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Synthesis, Characterization and Biological Activity of Imidazole Derivatives

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ABSTRACT: Substituted Imidazoles have received considerable attention during last two decades as they are endowed with variety of biological activities and have wide range of therapeutic properties. Imidazole derivatives are associated with many therapeutic fields. Some have been employed as anthelmintic, antibacterial and antiprotozoal. A literature survey indicates that imidazole derivatives possess different pharmacological and biological activities, out of which the most potent is anti-fungal activity. In view of this and literature survey we have planned design, synthesis of some novel imidazole derivatives and evaluation of biological activity
Keywords: Imidazole, Morpholine, Anti-microbial activity, Synthesis..

I. INTRODUCTION

A key part of pharmaceutical research is the finding of new with extra powerful proportionate of granules along-with previously formed actions. Modifying the parent compound increases compound efficacy, and removes the additional impacts or venomousness connected to the parent medicine in most cases.

A large amount of drug substances, mainly of synthetic origin[1], include alkaloids, xanthines, cardiac glycosides and vitamins, have been obtained from natural resources. Two nitrogen-oriented, 1-3 position-oriented heterocyclic derivatives contain a broad variety of organic activities [2]. Amount of sulfur and nitrogen in the live and non-living system containing [3-5] compounds. Among the sulfur and nitrogen heterocyclic compounds, six and five members are of utmost importance because they include many biological and industrial applications [6, 7]. They include the sulfur and the nitrogen heterocyclic compounds [6].

The compound containing the imidazole ring, like vitamin B12 and several pilocarpine alkaloids, are very important in the living system. The essential amino acid histidine includes imidazole; histitdines within enzymes are closely associated with catalysis, which involves the transfer of proteins. 1-Histidine, which is a dipeptide component of the mammalian body, and its relative carnosine. Histamine is a vasodilator and a big factor in allergic reaction such as hey-fever, structurally related hormone.

Any of them have physiological properties, such as priscal, privine or antihistamine. Azamycin is a 2-nitroimidazole antihistamine. The treatment of peptic ulcer is based on synthetic imidazoles and metronidazole, which is a bactericidal and protozociadal in the therapy of amenetic dysentery. The antifungal imidazole derivatives are miconazole, clotrimazole, ketaconzole and are currently in use. We prevent the synthesis of ergosterol, a key cell sterol on the fungal cell wall. The first reported oral action of imidazole was ketaconazole.

A variety of large adrenergic agents include imidazoline derivatives, for example, private hydrochloric acid, tetrahydrochloric acid, nasals, and occular mucous.

Chemistry of Imidazoles

In the last 30 years the imidazole ring has gained tremendous interest. That is, the industry started in the year 1970 with regard to its chemical structure, physical properties and the application of its various derivatives.

Imidazole, or imidazoline, is an azapyrrole, with one carbon atom separating the nitrogen atoms. This compound was earlier also called glyoxaline, since glyoxaline and ammonia were first prepared in 1858.

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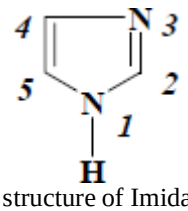


Figure 1 Basic structure of Imidazole

Place 1 is assigned to imino nitrogen while place 3 is assigned to tertiary nitrogen atom. Imidazoles are very stable compounds that don't autoxidize butpotassium permagnate destroys them. Imidazole also exists in tautomeric forms, which can bear the H^2 molecule on either of the N^2 molecule, resulting into 4-methyl imidazole is identical with 5-methyl imidazole and this compound may be designated either 4- or 5-methylimidazole, depending on the position of the amino hydrogen. All the tautomeric pairs like that are in separable.

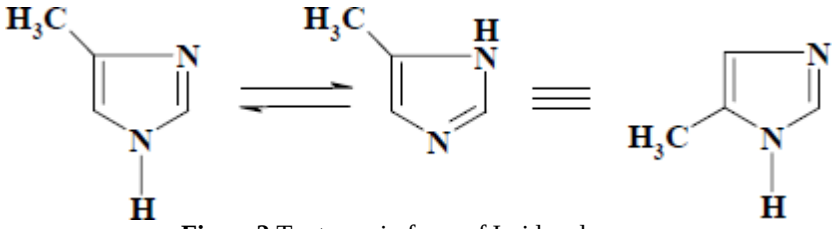
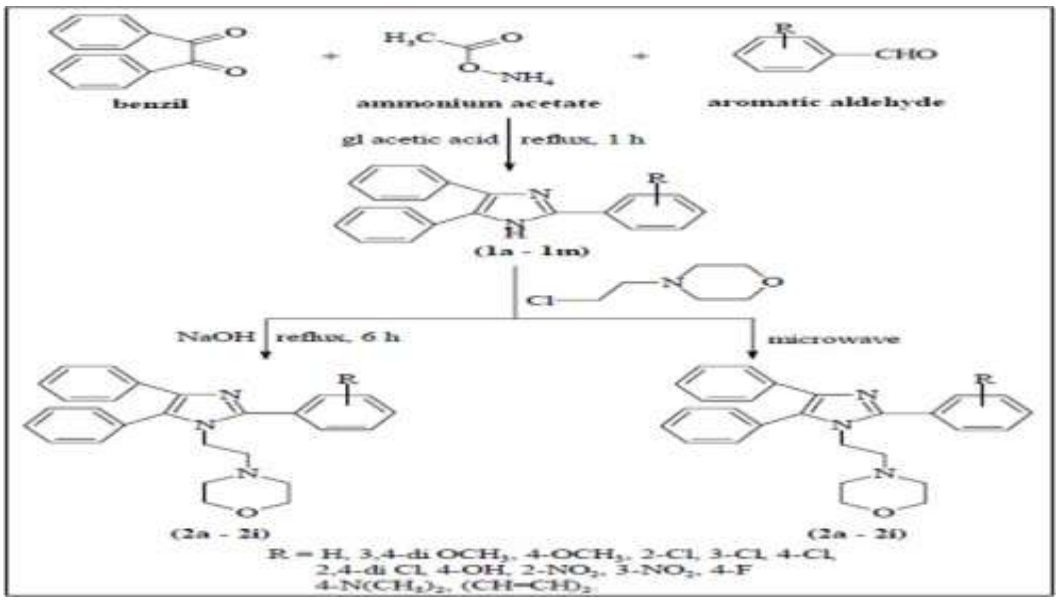


Figure2 Tautomeric form of Imidazole

The contribution of imidazole charged structures is significant over benzene. Therefore imidazole has increased reactivity to electrophillic attack.

Material and Method



2,4,5-triphenyl-1H-imidazole preparation process (1a):

Benzyl (0,01 mol), benzaldehyde (0,01 mol) and 25 mililitre attributed to acetate have been added to the clean and dry bottom flask and have been refluted in contents in favor of one hour.

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Reaction admixtures were calm and drained into 50 milliliter of water and filtered and dried the precipitate thus removed. Recycling from pure alcohol, the obtained 2,4,5- triphenyl-1H-Imidazole (1a), the output was 60%; melting point 272 ° C.

The other replaced imidazole derivatives of this series (1b-m) were made using the same method as above, and the information in Table No-I was given.

Preparation process (2a):

Conventional method:

10 milliliter of alcohol and sodium hydroxide (0.01mol) were added to a neat and arid circular bottom vial by stirring in consideration of 10 min, 2.4,5-triphenyl-1H- imidazole (0.01mol),(1a) added and stirred for ten minutes. In addition to the reaction mixture, the 2-chloro ethyl morpholine (0.01mol) was replanted for 360 minutes. The admixture of the chemical process was cleaned, then filtered followed by dried in the separated in tight form. Recrypted from absolute alcohol the compound (2a), its yield was 55 percent; m.p. 178 degrees Celsius.

Many substituted imidazole derivatives, i.e. (2b-i), were prepared using the same technique as above, and the data were given in Table No-II.

Microwave Method:

Stirred and radiated at 100 W for 4.5-5.0 min with a mixture of 2,4,5 triphenyl-1H-imidazole (0.01mol) (1a), 2-chlorinated ethyl morpholine (0.01mol) and sodium hydroxide (0.01mol) in ethanol (5 milliliter). The compound (2a) obtained was recrypted from absolute alcohol with an efficiency of 80%; m.p. 178 degrees Celsius.

In this sequence, other replaced imidazole derivatives, i.e. (2b-i) were generated using the same process.

SerialCount	Com-poundCode	R	MolecularThread	Molecu- lar Weight	Melt- ing Point (^{o}C)	Yiel d %
1	1a	H	$C_{21}H_{16}N_2$	296	272-274	61
2	1b	3,4-di OCH 3	$C_{23}H_{20}N_2O$ 2	356	140-160	64
3	1c	4- OCH 3	$C_{22}H_{18}N_2O$	326	222-224	58
4	1d	2-Cl	$C_{21}H_{15}N_2C$ l	330	176-180	59

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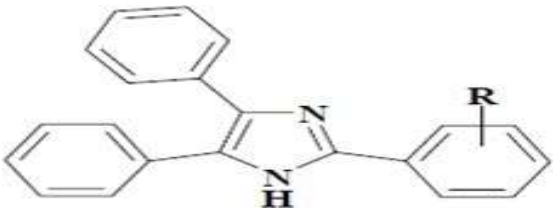
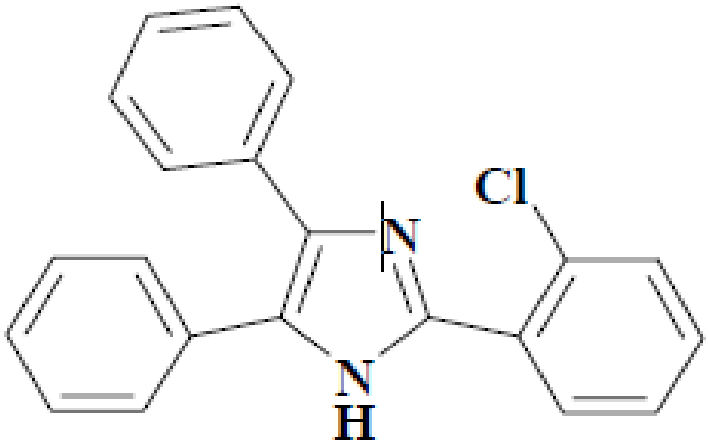
Table No-I: Structural properties information of formulated substances (1a - 1m)



SPECTRAL DATA
Compound (1d)



^{1}H NMR Spectra (δ ppm):

Value in δ ppm	**Nature of segments**	**No. of pro-tons**	**Type of proton**
10.24	Singlet	1H	1H of NH
7.3-8.5	Multiplet	14H	14H of Ar-H

MASS Spectra (m/z):
Molecular weight of the compound is 330; the granular ion peak appeared at 331 asM+1.
IR Spectra (cm-1):

Kind of oscillation	**Cluster recurrence at ripple count (cm^{-1})**
NH stretching	3190
Ar-CH=CH stretching	3065 and 2955

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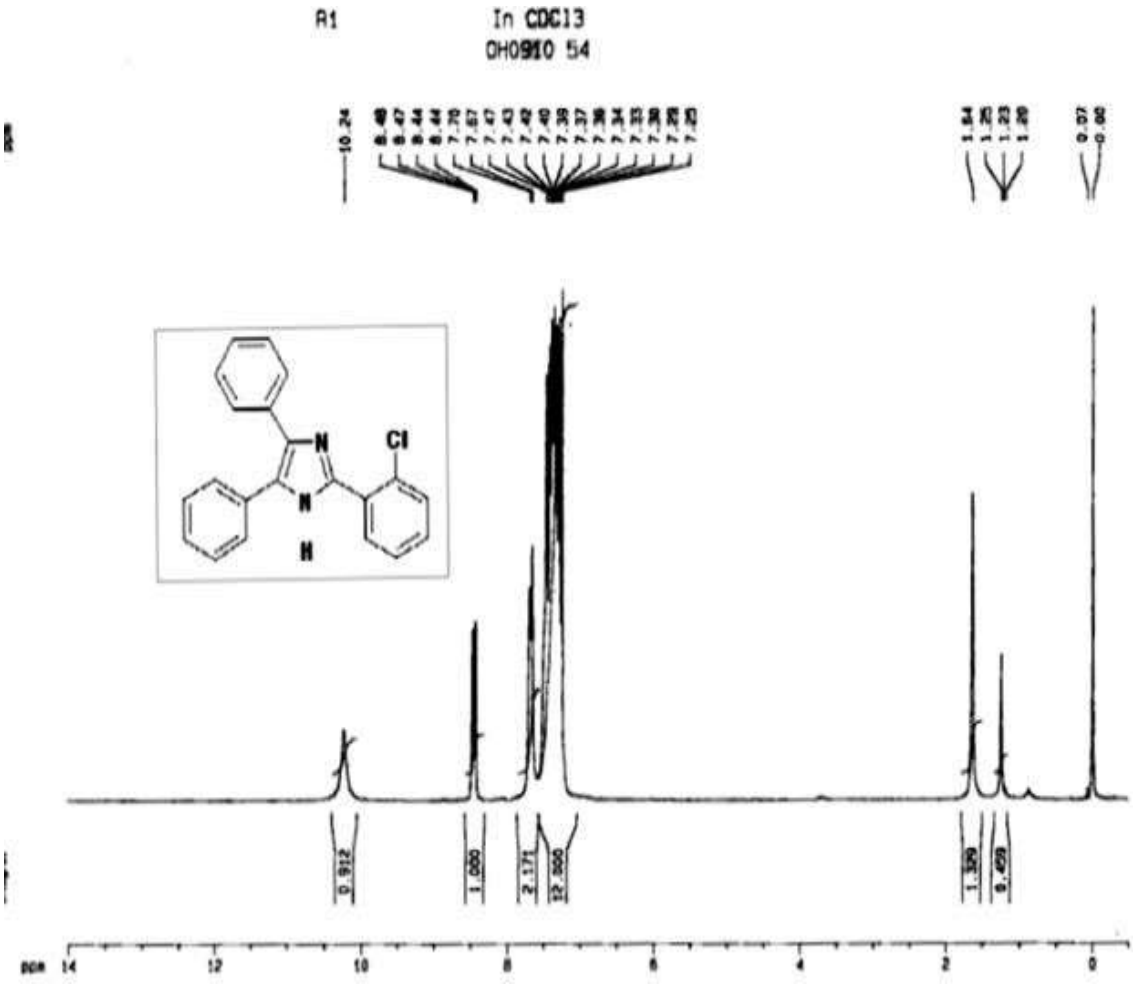
Ar-CH- bending	734

^{1}H Nuclear Magnetic Resonance order of Substance (1d)



MASS coloration of Substance (1d)

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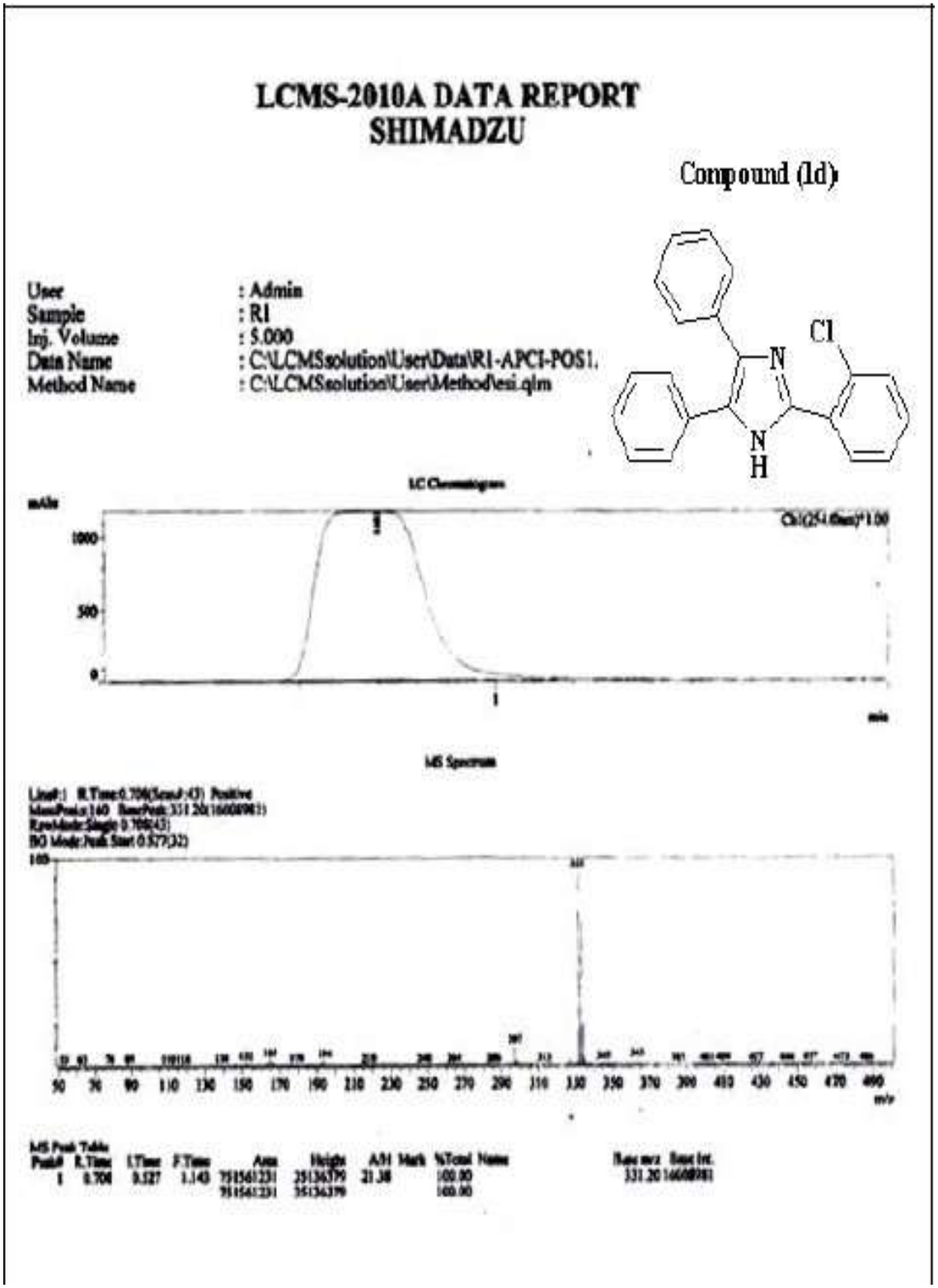

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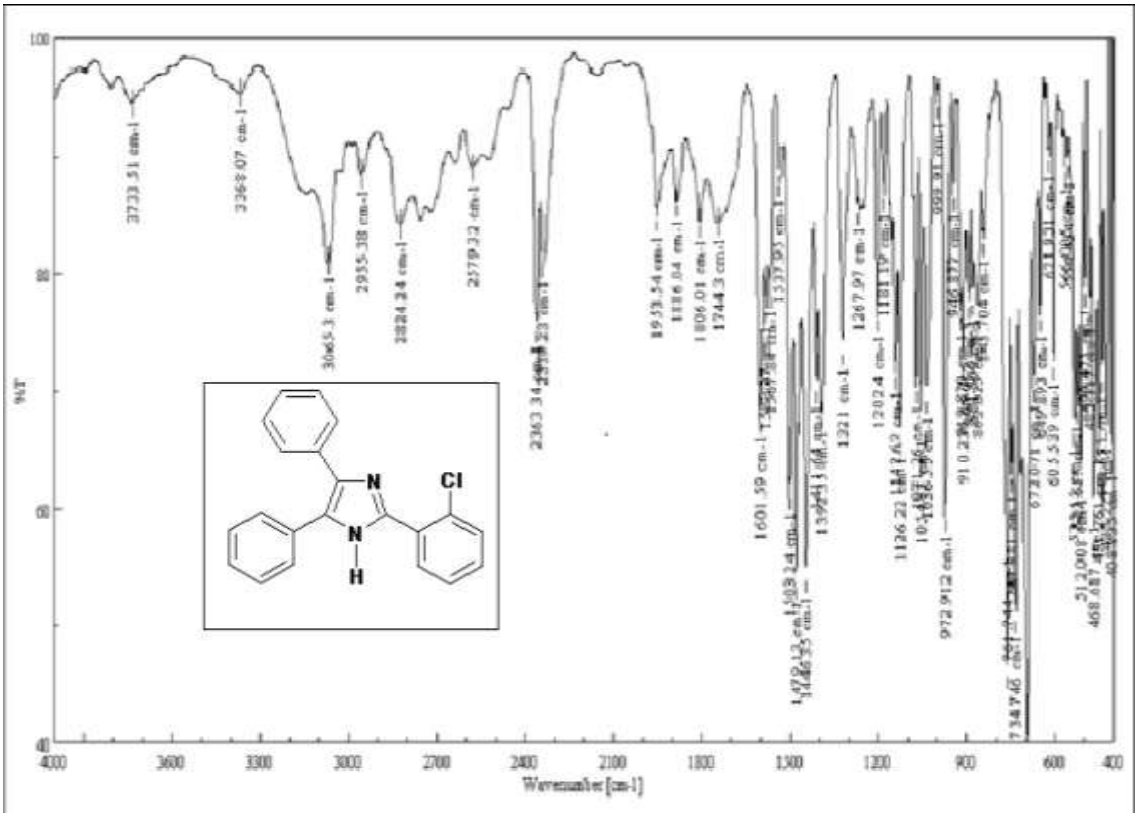
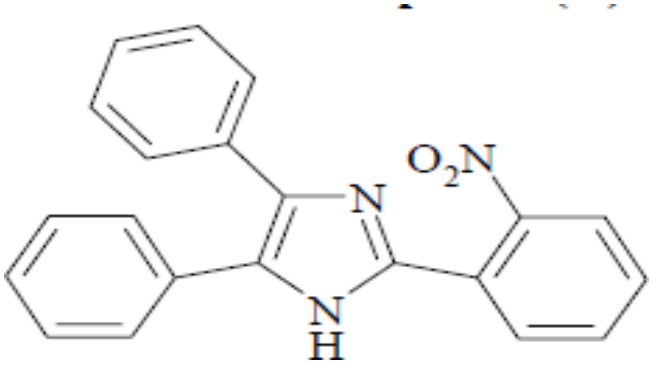
IR Spectrum of Substance (1d)



Compound (1i)



^{1}H Nuclear Magnetic Resonance Spectra (δ ppm):

Value in δ ppm	Nature of segments	No. of pro-tons	Type of pro-ton

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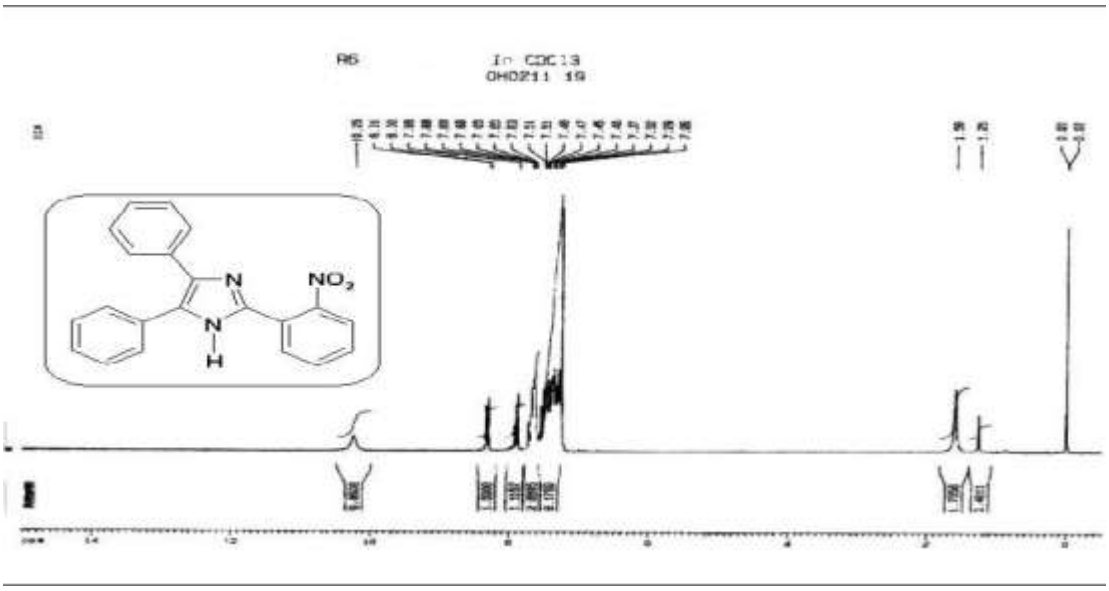
10.25	Singlet	1H	1H of NH
7.2-8.3	Multiplet	14H	14H of Ar-H

MASS Spectra (m/z):
Molecular weight of the substance is 341; the granular ion peak appeared of 343 asM+2.
IR Spectra (cm-1):

Kind of Oscillation	**Cluster recurrence at ripple count (cm^{-1})**
NH- stretching	3155
Ar-CH=CH-stretching	3027, 3082

^{1}H Nuclear Magnetic Resonance Spectrum of substance (1i)



MASS Spectrum of substance (1i)

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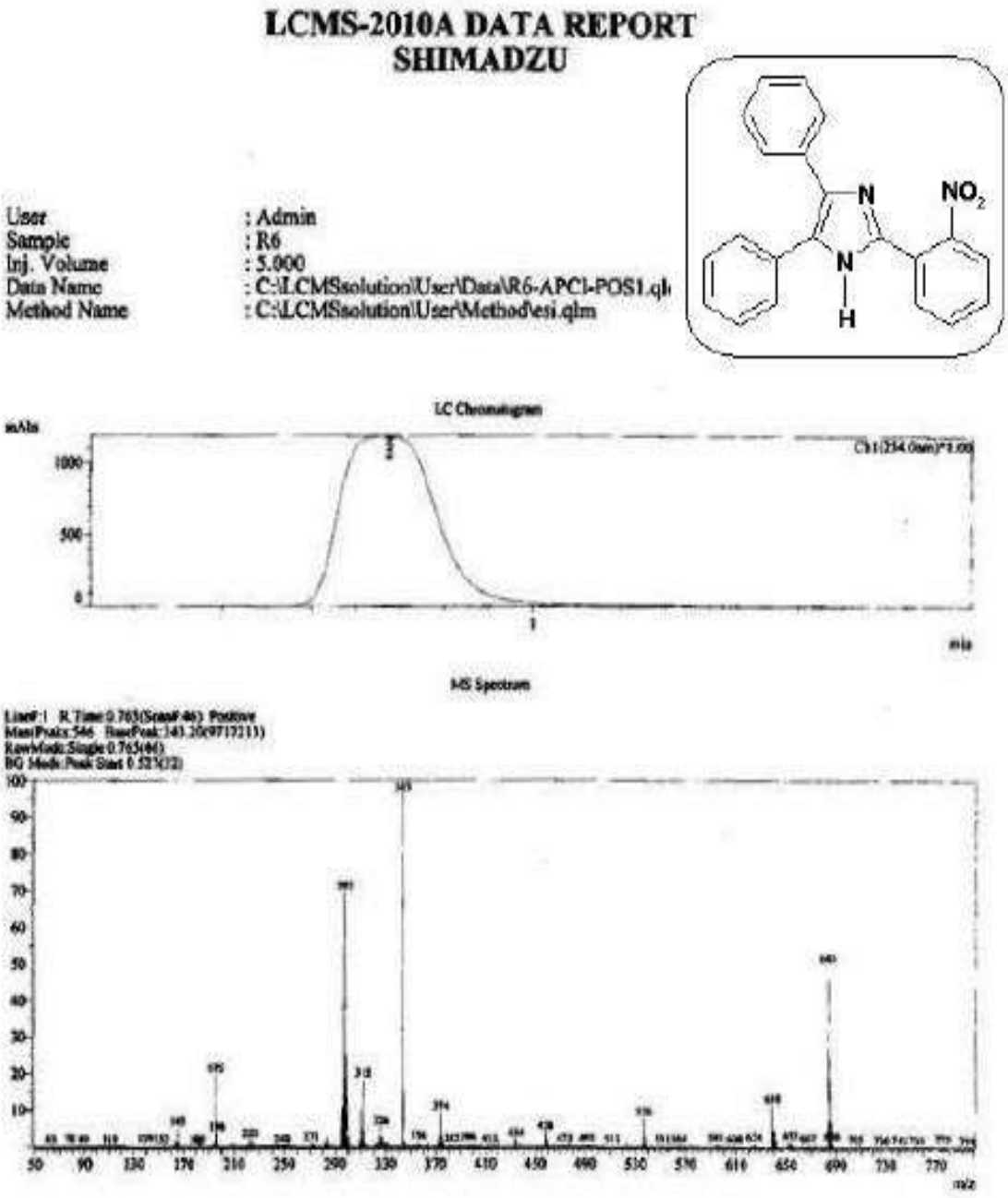

MASS Spectrum of Substance (1i)

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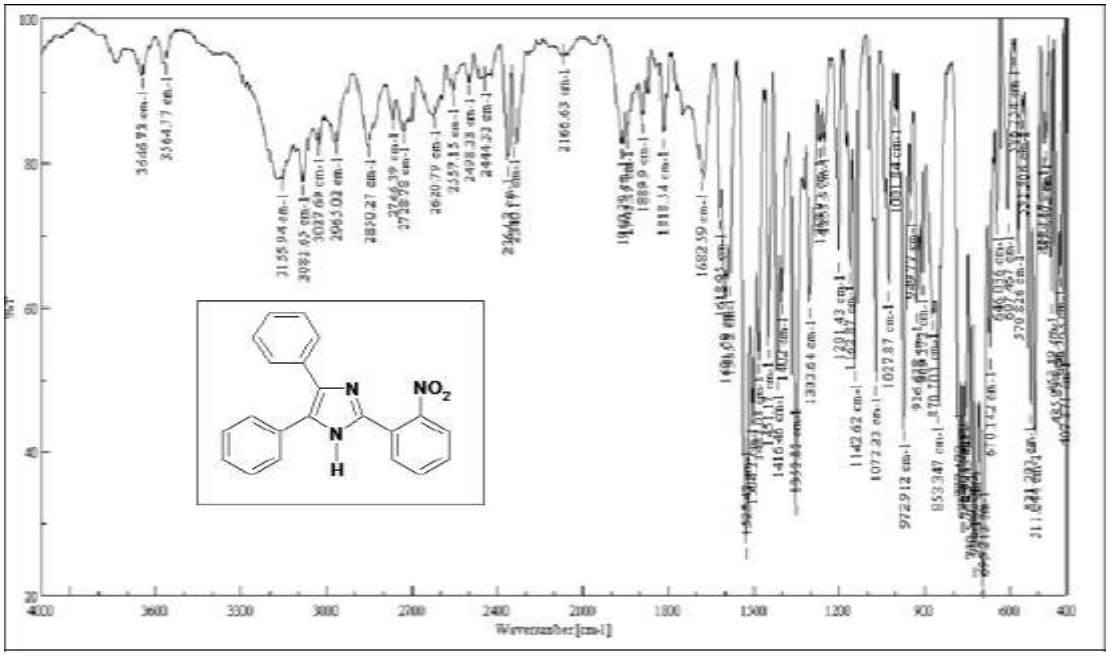
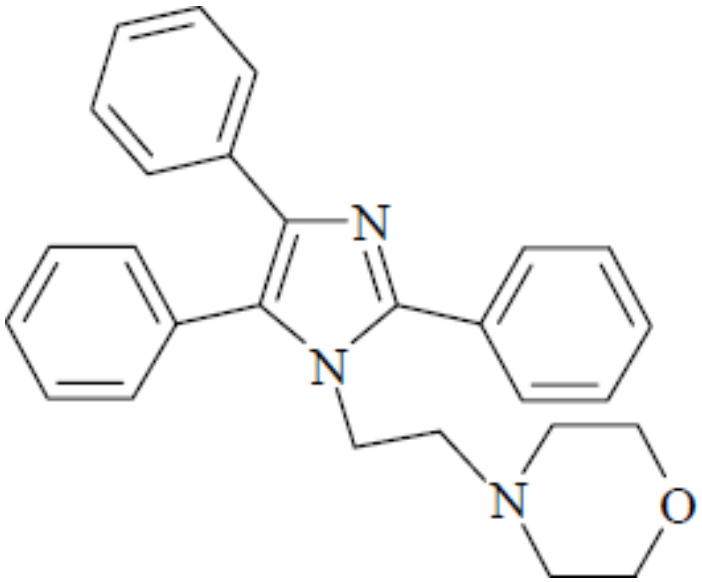


Compound (2a)



[1]H Nuclear Magnetic Resonance Spectra (δ ppm):

Value in δ ppm	Nature of segments	No. of pro-tons	Type of proton
7.3-8.1	Multiplet	15H	15H of Ar-H

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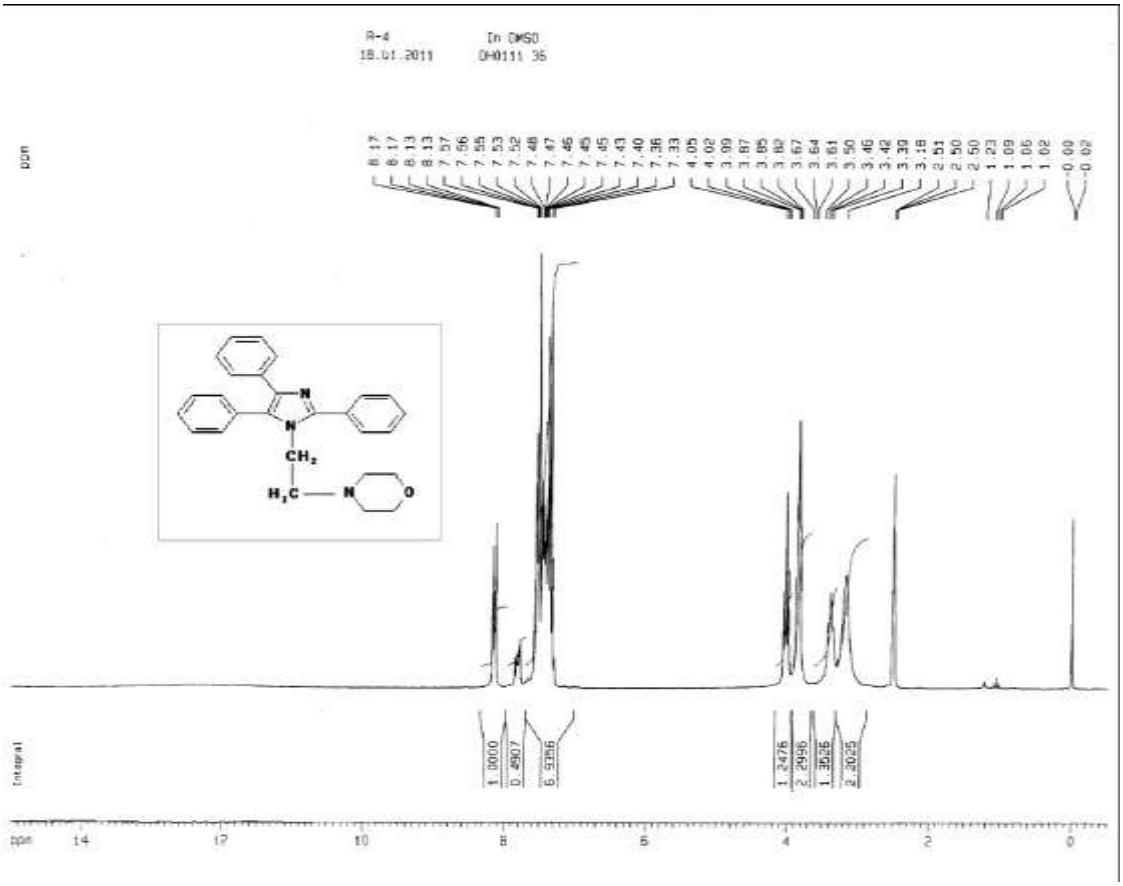
3.8-4.1	Multiplet	8H	4H of $N(CH_2)_2$-N & 4H of morpholine $N(CH_2)_2$
3.1-3.5	Multiplet	4H	4H of $O(CH_2)_2$ of morpholine

^{1}H Nuclear Magnetic Resonance Spectrum of Substance (2a)



Compound (2d)

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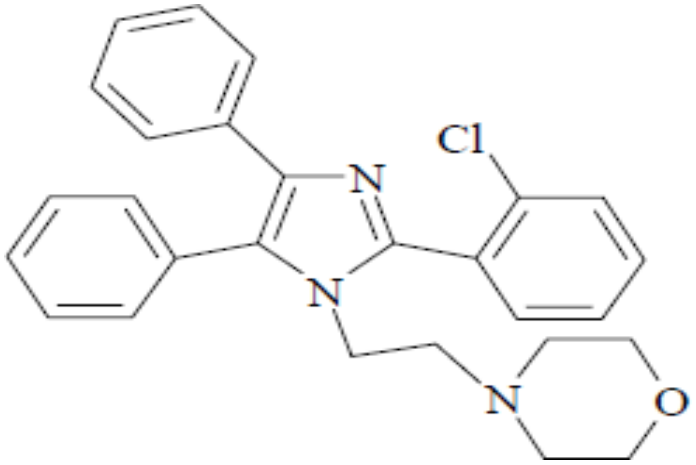

^{1}H Nuclear Magnetic Resonance Spectra (δ ppm):

Value in δ ppm	Nature of seg-ments	No. of pro-tons	Type of proton
7.1-8.2 Multi	plet 14 H		14H of Ar-H
3.8-4.1	Multiplet	8H	4H of $N(CH_2)_2$ & 4H of morpholine $N(CH_2)_2$
3.0-3.2	Multiplet	4H	4H of $O(CH_2)_2$ of morpholine

IR Spectra (cm-1):

Kind of Oscillation	Cluster recurrence at ripple count (cm^{-1})
Ar-CH=CH stretching	3064
CH-CH- stretching	2970
C-O-C-stretching	1253

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Ar-CH- bending	734

II. RESULTS

Antibacterial activity:

In consideration of bactericidal actions, studies on concentrations of 50 µg / milliliter and 100 µg / milliliter, synthesized compounds (2a-i) were tested with DMF as a control of nutritive gelatinous substance tool Bacillus species of subtilis family, Bacillus species of pumilus family, E. coli, with P. Aeruginosa. In contrast with Gm+ve and Gm-ve microbes are considered to use to analyse, ciprofloxacin was a normal drug. Annexure No-III data indicate that the compounds have a moderate and weak activity, while antibacterial activity has been observed with several imidazols, but that some synths failed to produce significant antibacterial activity. Compounds 2b and 2c display significant Bacillus subtilis activity, and compounds 2b, 2i show significant Pseudomonasaeruginosa activity, the majority of the compounds displayed poor activity relative to standard Ciprofloxacin.

Activities of antifungal drugs:

Both compounds were screened for the use of DI-METHYL-FORMAMIDE to monitor Aspergillus niger and Candida albicans with a concentration of 100 µg / milliliter in potato-dextrose agar media in antimicrobial activity studies. The standard application is clotrimazole 100 µg / milliliter. Data in Table No-IV show that Candida Albicans remaining compounds are significantly active in the 2d, 2e, 2 g and 2h compounds, Candida Albicans are low in activity and Aspergillus niger in the compounds 2d and 2i are significantly affected by the other Candida Albicans.

III. DISCUSSION

By having the bactericidal monitoring, Results suggests that the compounds depicts moderate to weak actions. The compounds 2b, 2c and 2i showed good response opposite to some of the micro-organisms considered in the analysis, rest of the mixturesshowed to depict weak and average in actions. In the midst of all these multiple mixtures the 2b, 2c with 2i depicted better response viz-a-viz, some other admixtures. Ideal Ciprofloxacin, was the drug that depict biggest inhibitory zone.

During the process of fungicidal actions, the synthesized compounds 2d, 2g, 2h and 2i has only shown significant fungicidal actions opposite to the albicans species of Candida family and niger species of Aspergillus family, rest of compound shown moderate activity.

The above results establish the fact that the substituted imidazole can be studied further to search for new antibacterial compounds.

8.1 USES OF IMIDAZOLES:

Among many uses, one usage of Imidazole is in purifying His labeled proteins in chromatography with immobilized metal affinity (IMAC). In order to evade the attached proteins which are connected to the Nickel ions that are linked to the bead stratum, Imidazole is used in the chromatography column. Extra amount of imidazole is crossed from the tube, the His-linked with Ni is displaced, with the His-linked long chains of amino acids free. Buffers can be prepared by using Imidazole on the normal room temperature within the pH scale of 6.2-7.8. Imidazole is suggested as a buffer ingredient for horseradish peroxides. This also acts as a binding molecule with affinity towards metal ions.

Imidazole consumption (orally) has positive results on skin diseases in seborrhoea. For a kind of skin disease in which it shows red patches, results showed post 45 days to 90 days. For skin inflammation, patients start with reduced symptoms within 1 to 1 and a half month. Positive outcomes of this process come without using ointment formulations and another treatment.

In drug discovery the nucleus of the Imidazole is an effective synthetic strategy. Multiple preparations were made like Moxonidine, Clotrimazole, Azomycin, Miconazole, Clonidine and Ergothionine pharmacological agents. Some imidazole derivatives' major uses as a drug in consideration of the therapy of dental stomatism. Imidazole has been a major component of many prescription substances. Synthetic Imidazoles are used in many fungicidal, anti-protozoal along-with hypertension- reducing drugs and fungicides. A small part of the molecule of theophylline present in tea leaves and coffee beans that activates the central nervous system.

This is available in mercaptopurine anti-

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carcinogenic medicine that was considered to be used in blood-cancer by mixing up with DNA actions. With some of the transition metals, Imidazole can be used as a Corrosion agent like Cu, in industry. Conductivity of Copper lessens because of corrosive oxides and sulfide. Most organizational and technically important compound contains byproducts of the imidazole. The not-so-affected-by-heat imidazole with other thermally and chemically azoles get fused in a benzene ring with serving like a substance that slows down or reduce the intensity of fire. Imidazole is present in many substances that are utilized in consideration of imaging and electronics.

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