



## A Review on Synthesis And Various Reaction Of Benzoxazole

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### ABSTRACT

A number of methods have been reported for the preparation of these heterocycles including the condensation of carboxylic acids, orthoesters, acid chlorides, nitriles amides, aldehydes and esters with *o*-substituted amino aromatics derivatives from orthoesters. 2 amino phenyl or 5-amino (*p*-substituted phenyl) benzoxazoles were obtained by heating substituted benzoic acid with 2-4-diamino phenol in PPA (polyphosphoric acid). rapid and efficient condensation of 2-amino phenol with various aldehyde were carried out using  $I_2$  in solvent free condition with or without microwave irradiation to afford corresponding 2-substituted benzoxazole in good yield. benzoxazole have been synthesized in non-polar high boiling solvent such as toluene and xylene in model reaction addition amino phenol react with acid chloride in present of base.

**KEYWORDS:** Benzoxazole, 2-chloroacetyl mercaptobenzoxazole, Nitro benzoxazoles.

### INTRODUCTION:

The approach to practice medicinal chemistry has developed from an empirical one involving organic synthesis of new compound, based largely on modification of structures of known activity. According to Manfred Wolf, present development of medicinal chemistry has resistance, stating that "underlying the new age in foundation that includes explosive development of molecular biology since 1960, the advances in physical chemistry and physical organic chemistry has made possible by high speed computers and new powerful analytical methods.

Numerous heterocyclic compounds, cyclic anhydrates, cyclic imides, cyclic acetals of dihydroxy alcohols, the solvents, dioxanes and tetrahydrofuran, in all of these, the chemistry is essentially that of their open-chain analogues. Heterocyclic intermediates are being used more and more in synthesis as protecting groups, readily generated, and readily removed.

Benzoxazole moieties have attracted special attention in chemistry and biochemistry. These heterocycles show various pharmaceutical properties such as antiviral<sup>33</sup>, antibiotic<sup>27</sup>, antibacterial<sup>25</sup>, antifungal<sup>28</sup>, antitumor<sup>34</sup>, anti-inflammatory, antiulcer<sup>35</sup>, antitubercular<sup>36</sup>, analgesic<sup>26</sup> activities. Furthermore, some of them have found applications as fluorescent whitening agents,

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Generally in the pharmaceutical field, new drugs are continuously discovered by molecular modification of lead compound of established activity. Molecular modification can possibly result in augmenting the activity. Molecular modification involves combination of separate group having similar activity in one compound by eliminating, substituting or adding new moiety to parent lead compound. In the survey of literature, it is seen that drug

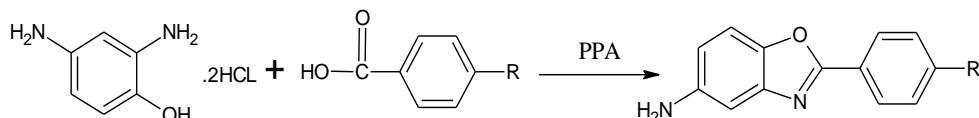
design by molecular modification is a productive source of new drug; therefore the need to synthesize new molecules as potential medicinal agents is more relevant today. Among medicinal agents, there is growing interest in the development of newer, effective antifungal and antimicrobial agents. Among the variety of compounds studied, benzoxazole derivatives form an important class.

## Benzoxazoles

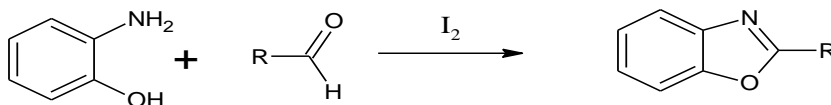
Oxazole is considered to be derived from furan by the replacement of  $-\text{CH}=\text{}$  (methane group) from the position - 3 by the azomethine nitrogen ( $-\text{N}=\text{}$ ). Oxazole ring system is numbered as follows.



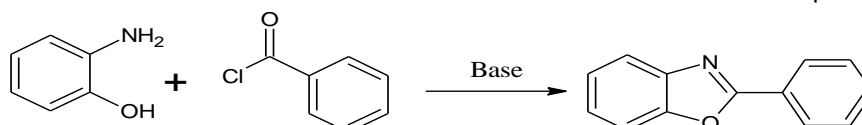
The chemistry of oxazoles began in 1876 with the synthesis of 2-methyloxazole., although parent oxazole 5 was synthesized in 1947.and 1962. The interest in the chemistry of oxazole was developed during the world war when the penicillin was consider to contains the oxazole ring system. But discovery of oxazoles as dienes in Diels-Alder reaction and in 1,3-dipolarcycloaddition reaction of mesotonic heterocycles gave impetus to the development of oxazoles chemistry.



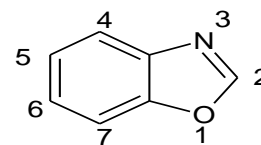
**2. Reaction of aldehydes:-** rapid and efficient condensation of 2-amino phenol with various aldehyde were carried out using  $\text{I}_2$  in solvent free



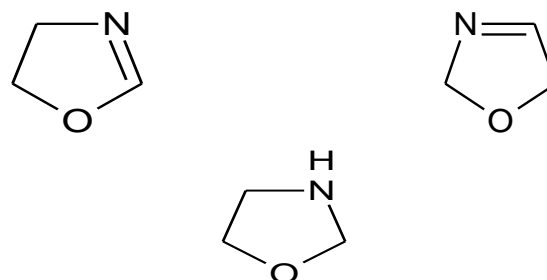
**3.Reaction with acid chloride:** - benzoxazole have been synthesized in non-polar high



The fusion of benzene ring to the 4,5-positions of the oxazole ring results in benzoxazole and numbering as follows.



Two partially saturated oxazoles with different position of double bond are possible and named as: 4,5-dihydro-(A) and 2,5-dihydro-(B) oxazoles. Fully saturated oxazoles are named as oxazolidine(C).



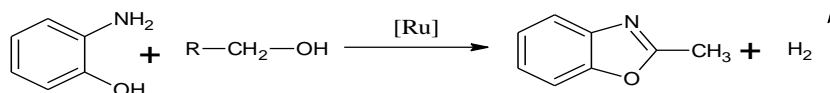
## 1.1 Synthesis of benzoxazole

**1. Reaction with Acid:** - 2 amino phenyl or 5-amino (p-substituted phenyl) benzoxazoles were obtained by heating substituted benzoic acid with 2-4-diamino phenol in PPA (polyphosphoric acid).<sup>20</sup>

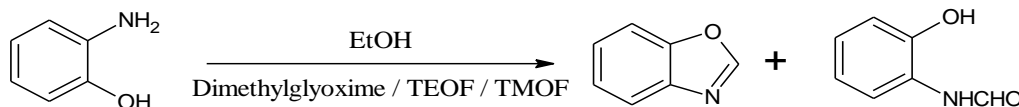
condition with or without microwave irradiation to afford corresponding 2-substituted benzoxazole in good yield.<sup>21</sup>

boiling solvent such as toluene and xylene in model reaction addition amino phenol react with acid chloride in present of base.<sup>22</sup>

4. **Reaction with alcohol:** - *O*-amino phenol reacts with alcohol in presence of a catalytic amount of a ruthenium complex to give 2-substituted benzoxazole in good yield.<sup>23</sup>

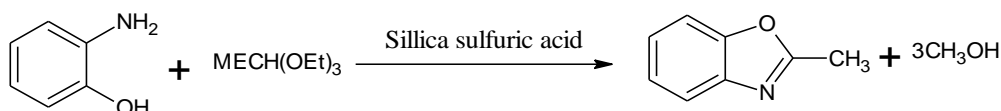


5. **Reaction with oximes:** - transformation of *o*-amino phenol with *O*-alkylated oxime in to benzoxazole.<sup>24</sup>



6. **Reaction with ester:** - A mixture of trialkyl orthoester, *o*-aminophenol, *O*-phenylenediamine or 2-amino-3-hydroxypyridine and silica sulfuric acid was stirred at room temperature or at 85 °C for the appropriate time. The progress of the reaction was monitored by TLC (eluent: *n*-hexane: ethyl acetate,

2:1). After completion of the reaction, the mixture was diluted with CHCl<sub>3</sub> (10 ml) and filtered. The solid material was washed with CHCl<sub>3</sub> and dried at 60 °C. The filtrate was evaporated and the residue was purified by recrystallization in *n*-hexane or by column chromatography on neutral alumina.<sup>25</sup>

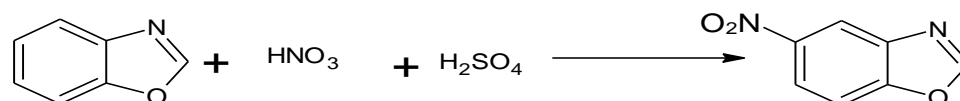


## 1.2 Reactions of Benzoxazoles:-

1. **Nitration:** The nitration of benzoxazole proceeds readily. In most cases nitration appears to take place preferentially in the 5 or 6 places. However the nitro

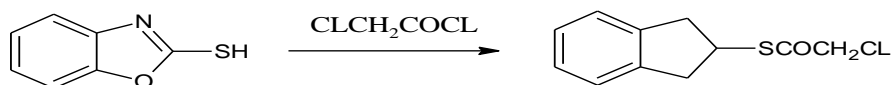
group may also enter 4 or 7- position, especially if 5 or 6 positions are blocked.

Nitro benzoxazoles that have been obtained by the nitration of benzoxazoles example is as under,



2. **Chloroacetylation:** 2-mercapto benzoxazole on chloroacetylation gave 2-chloroacetyl

mercaptobenzoxazole.<sup>26</sup>



3. **Alkylation:**

The reaction of sub. benzoxazole with butylcyclohexanol for 25 H gave

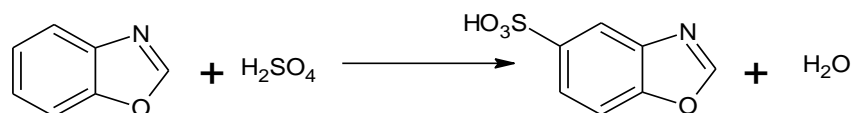
(2- butylcyclohexyloxy) benzoxazole.



4. **Miscellaneous reaction:**

Sulfonated benzimidazoles are obtained by the sulfonation of benzimidazoles with either sulfuric acid or chloro sulfonic acid. Treatment of benzimidazole with

concentrated sulfuric acid gives 5- benzimidazole sulfonic acid.



## Reported Pharmacological Activities of Benzoxazoles.

Benzoxazole and various derivatives of benzoxazoles possess a variety of Pharmacological activities. The few selected activity reported as under.

Large number of benzimidazoles are reported to possess trypanosomicidal and

pyrochitocidal action and active against diseases caused by protozoa. These compounds in most cases are derivatives of 2-(3H)-benzimidazole thione, or 2-(3H)-benzimidazolone.

The number of benzimidazoles related to the active anti-malarial activity these includes 2-benzimidazole propionic acid, 5-ethoxy benzimidazole 2-propionic acid and 5-ethoxybenzimidazolyl ethylamine.<sup>15-16</sup>

Benzimidazole shows anti-convulsant activity when administered in larger doses.

N-benzoyl benzimidazole shows only a trace of anti-convalescent activity.<sup>17</sup>

## CONCLUSION

From the above literature review concluded that these heterocycles show various pharmaceutical properties such as antiviral<sup>33</sup>, antibiotic<sup>27</sup>, antibacterial<sup>25</sup>, antifungal<sup>28</sup>, antitumor<sup>34</sup>, anti-inflammatory, antiulcer<sup>35</sup>, antitubercular<sup>36</sup>, analgesic<sup>26</sup> activities. Furthermore, some of them have found applications as fluorescent whitening agents.

1-dimethylaminoethylbenzimidazole and several related compounds containing substituents group in the second position of the benzimidazole were found to possess only slight anti-histaminic activity.<sup>18</sup>

Numbers of benzimidazoles and benzimidazole-2-thions have been tested for goitrogenic activity. In this main 2(3H) benzimidazole thione itself is a markedly goitrogenic.

A number of 5-benzimidazole sulfonamides have been prepared and tested for their antibacterial activity against *Pseudomonas aurigenosa*.<sup>19-20</sup>

A number of 2-alkylaminomethylbenzimidazoles have been prepared and is reported to be a local anaesthetic.<sup>21</sup>

2-(3H)-benzimidazolonecarboxylic acids as well hexahydro derivatives obtained by reduction of the benzene nucleus in these compounds have been investigated for antibiotic activity.<sup>22</sup>

The benzimidazole analog of pteric acid have been prepared and tested for their inhibitory active against *Streptococcus gaecalis* and *Lactobacillus casei*.<sup>23-24</sup>

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