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Synthesis, Characterization of Benzimidazole Containing Schiff Basederivatives and Theirantimicrobial Activity

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A B S T R A C T

New schiff base tagged benzimidazole compounds have been synthesized. This articles provides an introduction to Schiff base derivatives and general methods of synthesis, spectral characteristics and biological importance of a number of benzimidazole and its Schiff base derivatives. This also endeavor in this direction, in the synthesis and characterization of such novel compounds based on Melting point, IR, ^{1}H NMR and ^{13}C NMR spectral data.

Keywords: Synthesis, Schiff base, Benzimidazole, spectral analysis

1. Introduction

During the past decades, the human population affected with life threatening infectious diseases caused by multidrug resistant Gram-positive and Gram-negative pathogen bacteria increased to an alarming level around the world[1-5]. Due to this reason, it is imperative to design and develop new antibacterial or antifungal agents with novel chemical structure preferably having different modes of action rather than analogues of the existing ones[6-8].

The development of resistance to current anti-bacterial therapy continues to stimulate the search for more effective agents[7]. The increasing clinical importance of drug resistant and bacterial pathogens has lent additional urgency to microbiological research and development of novel biologically active compounds[8]. Many important biochemical compounds and drugs of natural origin contain heterocyclic ring structures. Among these eg: Carbohydrates, essential amino acids, vitamins, alkaloids, glycosides etc. the presence of heterocyclic structures in such diverse types of compounds is strongly indicative of the diverse types of the pharmacological activity and recognition of this is reflected in efforts to find useful synthetic drugs[9-13].

Heterocyclic compounds possess a cyclic structure with two or more different kinds of atoms in the ring[14]. These types of compounds are widely distributed in nature and are essential to life. It plays a vital role in the metabolism of all living cells e.g. the pyrimidine and purine bases of the genetic material DNA, the essential amino acids proline, hisitidine, the vitamins and coenzymes etc[15-20]. There are a vast number of pharmacologically active heterocyclic compounds, many of which are in regular clinical use. A wide range of synthetic and naturally occurring heterocyclic compounds find their use in medicine and also as pesticides, agrochemicals, polymers etc., paving the way for considerable amount of research leading to new heterocyclic molecules having an array of biological activities[21-25].

Now days, a wide variety of heterocyclic systems are known, but the nitrogen containing heterocycles are of great importance[26]. Among the all heterocycles, benzimidazole is one of the most important nitrogen containing heterocyclic species because of its synthetic utility and broad spectrum of pharmacological activity[27]. It is an important pharmacophores and a privileged structure in medicinal chemistry. Several of its derivatives possess pharmacological properties and have been marketed as commercial products[28-30].

Benzimidazole is a heterocyclic aromatic organic compound.This bicyclic compound consists of the fusion of benzene and imidazole[31]. The most prominent benzimidazole compound in nature is N-ribosyl-dimethylbenzimidazole, which serves as an axial ligand for cobalt in vitamin-B_{12}. Benzimidazole, is an extension of the well elaborated imidazole system, has been used as carbon skeletons for N-heterocyclic carbenes[32]. The N-

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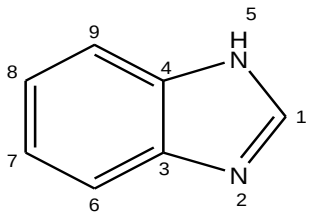
heterocyclic carbenes (NHC) are usually used as ligands for transition metal complexes. They are often prepared by deprotonating an N, N'-disubstitutedbenzimidazolium salt at the 2-position with a base[33].



Benzimidazoles **(1)**

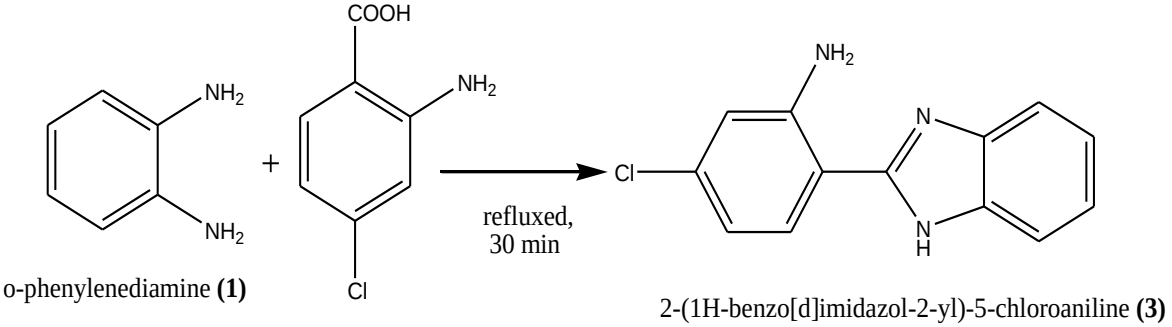
Taking into consideration of the above mentioned issues, a stepwise systematic approach is adopted to explore those above problems is the main objectives of this paper ,o prepare to derivatives from *o*-phenylenediamine and 2-amino-4-chlorobenzoic acid were condensed to get various substituted benzimidazole derivatives. Further it is condensed with various substituted aromatic aldehydes to get the final five Schiff base derivatives of benzimidazole, to characterize the synthesized compounds by melting point, IR, ^{1}H-NMR and ^{13}C-NMR spectral studies. Synthesized derivatives evaluated the antibacterial activity of N-(4-bromobenzylidene) -2-(1H-benzo[d]imidazol-2-yl)-5-substitutedbenzenamine against *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa* and *Escherichia coli* by using disc diffusion method. Ciprofloaxacin was used as reference standard. Further the antifungal activity of N-(4-bromobenzylidene-2-(1H-benzo[d]imidazol-2-yl)-5-substituted benzenamine against *Aspergillusflavus,Aspergillusniger and Trichodermaviride* by using the disc diffusion method. Amphotericin-B was used as reference standard.

2. Materials and Methods

Melting points of the synthesized compounds were determined in open-glass capillaries on a Stuart-SMP10 melting point apparatus and recorded in ^{0}C without correction. IR absorption spectra were recorded in the 4,000–400 cm^{-1} range on a Shimadzu FTIR-8400s using KBr pellets technique. ^{1}H-NMR &^{13}C-NMR spectra was recorded on a Bruker-400MHz spectrophotometer.

2.1 Synthesis of 2-(1H-benzo[d]imidazol-2-yl)-5-chloroaniline (3)

The synthetic strategyleading to the target compounds are illustrated in **scheme 1**. Equimolar quantities (0.01mol) of *o*-phenylenediamine (1), 2-amino-4-chlorobenzoicacid (2) (0.01mol) in 4N HCl(20mL) was refluxed for 30 min. The mixture was cooled and filtered off. The residue was the 2-(1H-benzo[d]imidazol-2-yl)-5-chloroaniline **(3)**. The product was recrystallized from absolute alcohol. This compound was obtained as a pale yellow solid; M.F: $C_{13}H_{10}ClN_3$; Yield 78%; mp 209^{0}C - 211^{0}C.



o-phenylenediamine **(1)**

2-amino-4-chlorobenzoicacid **(2)**

2-(1H-benzo[d]imidazol-2-yl)-5-chloroaniline **(3)**

Scheme - 1 Synthesis of 2-(1H-benzo[d]imidazol-2-yl)-5-chloroaniline **(3)**

The IR spectra of the synthesized derivative was characterized by the presence of a strong band at 1587 cm-^{1} for the ring C=N group. This is considered a strong confirmation for the benzimidazole nucleus formation. A peak is observed at 3479 cm^{-1}is due to NH_2 stretching. The peak observed at 3059 cm^{-1}is due to aromatic C-H- stretching. All the IR values characterized that the compound is 2-(*1H*-benzo[d]imidazol-2-yl)- -5-chloroaniline (3). The singlet observed at 5.61 ppm is due to NH_2 proton. The singlet observed at 4.41 ppm is due to (-NH) proton. The signals appearing 6.60 to 8.37 ppm are obviously due to aromatic protons. The ^{13}C-NMR spectra of 2-(*1H*-benzo[d]imidazol-2-yl)--5-chloroaniline(3) also supported the fact that cyclic C=N group present and a signal appeared in the range of 162.77 ppm. The chemical shift due to aromatic carbon can be readily sorted out by their characteristic absorption in the region 113.39-140.54 ppm.

2.2Synthesis of (E)-N-(4-fluorobenzylidene)-2-(*1H*-benzo-[d] -imidazol-2-yl)-5-chlorobenzenamine (5)

A mixture of equimolar quantities (0.01mol) of 2-(1H-benzo[d]imidazol-2-yl)-5-chloroaniline **(3)** and p-Fluoro -benzaldehydes was refluxed for 20 min in 20 mL of ethanol. The reaction mixture was cooled and kept for 24 hour. The crystals obtained was filtered and dried. The Schiff base (E)-N-(4-fluorbenzylidene)-2-(*1H*-benzo[d]imidazol-2-yl)-5-chlorobenzamine**(5)** recrystallized from ethanol. M.F: $C_{20}H_{13}ClFN_3$; Yield 81%; mp187 - 188^{0}C.

The IR spectra of the synthesized derivatives were characterized by the presence of a strong band at 1593 cm-^{1} for the ring C=N group. This is considered a strong confirmation for the Schiff base formation. A peak is observed at 3360 cm^{-1}and748 cm^{-1}is due to NH, C-Cl stretching. The peak observed at 1593 cm^{-1}is due to aromatic C-H stretching. All the IR values characterized that the compound is (E)-N-(4-fluorobenzylidene)-2-(*1H*-benzo[d]imidazol-2-yl)-5-chlorobenzenamine **(5).** The singlet observed at 4.25 ppm is due to (-NH) proton. The signals appearing 6.58 to 7.68 ppm are obviously due to aromatic protons. The singlet observed at 8.08 ppm is due to C=N proton. The ^{13}C-NMR spectra of compound also supported the fact that cyclic C=N group present and a signal appeared in the range of 155.32ppm. A signal appeared in the range of 163.84 ppm due to Schiff base C=N. The chemical shift due to aromatic carbon can be readily sorted out by their characteristic absorption in the region 115.59 to 140.48 ppm.

3. Conclusion

This articles provides an introduction to Schiff base derivatives and general methods of synthesis, spectral characteristics and biological importance of a number of benzimidazole and its Schiff base derivatives. This also endeavor in this direction, in the synthesis and characterization of such novel compounds based on Melting point, IR, 1H NMR and 13C NMR spectral data.

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