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RESEARCH ARTICLE

Microwave Assisted Synthesis of Napthaimidazoles Using Acid Catalyst & their Antimicrobial Activity

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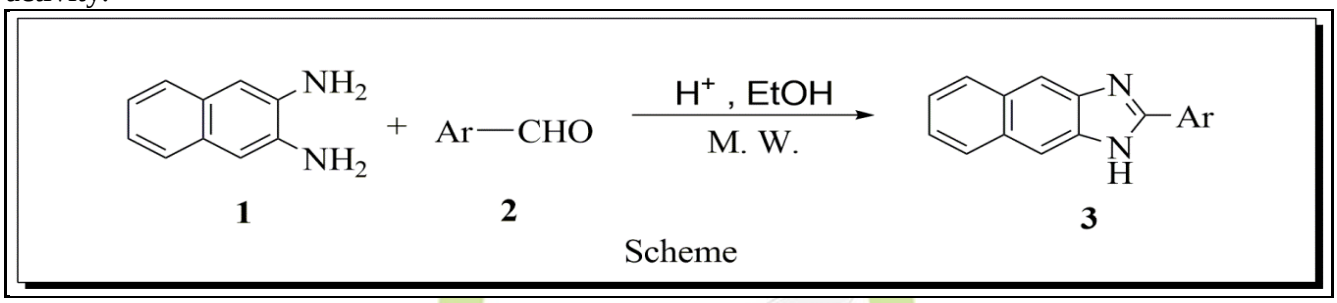
ABSTRACT

It deals with the synthesis of napthaimidazoles **3** by the condensation reaction between 2, 3-naphthalene diamine **1** and aromatic aldehydes **2** catalyzed by the optimized quantity of HCl as a catalyst in ethanol as the solvent. A series of compounds was synthesized by conventional route and under microwave irradiation (MWI) technique. All the synthesized compounds have been characterized by using ^{1}HNMR, ^{13}CNMR, IR and Mass spectroscopy. All the synthesized compounds were tested for their biological activity.



Scheme

KEYWORDS

Napthaimidazoles, Antimicrobial Activity, Microwave, Spectroscopy

INTRODUCTION

Benzimidazole is a heterocyclic aromatic organic compound. It is very important skeletal in medicinal chemistry. Today this moiety bearing various medicinal characteristics.

The most famous benzimidazole derivative in practice is *N*-ribosyl-dimethylbenzimidazole, which act as ligand bind with Co metal in vitamin B_{12}[1]. The application of Benzimidazole records many year back[2].

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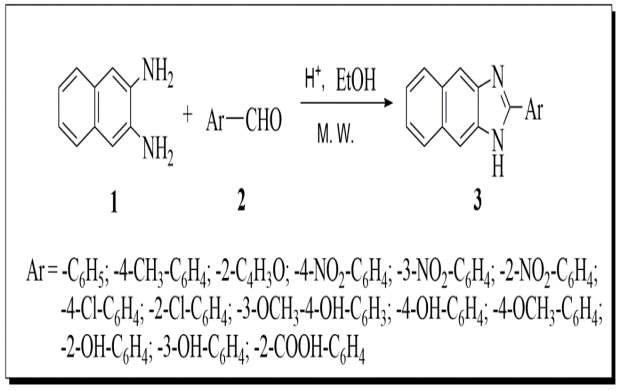
In 1990 different benzimidazole moiety were prepared with different group such as fluorine, tetrahydroquinoline, propylene & ring compoundwhich resulted in drug with bioavailability, increased stability & significant biological potency[3,4]. In 1991 benzimidazole derivatives were synthesized by derivatization at N-H of benzimidazole by electron donating group and substitution with long chain of propyl, acetamido, thio, thiazole-amino, tetramethyl piperidine on pyridine resulting in good antiulcer activity[5,6]. Nowadays infectious microbial diseases are causing problems worldwide, because of resistance to number of antimicrobial agents (β-lactam antibiotics, macrolides, quinolones, and vancomycin). A variety of clinically significant species of

microorganisms has become an important health problem globally[7]. One way to fight with this challenge is the appropriate usage of the available marketed antibiotics the other is the development of novel anti-microbial agents[8]. There is always scope to determine novel chemotherapeutic to remove the emergency need and also release shortage problem of therapy. Due to the structural similarity to purine, antibacterial ability of benzimidazoles are explained by their competition with purines resulting in inhibition of the synthesis of bacterial nucleic acids and proteins[9,10].

A number of Synthetic strategies have been developed for the preparation of substituted napthaimidazoles. The most common method involve the condensation of an aryl-1,2-diamine with various aldehydes compound in refluxing ethanol for 2–12 h, and this typically gives yields of 34–70 %. Hence, the search for the better method, therefore we have plane reported protocol for one-pot synthesis of naphthaimidazole derivatives from readily available 2, 3-naphthalenediamines and aldehyde under acidic conditions. A wide range of functional groups can be tolerated in the building blocks.

REACTION SCHEME

The cyclocondensation reaction between naphthalene-2,3-diamine (0.0105 mole) and bbenzaldehydes (0.01 mole) in ethanol (10 mL) under Microwave to afford naphthaimidazole **A** using 5mmol % HCl with respect to naphthalene-2,3-diamine (**Scheme 1**).



Scheme 1

RESULT AND DISCUSSION

Optimization of reaction condition

The cyclocondensation reaction between naphthalene-2,3-diamine (0.0105 mole) **1** and benzaldehyde **2** (0.01 mole) in ethanol (10 mL) under Microwave to afford Napthaimidazoles **3** (Scheme 1) was chosen as the model reaction for optimization. The amount of HCl was used in the ratio of mmole % with respect to naphthalene-2,3-diamine. The reaction was studied under Microwave at power level 240 Watt. Reaction was also optimized by varying HCl (Table 4.1, entries 1-5). It was observed that 5 mmole % amount of catalyst on the basis of naphthalene-2,3-diamine is suitable to complete.

Table 1: Effect of different catalyst on the condensation of naphthalene-2,3-diamine and benzaldehydes in ethanol under microwave.

Entry	Catalyst	Under Microwave.	
		Time[a] (min)	Yields[b] (%)
1	1mmol % HCl	2	82
2	2mmol % HCl	2	82
3	3mmol % HCl	2	82
4	4mmol % HCl	3	80
5	5mmol % HCl	3	85
6	6 mmol% HCl	3	80

[a] Reaction was monitored by TLC, [b] Isolated yields.

Our next target of the present work was to synthesize all the napthaimidazole derivatives by taking the assistance of microwave irradiation (MWI) technique using ethanol as

the solvent. These series of experiments were also optimized with respect to power levels. The reactions as presented in **Scheme 1** were carried out under microwave irradiation. The MWI reactions were carried out in the Scientific Microwave system CATA-R CATALYST SYSTEM. The optimization of the power levels was checked with reference to duration of reaction, yield improvement. The characteristic data are given in **Table 2**.

Table 2: Data representing the optimization for synthesis of Napthaimidazoles by the assistance of MWI technique.[a, b]

Power Levels in Watt	Reaction Time (min)[a]	% Isolated Yield[b]
140	4	65
210	4	80
240	**3**	**85**
280	3	75
350	3.5	75

[a]Reaction was monitored by TLC.; [b]Isolated yields.

From the above experimental data, it becomes clear that more efficient results were obtained at 240 W power level of the MW instrument. At this power level Naphthaimidazole derivative were obtained in 85% yield with very good purity in 3 min.

EXPERIMENTAL

Chemicals and Reagents

All chemicals used were of laboratory reagent grade and used without further purification. 2,3-naphthalenediamines, HCl and Aldehydes were obtained from Samir Tech Chem. Pvt. Ltd., Vadodara, India. All the solvents were supplied by Sisco Chem. Pvt. Ltd., Mumbai, India.

Analytical Methods

Determination of M. P. was done by open capillary process and it is uncorrected. ^{13}C NMR & ^{1}H NMR spectra were measure by solutions in DMSO-d_6 using Bruker Avance 400 spectrometer having radiofrequency 400 MHz for ^{1}H NMR, & 100 MHz for ^{13}C NMR. Chemical shifts (δ) are expressed in parts per million (ppm) and referenced to the residual protic solvent. FT-IR spectra were recorded on ABB Bomem Inc. FT-IR 3000 spectrophotometer and are expressed in wave numbers (cm^{-1}). The mass spectra (ESI-MS) were recorded on Shimadzu LCMS-2010 spectrometer and Carbon, Hydrogen and Nitrogen were estimated on a PerkinElmer 2400 Series II CHNS/O Elemental Analyzer. All the reactions were monitored by TLC using aluminum sheet precoated with silica gel 60 f254 (Merck).

General Experimental procedure

To a mixture of an 2,3-naphthalenediamine (1 mmol) and benzaldehyde (1 mmol) in ethanol (5mL), 5% w/w HCl with respect to 2,3-naphthalenediamine was added and the mixture was reflux under microwave at optimum power level. The progress of the reaction was monitored by TLC using aluminum sheet precoated with silica gel 60 f_{254} (Merck). After completion of the reaction, ethyl acetate was added to the solidified mixture. The filtrate was dried over anhydrous Na_2SO_4. The solvent was evaporated with care and the pure product was obtained. The product obtained had been characterized by FT-IR, ^{1}HNMR, ^{13}CNMR and GC-MS.

(I) Against Staphylococcus aureus:

Maximum activity were found in compounds (C, B &H) zone of inhibition-10.0 m.m. and minimum activity were found in compound (A) zone of inhibition -6.0 m.m

(II) Against Bacillus megaterium:

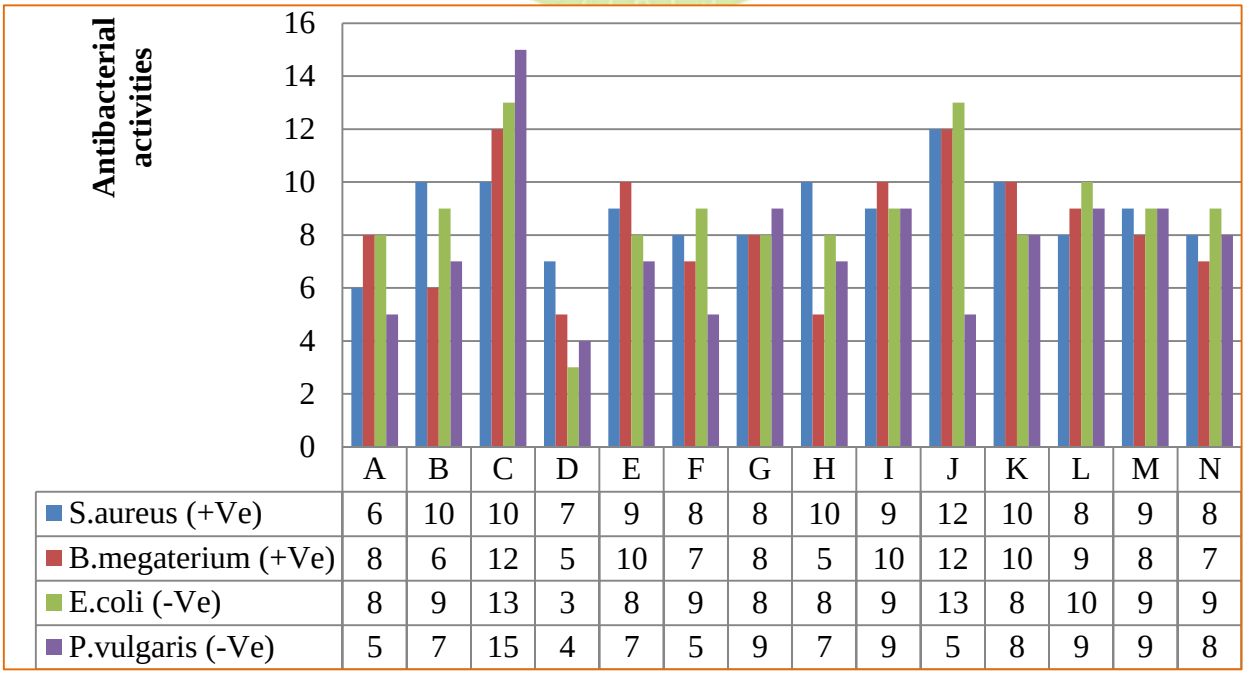
Maximum activity were found in compounds (C & J) zone of inhibition -12.0 m.m where as minimum activity were found in compound (D) zone of inhibition -5.0 m.m.

Table 3: The characteristic data showing the synthesis of Napthaimidazoles

Code	Ar	Thermal Conditions		Microwave Irradiation 240 W	
		Reaction Time[c] (h)	Yield (%)	Reaction Time[c] (min)	Yield (%)
A	C6H5-	3	88	3	85
B	4-CH3-C6H4-	4	70	3	75
C	4-Cl-C6H4-	3	80	3	90
D	2-Cl-C6H4-	3.5	78	3	88
E	4-NO2-C6H4-	3	90	3	90
F	2-NO2-C6H4-	3	84	3	89
G	3-NO2-C6H4-	3	90	3	90
H	2-C4H3O-	3	85	3	85
I	4-OCH3-C6H4-	4	78	4	74
J	2-OH-C6H4-	3.5	78	3.5	74
K	3-OH-C6H4-	3	80	3.5	80
L	4-OH-C6H4-	3.5	77	3.5	82
M	2-COOH-C6H4-	3.5	81	3	82
N	4-OH-3-OCH3-C6H3-	4	76	3.5	75

[a]Reaction was monitored by TLC.; [b]Isolated yields.

Antimicrobial activity of Compounds A-N



	A	B	C	D	E	F	G	H	I	J	K	L	M	N
S.aureus (+Ve)	6	10	10	7	9	8	8	10	9	12	10	8	9	8
B.megaterium (+Ve)	8	6	12	5	10	7	8	5	10	12	10	9	8	7
E.coli (-Ve)	8	9	13	3	8	9	8	8	9	13	8	10	9	9
P.vulgaris (-Ve)	5	7	15	4	7	5	9	7	9	5	8	9	9	8

(III) Against Escherichia coli:

Maximum activity were found in compounds (C,B & F) zone of inhibition -13.0 m.m and minimum activity were found in compound (D zone of inhibition -3.0 m.m

(IV) Against Proteus vulgaris

Maximum activity were found in compound (C) zone of inhibition -15.0 m.m (near to standard drug) and minimum activity were found in compounds (D) zone of inhibition 4.0 m.m.

CHARACTERIZATION

2-phenyl-1H-naphtho[2,3-d]imidazole A

IR (KBr): 3433 (w), 3050, 1446, 1412, 1280, 970, 750 cm^{-1}; ^{1}H NMR (400 MHz, DMSO, δ ppm): 12.94 (s, 1H, NH), 8.21 (d, 2H, *J*=7.6 Hz, Ar-H), 7.62-7.21 (m, 9H, Ar-H); ^{13}C NMR (DMSO-*d6*, δ ppm): 151.7, 140.1, 130.6, 130.2, 129.4, 126.9, 122.5, 116.4; ESI-MS: m/z $(M+H)^{+}$ 312.10; Anal. Calcd. for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95; N, 11.47 ; Found: C, 83.52; H, 4.96; N, 11.53.

CONCLUSION

We have reported green protocol for one-pot synthesis of napthaimidazoles from readily available 2,3-naphthalenediamines and various aromatic aldehydes by a simple and convenient protocol. The conditions are mild and a wide range of functional groups can be tolerated in the building blocks for synthesized products. Antimicrobial activity of all the synthesized compounds was done and compare with standards. Compounds C, B, H and F shows good activity.

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