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Review Article

STUDY ON MANNICH BASES OF BENZIMIDAZOLES: A REVIEW

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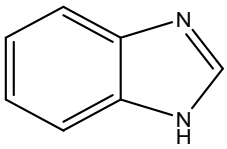
Nowadays, nitrogenous heterocyclic molecules have attracted a great deal of interest among medicinal chemists. Among these potential heterocyclic drugs, benzimidazole scaffolds are considerably prevalent. Due to their isostructural pharmacophore of naturally occurring active biomolecules, benzimidazole derivatives have significant importance as chemotherapeutic agents in diverse clinical conditions. Researchers have synthesized plenty of benzimidazole derivatives in the last decades, amidst a large share of these compounds exerted excellent bioactivity against many ailments with outstanding bioavailability, safety, and stability profiles. In this comprehensive review, we have summarized the bioactivity of the benzimidazole derivatives reported in recent literature with their available structure-activity relationship. Compounds bearing benzimidazole nucleus possess broad-spectrum pharmacological properties ranging from common antibacterial effects to the world's most virulent diseases. Several promising therapeutic candidates are undergoing human trials, and some of these are going to be approved for clinical use. However, notable challenges, such as drug resistance, costly and tedious synthetic methods, little structural information of receptors, lack of advanced software, and so on, are still viable to be overcome for further research.

Key words :- nitrogenous heterocyclic molecules, benzimidazole, active biomolecules, bioavailability, pharmacological properties, antibacterial effects.

INTRODUCTION

The benzimidazoles contain a phenyl ring fused to an imidazole ring as indicated in the structure. This important group of substances has found practical applications in a number of fields. Benzimidazole, which is a heterocyclic nucleus, plays an important role in various medicines.[1]



Historically, the first benzimidazole was prepared in 1872 by Hoebrecker, who obtained 2, 5 or (2, 6)-dimethyl benzimidazole by the reduction of 2-nitro-4-methylacetanilde. Since compounds of this type were formed by the loss of water, they were called "anhydrobases". The benzimidazoles are also called as benzoglyoxalines, this tautomerism is analogues to that found in the imidazole and amidines. The benzimidazoles, in fact, may be considered as cyclic analogs of the amidines.The benzimidazole is also called as 1,3-benzodiazole, aolzinde, benzoglyoxaline, 3-

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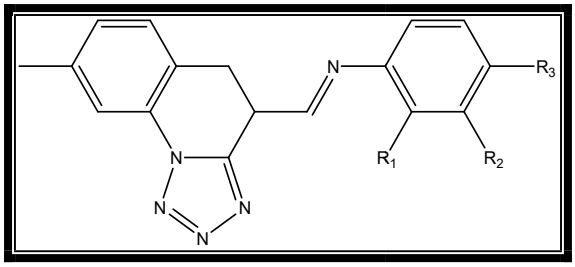
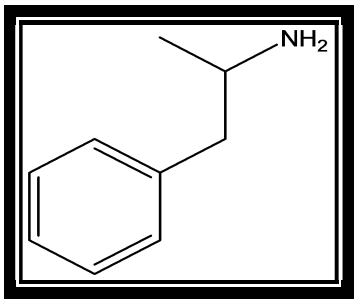
azaindole, 1H-benzimidazole, o-benzimidazole, BZI, 1, 3-diazaindene, NSC 7591 with melting point of 170-172°C and occurs as white crystals. It is highly stable, combustible but incompatible with strong oxidizing agents. It is harmful if swallowed, inhaled or absorbed through the skin. It is used as muscle relaxant.

Review of literature

Bhargava S., *et.al.* (2010, 2008) have synthesized synthesis of schiff's bases of 8-methyl – tetrazolo(1,5-a) quinoline as potential anti- inflammatory and antimicrobial agents.[2]



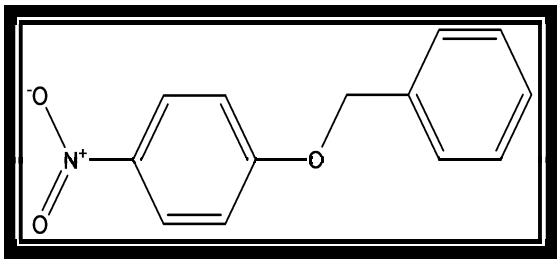
Andrew A., *et.al.* (2010) Worked on synthetic reductions in clandestine amphetamine and methamphetamine laboratories.[3]



This review summarizes the synthetic methods, reactions and biological applications of 2-chloroquinoline-3-carbaldehydes during the period from 1999 to 2011. The reactions are subdivided in groups that cover reactions at the chloro or aldehyde substituent and reactions which involve both groups. Most reaction types have been successfully applied and used in the production of biological active compounds.[4]

Lee. J. C., *et.al.* (2009), have synthesize 1-(benzyloxy)-4-nitrobenzene by alkylation of benzyl bromide. The biosynthetic pathways to a number of natural products have been reconstituted*in* vitro using purified enzymes.

Many of these molecules have also been synthesized by organic chemists. Here we compare the strategies used by nature and by chemists to reveal the underlying logic and success of each total synthetic approach for some exemplary molecules with diverse biosynthetic origins.[5]



Rajput. A.P., *et.al.* (2009) have synthesized benzaldehyde substituted phenyl carbonyl Benzimidazoles and their formyl derivatives using vilsmeier-Haack-reaction. A series of benzaldehyde substituted phenyl carbonyl

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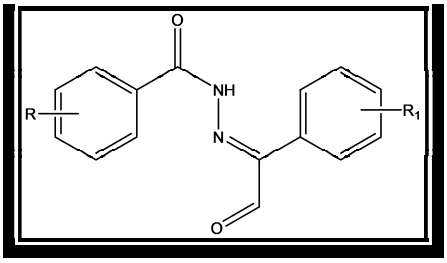
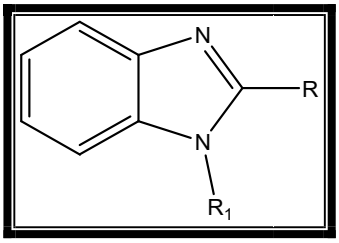
Benzimidazoles has been synthesized and their formylation has been carried out by using Vilsmeier-Haack reaction. All the Benzimidazoles and their formyl derivatives were screened for antibacterial activity.



Mishra A., *et.al.* (2006)) have reported the synthesized 1-substituted isochromanes with phenyl acetic acid esters. A series of 1-substituted isochromanes has been synthesized from the corresponding alkyl 2-acylphenylacetates 3, by reduction and cyclization with a catalytic amount of p-toluenesulfonic acid monohydrate (PTSA), as compounds with potential ntitumor activity and N-bearing heterocyclic analogues.



Synthesis of benzimidazole

Step A: o-pheylenediamine (13.5 gm, 0.12 mol) was placed in a 250 ml round-bottomed flask and 85 % formic acid (9.2 gm, 8.4 ml, 0.17 mol) was added to it. The mixture was heated on a water bath for 100°C for 3 hours. The mixture was cooled, 10 percent sodium hydroxide solution was added slowly, with constant rotation of the flask, until the mixture was just alkaline to litmus. The crude product was filtered washed with ice cold water and dried. The product was dissolved in 200 ml of boiling water and about 1 gm decolorizing carbon was added and digested for 15 minutes. Then it was filtered, the filtrate was cooled to about 10°C, benzimidazole was filtered and washed with water and dry at 100°C. The completion of reaction was monitored by running TLC.

Solvent system: Ethylacetate: chloroform - (8:2)

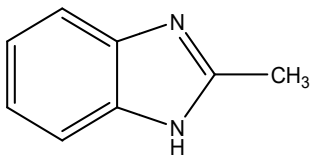
Melting Point: 178-180°C

Yield: (8.25 gm) 56%

R_f value: 0.19

Step B: Synthesis of 2-methylbenzimidazole

The mixture of o-pheylenediamine dihydrochloride (5.43 gm, 0.03 mol), 20 ml of water, acetic acid (5.4 gm, 5.67ml, 0.09 mol) was refluxed for 4 hours. The reaction mixture was cooled and basified with gradual addition of



concentrated ammonia solution, the precipitate was filtered, dried and recrystallised from 10 % aqueous ethanol. The completion of reaction was monitored by running TLC.

Solvent system: Ethylacetate : chloroform - (8:2)

Melting Point: 184-186ºC.

Yield: (2.3 gm) 58%

R_f value: 0.22

Summary and Conclusion

It is an attempt to review the literature on substituted Benzimidazole derivatives for their medicinal significance with help of chemical abstract, journals and internet sites. All synthesized compounds will tested for the preliminary tests, physical constants and TLC.

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.Conflict of Interest

The authors declare that they have no conflict of interest