International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.12 No.04, pp 271-276, 2019

Synthesis and Pharmacological Screening of 2-Substituted Benzimidazole Derivatives

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Abstract : The methods for the synthesis of benzimidazoles have become a focus of synthetic organic chemists, as they are useful building blocks for the development of important therapeutic compounds in medicine. Confirmation of the chemical structure of the novel synthesized compound benzimidazole was substantiated by TLC, different spectral IR data. The synthesized compounds were evaluated for in-vitro antimicrobial and against Staphylococcus aureus and Escherichia coli. The compounds exhibited weak, moderate, or high in-vitro antimicrobial activity. It may be the medicine to prevent and treat many bacterial diseases.
Keywords : Benzimidazole, Antibacterial; activity, S. aureus and E. coli.

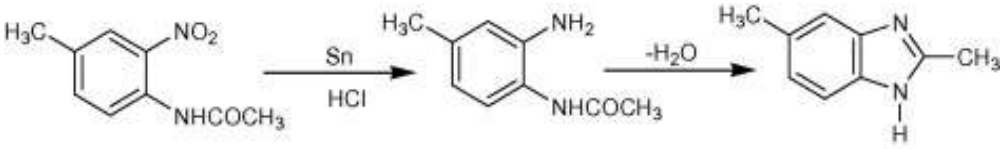
Introduction:

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-4methylacetanilide**.** Despite of the availability of a number of antimicrobial agents the main matter of concern in the treatment of microbial infections is the limited number of efficacious antimicrobial drugs. Many of the currently available drugs are toxic, enable recurrence because they are bacteriostatic/ fungistatic and not bactericidal/fungicidal or lead to the development of resistance due in part to the prolonged periods of administration. The impact is more acute in developing countries due to non availability of desired medicines. There is a real perceived need for the discovery of new compounds that are endowed with antibacterial and antifungal activities, possibly acting through mechanism of actions, which are distinct from those of well known classes of antimicrobial agents to which many clinically relevant Pathogens are now resistant.[1-2]

Synthesis of Benzimidazole

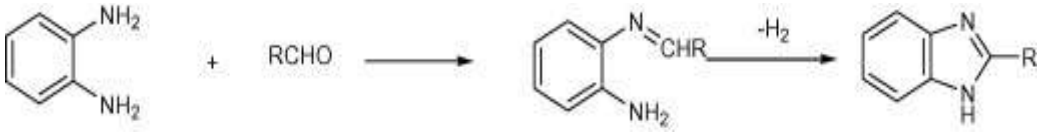
The first benzimidazole was prepared by Hoebrecker, who obtained 2,5-dimethylbenzimidazole by the reduction and dehydration of 2-nitro-4-methylacetanilide)[3].

DOI= http://dx.doi.org/10.20902/IJCTR.2019.120432



Almost all syntheses of benzimidazoles start with benzene derivatives possessing nitrogen-containing functions ortho to each other that is, the starting material possesses the function designated by formula many methods have been reported for the synthesis of benzimidazols. Most of these methods involve the condensation of ortho-phenylenediamine, and its derivatives with carboxylic acid , or aldehyde[4].

By reaction with aldehyde



List of Derivatives

1)3,5 dinitrophenyl benzimidazole
2)P– chlorophenyl benzimidazole

Material:

Melting points were taken by open capillary method. TLC was used to assess the course of reaction using various solvent systems. Visualization of spot on plate was done by exposure to iodine vapours. Infrared (IR) spectra were used to confirm the structures of all synthesized compounds. IR spectra were recorded using KBR disc on a jasco FTIR-410[5]

Chemicals:

All chemicals and solvents were procured from commercial sources purified and dried using standard procedures from literature whenever required .chemicals used for the synthesis were enlisted below with their manufacturer mentioned in parentheses. o-pheneylene diamine, hydrochloric acid, ethanol, ammonia [6]

List of Derivatives

1) 3,5 dinitrophenyl benzimidazole

2) P– chlorophenyl benzimidazole

Microwave Technique:

Same derivatives were synthesized by using microwave technique. By this technique required time was less and yield was higher as compared to conventional technique table.

Table no. 1

Compound code	Time and watt	% yield
A_1	210 watt,25min	48.90
A_2	210 watt,25min	63.17

Pharmacological Screening

Antibacterial Activity:

All the compound synthesized in the present investigation were screened for their anti bacterial activity by cup plate method. Antibacterial activities were were tested on nutrient medium against staphylococcus aureus and E. Coli. All chemicals and solvents were procured from commercial sources, purified and sterilized using standard procedures from literatures whenever required.[7]

Method:

1) Dilution of the Compounds-

All the synthesized compounds were dissolved in dimetyl sulphoxide (DMSO) so as to get concentration of 5 mg/ml, 10mg/ml, and standard drugs chloramphenicol in DMSO as concentration of 10mg/ml .

2) Sterilization of Equipments and the Chemicals-

Nutrient agar medium and normal saline solution were sterilized in autocalve at 15 lbs pressure (121^0C) for 15 mins. Petri plates, whattman filter paper ,discard cotton swab were sterilized in oven at 160 ^{0}C for 2 hrs

3) Preparation of Nutrient Agar Medium Slant-

Nutrient agar medium 112 mg and agar powder 100 m g was dissolved in 4ml distilled water, boiled and then poured in the conical flask then plugged with cotton and sterilized in autoclave at 15lbs for 15 min After sterilization the conical flask containing the nutrient medium were kept in inclined position for 30 min .sterilised agar media poured into the petri plate .Then on the surface of slant pure culture of S. Aureus, Escherica coli were streaked in aseptic condition and incubated at 37° c for 24 hrs

4) Preparation of Suspension of Test Bacteria

Using the 24 hrs old growth of test bacteria from the slant, suspension of the bacteria was made separately in sterile normal saline solution (0.85%Nacl in distilled water) in aseptic condition to get moderate turbidity.[10]

Table No. 2: Zone of Inhibition

Code of compound	E. Coli		S. Aureus	
	5 mg/ml	10 mg/ml	5 mg/ml	10 mg/ml
Standard (Cholramphinicol)	2	2	2	2
A_1	-	-	0.9	-
A_2	-	-	-	1.2

S . Aureus A_1 (5mg/ml)

E. coli A_1 (5mg/ml)

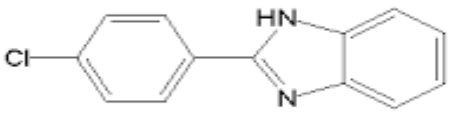
S . Aureus A_2 (10 mg/ml)

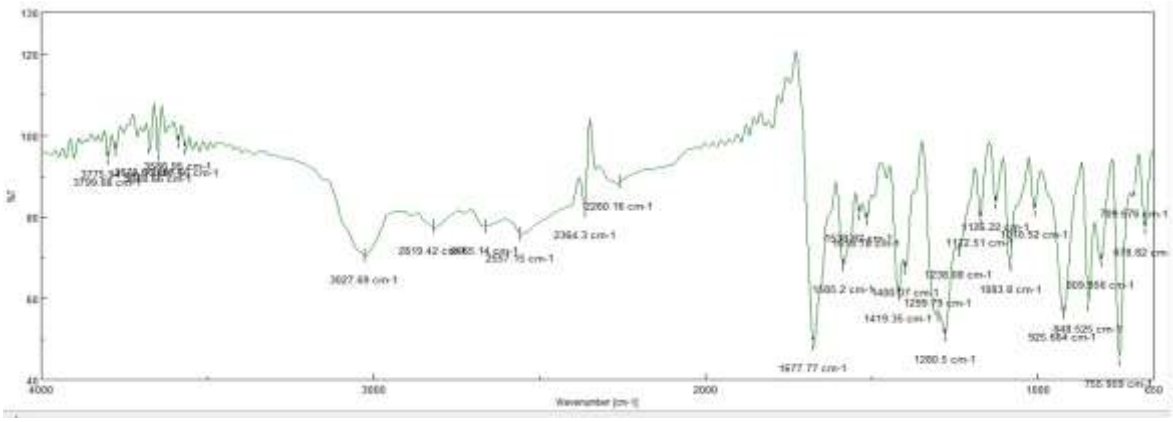
E. coli A_2 (10mg/ml)

Spectral Analysis[8]

IR Spectral analysis of

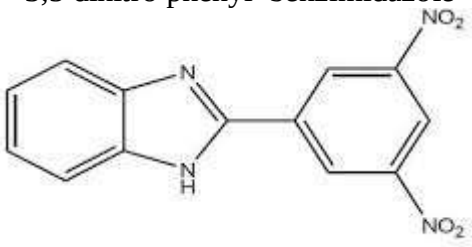
P – chloro phenyl benzimidazole

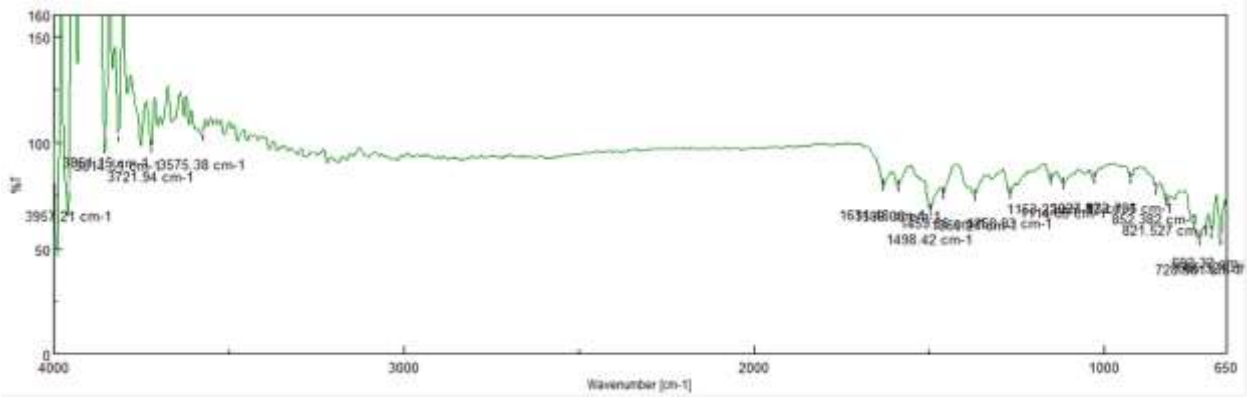




Functional group	**Absorption (cm^{-1})**
Aromatic carbon	1585-1600
N-H	3200
C-cl	1419
C-C	1124
-CH Bending	3349
Aromatic amine	3000-3200

3,5 dinitro phenyl benzimidazole





Functional group	**Absorption (cm^{-1})**
Aromatic carbon	1600-1585
N-H	3200
C-NO_2	1307
C-C	1124
-CH Bending	3349
Aromatic amine	3000-3200

Results and Discussion:

The antibacterial activity of synthesized compound (A_1-A_2) was carried out by using Cup plate method and screened against E.coli and S. aureus using standard chloramphenicol (10ug/ml)and test compounds 5,10 mg/ml in (DMSO).

Conclusion:

An efficient of synthesis different novel 2-Substitiuted derivatives by the Phillips condensation by condensing the o-phenylene diamine and carboxylic acid derivatives in 4N HCL. 2- Substituted derivatives have been synthesised by reaction with alkyl halide in presence of base Hydrochloric acid the yield of product A_1 microwave irradiation is 48.90% w/w and A by microwave irradiation is 63.17% w/w . The entire synthesised compounds were screened for antimicrobial activity . R_F value of 3,5 dinitrophenyl benzimidazole was found to be 0.8 and R_F value of p - chlorophenyl benzimidazole was found to be 0.9.

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