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Review Article

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A REVIEW ON PHARMACOLOGICAL AND SYNTHETIC METHODS OF BENZIMIDAZOLE NUCLEUS

Sanjay Singh[1]*, Gaurav Kumar[2], Manisha Negi[2] and Salman[3]

Department of Pharmaceutical Sciences, Siddhartha Group of Institutions, Sahasthadhara Road, Uttarakhand (India), Affiliated to Uttarakhand Technical University, Dehradun.

***Corresponding Author: Dr. Sanjay Singh**
Department of Pharmaceutical Sciences, Siddhartha Group of Institutions, Sahasthadhara Road, Uttarakhand (India), Affiliated to Uttarakhand Technical University, Dehradun.

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ABSTRACT

Benzimidazole is an organic compound which consists of benzene ring fused with imidazole heterocyclic ring and shows aromaticity. Benzimidazole moiety has been showed more potent role in the field of research. It is an amphiprotic compound, its pseudo acidic in character and alkali molecule is show planner properties. Reported moiety is a constituent of Vitamin B_{12}. Benzimidazoles are regarded as a promising types of bioactive heterocyclic moiety that showed a various types of biological activity like antibacterial, antiviral, analgesic, antitubercular, anti HIV, anticonvulsant, anti proliferative, anti inflammatory, anti-helmintics, antioxidant, anti neoplastic, proton pump inhibitor and antihypertensive. In this review article has been discussed about introduction, preparation, physical properties, chemical properties and uses.

KEYWORDS: Benzimidazole, FT-NMR, FT-IR and UV.

INTRODUCTION

Introduction of benzimidazole

Benzimidazole it is a heterocyclic aromatic compound. It is an important Pharmacophore &it is a bicyclic in nature. The term imidazole contain a phenyl ring fused to an imidazole ring as indicated that the structure of benzimidazole. It is bicyclic compound having imidazole ring containing 2-N atom at non adjacent position. Its molecular formula $C_7H_6N_2$. It plays a very important with plenty of useful therapeutic activities. It play vital role in biological field such as anti-microbial, anti-viral anti-diabetic &anti-cancer activity.

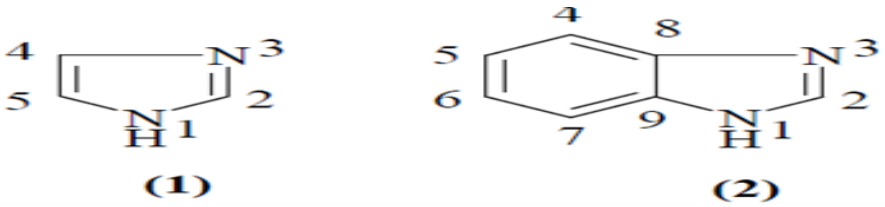

Fig. 1, 2: Structure of imidazole ring.

Five membrane heterocyclic ring system containing imino group and addition to a 3^0 N atom located at position 1-3, benzene ring is fused to 4-5 position of imidazole ring.[1] In 1990 various benzimidazole derivatives were synthesized and substitution of fluorine, propylene, tetrahydroquinoline and cyclized compound and those resultant the compounds with increased stability, bioavailability and significant biological activity Different heterocyclic moiety to produce molecules with enhanced biological properties.[2]

Introduction to Benzimidazoles and *N*-heterocyclic carbenes:

Benzimidazoles are a class of heterocyclic, aromatic chemical compounds which share a fundamental structural characteristic of six-membered benzene fused to five-membered imidazole [Fig3].

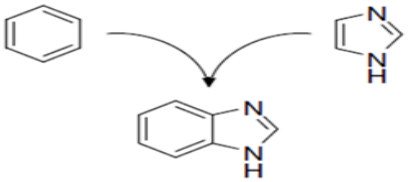

Fig. 3: The benzimidazole Skelton is the fusion of Benzene and Imidazole.

In biomedical research, benzimidazoles also have prominent place in organ catalysis, organ metallic 3, and medicinal chemistry for two reasons stemming from their molecular architecture:

The imidazole is precursor to n-heterocyclic carbenes. The benzene ring provides a convenient scaffold and modifies the spatial and electronic characteristics of a benzimidazole derivative.

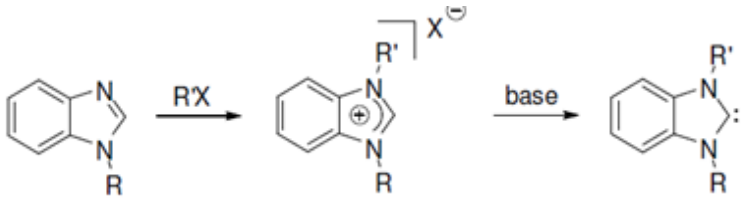

Fig. 4: Reaction of N-substituted benzimidazole with a alkyl or arylhalide yields a benzimidazole salt that when treated with strong base (eg:NaH, KO'Bu)yields N-heterocyclic carbenes.

Use of benzimidazole and their N-heterocyclic carbenes in combination of reactive carbenes with modify backbone. '5&6' heterocyclic structure is shared by another class of chemical compounds, the purines [Fig5].

All the members of this group are several very well known and important bimolecular, such as adenine and guanine, two of the four nucleic acid bases, uric acid, and caffeine.[4]

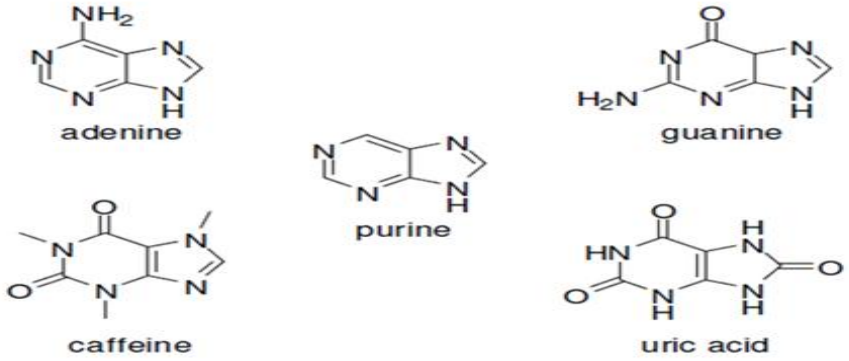

Fig. 5: Purine is well bimolecular and share 5, 6 heterocyclic structure with benzimidazole.

Prepration

1. Benzimidazole is made by condensation of o-phenylenediamine with formic acid, or the equivalent tri methyl ortho formate.
   $C_6H_4(NH_2)_2 + HC(OCH_3)_3 \rightarrow C_6H_4N(NH)CH + 3CH_3OH$
2. When the condensation is conducted with aldehyde in place of formic acid by oxidization, then obtained 2-substituted derivatives.
   Synthesis of benzimidazole by (OPD) organic compound.

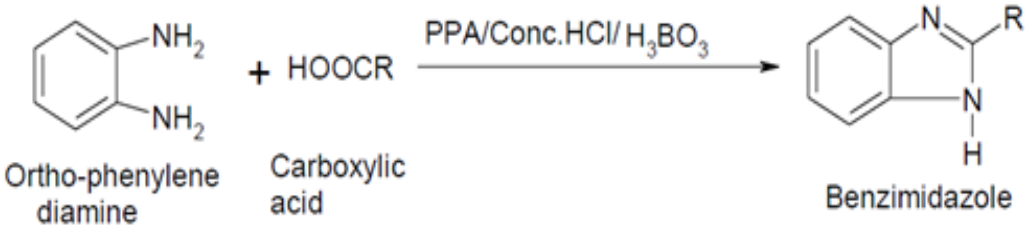

Fig. 6: Synthesis of benzimidazole.

Physical properties

- Benzimidazoles with organic compound gas are sometimes soluble in polar solvents or less soluble in organic solvents
- It general soluble in dilute acids.
- N-metallic compound are acidic or additional acidic.
- Non-polar substituents in varied positions of the benzimidazole ring, the solubility in non-polar solvents are increased or augmented.
- However another espect the polar substituent's hooked up in varied position then molecule increases solubility in polar solvents. Benzimidazole distils unchanged higher than 300℃.
- Benzimidazoles are sufficiently acidic, they are soluble in aqueous alkali and N-metallic.
- Additional acidic benzimidazoles are soluble in less basic resolution, eg : like K_2CO_3resolution.
- Benzimidazole are sufficiently acidic are soluble in aqueous alkali.

Chemical properties:

Reaction of benzimidazole ring

Benzimidazole ring possess a high degree of stability. Benzimidazole isn't stricken affected by conc. H_2SO_4 acid, hot HCL likewise alkalizes.

Oxidation cleaves the benzol ring of benzimidazole solely vigorous conditions. The benzimidazole ring is additionally quite resistant to reduction except underneath considerations.

Reactions involving 1 and 3-positions: Benzimidazoles kinds salts e.g. with acids from to monohydrochloride, mononitrate, monopicrate, monoacetate.

Alkylation's: In which during alkylation with alkyl halides, and react underneath more vigorous condition with1-alkylbenzimidazoles and formed 1, 3-dialkylbenzimidazolium halides. Benzimidazole additionally forms Mannich bases by reacting with gas formaldehyde and piperidine and acylating, Grignard chemical agent, metal.

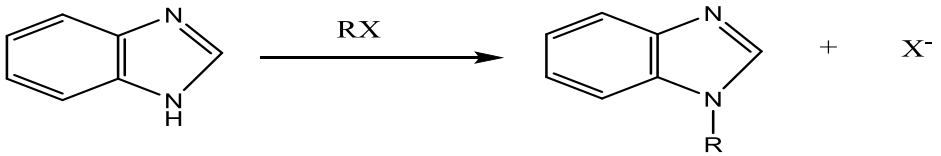

Fig. 7: Alkylation of benzimidazole with alkylhalide.

Hydrogenation and dehydrogenation reactions: Benzimidazole are stable in reduction form but in Chemical action in under high pressure in presence of nickel & Ni use as the catalyst give show negative results. E.g.: 2-Phenylbenzimidazole provides 2-cyclohexylbenzimidazole.Hydrogenation of 2-(*p*-dimethylaminostyryl) benzimidazole presence of nickel at air saturates only the olefinic linkage in the 2-positions.[6]

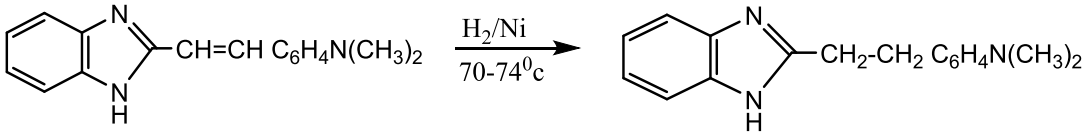

Fig. 8: Hydrogenation and Dehydrogenation reaction.

Stereochemistry

Benzimidazole possessing a free imino hydrogen and 3^0N are tautomeric systems [**3]** and [**4**]. The 2 possible tautomeric forms of the benzimidazole are a unit identical.

Fig. 9: Tautomeric system of benzimidazole.

Substitution of the imino gas eliminates the possibility the chance for tautomerism and outline structure becomes potential.[5]

In 1960 Wanzlick was studies NHC group was stable and isolable to carbenes centre, when saturated imidazoline ring was hooked up to NHC group, and is found 2-position of the alkali ring , it also stable when the electron donating effects of close N-atom. Carbenes are unit extraordinarily reactive species due to electron deficiency, divalent carbon atom with two non-bonding electrons that are covalent bond to 2-adjacent groups. However usually carbenes exist for brief periods of time and they aren't secured.[4]

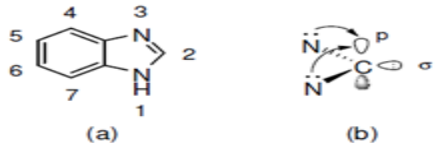

Fig. 10 (a): The numbering for benzimidazole: 2-position carbon becomes the NHC carbenes centre. (b): The singlet ground state has a vacant p-orbital into which neighboring substituents may donate electron to stabilize the carbenes centre.

G.Spectral Properties of Benzimldazole:

Chemical analysis studies of benzimidazole: Benzimidazole is amphiprotic compound, its pseudo acidic in character and alkali molecule is show planner properties and additionally exhibit aromaticity. It associates the 6Negatron 1 atom from every C, one from the pyridine nitrogen and 2 from the pyrrole nitrogen. But in benzimidazole are often envisaged 2 overlapping having 10 electron and the basic properties result from its ability of pyridine N to accept Nucleon. Benzimidazole (pk_b-5.5) is base is weaker then imidazole (pk_b-6.95).

Ultraviolet (UV) spectroscopy: The ultraviolet spectra of benzimidazole and its derivative were studied in alkaline, neutral and acidic media. The bands as curtained with in the case of benzimidazole are given below

Solvent	λ_{max} (logε) m μ
Ethanol	280 (3.89), 272 (3.91), 243 (3.80)
0.01 N HCl	274 (3.91), 268 (3.92), 235 (3.61)
0.01 N NaoH	277 (3.75), 271 (3.74), 240 (3.63)

Table 1: Showed λ_{max} value.

Infra Red (IR): The infra red spectra of benzimidazole ring system has strong absorption band around 1400–1650 cm^{-1} for –C=N– stretching. It is very difficult to distinguish the C–H stretching and –NH stretching vibration range occur 3300-3100 cm^{-1}& from around 3300–2800 $cm^{-1.}$

Nuclear Magnetic Resonance (NMR): The chemical shifts of benzimidazole are manifested at lower field δ 7.71 (C_2–H), 7.67 (C_4–H), 7.17 (C_5–H), 7.24 (C_6–H) and 7.32 ppm (C_7–H) respectively. The overlapping signals ascribable to aromatic proton and –NH proton have been observed at δ 3.0–8.2 ppm, which are disappeared on $_{D2}$o addition. The chemical shift of C_4–H and its deviation is because of various substituents to the magnetic property of the unsaturated N lone pair, 17 that removed once protonation appears.

C^{13} Magnetic Resonance Spectroscopy: The C^{13} NMR chemical shifts that are performed by Pugmire and Grant18 for benzimidazole ion, benzimidazole and benzimidazole cations as follows.[7]

Uses:

- Several benzimidazole derivatives have found use with in the preparation of sunburn preventatives.
- These compounds protect the skin by exciting ultraviolet rays.
- The benzimidazole opioid family includes a variety of study agents e.g. etonitazene whose article discusses the family in some depth.
- Benzimidazole is often used as a organic sold out preservative.
- Many dyes are square measure derived from benzimidazoles.
- Benzimidazole is involved in the synthesis of the antiandrogen Galeterone.

- Benzimidazole drugs are widely used for the interference and treatment of parasitic infection for e.g. Omeprazole, rabeprazole, lansoprazole, pantoprazole and esomeprazole.
- Benzimidazole derivatives are use within the textile industry as wetting, emulsifying, foaming and softening agents and are also used in colouring.
- Impropriation of fluorescent dyes to be use in such preparations as inks for creating clothes to be dried cleaned the marks becomes visible below UV light.

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