescent whitening agent dyes such as bisbenzoxazolylethylenes and arenes .[21] Several synthetic methodologies were available for the synthesis of benzoxazoles .Generally the condensation of 2-aminophenol with different aromatic aldehyde , aromatic acids and their nitrile,imide and orthoesters derivatives have been widely used for benzoxazoles

## 2. EXPERIMENTAL

2.1The melting points of all synthesized compound were recorded using hot paraffin bath and are uncorrected. $^{1}$H NMR spectra ($CDCl_3$) were recorded on Bruker Advance II 400 NMR spectrophotometer using TMS as internal standard. IR spectra were recorded on Perkin-Elmer-1800 FTIR spectrophotometer in the frequency range 4000-450 cm$^{-1}$ in Nujol mull and as KBr pellets. Mass spectra were recorded on a LC-MS Q-Tof Micro, Mass analyzer (Shimadzu). Chemicals used were of AR grade. The purity of the compound was checked on silica gel-G plates by TLC.

2.2 **General procedure for the preparation of 2-(4-chlorophenyl) benzooxazole.**

Preparation of 2-(4-chlorophenyl)benzooxazole was carried out by 2-aminophenol (1.09 gm) and p-chlorobenzoic acid (1.56 gm)in presence of ammonium chloride (0.5 gm) as catalyst in 4-5 ml of ethanol. The resulting mixture was stirred for 6-8 hr at 80$^{0}$c. After complition of reaction, the reaction mixture was poured into ice cold water and product was precipited out as brownish solid. It was crystallized from ethanol to yield 2-(4-chlorophenyl) benzo[d] oxazole, yield 88% m.p 270$^{0}$C. The molecular formula was established as $C_{13}H_9ClNO$.IR(KBr) , ν = 1515 (C=N), ν =1587(C=C),ν = 1276(C-O), ν =807 1,4-disub Aromatic ring & ν =743 1,2-disub Aromatic ring cm$^{-1}$. $^{1}$H NMR ($CDCl_3$) 7.9 ppm (2H, m, Ar-H), δ7.6 ppm (2H, m, Ar-H), δ6.4 ppm (2H, m, Ar-H), δ6.6ppm (2H, m, Ar-H).Mass (m/z) 229 ($M^+$).

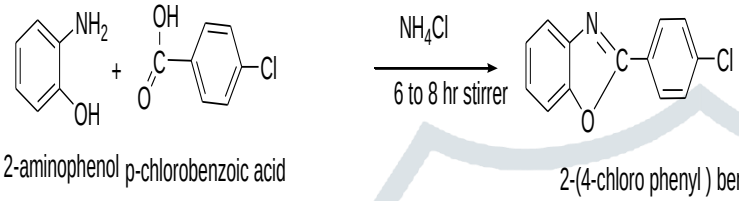
2.3**General procedure for preparation of 2-benzo oxazole 2-yl phenol.**

2-aminophenol (0.01 mole ) and salisylic acid (0.01 mole) both in stoichiometric proportion were taken in ethanol as solvent in presence of $NH_4Cl$ as catalyst .The reaction mixture was stirred for 6 to 8 hr at 80$^{0}$c on hot plate. After the completion of reaction, the reaction mixture was cooled and poured in the ice cold water. The granular solid was obtained. It was crystalized from the alcohol,yield 85% m.p 180$^{0}$c.IR(KBr) ν = 1509 (C=N), ν =1594(C=C),ν = 1244(C-O), $^{1}$H NMR ($CDCl_3$) 7.9 ppm (1H, m, Ar-H), δ7.6 ppm (1H, m, Ar-H), δ6.6 ppm (4H, m, Ar-H), δ6.3ppm and 6.4 ppm (1H, m, Ar-H).Mass (m/z) 211.6($M^+$).
All other compounds (3c-e) were synthesized in similar manner by treatment of (1) with substituted aromatic acids (2c- e) respectively **Table No.1**

**Table No.1: Reaction of o-phenylenediamine (1) (0.01 mole) with different aromatic acids (2) (0.01 mole) :**

| Sr. No | Product (3) | -R (2a-e) | Yield (%) | Melting Point$^0$C | Molecular Formula | Elemental analysis of N Found (Calcd.) (%) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N | 0 |
| 1 | 3a | p-chlorobenzoic acid | 88.78 | 270 | $C_{13}H_9ClNO$. | 66.12 (67.99) | 3.20 (3.51) | 6.00 (6.11) | 6.54 (6.97) |
| 2 | 3b | Salicylic acid | 89.18 | 180 | $C_{13}H_{10}O_2N$ | 73.23 (73.92) | 4.01 (4.29) | 6.22 (6.63) | 15.00 (15.15) |
| 3 | 3c | Benzoic acid | 78.08 | 70 | $C_{13}H_9NO$ | 79.56 (79.98) | 4.21 (4.65) | 6.98 (7.17) | 8.11 ( 8.20) |
| 5 | 3d | Cinnamic acid | 75.15 | 80 | $C_{15}H_{11}NO$ | 74.25 (74.47) | 4.56 (4.86 ) | 9.58 (9.65) | 10.85 ( 11.05) |
| 6 | 3e | Chloro acetic acid | 70.88 | 90 | $C_8H_6ClNO$ | 57.11 (57.33) | 3.50 (3.61) | 8.02 ( 8.36) | 9.35 ( 9.55) |

**REACTION SCHEME**




2-aminophenol p-chlorobenzoic acid

2-(4-chloro phenyl ) benzoxazole

**3.RESULTS AND DISCUSSION**

In order to synthesized substituted Benzaoxazole derivatives (3), a relatively more versatile yet simplified procedure was perceived. Our argument have been that an instantaneous condensation of 2-amino phenol and aromatic acid at 80- 90 $^oC$ to affords substituted Benzaoxazolewith the use of $NH_4Cl$ as catalyst. The strategy worked well affording the desired product in respectable yields. (Table No.1), the present reaction have been relatively faster, as anticipated, comp aired to those in conventional solution phase synthesis. It is necessary to mention that in all cases the conversion was never 100 %. Some amount of starting material recovered after each reaction.

**4.CONCLUSION**

In conclusion we have developed a simple methodology for the preparation of substituted Benzaoxazole derivatives (3).The advantage of this method are extremely mild reaction conditions , short reaction time , high yield , simple experimental technique and compliance with green chemistry protocols.

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