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Research Paper

A Research on Synthesis and Biological Evaluation of Substituted Benzimidazole Derivative

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ABSTRACT

Benzimidazoles are an important class of composites with a wide diapason of natural exertion ranging formant-microbial, anti-fungal, and anthelmintic exertion. Benzimidazole rings are the most important nitrogen- containing heterocycles, which are extensively explored and employed by the pharmaceutical assiduity for medicine discovery. The identification and characterization of the synthesized composites were carried out by essential analysis, melting point, Thin Subcaste Chromatography, FT- IR, NMR and Mass data. The synthesized composites were estimated for anti-microbial exertion. Among these implicit heterocyclic medicines, benzimidazole and imidazopyridine pulpits are the most current. Over the once many decades, it has gained immense attention. Both are important classes of motes owing to their wide diapason of natural conditioning and clinical operations. Both are used in fashion design and the development of new synthetic analogy for colourful remedial diseases. A wide variety of derivations have been developed as implicit anticancer, antimicrobial, antiviral, and anti-inflammatory agents in addition to other chemotherapeutic agents. A library of 53 benzimidazole derivations, with substituents at positions 1, 2 and 5, were synthesized and screened against a series of reference strains of bacteria and fungi of medical applicability. The SAR analyses of the most promising results showed that the antimicrobial exertion of the composites depended on the substituents attached to the bicyclic heterocycle

INTRODUCTION

In nature, heterocyclic chemical composites have a wide distribution and necessary for life. Heterocyclic substances have been involved in the metabolism of all living cells in an important manner. Heterocyclic composites grounded on nitrogen are pivotal to humankind. Particularly within the entire class of nitrogen- grounded heterocyclic composites, benzimidazole has a

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significant impact on both natural and artificial processes. Benzimidazole is an important heterocyclic system, according to expansive study, since it has natural action against a variety of infections and physical ails. In remedial composites including antimicrobial, antifungals, proton pump impediments, and anticoagulants, among others, benzimidazole derivations play an active part. Despite a multitudinous attempt to develop new structural prototype in the hunt for further effective antimicrobials, the benzimidazoles still remain as one of the most protean class of composites against microbes and, thus, are useful substructures for farther molecular disquisition. lately, the chemistry and natural biographies of colourful pharmacophores of 1N-substituted and 2- substituted benzimidazoles derivations have been worked out in detail. On the other side, literature check revealed that-thiadiazole and 2- azetidinones are also associated with pharmacological conditioning like antimicrobial, antiviral, aesthetic, anticonvulsant, etc. The current use of these classical antimicrobial agents has redounded in emergence of multi-drug resistant(MDR) bacterial strains and methicillin- resistant Staphylococcus aureus(MRSA) is one the utmost disturbing source for nosocomial infections. Benzimidazole is a heterocyclic sweet organic emulsion. It's an important pharmacophore and a privileged structure in medicinal chemistry. This emulsion is bicyclic in nature which correspond of emulsion of benzene and imidazole. Benzimidazole derivations were reported to retain analgesic and anti-inflammatory exertion, antimicrobial, anticancer, anticonvulsant, antiviral, antioxidant, antihypertensive, anti-tubercular, anthelmintic, proton pump asset exertion. In this present study benzimidazole derivations of Schiff bases containing colourful aldehydes have synthesized. A pivotal problem presently is the rise of bacterial resistance to antibiotics. Due to bacterial resistance, multitudinous antibacterial specifics are insignificant against origins. The World Health Organization recently released an antibiotic resistance bacterium priority list. An important heterocyclic sweet chemical with a benzene and imidazole ring is benzimidazole. The protocols generally followed for their emulsion involve condensation of ortho- esters, nitriles, aldehydes, carboxylic acids, amides and esters with ortho-substituted amino aromatics, in the presence of different acids or catalysts. Benzimidazole ring displays an important heterocyclic pharmacophore in drug discovery. These mixes carrying different substituents in the benzimidazole structure are associated with a wide range of natural exertion including anti--- bacterial,-- seditious, antihistaminic, proton pump-- hypertensive and anti- coagulant parcels. This review enlightens about the chemistry of different derivatives of substituted benzimidazoles along with their pharmacological exertion. Antimicrobial agents Antibiotics are antibacterial substances produced by various species of micro- organism(bacteria, fungi, and actinomycetes) that suppress the growth of other micro- organisms. As the microorganisms are swiftly witnessing heritable changes and developing resistance against multitudinous antibiotics and remedial agents for various conditions more snappily than new drugs are being made available so the war against the contagious conditions has come a no way ending process. The conformation of a Schiff base from aldehydes of ketones is a reversible response and generally takes place under acid or base catalysis. The conformation is generally driven to the completion by separation of the product or dumping of water or both. multitudinous Schiff bases can be hydrolysed back to their aldehydes or ketones and amines by arid acid or base. The medium of conformation of Schiff base is another variation on the theme of nucleophilic addition to the carbonyl group. In this case, the nucleophile is

the amine. In the first part of the medium, the amine reacts with the aldehyde or ketone to give an unstable carbinolamine conflation. Schiff bases have also displayed a broad range of natural exertion including anti-- bacterial parcels.

MATERIALS AND METHODS:

Nuclear glamorous Resonance(1HNMR) gamut's were recorded on a Bruker using CDCl3. The Chemical shift values are reported in corridor per million (ppm) relative to Tetra methyl silane as internal reference. Infra-red (IR) gamut's were recorded with a Bruker spectrophotometer. The melting point ranges of recently synthesized composites were determined by open glass capillary tube using Lab India's visual melting point outfit and were uncorrected. All the commercially available reagent grade chemicals were used as entered. chastity of the emulsion and progress of the response were covered by thin subcaste chromatography (TLC), with discovery by Ultra-violet (UV) light and/ or spots were imaged by exposure to iodine vapours 27.

General Procedure for Synthesis of Benzimidazole from 0-phenylenediamine.

Procedure:

Place 2.7 g of o- phenylenediamine (OPD) in 250 ml round bottom beaker and add 16 ml of 90 formic acid. toast the admixture on water bath at 100c for 2 hrs. Cool, and 10 sodium hydroxide result sluggishly, with constant gyration of the beaker, until the admixture is just alkaline to litmus test (PH = 8) Filter off the crude benzimidazole at the pump, marshland with sufficient ice-cold water, drain well wash again with 10 ml of cold water.

Fig 1. Synthesis of Benzimidazole from 0-phenylenediamine.

Recrystallization:

Dissolve crude product in 40 ml of boiling water. Add 0.2 g of snowing carbon and condensation for 15 min. Sludge fleetly through a preheated Buchner channel and beaker at the pump. Cool the filtrate to about 10c sludge off recrystallized benzimidazole, marshland with 25 ml of cold water and dry at 70c in oven Record the practical yield and report melting point.

Fig 2. Recrystallization:

Synthetic Scheme 1:

The title composites were synthesized using synthetic strategy described in Fig. 1. Benzimidazole composites were synthesized starting from o- phenylenediamine and benzoic acid.

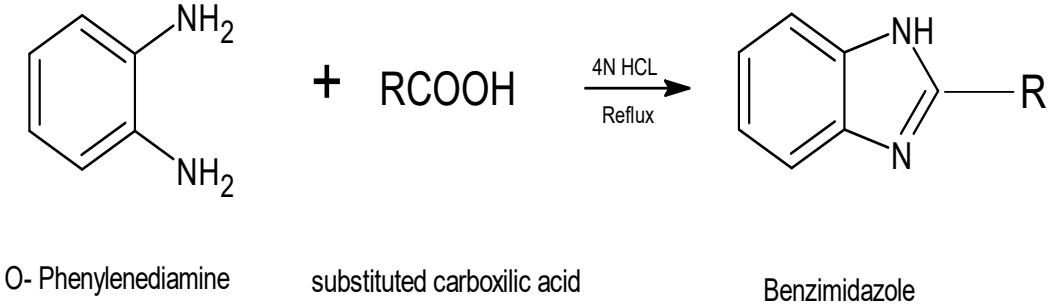


FIG. 1: SYNTHESIS OF BENZIMIDAZOLE

Substituted carboxylic acid: Formic acid, Benzoic acid, 2-amino benzoic acid, 3, 4-dimethoxybenzoic acid, 3, 4, 5trimethoxybenzoic acid, 2-chloro-4-nitro benzoic acid, 2-chloro-5-nitro benzoic acid, 2- Iodo benzoic acid, 4-methoxyphenyl acetic acid, 4-ethyl benzoic acid, 2, 4, 5-trifluoro benzoic acid, 4-chloro-3, 5-dinitro benzoic acid

General Procedure for Synthesis of 2(-2,4-Dichlorophenyl) benzimidazole from 0-phenylenediamine.

Procedure:

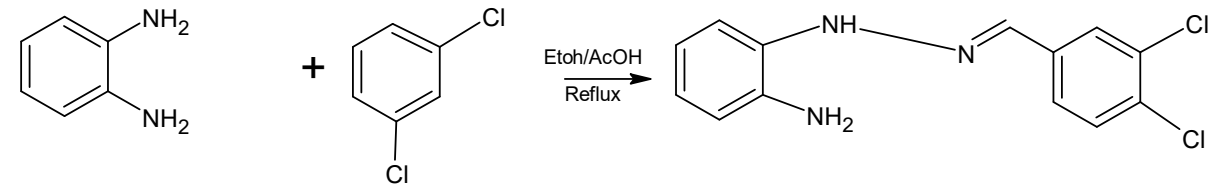
1. Take o- phenylenediamine(0.01 spook) in a round bottom beaker.
2. Add 2,4- Di chlorobenzaldehyde(0.01 spook) to the beaker.
3. Add 20 – 30 mL ethanol as detergent.
4. Add 2 – 3 drops of glacial acetic acid as catalyst.
5. Reflux the response admixture for 2 – 3 hours with nonstop shifting.
6. Cover the response progress using TLC.
7. After completion, cool the admixture to room temperature.
8. Pour into ice-cold water to precipitate the product.
9. Filter the solid and wash with cold water.
10. Recrystallize the crude product using ethanol to gain pure 2-(2,4- dichlorophenyl) benzimidazole.

Fig 3. Synthesis of 2(-2,4-Dichlorophenyl) benzimidazole

Synthetic Scheme 2:

The title compounds were synthesized using synthetic strategy described in Fig. 2 . of 2(-2,4-Dichlorophenyl) benzimidazole compounds were synthesized starting from o-phenylenediamine and 2,4 Dichlorobenzaldehyde

Step 1 Starting material Step 2 : Condensation

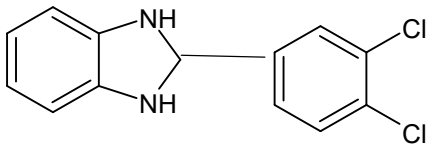


o- Phenylenediamine

2,4-Dichlorobenzaldehyde

Schiff Base Intermediate
(Imine)

Step 3 : Cyclization And Oxidation



2-(2,4-Dichlorophenyl Benzimidazole

FIG. 2: SYNTHESIS OF BENZIMIDAZOLE DERVATIVES

Characterization:

1.Melting Point Determination of Benzimidazole Derivatives.

Principle:

The temperature at which a solid turn into a liquid is known as the melting point. The melting point range of an imperfect emulsion is broad and depressed, whereas that of a pure emulsion is acute and narrow. Two popular methods for figuring out the melting point are described.

1. Meltem apparatus
2. Thiele sock configuration

Method for melting point

1. Take a burette stand, Thiele tube, thread, liquid paraffin, thermometer, and one-sided seal capillary.
2. Fill one side of the capillary, seal it, and attach it to the thermometer.
3. The liquid paraffin is contained in the capillary and deep thermometer in Thiele.
4. Use a burner to heat the tube.
5. Check the temperature at which the substance begins to melt.
6. Make a note of the melting point

Fig 4. Melting point

2.Thin Layer Chromatography of Benzimidazole.

Principle:

TLC uses polarity differences and adsorption to separate substances.

Polar silica gel = stationary phase

The mobile phase is the solvent.

Compounds that are less polar move more quickly (higher Rf).

Materials Needed:

TLC plate (G silica gel)

Tubes of capillaries
Developing chamber (lidded jar)
The solvent system
Hexane: Ethyl acetate (7:3), which is frequently utilized
An example of a solution
Benzimidazole, a crude product
o-phenylenediamine is the starting ingredient.

Method:

1. Chamber preparation
Fill the chamber with the mobile phase (approximately 0.5–1 cm deep).Close and let it saturate for ten to fifteen minutes.
2. TLC Plate Preparation Draw a pencil line about 1 cm from the origin. Identify the spotting points.
3. Preparing the Sample
dissolve a tiny quantity of:
Methanol containing crude benzimidazole
o-phenylenediamine in isolation
4. Spot Application
Utilize a capillary tube to place small drops on designated points. Allow the drops to dry completely.
5. Chromatography Development
Carefully position the plate in the chamber. Make sure the solvent level remains below the origin line. Allow the solvent to ascend approximately 8–10 cm.
6. Drying Process
Take out the plate and let it air dry.

Calculation of Rf Value:
Standard Solvent System:
Benzene: Acetone =(7:3)
Rf value for Benzimidazole: 0.39

Thin Layer Chromatography of 2(-2,4-Dichlorophenyl) benzimidazole extracted from o-phenylenediamine.

Principle:
Stationary Phase
Silica gel TLC plate (most frequently utilized)
Mobile Phase (Solvent System)
A moderately non-polar to slightly polar system is required, as this compound contains both aromatic rings and heteroatoms. Suggested solvent systems include:
Toluene: Ethyl acetate (7:3)
Hexane: Ethyl acetate (6:4)
Chloroform: Methanol (9:1)
(if the compound exhibits higher polarity)

Procedure:
Dissolve a small quantity of your compound in ethanol or methanol.
Use a capillary tube to apply the solution onto the TLC plate.
Insert the plate into a saturated TLC chamber containing the mobile phase.
Allow the solvent to ascend approximately 70–80% of the plate.
Take out the plate and let it dry.

Calculation of RF value:
Standard Solvent System:
toluene: ethyl acetate = (7:3)
Rf value: 0.4

3. Agar Diffusion Method (for Benzimidazole Derivatives)

The agar diffusion method—often referred to as the disc diffusion method—is utilized to assess the antimicrobial effectiveness of compounds such as benzimidazole derivatives by measuring the zone of inhibition.

Principle:
When a solution of a drug (for instance, a benzimidazole derivative) is applied to agar that has been inoculated with microorganisms, the compound will diffuse into the medium. If it possesses antimicrobial properties, it will inhibit the growth of the microorganisms, resulting in the formation of a zone of inhibition.

Method:
1. Agar Medium Configuration

Sterilize and prepare the nutrient-rich agar. Put them in sterile petri dishes and let them solidify.

2. Immunization

Using a sterile swab, evenly distribute the microbial culture across the agar surface.

3. Utilizing Test Materials

Two strategies:

The Disc Diffusion Method involves soaking sterile paper discs in benzimidazole derivative solutions.

Put them on the surface of the infected agar. For a full day, or longer if needed, plates should be incubated at 37°C.

5. Investigation

Calculate the inhibitory zone (in millimetres) around the discs or wells.

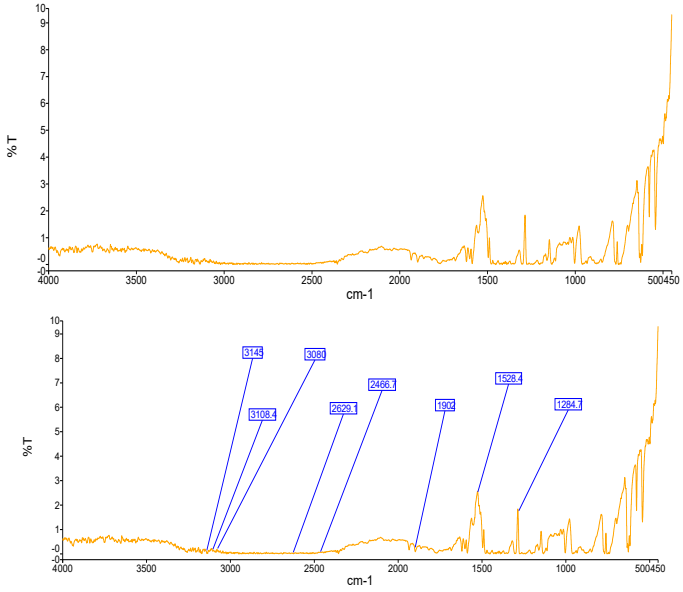
Analysis of the Findings

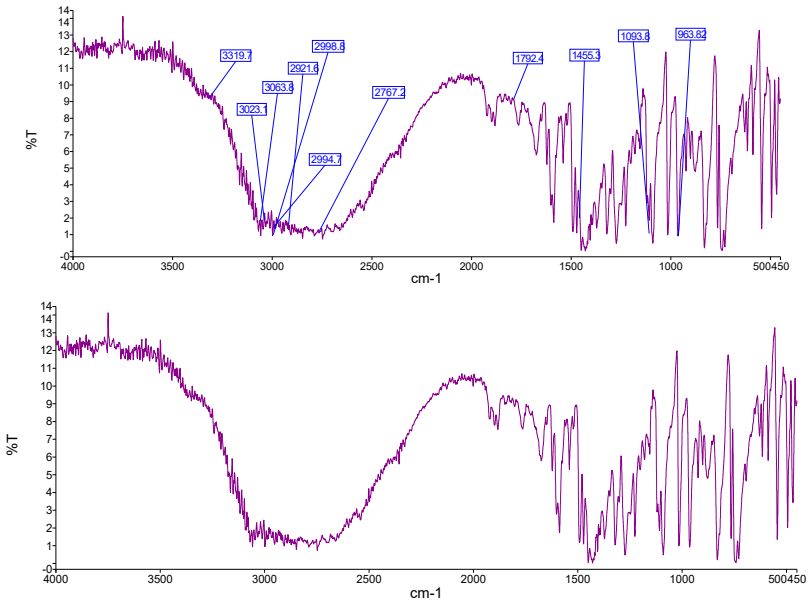
Enhanced antibacterial activity in a larger region

Due to reduced or non-existent activity, the zone is smaller or non-existent.

RESULT:

Conflation of Benzimidazole from 0-phenylenediamine. Practical yield85, Melting point172- 174, RF value 0.39 2. 2(-2,4-Dichlorophenyl) benzimidazole from 0-phenylenediamine. Practical yield72, Melting point227- 230, RF value 0.4 3. IR Spectrum Peaks of Benzimidazole Derivative





Peaks and Their Assignments Wavenumber(cm $^{-1}$) Functional Group Interpretation 3149 cm $^{-1}$ N – H stretching Presence of imidazole N – H group 3108 cm $^{-1}$ sweet C – H stretching Indicates sweet benzene ring 3080 cm $^{-1}$ sweet C – H Confirms substituted sweet system 2629 cm $^{-1}$ Weak O – H/ hydrogen clicked N – H Conceivably due to intermolecular commerce 2468 cm $^{-1}$ Broad band May indicate hydrogen cling 1903 cm $^{-1}$ Undertone/ combination bands Typical of sweet composites 1528 cm $^{-1}$ C = C stretching sweet ring vibration 1284 cm $^{-1}$ C – N stretching Characteristic of benzimidazole ring 1000 – 1200 cm $^{-1}$ C – N/ C – H bending point region 500 – 800 cm $^{-1}$ C – Cl stretching Indicates chloro-substituted secondary

CONCLUSION

The present study successfully demonstrated the conflation of substituted benzimidazole derivations using suitable condensation responses involving o- phenylenediamine and substituted aldehydes or carboxylic acids. The synthesized composites were purified and characterized using standard ways similar as melting point determination and thin- subcaste chromatography(TLC), attesting their identity and chastity. Biological evaluation of the synthesized derivations revealed that structural revision on the benzimidazole nexus significantly influences antimicrobial exertion. composites containing electron- withdrawing substituents (similar as chloro or nitro groups) displayed enhanced antibacterial and antifungal exertion compared to unsubstituted derivations. This suggests that negotiation plays a crucial part in perfecting pharmacological eventuality. Overall, the study confirms that benzimidazole is an important heterocyclic altar with promising natural parcels. The synthesized derivations may serve as implicit lead composites for the development of new antimicrobial agents. farther studies, including advanced spectroscopic characterization and in vivo evaluation, are recommended to explore their full remedial eventuality.

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