IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
March 2020 Vol.:17, Issue:4

Synthesis, Characterization of Benzimidazole Derivatives as Potent Antimicrobial Agents

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

Rajput M. D.*, Yadav A. R, Mohite S.K.

Rajarambapu College of Pharmacy Kasegaon, Tal-Walwa, Dist.Sangli 415404, Maharashtra, India.

Submission: 22 February 2020
Accepted: 29 February 2020
Published: 30 March 2020

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Benzimidazole derivatives, microwave, substituted acids, spectral characterization, antifungal activity

ABSTRACT

Benzimidazole derivatives were synthesized with an approach to develop more potent and side effects having antimicrobial activity. The Benzimidazole and their subordinates with proper substitution example can likewise as of late orchestrated by eco accommodating microwave to upgrade the pace of response. Incorporated compound shows tasteful IR, NMR, and mass spectra. Further, the orchestrated mixes demonstrated promising calming movement and antimicrobial action. A blend of o-phenylenediamine and substituted acids was refluxed in for hours on a warming mantle and with help of substituted halides gives novel benzimidazole derivatives. Result indicated that compounds (b1-b6) Showed promising antifungal, anti-bacterial activity in comparison to standard drugs.

1. INTRODUCTION

Among heterocyclic pharmacophores, the benzimidazole ring framework is very normal. These substructures are frequently called special because of their wide repeat in bioactive mixes. In spite of incredible enthusiasm for benzimidazole ligands and basic science, the principle intrigue is in their organic exercises. The mid 1950s was a significant period with respect to revelation of the natural importance of benzimidazole containing structures and the firmly related purines. Along these lines various natural exercises because of changing the gatherings on the center structure. These organic exercises incorporate enemy of disease, bactericidal, fungicidal and pin relieving and hostile to viral properties. While a few subsidiaries have been orchestrated and assessed for restraint[1].

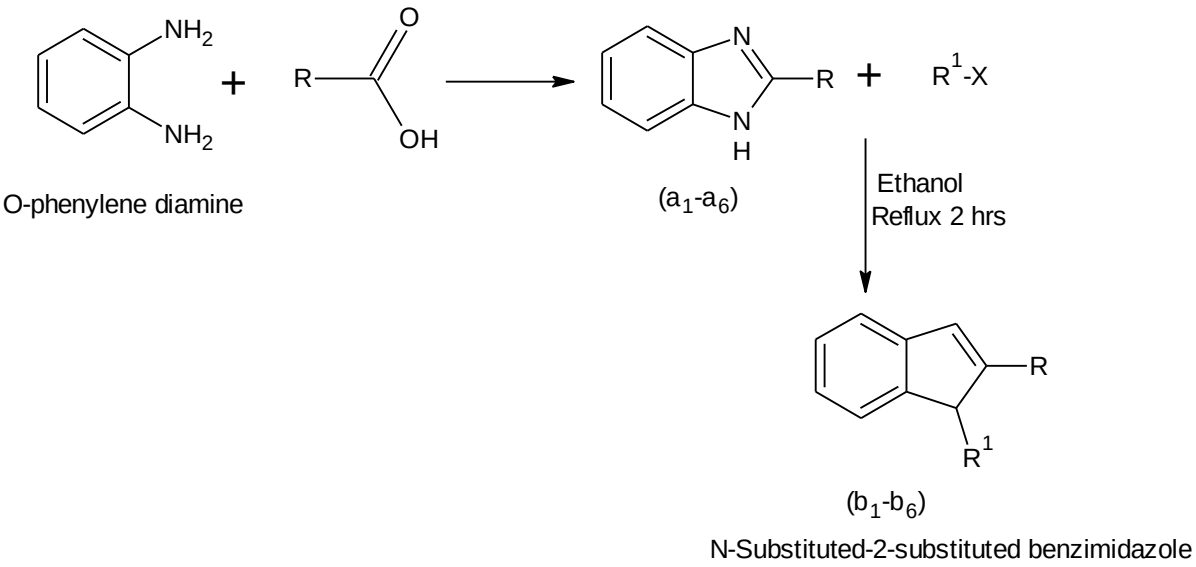
Synthesis of benzimidazole

Monobasic acids

O-phenylenediamines responds promptly with most carboxylic acids to give 2-substituted benzimidazole, as a rule with awesome yields. The response is completed as a rule by warming the reactants together on a steam shower, by warming together under reflux or at a raised temperature or by warming in a fixed cylinder. Benzimidazole might be set up in 83-85% yield by utilizing 90% formic corrosive[2].

2. MATERIALS AND METHODS

Melting points were determined by open capillary tube method and are uncorrected. IR spectra were obtained using FTIR Jasco-4100 spectrophotometer. ^{1}H NMR spectra were recorded on Bruker 300MHz instrument using $CDCl_3$ as a solvent with tetramethylsilane (TMS) as internal standard. Mass spectra were recorded on a QP 2010 Shimadzu, Shivaji University, Kolhapur. Reactions were monitored by TLC using 0.25mm silica gel G.



Scheme 1.

Compound	R
b1	3,5-dimethylbenzoic acid
b2	5-chlorosalicyclic acid
b3	4-nitrobenzoic acid
b4	3-nitrobenzoic acid
b5	5-bromobenzoic acid
b6	2-bromobenzoic acid

Where, R^1=aryl halide

General procedure for synthesis of 2-substituted benzimidazole

A O-phenylenediamine (0.04 mol, 4g) and substituted acids (0.03 mol) was refluxed in 4 N HCl for 20 min on a warming mantle. After finish of response, arrangement was poured onto squashed ice, smelling salts arrangement was added drop savvy to kill and the subsequent strong was separated, washed dried and recrystallized.

General procedure for synthesis of N-substituted2-substituted benzimidazole

Ethanol was added to aryl halide (5.0 mmol) affected by attractive stirrer until a total clear arrangement was achieved. At that point fitting 2-substituted benzimidazole (a1-a7) (5.4mmol) was added carefully to the arrangement and blend was warmed under reflux for 20 min. for crystallization and Melting point and percentage yields reported[3-5].

Spectroscopic data

i] 1-(4-chlorophenyl)-2-(3,5-dimethylphenyl)-1*H*-benzimidazole

IR (KBr): 3426(-NH), 3042(Ar-CH), 1742, 1631(-C = N) cm^{-1}; NMR (δ, ppm): 6.06 (bs, 1H, NH), 6.82 (d, 2H, aromatic), 6.98 (d,2H, aromatic), 7.06 (t,1H, aromatic),7.28 (m, 2H, aromatic), 7.52 (m, 2H, aromatic; Mass : *m/z* 195 (M^+ + H).

ii] 4-chloro-2-[1-(4-chlorophenyl)-1*H*-benzimidazol-2-yl]phenol

IR (KBr):3379(-NH), 3211(-OH), 3078(-Ar-CH), 1461(C = N) cm-1; NMR (δ, ppm):δ 6.06 (bs, 1H, NH), 6.82 (d, 2H, aromatic), 6.98 (d,2H, aromatic), 7.21 (d,2H, aromatic),7.52 (d, 2H, aromatic); Mass : *m/z* 211 (M^+ + H).

iii] 1-(4-chlorophenyl)-2-(4-nitrophenyl)-1*H*-benzimidazole

IR (KBr):3211(-NH), 2984(Ar-CH), 1552(-NO_2), 1529 (-C=N) cm^{-1}

NMR (δ, ppm): δ 6.08 (bs, 1H, NH), 6.90 (d, 2H, aromatic), 6.96 (d,2H, aromatic), 7.05 (t,1H, aromatic), 7.54 (d,1H, aromatic),8.12 (d, 1H, aromatic), 8.44 (s, 1H, aromatic); Mass : *m/z* 240 (M^+ +H).

iv] 2-(3-chlorophenyl)-1-(4-chlorophenyl)-1*H*-benzimidazole

IR (KBr):3294(-NH), 3103(Ar-CH), 1184 (-OCH_3), 1588(-C=N) cm-1;

NMR (δ, ppm):3.70 (d,3H, OCH_3), 6.12 (bs, 1H, NH), 6.94 (d, 2H, aromatic), 6.98(d,2H, aromatic), 7.20 (d,2H, aromatic), 7.58 (d,2H, aromatic); Mass : 225 (M^+ +H).

v] 2-(3-bromophenyl)-1-(4-chlorophenyl)-1*H*-benzimidazole

IR (KBr):3346(-NH), 3024(Ar-CH), 2923(-CH_3), 1575(-C=N) cm-1

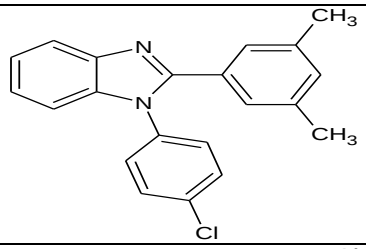
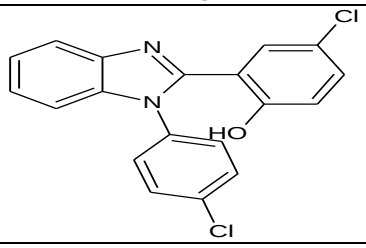
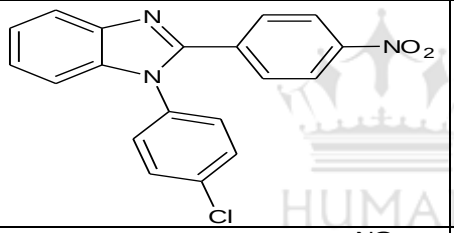
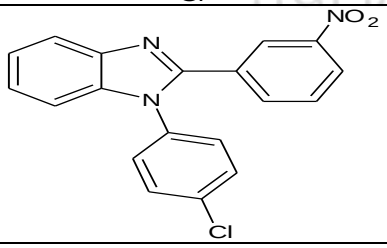
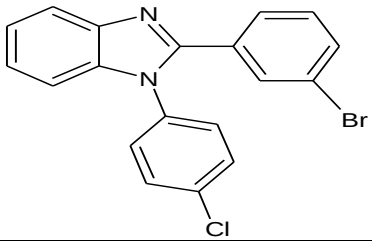
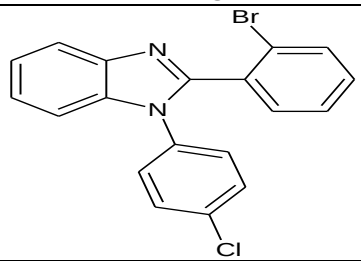
NMR (δ, ppm):δ 2.54 (d, 3H, CH_3),6.06 (bs, 1H, NH), 6.84 (d, 2H, aromatic), 6.96 (d,2H, aromatic), 7.18 (d,2H, aromatic),7.58 (d, 2H, aromatic); Mass : *m/z* 209 (M^+ +H).

vi] 2-(2-bromophenyl)-1-(4-chlorophenyl)-1*H*-benzimidazole

IR (KBr):3402(-NH), 3054(Ar-CH), 1534(-C=N), 1524(-NO_2) cm-1

NMR (δ, ppm):δ 2.56 (d, 3H, CH_3),6.10 (bs, 1H, NH), 6.80 (d, 2H, aromatic), 6.86 (d,2H, aromatic), 7.54 (d,1H, aromatic),8.08 (d, 2H, aromatic); Mass : *m/z* 254 (M^+ +H).

Table No. 1: Physicochemical data of compounds (b1-b6)

Sr. No.	Name	Molecular formula	formula Melting Point [ºC]	% yield	Rf value	Mobile phase
1	b1		120-122 ºC	67%	0.6	T:EA
2	b2		127-129 ºC	80%	0.52	T:EA
3	b3		116-118 ºC	64%	0.71	T:EA
4	b4		132-134 ºC	76%	0.65	T:EA
5	b5		138-140 ºC	72%	0.62	T:EA
6	b6		131-133 ºC	69%	0.74	T:EA

3. Pharmacological activity:

Antimicrobial activity

The compounds (B1-B6) were evaluated for their antimicrobial activity against E.coli, *S.aureus, B.substilis* and *C.albicans* by disk diffusion method was performed using Mac Conkeys agar and Nutrient agar medium. Each compound was tested at a concentration at different concentration and zone of inhibition was measured after 24h incubation at 37ºC [6-10].

4. RESULTS AND DISCUSSION

Pharmacological Studies;

E.coli, S.aureus, B.substilis and Candida albicans and compound b4 shown significant activity. As compared to standard drug Ciprofloxacin and Fluconazole.

Compound no.	Antibacterial activity data in MIC (µg/ml)			Antibacterial activity data in MIC (µg/ml)
	E.coli	***S.aureus***	***B.substilis***	***C.albicans***
b1	6	6	6	6
b2	6	6	6	6
b3	6	6	6	6
b4	12.5	12.5	6	6
b5	6	6	12.5	3
b6	6	6	12.5	3
Ciprofloxacin (std)	12.5	12.5	12.5	Fluconazole (std) 6

5. ACKNOWLEDGEMENT

Authors acknowledge Dr. C. S. Magdum principle of Rajarambapu College of Pharmacy, Kasegaon. For providing the necessary facilities and infrastructure to perform this study.

6. REFERENCES

1. Soni B, Singh M, Bhandari A, Verma R. Synthesis and Antimicrobial activity of some novel N- substituted-2-substituted benzimidazole derivatives. J. Pharm Res. 2012; 5(7), 3523- 3526.
2. Bhardwaj S. Microwave Assisted Synthesis and Pharmacological Evaluation of Some 1, 3, 4- Oxadiazole Derivatives. Sch Res Lib. 2011; 3(2), 556-567.
3. Desai N. Synthesis and Antimicrobial Screening of 1, 3, 4-Oxadiazole and Clubbed Thiophene Derivatives. J Saudi Chem Soc. 2014; 18(1):255-261.
4. J.E.Cheong, M. Zaffagni, I. Chung, Y. Xu, Wang, F.E. Jernigan, B.R. Zetter, L. Sun. Synthesis and anticancer activity of novel water soluble benzimidazole carbamate, Eur.J. Med. 2018; 4: 212-219.
5. Wang M. Design, synthesis and antifungal activities of novel pyrrole alkaloid analog. Eur.J. Med. (2011) 46, 1463-1472.

6. Patel T. Study of novel pyrrole derivatives, Int. j. pharm, 2012, 36-39.
7. Kokare C. Pharmaceutical microbiology experiments and technique. 3rd edition; 2010.
8. Idhayadhulla A. synthesis of some new pyrrole derivatives and there Antimicrobial activity. Der Pharma Chemica. 2011; 3, 210-218.
9. Kumari N. Synthesis and antimicrobial activity of some new 2-Mercapto-3-phenyl-4-oxo-(3H)-quinazolinyl substituted 1, 3, 4oxadiazoles. Ind J Hetro Chem. 2008; 17(5), 331-346.
10. Basavapatna N. Synthesized and In Vitro Antimicrobial Evaluation of New 1, 3, 4- Oxadiazole Bearing 5-chloro- 2 methoxyphenyl Moiety. Inter J Med Chem.2013; 17(2), 11-17.