SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL IMIDAZOLE BASED COMPOUNDS

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Abstract

This study focuses on synthesis and biological evaluation of a diverse library of more than fifty novel imidazole-based compounds. The objective was to investigate their potential as antibacterial and antifungal agents. Heterocyclic and fused heterocyclic compounds have been extensively explored in drug development due to their biological and synthetic utility. Imidazole compounds, in particular, hold great importance in medicinal chemistry. The research comprises three main parts. Firstly, an extensive literature survey was conducted to identify biologically active imidazole compounds associated with antibacterial and antifungal activities. Based on this knowledge, the second part involved the rational design of target compounds using well-known drugs such as clemizole, etonitazone, envioroximal, astemizole, omeprazole, pentoparazole, and thiabendazole, which possess imidazole/benzimidazole heterocyclic or imidazole nucleus as the pharmacophoric group. In the third part, various substituted imidazole derivatives were synthesized using different synthetic schemes. Conventional methods were employed for the synthesis, and the structures of the newly synthesized compounds were confirmed using modern analytical techniques such as IR, NMR, and mass spectrometry. The synthesized compounds were then subjected to antibacterial and antifungal screening. The synthetic protocols outlined in the study were successfully applied to synthesize the proposed compounds. For instance, compounds 2a-j and 3a-j were synthesized via scheme-1, which involved the reaction of 1-(4-chlorophenyl) ethanone with selenium dioxide to obtain 2-(4-chlorophenyl)-2-oxoacetaldehyde (1), followed by treatment with various benzaldehydes and ammonium acetate to obtain 4-(4chlorophenyl)-2-(substituted) phenyl-1H-imidazole (2a-j). Compound 2a-j was further reacted with tetrahydrofuran and chlorobenzene to yield the final products, 4-(4chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazole (3a-j). Similar synthetic schemes were employed for the synthesis of compounds 3i-xii (scheme-2) and 4i-xii (scheme-3), resulting in the successful preparation of twelve new imidazole derivatives in each case. The structures of the newly synthesized compounds were confirmed by analytical techniques, and their purity was assessed through TLC examination.

Keywords: Novel Imidazole, Anti-bacterial and Anti-fungal agents, IR, NMR.

Introduction:

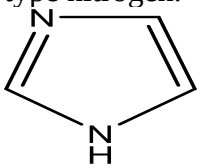
Imidazole (ImH) is an organic compound with the formula $C_3N_2H_4$. It is a white or colourless solid that is soluble in water, producing a mildly alkaline solution. In chemistry, it is an aromatic heterocyclic, classified as a diazole, and has non-adjacent nitrogen atoms in meta substitution. Imidazole has occupied a unique position in heterocyclic chemistry, and its derivatives have attracted considerable interests in recent years for their versatile properties in chemistry and pharmacology. Imidazole is nitrogen-containing heterocyclic ring which possesses biological and pharmaceutical importance. Thus, imidazole compounds have been an interesting source for researchers for more than a century. The imidazole ring is a constituent of several important natural products, including purine, histamine, histidine, and nucleic acid.

Chemistry of Imidazole:

Imidazole is incorporated into many important biological molecules. The most pervasive is the amino acid histidine, which has an imidazole side chain. Histidine is present in many proteins and enzymes and plays a vital part in the structure and binding functions of hemoglobin. Histidine can be decarboxylated to histamine, which is also a common biological compound. One of the applications of imidazole is in the purification of His tagged proteins in immobilised metal affinity chromatography (IMAC). Imidazole has become an important part of many pharmaceuticals. Synthetic imidazoles are present in many fungicides and antifungal, antiprotozoal and antihypertensive medications. Imidazole is part of the theophylline molecule, found in tea leaves and coffee beans, which stimulates the central nervous system. Apart of its use for pharmaceutical purpose it also have varying applications in industries, the imidazole has been used extensively as a corrosion inhibitor on certain transition metals, such as copper. Preventing copper corrosion is important, especially in aqueous systems, where the conductivity of the copper decreases due to corrosion. Many compounds of industrial and technological importance contain imidazole derivatives. The thermostable polybenzimidazole (PBI) contains imidazole fused to a benzene ring and linked to benzene, and acts as a fire retardant. Imidazole can also be found in various compounds which are used for photography and electronics. This review mainly enlights the pharmaceutical importance of the imidazole moiety

Structure of Imidazoles:

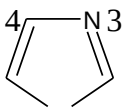
Imidazole is a five-membered heterocyclic moiety that possesses three carbon, two nitrogen, four hydrogen atoms, and two double bonds. It is also known as 1, 3diazole. It contains two nitrogen atoms, in which one nitrogen bear a hydrogen atom, and the other is called pyrrole type nitrogen.



Imidazole

Nomenclature and Structure of Imidazole:

Imidazole is the accepted name for the parent compound of the series, although other names such as glyoxalline, imidazole and 1, 3-diazole are frequently encountered. The numbering of the imidazole ring follows the accepted pattern for heterocyclic compound. Imidazole was first prepared by Debus[2] in 1858. Structure of Imidazoles is best demonstrated by its mesmeric structure or by a set of resonance structure.



Materials and Methods:

Used Equipments:

The analysis of the synthesized compounds was done using various equipments which are listed below:

IR: The IR spectra were recorded in KBr pellets on Shimadzu FT-IR Spectrometer FTS 135.

^{1}H NMR: The Proton Magnetic resonance spectra (^{1}H NMR) were recorded on Brucher

300MHz & 400 MHz instrument using $CDCl_3$ and DMSO as solvent and TMS as internal standard.

M.S.: The Mass spectra were recorded on UPLC-MS/MS-ESI-Q-TOF, waters SYNAPT (Software-Mass Linux V4.1).

Mp.: Melting point of compounds was determined in open glass capillaries using Kjeldhal flask containing liquid paraffin and are uncorrected.TLC: Iodine chamber and U.V Lamps were used for visualization of TLC spots.

Used Chemicals:

All the chemicals were procured from Central Drug House (P) Ltd. New Delhi, S.D. fine chemical Ltd. New Delhi, Qualigens fine chemicals Delhi and C.D.H. Labs, Mumbai etc. Chemicals were of L.R. grade. The chemical procured and made available for the synthetic procedure are listed below:

1) *o*-Chloro benzoic acid from Central Drug House (P) Ltd. New Delhi.
2) Aniline and their derivatives from Central Drug House (P) Ltd. New Delhi.
3) Anhydrous potassium carbonate from S.D. fine chemical Ltd. New Delhi.
4) Copper powder from C.D.H. Lab New Delhi.
5) N, N-dimethyl formamide from S.D. fine chemical Ltd. New Delhi.
6) Thionyl chloride from C.D.H. Lab New Delhi.
7) Ammonia solution from S.D. fine chemical Ltd. New Delhi.
8) Pyridine from Qualigens fine chemicals Delhi.
9) Acetonitrile from S.D. fine chemical Ltd. New Delhi.
10) 1, 4-dioxane from Qualigens fine chemicals Delhi.
11) Triphenyl phosphine Qualigens fine chemicals Delhi.
12) Acetyl chloride from C.D.H. Lab Delhi.
13) Chloroacetyl chloride from S.D. fine chemical Ltd. New Delhi.
14) Benzoyl chloride from S.D. fine chemical Ltd. New Delhi.
15) Transcinnamoyl chloride from Qualigens fine chemicals Delhi.
16) Phenylacetyl chloride from S.D. fine chemical Ltd. New Delhi.
17) Sodium bicarbonate- from C.D.H. LAB New Delhi.
18) Sodium hydroxide- from S.D. fine chemical Ltd. New Delhi.
19) Chloroform- from C.D.H. lab Delhi.
20) Hydrochloric acid- from C.D.H. lab Delhi.
21) Sulfuric acid- from C.D.H. lab Mumbai.
22) Diethyl ether- from C.D.H. lab Delhi.
23) Methanol- from Merck Ltd. Delhi.
24) Acetone- from Qualigens fine chemicals Delhi.
25) Benzene- from Qualigens fine chemicals Delhi.
26) Silica gel- from Qualigens fine chemicals Mumbai.
27) Triethyl amine- from S.D. fine chemical Ltd. Delhi.
28) Cupper bromide from S.D. fine chemical Ltd. Delhi.
29) Copper turning from Thomas Baker chemical (P) Ltd Mumbai

Thin Layer Chromatography:

Chromatography is an important technique to identify the formation of new compounds and also to determine the purity of the compound.

Preparation of Chromatoplate:

Clean and dry the glass plate was taken. Silica gel G uniform slurry in water at a ratio of 1:2 was prepared. Plate glass plate to obtain a uniform coating of the solution on the applicator moved down easily. Plate is activated for 1hour prior in Hot Air Oven at 110℃ temperature.

Preparation of Solvent System and Saturation of Chamber:

Chromatogram of the solvent system used for development related solvents were carefully designed to blend on trial basis to get maximum revolution of components.

Application of Sample:

The solution of the parent compounds and its derivatives were taken in small bored capillary tube and spotted at 2cm from the base end of plate. After spotting the plate was allowed to dry at room temperature and plates were transferred to chromatographic chamber containing solvent for development.

Development of Chromatogram:

Plate were developed by ascending technique when solvent front had reached a distance of 75% max., they were taken out and dried at room temperature.

Detection of Spots:

The developed spots were detected by exposing them to iodine vapors.

Calculation of R_f values

R_f values of the compounds of formula were calculated.

R_f value = Distance travelled by sample/Distance travelled by solvent fronts.

Pattern seen with the parent compound was found to be different from that in all cases the distance travelled by sample and distance travelled by solvent fronts.

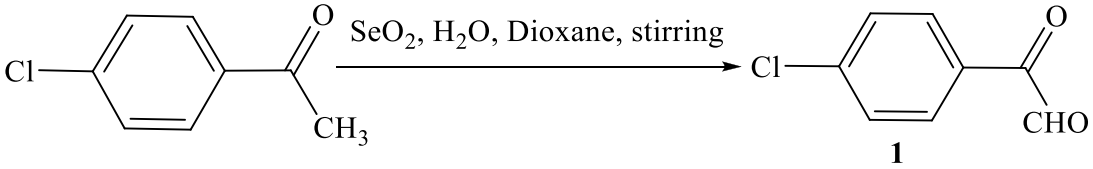
The Rf values of compounds were reported.

Synthetic Part:

Synthetic Series-1:

Synthesis of 2-(4-chlorophenyl)-2-oxoacetaldehyde (1):

A solution form of 1-(4-chlorophenyl) ethanone (0.5mol) and selenium dioxide (0.5mol) in water (10 ml) and dioxane (300ml) in a round bottom flask at 50-55ºC with stirring. The mixture was further refluxed with stirring for 4 hrs, during refluxing small amount of selenium was precipitated. The reaction mixture was decanted to remove the precipitate. The clear solution so obtained was distilled to remove excess of dioxane and water. A yellow liquid was left behind, which was found pure TLC examination (TEF 5:4:1).

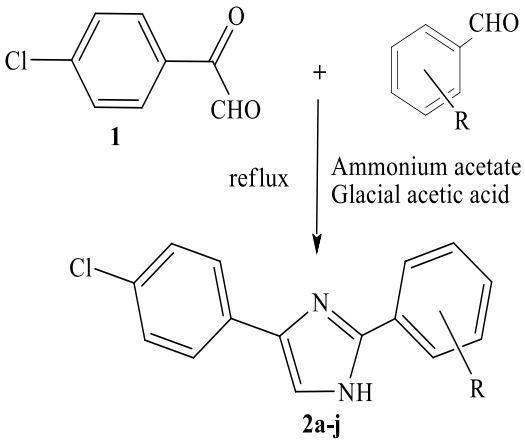


1

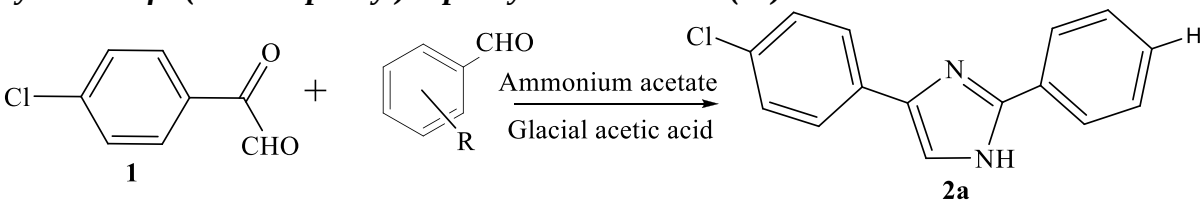
Color; Yellowish, State; Crystalline solid, Mp; 144-148°C, Yield; 70%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.51.

General procedure for the synthesis of 4-(4-chlorophenyl)-2-(substituted) phenyl-1H-imidazole (2a-j):

A mixture of compound **1** (0.025mol), different types of benzaldehyde (0.025mol) and ammonium acetate (10gm) in glacial acetic acid (50ml) was refluxed in round bottom flask for 5-6hrs. After completion of the reaction, the reaction mixture was cooled to room temperature and the contents were poured into the cold water (250ml). The precipitates so obtained were filtered, washed with water, dried and recrystallized from acetone to get the desired product. The compound was found pure on TLC examination.

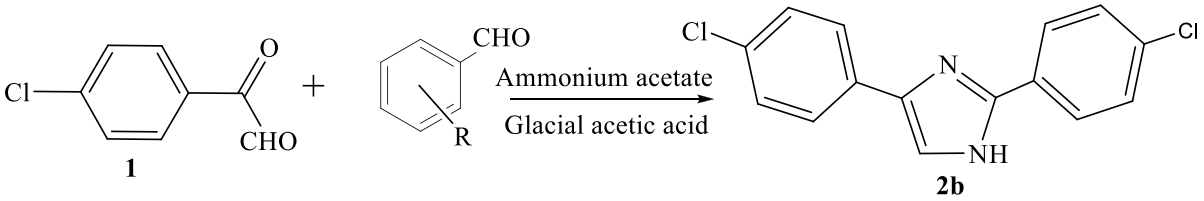


Synthesis of4-(4-chlorophenyl)-2-phenyl-1H-imidazole (2a):



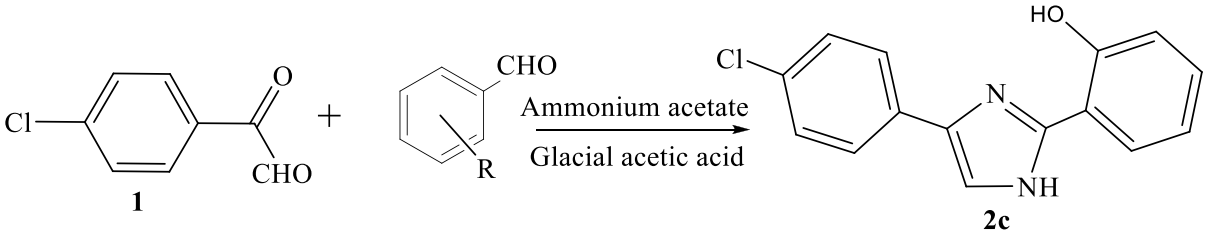
Color; Yellowish, State; Crystalline solid, Mp; 144-148°C, Yield; 75%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.51.

Synthesis of2, 4-bis (4-chlorophenyl)-1H-imidazole (2b):



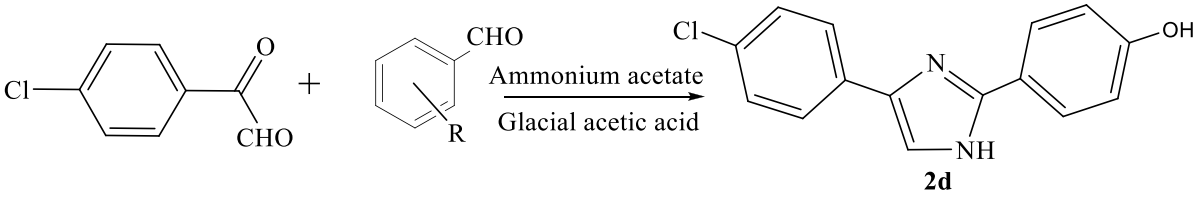
Color; Light Yellowish, State; solid, Mp; 148-150°C, Yield; 68%.On TLC examination in T:E:F (5:4:1), it was found to be pure, R_f= 0.47.

Synthesis of2-(4-(4-chlorophenyl)-1H-imidazol-2-yl) phenol (2c):



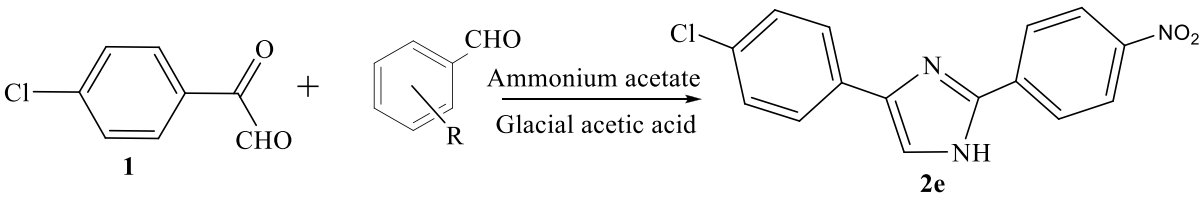
Color; Cream, State; Crystalline solid, Mp; 140-144°C, Yield; 81%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.54.

Synthesis of 4-(4-(4-chlorophenyl)-1H-imidazol-2-yl) phenol (2d):



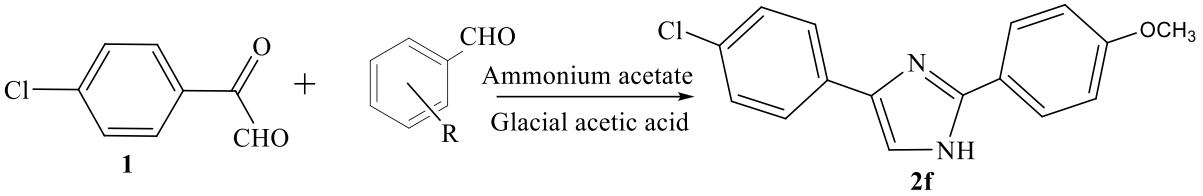
Color; Cream, State; Crystalline solid, Mp; 143-146°C, Yield; 75%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.53.

Synthesis of 4-(4-chlorophenyl)-2-(4-nitrophenyl)-1H-imidazole (2e):



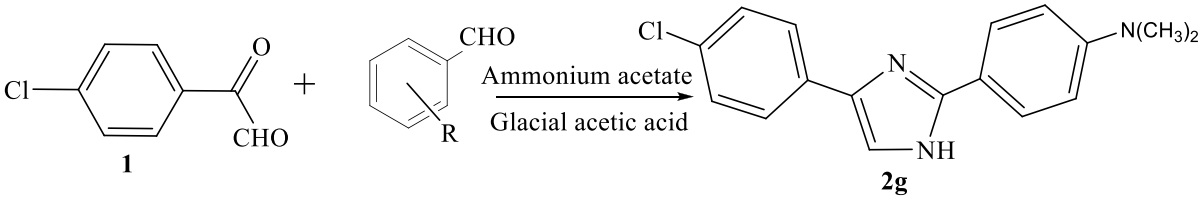
Color; Yellow, State; Crystalline solid, Mp; 161-163°C, Yield; 78%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.41.

Synthesis of 4-(4-chlorophenyl)-2-(4-methoxyphenyl)-1H-imidazole (2f):



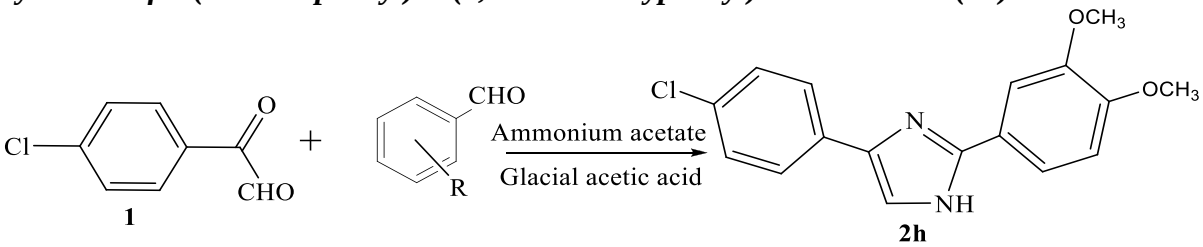
Color; White, State; Crystalline solid, Mp; 143-145°C, Yield; 73%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.57.

Synthesis of 4-(4-(4-chlorophenyl)-1H-imidazol-2-yl)-N, N-dimethylaniline (2g):



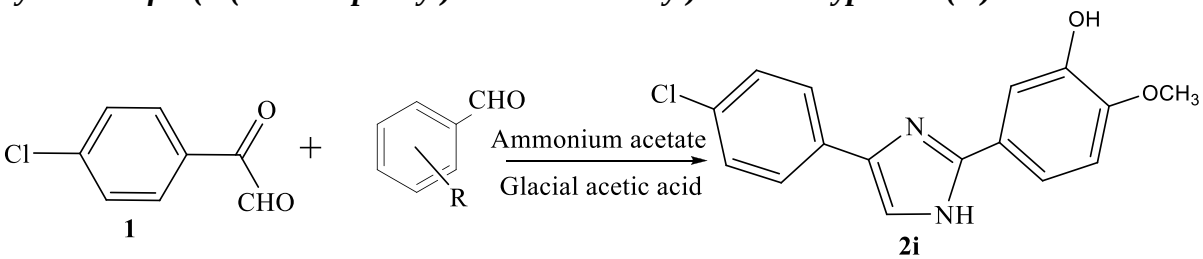
Color; Light yellow, State; Crystalline solid, Mp; 157-161°C, Yield; 75%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.52.

Synthesis of 4-(4-chlorophenyl)-2-(3, 4-dimethoxyphenyl)-1H-imidazole (2h):



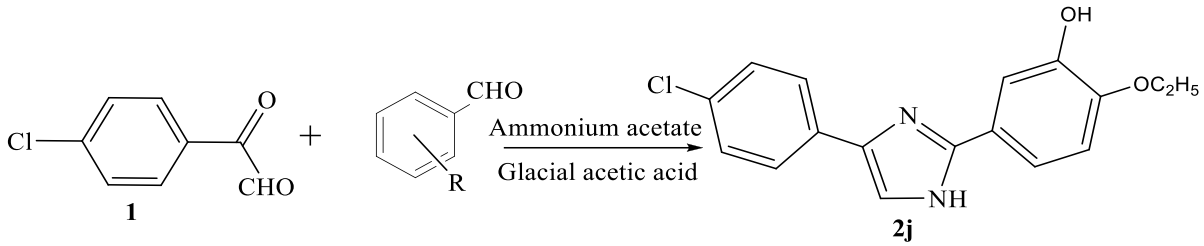
Color; White, State; Crystalline solid, Mp; 158-160°C, Yield; 74%. On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.55.

Synthesis of 5-(4-(4-chlorophenyl)-1H-imidazol-2-yl)-2-methoxyphenol (2i):



Color; Yellow-whitish, State; Crystalline solid, Mp; 151-153°C, Yield; 70%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.51.

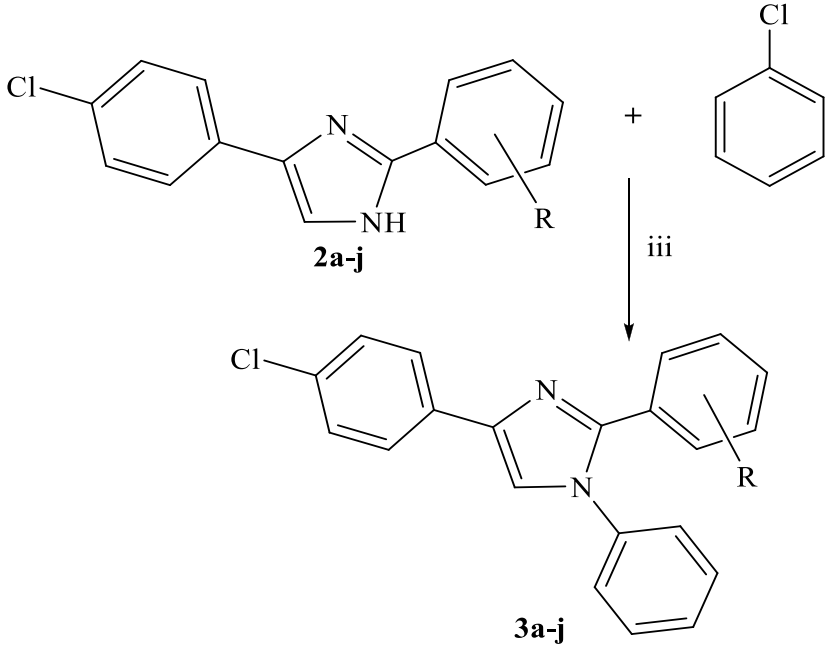
Synthesis of 5-(4-(4-chlorophenyl)-1H-imidazol-2-yl)-2-ethoxyphenol (2j):



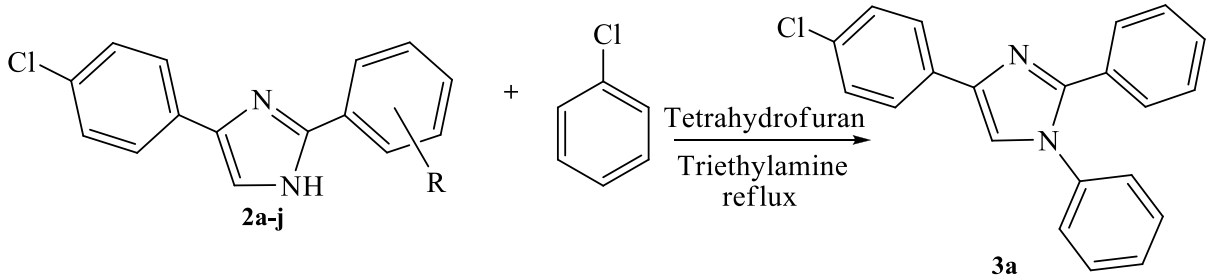
Color; Light Yellowish, State; Crystalline solid, Mp; 137-141°C, Yield; 72%.On TLC examination in T: E: F (5:4:1), it was found to be pure, R_f= 0.52.

General procedure for the synthesis of 4-(4-chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazol (3a-j):

Compound (**2a-j)** (0.01mol) was suspended in tetrahydrofuran (20ml) and refluxed with the excess of chlorobenzene (2ml) in the presence of 2 to 3 drops of triethylamine for 8 hrs. After refluxing, acetone was added to reaction mixture and kept at room temperature for overnight. A precipitate was formed, which was filtered, dried and recrystallized from ethanol and to get the final compounds (**3a-j**). The compound was found pure on TLC examination.

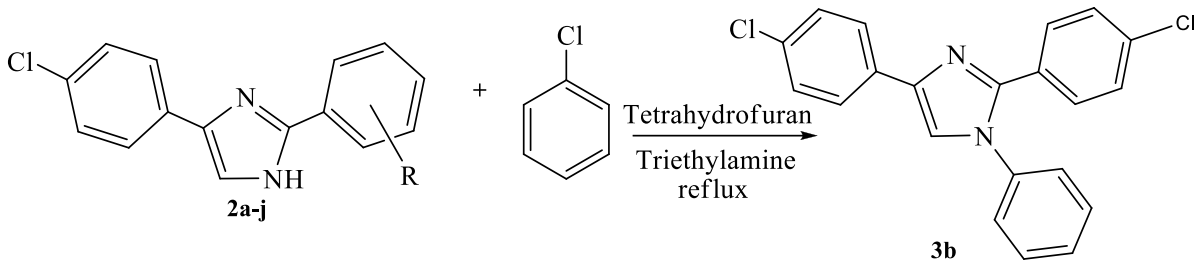


Synthesis of 4-(4-chlorophenyl)-1, 2-diphenyl-1H-imidazole (3a):



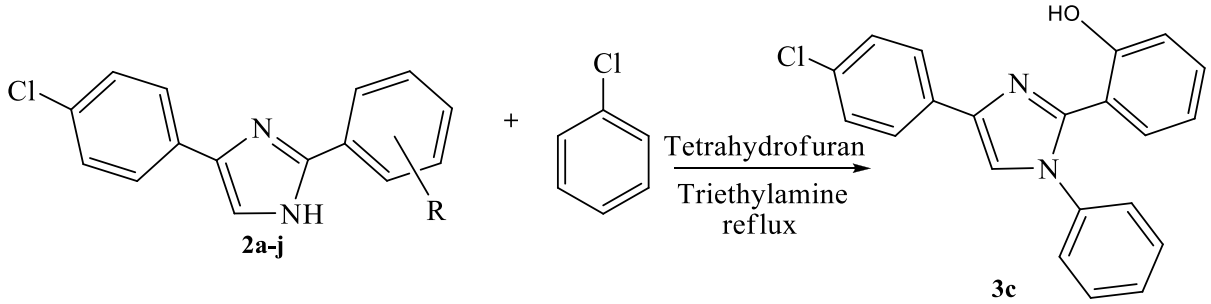
Yield: 75%, Mp: 167-170ºC, R_f = 0.61. Analcalcd. for $C_{21}H_{15}ClN_2$: C, 60.20; H, 6.73; N, 12.38. Found: C, 60.24; H, 6.71; N, 12.35.

Synthesis of 2, 4-bis (4-chlorophenyl)-1-phenyl-1H-imidazole (3b):



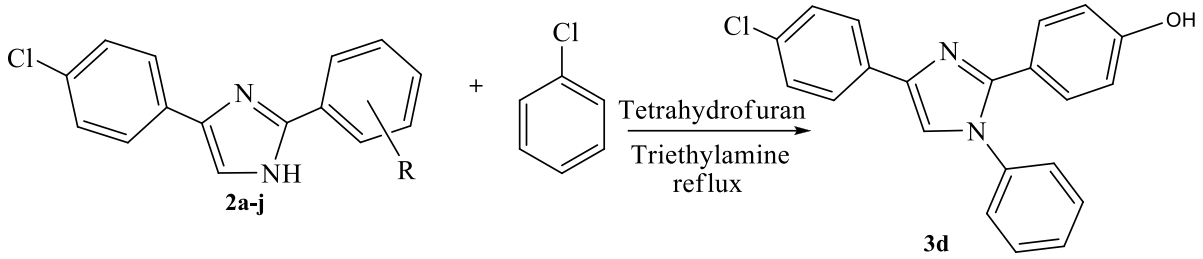
Yield: 65%, Mp: 175-178 ºC, R_f = 0.51. Anal. calcd. for $C_{21}H_{14}Cl_2N_2$: C, 56.80; H, 6.21; N, 24.17. Found: C, 56.76; H, 6.27; N, 24.21.

Synthesis of 2-(4-(4-chlorophenyl)-1-phenyl)-1H-imidazol-2-yl) phenol (3c):



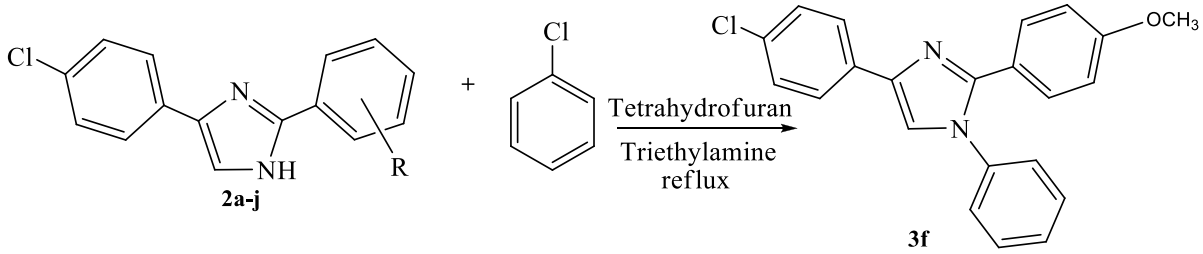
Yield: 71%, Mp: 160-165°C, R_f= 0.54. Anal. calcd. for $C_{21}H_{15}ClN_2O$: C, 52.71; H, 4.81; N, 19.23. Found: C, 52.74; H, 4.90; N, 19.30.

Synthesis of 4-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl) phenol (3d):



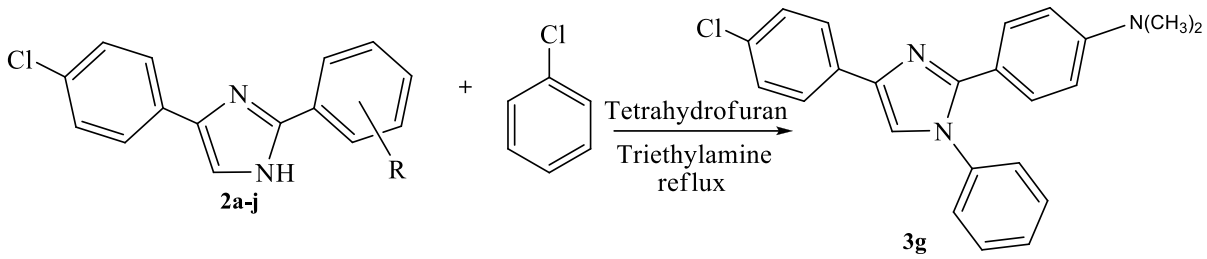
Yield: 70%, Mp: 164-167°C, R_f = 0.51. Anal. calcd. for $C_{21}H_{15}ClN_2O$: C, 53.63; H, 5.71; N, 17.35. Found: C, 53.71; H, 5.75; N, 18.41.

Synthesis of 4-(4-chlorophenyl)-2-(4-methoxyphenyl)-1-phenyl-1H-imidazole (3f):



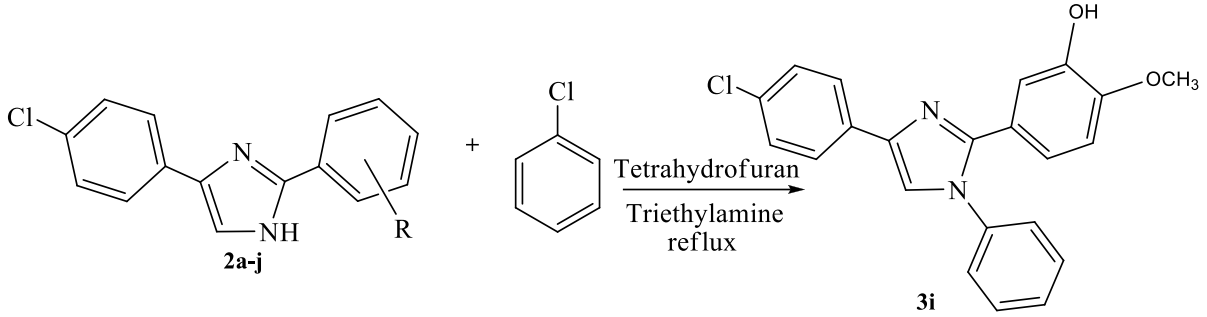
Yield: 64%, Mp: 172-176°C, R_f = 0.61. Anal. calcd. for $C_{22}H_{17}ClN_2O$: C, 54.52; H, 4.88; N, 32.32. Found: C, 54.86; H, 4.97; N, 32.47.

Synthesis of 4-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-N, N-dimethylaniline (3g):



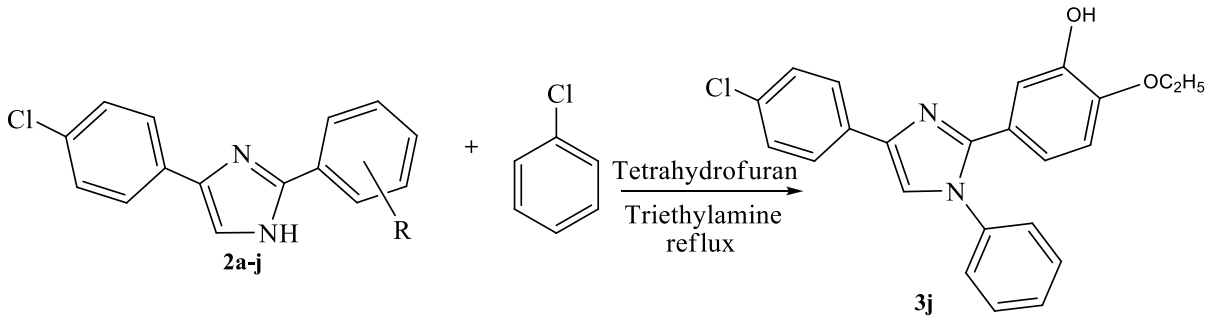
Yield: 71%, Mp: 185-189°C, R_f = 0.63. Anal. calcd. for $C_{23}H_{20}ClN_3$: C, 55.30; H, 4.61; N, 27.71. Found: C, 55.41; H, 4.75; N, 27.92.

Synthesis of 5-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-2-methoxyphenol (3i):



Yield: 68%, Mp: 178-186°C, R_f = 0.51. Anal. calcd. for $C_{22}H_{17}ClN_2O_2$: C, 56.72; H, 3.05; N, 30.23. Found: C, 56.75; H, 3.13; N, 30.39.

Synthesis of 5-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-2-ethoxyphenol (3j):



Yield: 67%, Mp: 180-183°C, R_f = 0.53. Anal.calcd. for $C_{23}H_{19}ClN_2O_2$: C, 60.31; H, 4.23; N, 25.17. Found: C, 60.35; H, 4.57; N, 26.41.

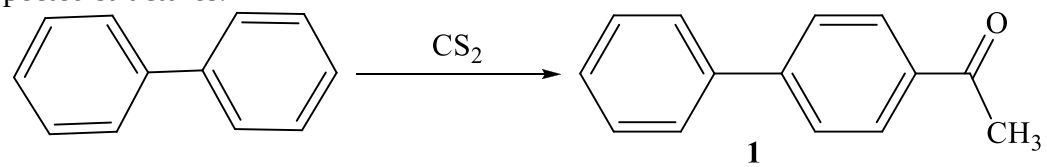
Synthetic Series-2:

Synthesis:

The compounds of the synthetic protocol scheme were obtained in the following steps

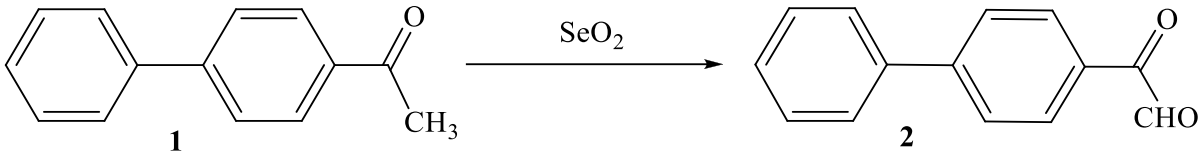
Synthesis of 1-(Biphenyl-4-yl) ethanone (1):

The starting material biphenyl ethanone (**1**) was prepared by heating biphenyl with anhydrous $AlCl_3$ in presence of CS_2 and acetic anhydride. The usual work up of the reaction mixture followed by recrystallized from ethanol gave pure compound. The purity of the compound was verified with the help of TLC (B:A, 9: 1). Percentage yield was found 85% and noted Mp.158-160°C. IR spectra are very informative and provided evidence for the formation of the expected structures.



Synthesis of 2-(Biphenyl-4-yl)-2-oxoacetaldehyde (2):

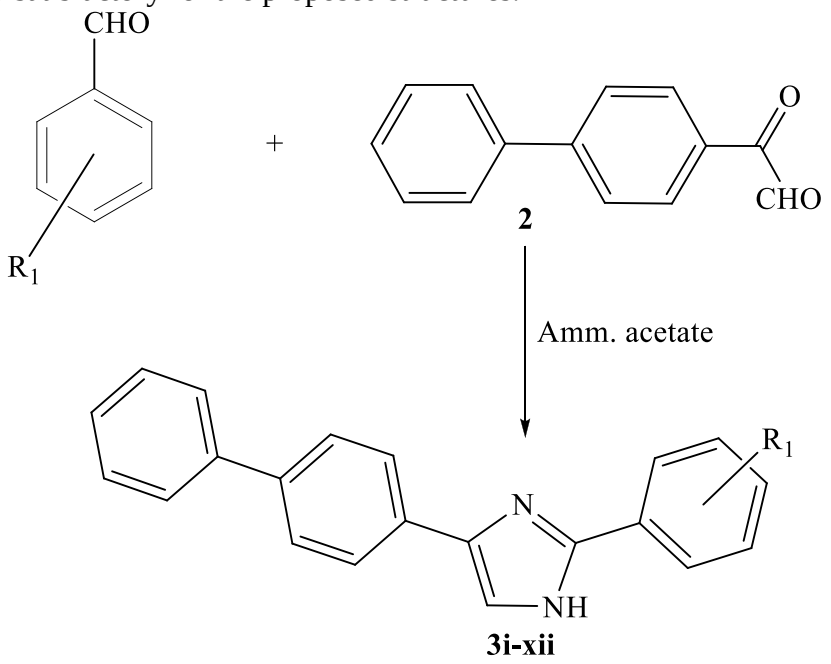
Compound 2-(Biphenyl-4-yl)-2-oxoacetaldehyde (**2**) was synthesized from biphenyl ethanone (**1**) in presence of selenium dioxide, usual work up of the reaction mixture gave a yellow liquid which was found pure on TLC examination (TEF 5:4:1). The structure of compound was confirmed on the basis of spectral studies.



1 **2**

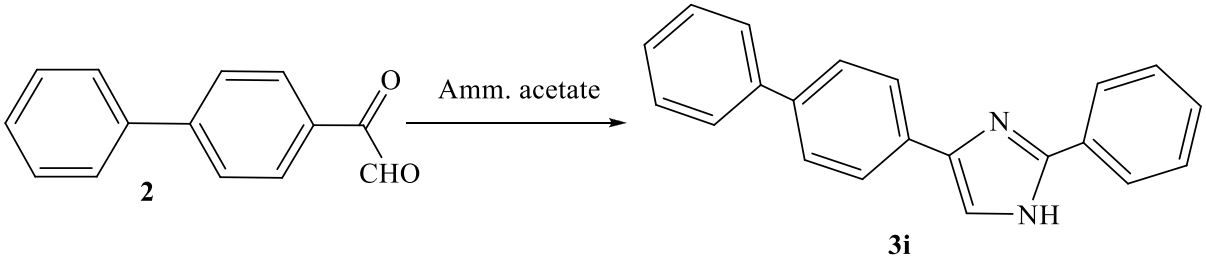
General procedure for synthesis of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1*H*-imidazole (3i-xii):

Biphenyl-2-oxoacetaldehyde (**2**) was refluxed with different aromatic aldehyde in presence of ammonium acetate and glacial acetic acid. The usual work up of the reaction mixture followed by recrystallized from acetone to get the desired products (**3i-xii**). The structures of compounds were confirmed on the basis of their IR and ^{1}H-NMR spectral studies. The compound was found pure on TLC examination (BA 9:1) and (TEF 5:4:1) and its spectral data was found satisfactory for the proposed structures.



3i-xii

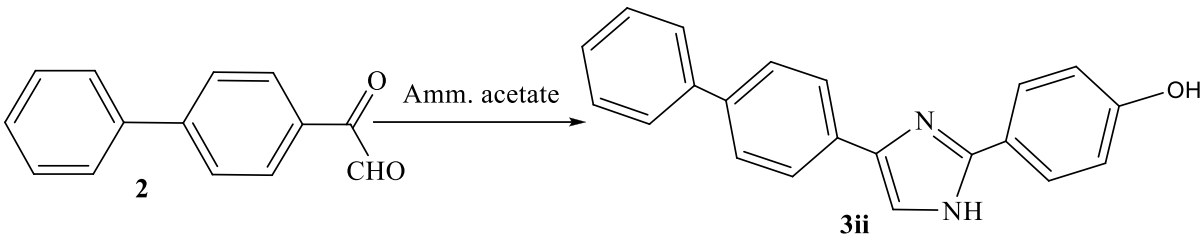
Synthesis of 4-(biphenyl-4-yl)-2-phenyl-1H-imidazole (3i):



3i

Yield: 70%, Mp: 134-137ºC, R_f = 0.53. Anal.calcd. for $C_{21}H_{16}N_2$: C, 65.11; H, 5.44; N, 9.45. Found: C, 75.11; H, 4.44; N, 9.51.

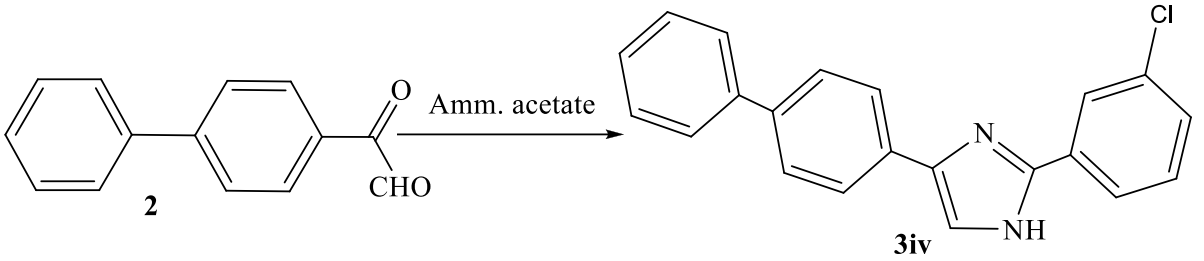
Synthesis of 4-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3ii):



2 **3ii**

Yield: 75%, Mp: 151-154°C, R_f = 0.54. Anal.calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.79; H, 4.11; N, 8.95.

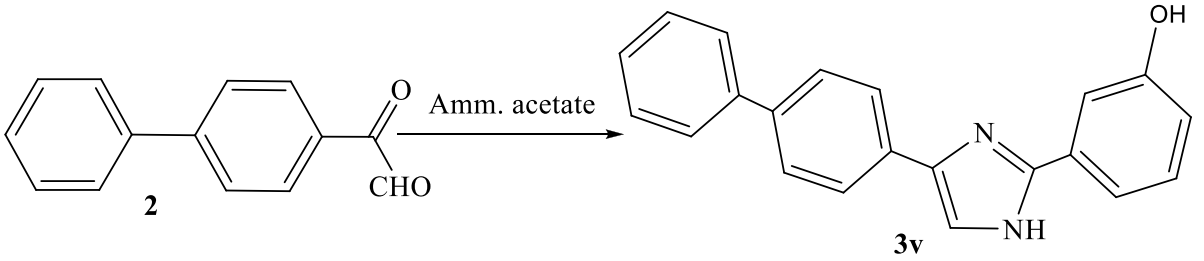
Synthesis of 4-(biphenyl-4-yl)-2-(3-chlorophenyl)-1H-imidazole (3iv):



2 **3iv**

Yield: 77%, Mp: 148-151°C, R_f = 0.47. Anal. calcd. for $C_{21}H_{15}ClN_2$: C, 76.24; H, 4.57; N, 8.47. Found: C, 76.27; H, 4.54; N, 8.37.

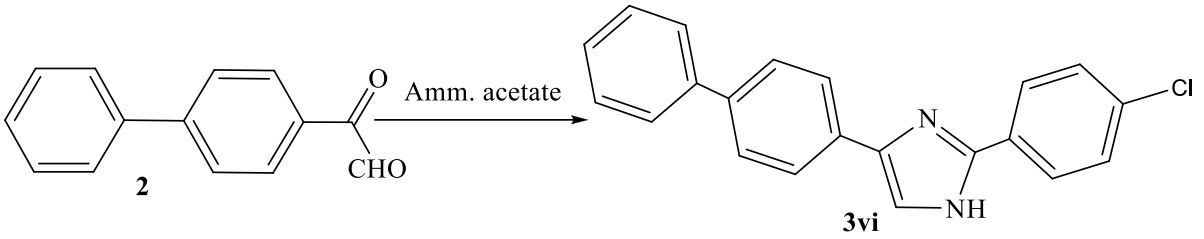
Synthesis of 3-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3v):



2 **3v**

Yield: 64%, Mp: 132-133°C, R_f = 0.53. Anal. calcd. for $C_{21}H_{16}N_2O$: C, 64.75; H, 5.16; N, 8.97. Found: C, 60.79; H, 5.21; N, 8.95.

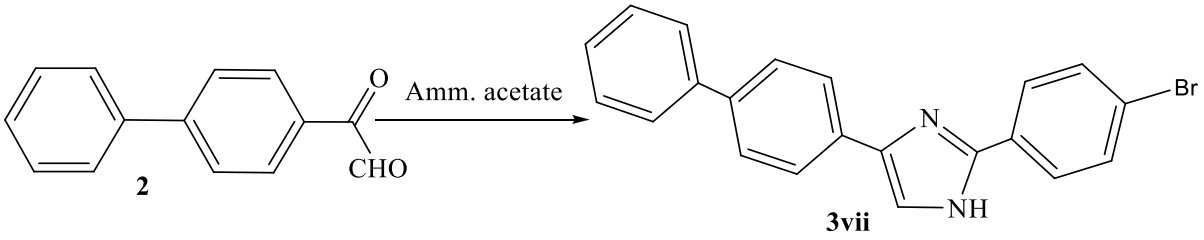
Synthesis of 4-(biphenyl-4-yl)-2-(4-chlorophenyl)-1H-imidazole (3vi):



2 **3vi**

Yield: 72%, Mp: 185-187°C, R_f = 0.47. Anal.calcd. for $C_{21}H_{15}ClN_2$: C, 55.30; H, 4.61; N, 15.71. Found: C, 55.41; H, 4.75; N, 15.92.

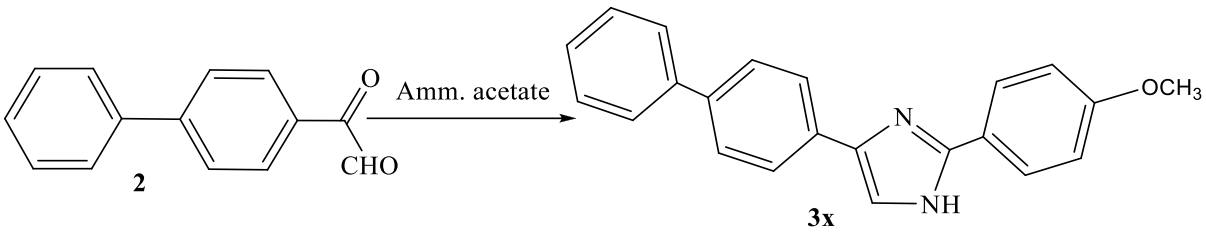
Synthesis of 4-(biphenyl-4-yl)-2-(4-bromophenyl)-1H-imidazole (3vii):



2 **3vii**

Yield: 81%, Mp: 142-145°C, R_f = 0.57. Anal. calcd. for $C_{21}H_{15}BrN_2$: C, 57.21; H, 4.03; N, 7.47. Found: C, 56.79; H, 4.07; N, 7.51.

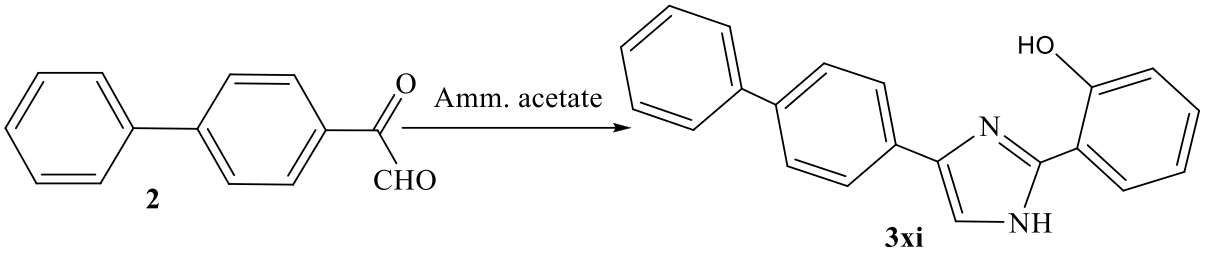
Synthesis of 4-(biphenyl-4-yl)-2-(4-methoxyphenyl)-1H-imidazole (3x):



2 **3x**

Yield: 71%, Mp: 160-163°C, R_f = 0.63. Anal. calcd. for $C_{22}H_{18}N_2O$: C, 68.91; H, 5.56; N, 8.51. Found: C, 68.79; H, 5.51; N, 8.58.

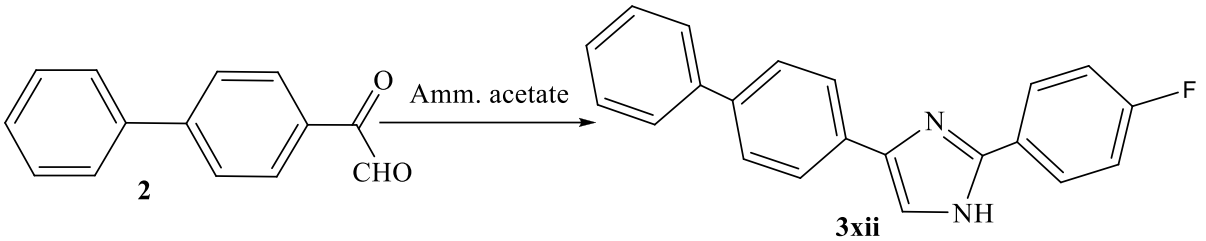
Synthesis of 3-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3xi):



2 **3xi**

Yield: 78%, Mp: 140-143°C, R_f = 0.55. Anal. calcd. for $C_{21}H_{16}N_2O$: C, 55.45; H, 5.19; N, 9.13. Found: C, 55.51; H, 5.21; N, 9.21.

Synthesis of 4-(biphenyl-4-yl)-2-(4-fluorophenyl)-1H-imidazole (3xii):



2 **3xii**

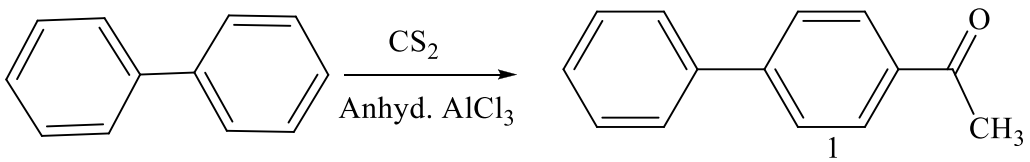
Yield: 67%, Mp: 171-175 ºC, R_f = 0.45. Anal.calcd. for $C_{21}H_{15}FN_2$: C, 52.35; H, 4.81; N, 8.91. Found: C, 53.21; H, 4.93; N, 8.97.

Synthetic Series-3:

The compounds of the scheme-3 were obtained in the following steps

Synthesis of 1-(Biphenyl-4-yl) ethanone (1):

The starting material biphenyl ethanone (**1**) was prepared by heating biphenyl with anhy. $AlCl_3$ in presence of CS_2 and acetic anhydride. The usual work up of the reaction mixture followed by recrystallized from ethanol gave pure compound. The purity of the compound was verified with the help of TLC (B: A, 9:1). % age yield- 80%, m.p.- 158-160 °C. IR spectra are very informative and provided evidence for the formation of the expected structures. In general, IR spectra of acetophenone showed a strong band of C=O at 1683 cm^{-1}. Whereas ^{1}H-NMR further confirmed the structure due to the presence of a singlet of CH_3 at 2.61 ppm.

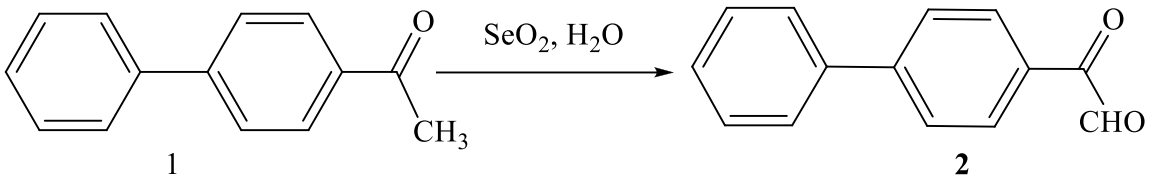


1

Synthesis of 2-(Biphenyl-4-yl)-2-oxoacetaldehyde (2):

Compound 2-(Biphenyl-4-yl)-2-oxoacetaldehyde **(2)** was synthesized from biphenyl ethanone (**1**) in presence of selenium dioxide, usual work up of the reaction mixture gave a yellow liquid which was found pure on TLC examination. (TEF 5:4:1). The structure of compound was confirmed on the basis of spectral studies. In IR spectra a band at 2850 cm^{-1}

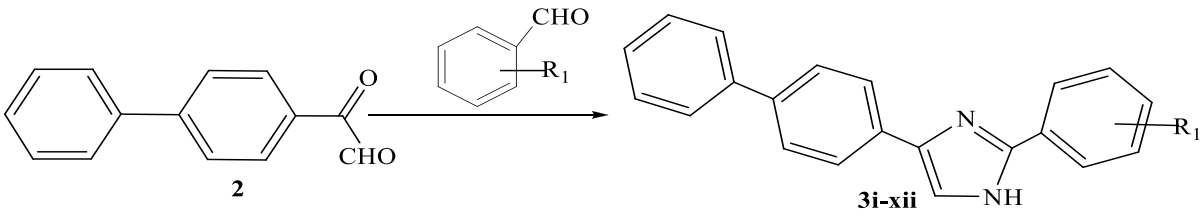
for aldehydic C-H stretching was very clear. The ^{1}H-NMR spectra left no doubt with singlet of aldehydic proton at 10.03ppm.



1 **2**

General procedure for synthesis of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1*H*-imidazole (3i-xii):

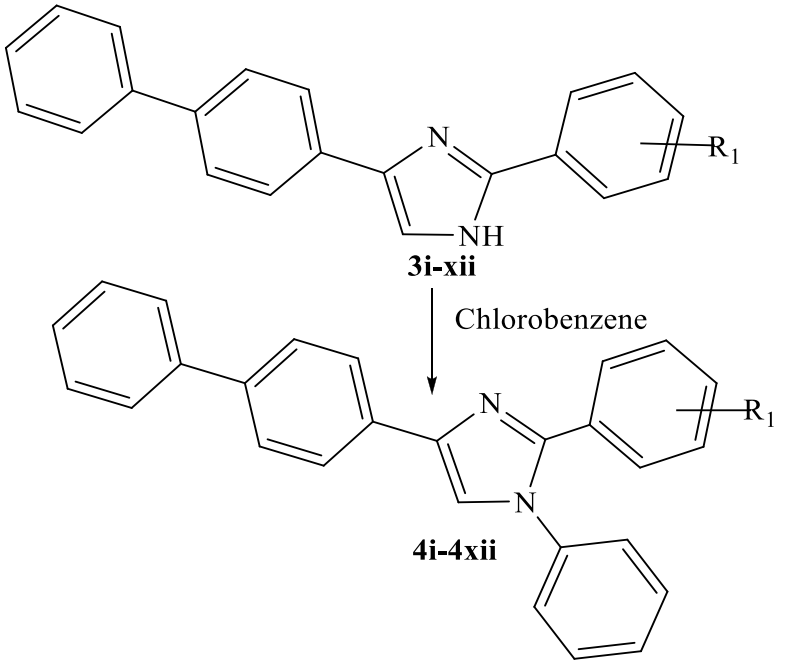
Biphenyl-2-oxoacetaldehyde **(2)** was refluxed with different aromatic aldehyde in presence of ammonium acetate and glacial acetic acid. The usual work up of the reaction mixture followed by recrystallized from acetone to get the desired products **(3i-xii)**. The compound was found pure on TLC examination (TEF 5:4:1). The structures of compounds were confirmed on the basis of their IR and ^{1}H-NMR spectral studies. In IR spectral studies, the compounds showed intense bands in the region 1541-1647 cm^{-1} of (C=N) stretching due to the ring closure. In addition, the absorption bands at 1331-1379 cm^{-1}are attributed to the (C-N) stretching vibrations, which also confirm the formation of desired imidazole ring in the compounds. Whereas ^{1}H-NMR spectra further confirm the structure due to disappearance of the peak of aldehydic proton and appearance of a single peak of NH (imidazole ring) at 12.03 ppm due to ring closure.



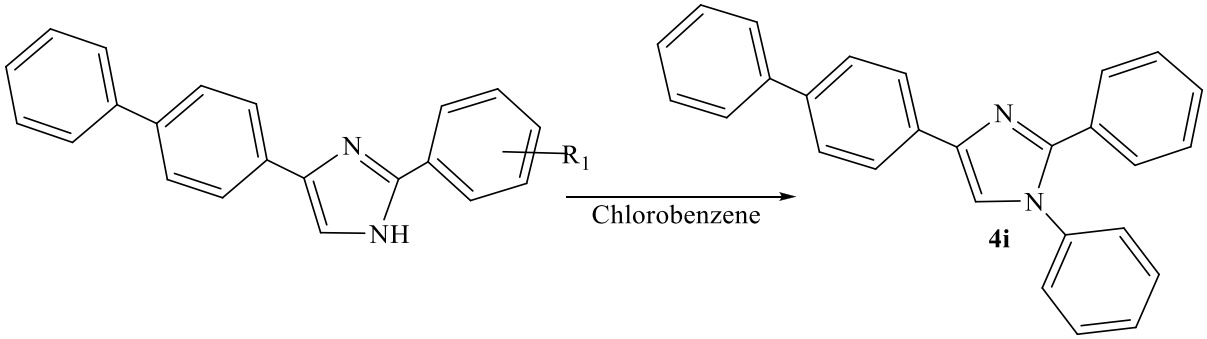
2 **3i-xii**

General procedure for synthesis of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1-phenyl-1*H*-imidazoles (4i-xii):

4-(Biphenyl-4-yl)-2-(substituted phenyl)-1-phenyl-1*H*-imidazoles (**3i-xii**) were refluxed with chlorobenzene in THF. The usual work up of the reaction mixture followed by recrystallized from ethanol gave pure compounds (**4i-xii**). The compound was found pure on TLC examination (B:A, 9:1), and its spectral data was found satisfy.

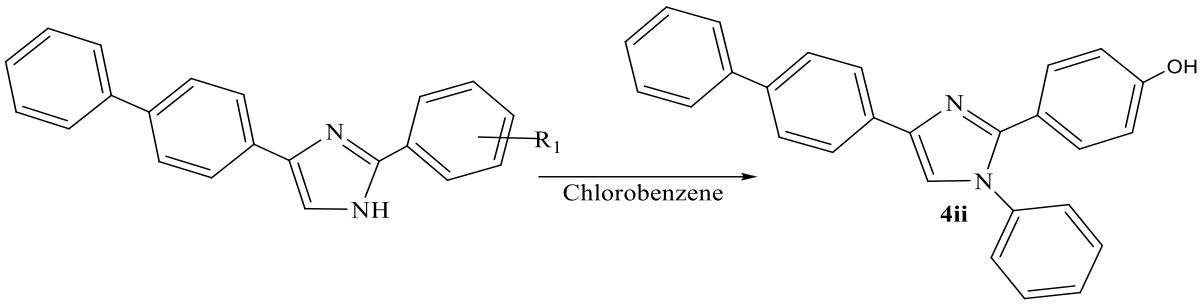


Synthesis of 4-(biphenyl-4-yl)-1,2-diphenyl-1H-imidazole (4i):



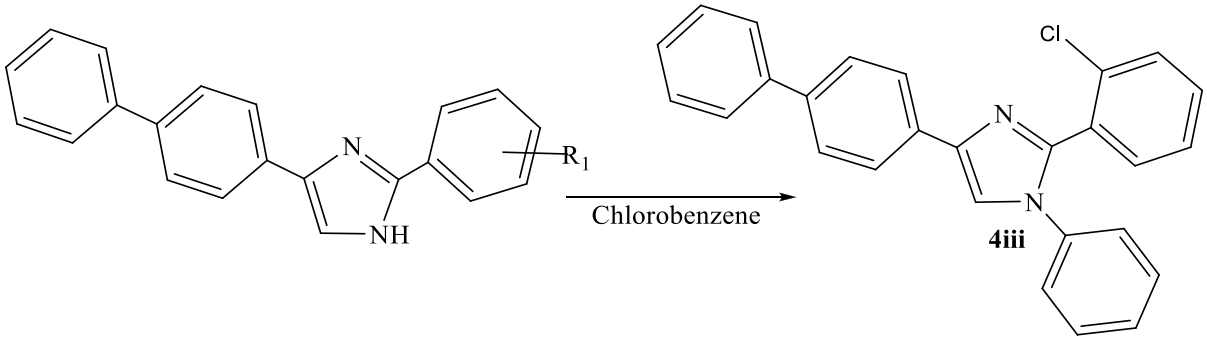
Yield: 73%, Mp: 198-203ºC, R_f = 0.57. Anal.calcd. for $C_{27}H_{20}N_2$: C, 57.12; H, 5.41; N, 10.51. Found: C, 60.11; H, 4.67; N, 9.71.

Synthesis of 4-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl) phenol (4ii):



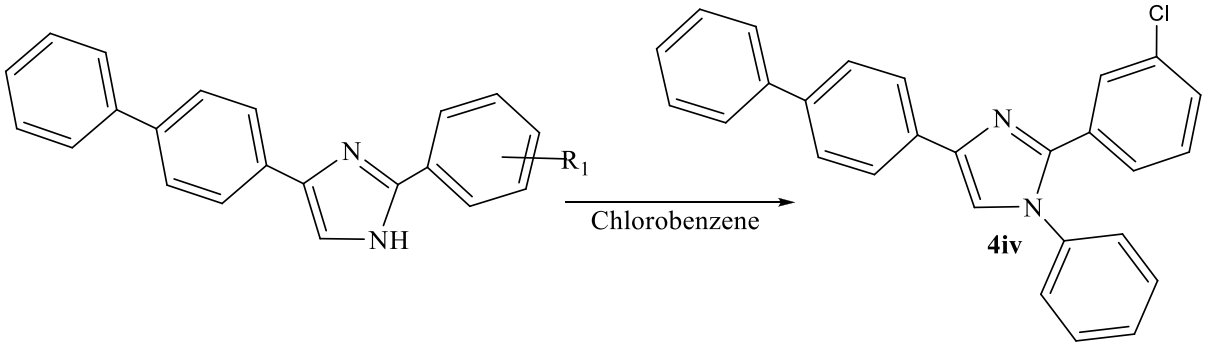
Yield: 71%, Mp: 192-195°C, R_f = 0.56. Anal. calcd. for $C_{27}H_{20}N_2O$: C, 83.48; H, 5.19; N, 7.21. Found: C, 83.51; H, 5.23; N, 7.27.

Synthesis of 4-(biphenyl-4-yl)-2-(2-chlorophenyl)-1-phenyl-1H-imidazole (4iii):



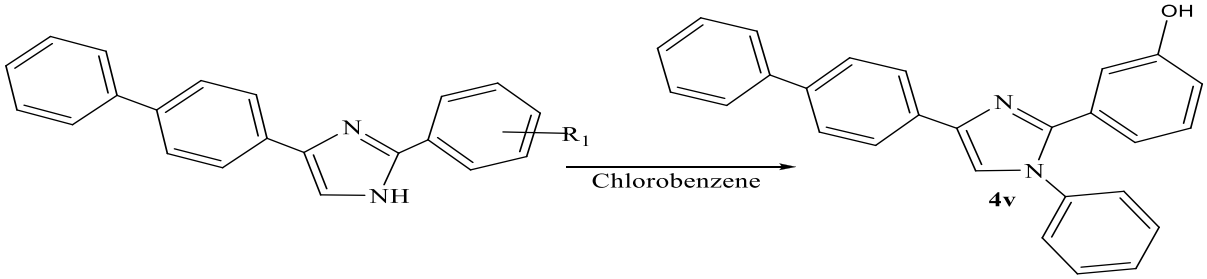
Yield: 77%, Mp: 205-207°C, R_f = 0.45. Anal.calcd. for $C_{27}H_{19}ClN_2$: C, 71.70; H, 4.71; N, 8.75. Found: C, 71.27; H, 4.54; N, 8.41.

Synthesis of 4-(biphenyl-4-yl)-2-(3-chlorophenyl)-1-phenyl-1H-imidazole (4iv):



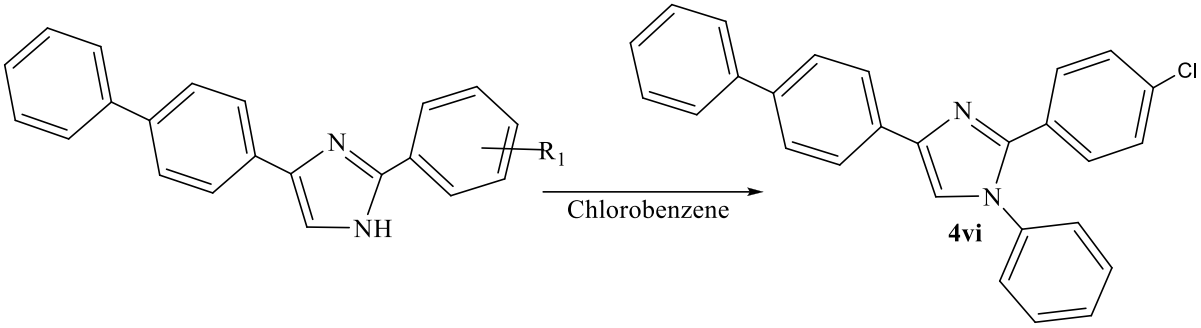
Yield: 75%, Mp: 220-223°C, R_f = 0.43. Anal.calcd. for $C_{27}H_{19}ClN_2$: C, 69.53; H, 5.72; N, 9.58. Found: C, 69.57; H, 5.74; N, 9.47.

Synthesis of 3-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl) phenol (4v):



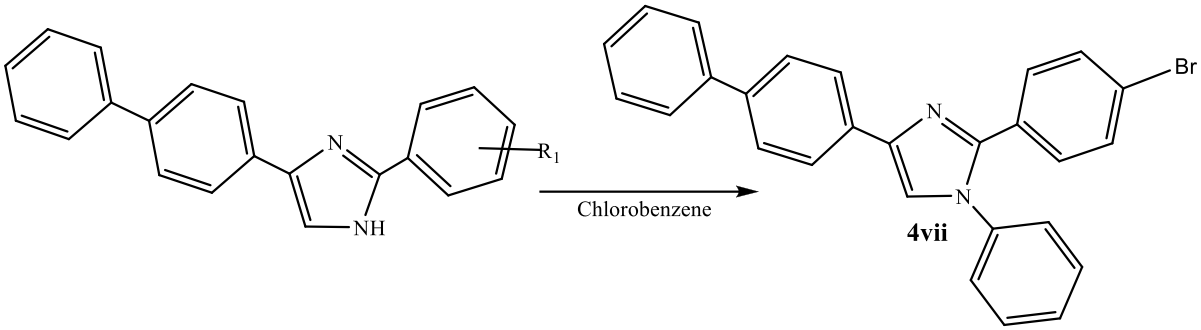
Yield: 64%, Mp: 132-133°C, R_f = 0.53. Anal. calcd. for $C_{27}H_{20}N_2O$: C, 63.48; H, 5.19; N, 7.21;. Found: C, 63.51; H, 5.23; N, 7.25.

Synthesis of* 4-(biphenyl-4-yl)-2-(4-chlorophenyl)-1H-imidazole *(4vi):



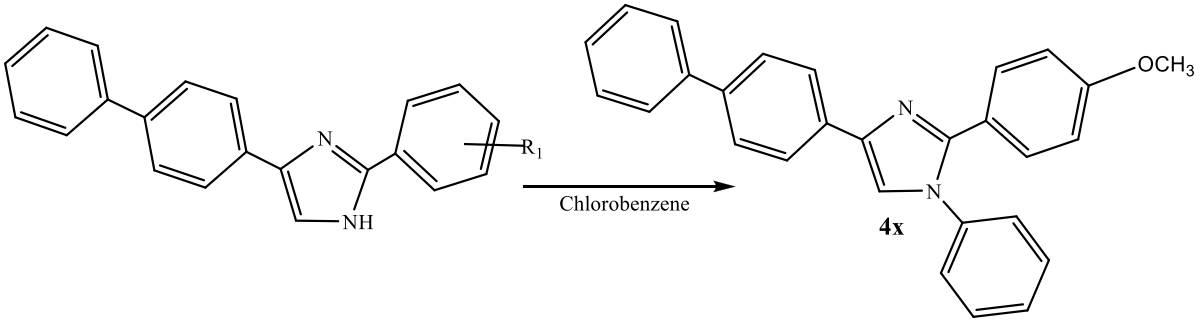
Yield: 68%, Mp: 192-193°C, R_f = 0.41. Anal. calcd. for $C_{27}H_{19}ClN_2$: C, 65.31; H, 4.68; N, 13.61. Found: C, 65.41; H, 4.75; N, 13.65.

Synthesis of 4-(biphenyl-4-yl)-2-(4-bromophenyl)-1-phenyl-1H-imidazole (4vii):



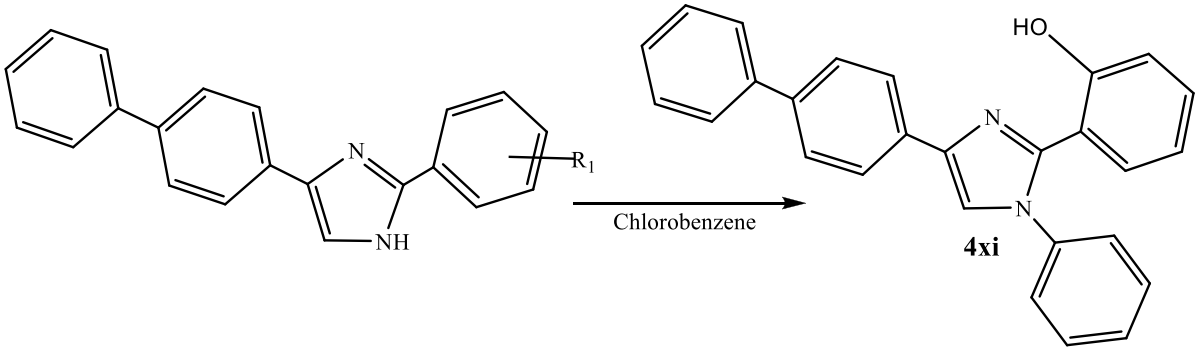
Yield: 83%, Mp: 215-219°C, R_f = 0.55. Anal. calcd. for $C_{27}H_{19}BrN_2$: C, 67.85; H, 4.24; N, 9.21. Found: C, 67.89; H, 4.27; N, 9.25.

Synthesis of* 4-(biphenyl-4-yl)-2-(4-methoxyphenyl)-1H-imidazole *(4x):



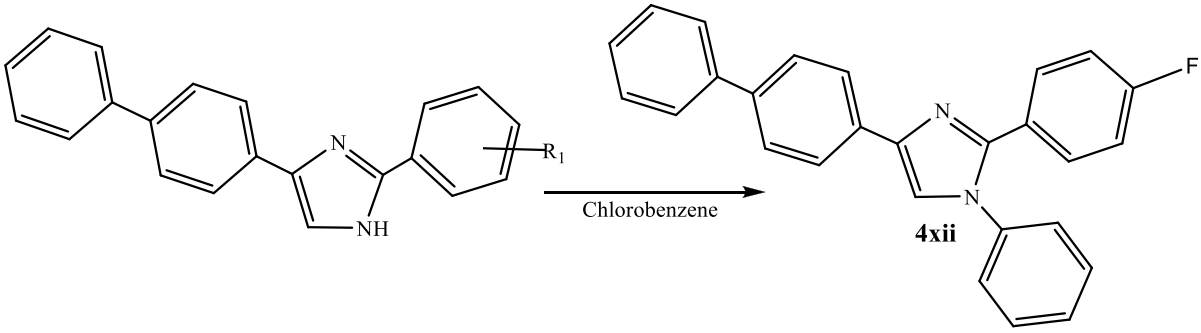
Yield: 71%, Mp: 160-163°C, R_f = 0.63. Anal. calcd. for $C_{28}H_{22}N_2O$: C, 73.56; H, 5.51; N, 8.91. Found: C, 73.51; H, 5.56; N, 8.93.

Synthesis of 2-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl)phenol (4xi):



Yield: 78%, Mp: 140-143°C, R_f = 0.55. Anal.calcd. for $C_{27}H_{20}N_2O$: C, 57.61; H, 4.39; N, 10.12. Found: C, 57.67; H, 4.43; N, 10.15.

Synthesis of 4-(biphenyl-4-yl)-2-(4-fluorophenyl)-1-phenyl-1H-imidazole (4xii):



Yield: 67%, Mp: 171-175 ºC, R_f = 0.45. Anal. calcd. for $C_{27}H_{19}FN_2$: C, 57.31; H, 4.91; N, 9.73. Found: C, 57.41; H, 4.93; N, 9.75.

Biological Evaluation:

Antimicrobial Activity:

Anti-bacterial Activity:

Shri B.M. Patil medical collages have reported different method for evaluation of anti-bacterial activity. Few of the most widely used method were as follows.

Agar diffusion method:

Cup plate method:

Preparation of Nutrient Agar Media:

Nutrient agar medium was used to incubate microorganism and was prepared in autoclaved distilled water to prevent any microbial contamination. After mixing all ingredients the mixture was autoclaved and poured in the Petri plate in laminar flow and kept in room temperature for solidifying.

Media composition and procedure:

The nutrients agar media was prepared by using the following ingredients.

(1) Agar	20gm
(2) Beef extract (Bacteriological)	5gm
(3) Peptone (Bacteriological)	20gm
(4) Sodium chloride	5gm
(5) Distilled water up to	1000ml

Weighed quantities of peptone and beef extract were dissolved in distilled water by gentle warming and then specified amount of agar was dissolved by heating on water bath. Then the pH of the solution was adjusted to 7.2 to 7.4 by adding the sodium chloride and the volume of the final solution was made up to 1000ml with distilled water. Then it was transferred in to a suitable container, plugged with non-adsorbent cotton and the media was sterilized by in autoclave at 121°C for 20 minutes at lbs pressure.

Preparation of the Inoculums:

A loop ful of culture from frozen agar slant was introduced into 10ml of sterilized nutrient broth and incubated at 30-35°C for 24hrs to obtain the stock culture. The stock solution of the culture was diluted by serial dilution method to a dilution factor which has given 25% light transmission at 530 nm. The suspension was stored under refrigerator.

Preparation of Solution:

10mg of the compound was dissolved in 10ml of DMF. From this 1ml of solution was taken and diluted up to 10ml with DMF. Now the concentration of the test solution was 100ug/ml. From the stocks solution 1ml of solution was taken and diluted with 1ml of DMF.

Preparation of Standard Antibiotic Solution:

Ciprofloxacin was used as standard antibiotic for comparison and solution were prepared by using sterile water, as they were water-solution. The solution are diluted by using sterile water so that the concentration of the solution 100ug/ml and 50ug/ml.

Preparation of Discs:

Discs of 6-7 mm in diameter were punched from No:1 Whattmann filter paper with sterile corks borer of same size. These discs were satirized by keeping in oven at 140^0C for 60 minutes. Then standards and test solutions were added to each disc and discs were air-dried.

Microbial Strain:

Name of micro-organism used

Escherichia coli (E. coli, MTCC 2961*), Staphylococcus aureus (S. aureus*, MTCC 3160*), Bacillus subtilis (B. subtilis*, MTCC 121*), Klebsiella pneumoniae (K. pneumoniae, MTCC 3040) and Micrococcus luteus (M. luteus*, MTCC 7527*).*

Stock Culture:

A loopful of culture from frozen agar slants will be introduced into 10ml of sterilized nutrient broth and incubated for 24hrs to obtain stock culture. This stock culture solution will be diluted by serial dilution method and the incubation size of 1:100 will be used for further studies. The cells of the inoculums will be suspended in normal saline to get sharp inhibition zones.

Experimental Procedure:

The antibacterial activity of the test compounds was done using cup-plate method. The nutrient agar medium was prepared and autoclaved at 15.1 lbs pressure for 20 minutes. This media was poured into plates and allowed to solidify. On the surface of media microbial suspension was spread with the help of sterilized cotton swab. Cups were made by boring into agar surface with a previously sterilized cork borer and scooping out the punched part of agar. Four cups were made in each Petri dish and into these cups were added the concentration (100, 50 and 25μg/ml) of the test compounds. In another plate each cup was filled with standard antibiotic Ciprofloxacin (100, 50 and 25 μg/ml) for antibacterial activity. In another plate each cup was filled with pure solvent (DMSO) as control. The plates were kept in cold for one hour to allow the diffusion of test compounds and then incubated at 37 ± 0.5^0C for 24 hours for antibacterial activity. The zone of inhibition formed around the cups after respective incubation was measured and percentage inhibition of the compound were evaluated [4-6].

Antifungal Activity:

Agar Dilution Method:

In agar dilution system the test compound is incorporated in a molten agar medium, plate is poured and subsequently inoculated. Using a multipoint inoculator's a large number of different organisms can be tested on a single plate. Following incubation plates are read visually scoring for each organism normal growth, reduced growth or no growth, where activity is found the test can be repeated using plates containing serial dilution of the compound.

Preparation of the inoculums:

The spores of fungal species were collected by sterile loop and placed in the autoclaved distilled water. Tubes were incubated at 20-25°C for 24hrs. After incubation 100μL medium were spread over the sterile malt extract agar plates and incubated for 24hrs.

Preparation of media:

The malt extract agar medium was prepared in autoclaved distilled water to prevent any microbial contamination. After mixing all ingredients the mixture was autoclaved and poured in the petri plate in laminar flow and kept in room temperature for solidifying.

Preparation of Standard Antibiotic Solution:

Fluconazole was used as standard antibiotic for comparison and solution were prepared by using sterile water, as they were water-solution. The solution are diluted by using sterile water so that the concentration of the solution 100 ug/ml and 50 ug/ml.

Microbial Strain:

Name of micro-organism used
Candida albicans (C. albicans, MTCC 227*), Aspergillus niger (A.niger,* MTCC 277*) and Aspergillus flavus (A. flavus,* MTCC 418*).*

Experimental Procedure:

The nutrient agar medium was prepared and autoclaved at 15 lbs pressure for 20 minutes. This media was poured into petri plates and was allowed to solidify. On the surface of media microbial suspension was spread with the help of sterilized cotton swab. Cups were made by boring into agar surface with a previously sterilized cork borer and scooping out the punched part of agar. Four cavities or cups were made in the medium and different concentrations of the test compounds and standard drug Fluconazole were poured in these cavities. The plates were kept at room temperature for 1 hr and then incubated at 37±0.5 $^{\circ}$C for 24 hrs. The diameter of the zone of inhibition formed around the cavities (cups) after 24hrs incubation was measured and percentage inhibition of the compound were evaluated. A solvent control was also run to know the activity of the blank [4-7].

Results and Discussion:

Synthetic Series-1:

Compounds **(3a-j)** 4-(4-chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazol were prepared from Scheme 1.

Structural Investigations:

2-(4-chlorophenyl)-2-oxoacetaldehyde (**1**) was synthesized from 1-(4-chlorophenyl) ethanonein presence of selenium dioxide, usual work up of the reaction mixture gave a yellow liquid which was found pure on TLC examination. (TEF 5:4:1). IR spectra are very informative and provided evidence for the formation of the expected structures. In IR spectra a band at 2810 cm^{-1} for aldehydic C-H stretching was very clear. The ^{1}H-NMR spectra left no doubt with peaks of aldehydic proton (9.87 ppm). 2-(4-chlorophenyl)-2-oxoacetaldehyde (**1**) was refluxed with different types of aromatic aldehyde in presence of ammonium acetate and glacial acetic acid. The usual work up of the reaction mixture followed by recrystallized from acetone to get the desired products **(2a-j)**. The compound was found pure on TLC examination (TEF 5:4:1). The structure of this compound was confirmed on the basis of their IR and ^{1}H-NMR spectral studies. In IR spectral studies, the compounds showed intense bands in the region 1542-1610 cm^{-1} of (C=N) stretching due to the ring closure. In addition, the absorption bands at 1320-1350 $cm^{-1}$are attributed to the (C-N) stretching vibrations, which also confirm the formation of desired imidazole ring in the compounds. Whereas ^{1}H-NMR spectra further confirm the structure due to disappearance of the peak of aldehydic proton and appearance of a single peak of NH (imidazole ring) at 11.36 ppm due to ring closure. 4-(4-chlorophenyl)-2-(substituted) phenyl-1H-imidazole (**2a-j**) were refluxed with chlorobenzene in THF. The usual work up of the reaction mixture followed by recrystallized from ethanol gave pure compounds (**3a-j**). The compound was found pure on TLC examination (B: A, 9: 1) and its spectral data was found satisfactory for the proposed structures.

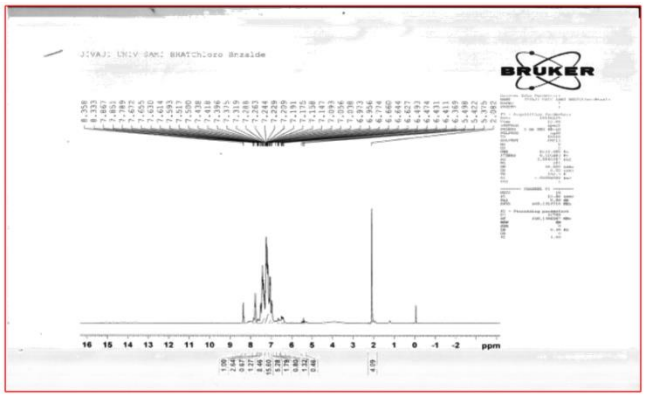


Fig.1: Structural investigation of 4-(4chlorophenyl)-2-(substituted) phenyl-1H-imidazole by H-NMR

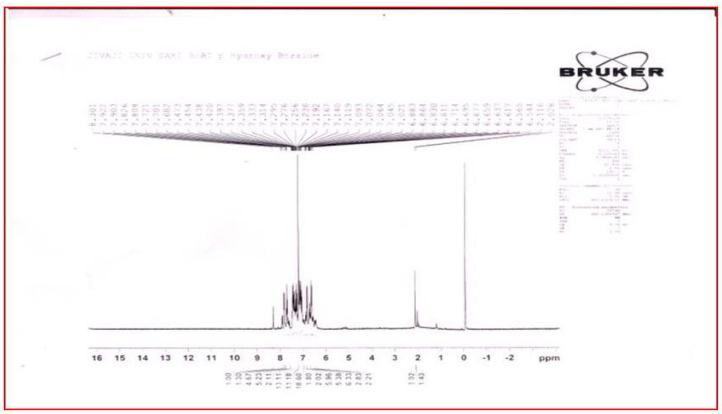


Fig.2: Structural investigation of 4-(4-chlorophenyl)-2-(substituted) phenyl-1H-imidazole by ^{13}C-NMR

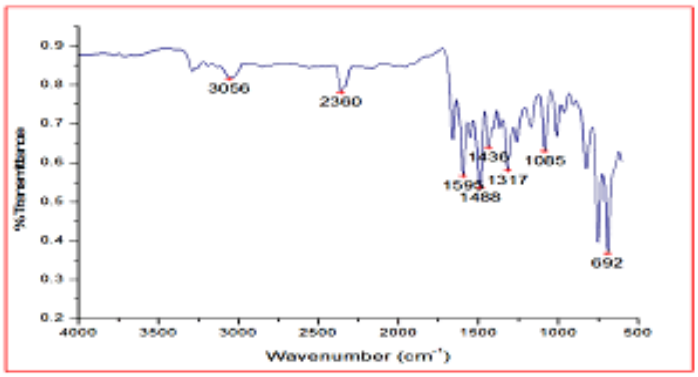


Fig.3: Structural investigation of 4-(4chlorophenyl)-2-(substituted) phenyl-1H-imidazole by FTIR

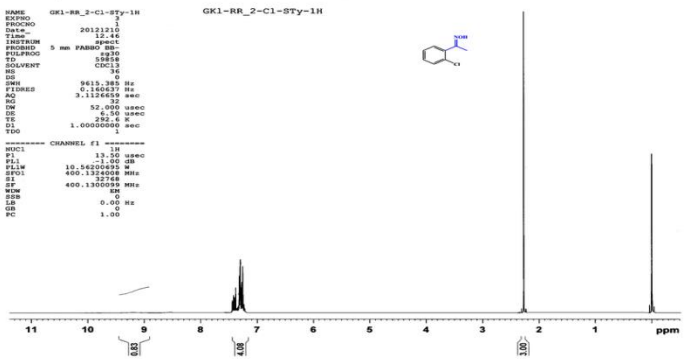


Fig.4: Structural investigation of 4-(4-chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazol by H-NMR

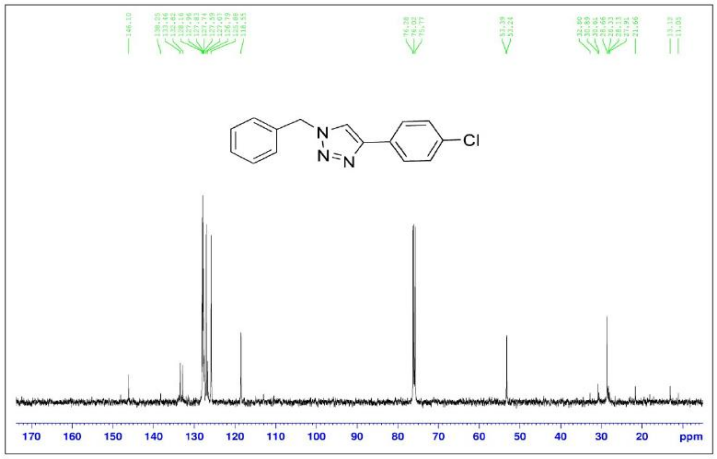


Fig.5: Structural investigation of 4-(4-chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazol by ^{13}C-NMR

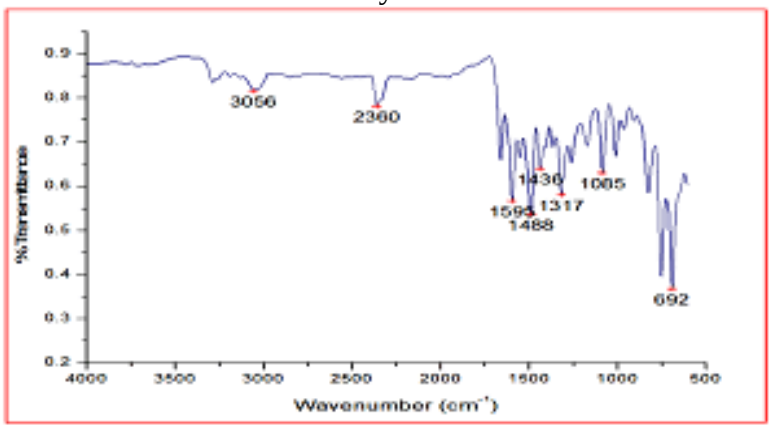
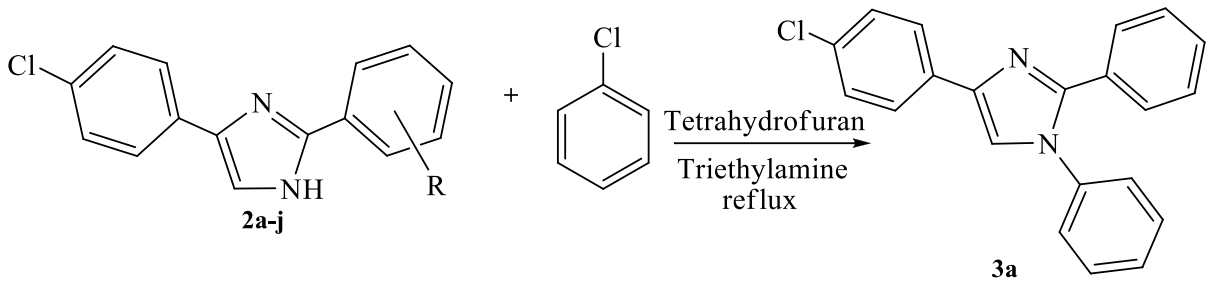
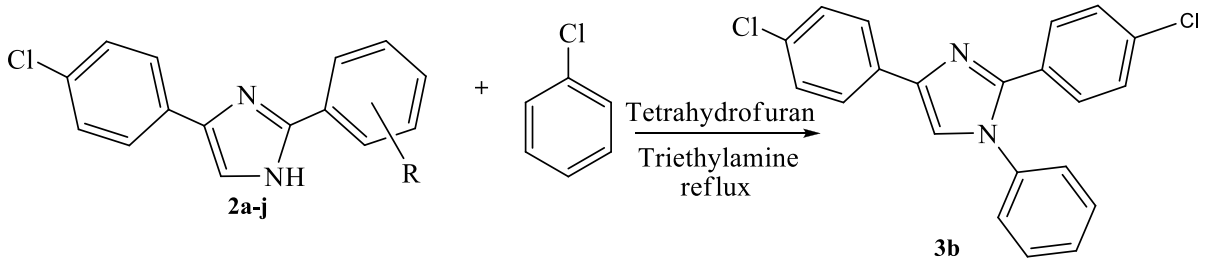


Fig.6: Structural investigation of 4-(4-chlorophenyl)-1, 2-(substituted phenyl)-1-phenyl-1H-imidazol by FTIR

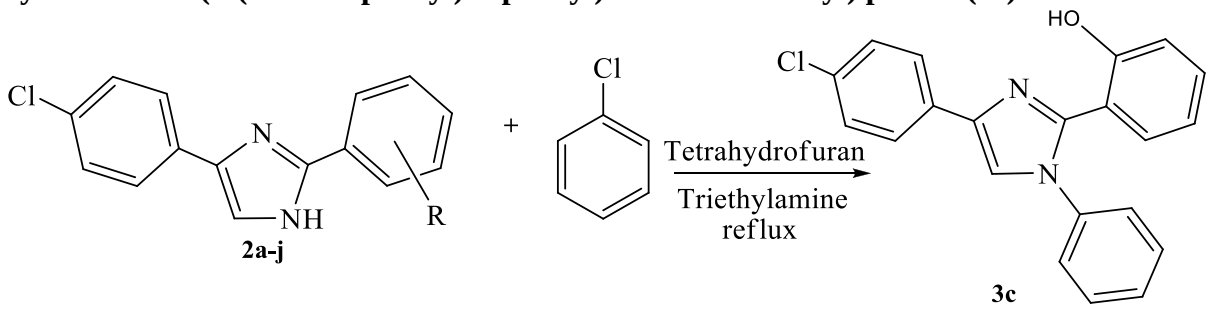
Synthesis of 4-(4-chlorophenyl)-1, 2-diphenyl-1H-imidazole (3a):



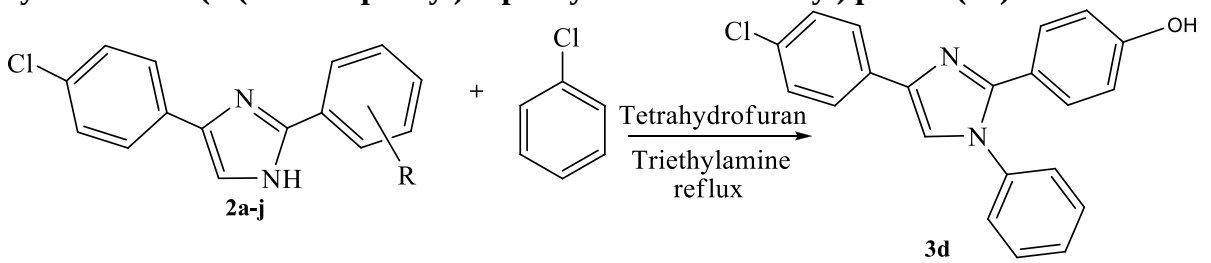
5.2.2.1 Synthesis of 2, 4-bis (4-chlorophenyl)-1-phenyl-1H-imidazole (3b):



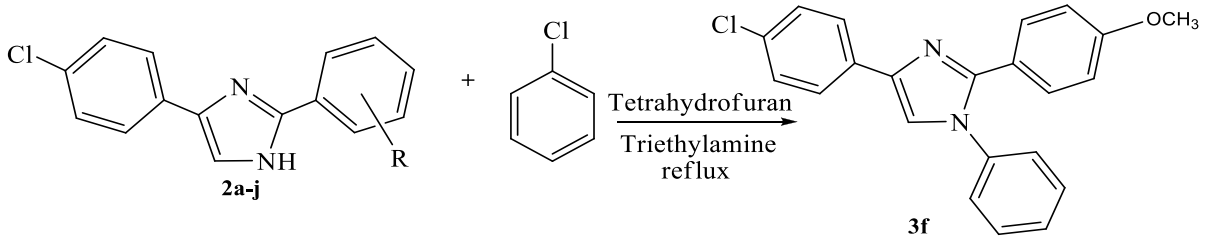
Synthesis of 2-(4-(4-chlorophenyl)-1-phenyl)-1H-imidazol-2-yl) phenol (3c):



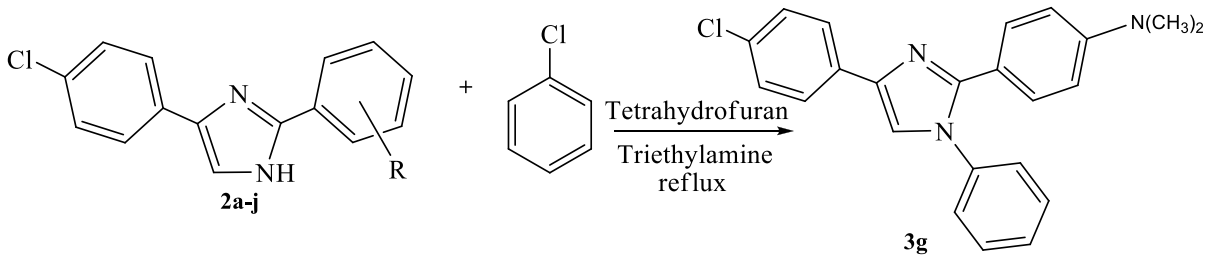
Synthesis of 4-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl) phenol (3d):



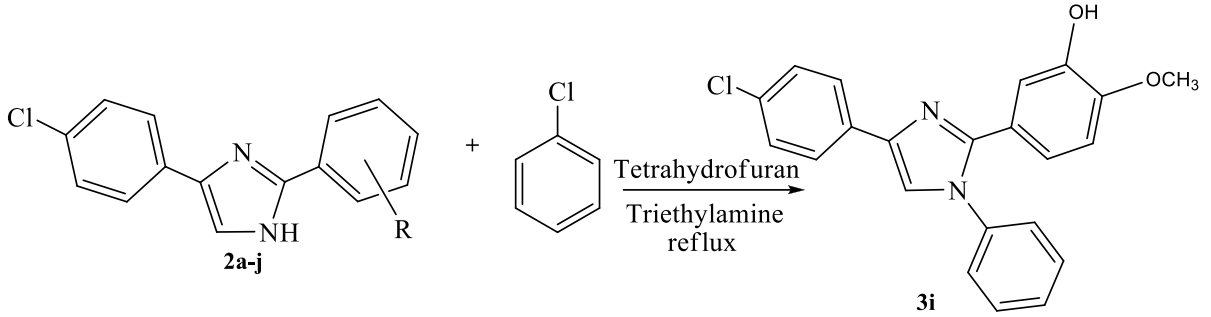
Synthesis of 4-(4-chlorophenyl)-2-(4-methoxyphenyl)-1-phenyl-1H-imidazole (3f):



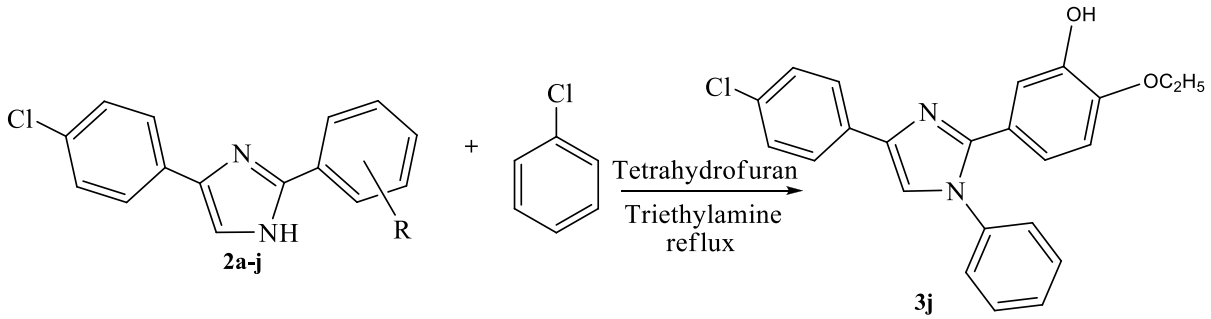
Synthesis of 4-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-N, N-dimethylaniline (3g):



Synthesis of 5-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-2-methoxyphenol (3i):



5.2.2.7 Synthesis of 5-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl)-2-ethoxyphenol (3j):



Synthetic Series-2:

Compounds **(3i-xii)** 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1H-imidazole were prepared from Scheme 1.

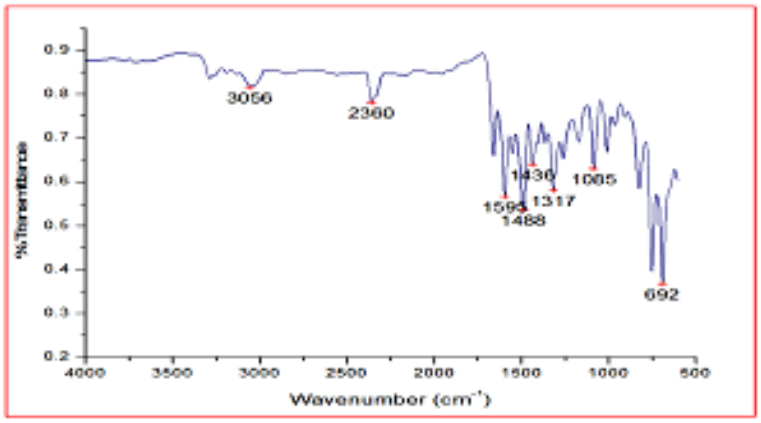


Fig.7: Structural investigation of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1H-imidazole by FTIR

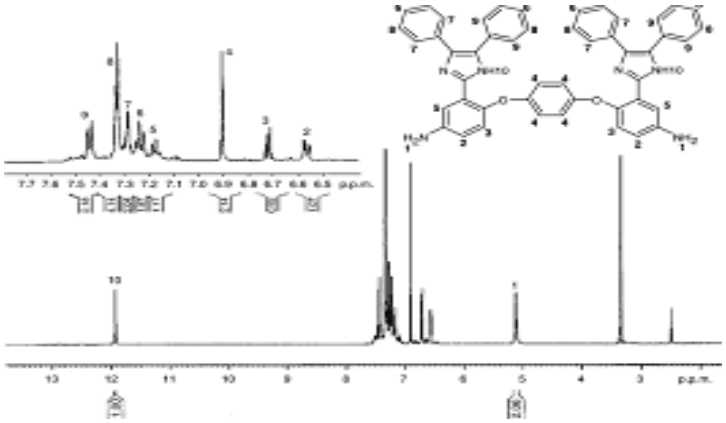
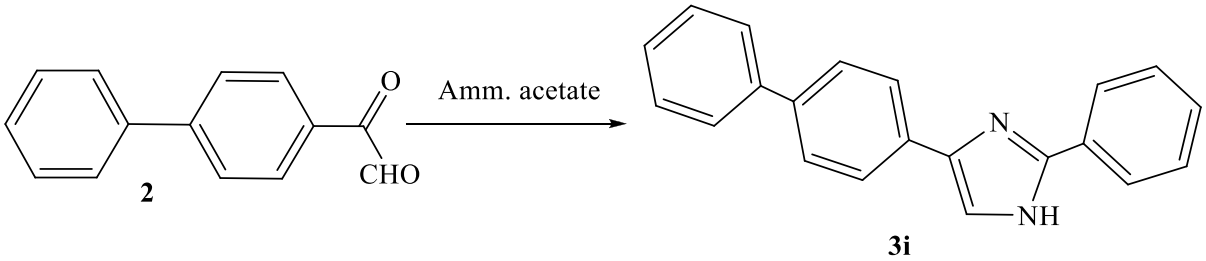


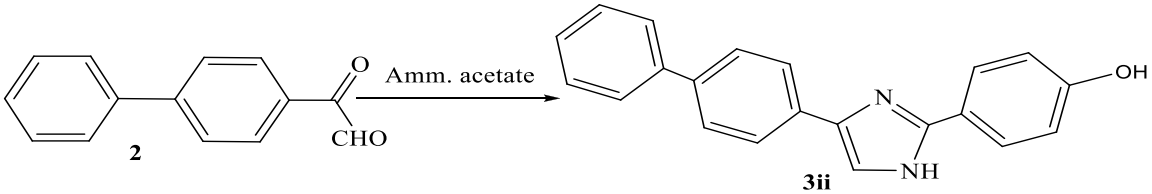
Fig.8: Structural investigation of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1H-imidazole by ^{1}H-NMR

Synthesis of 4-(biphenyl-4-yl)-2-phenyl-1H-imidazole (3i):



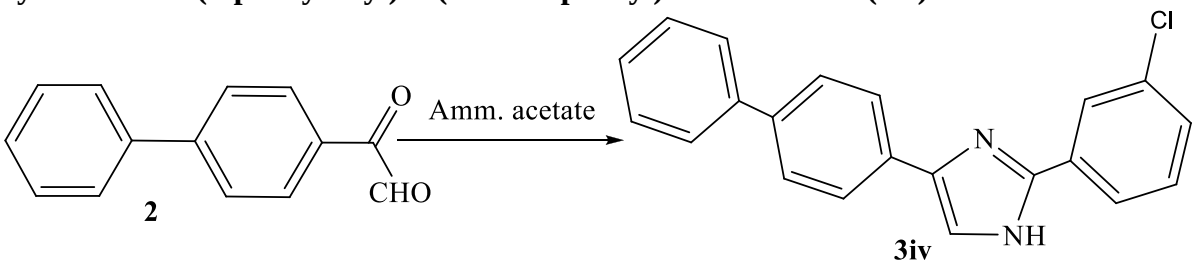
2 3i

Synthesis of 4-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3ii):



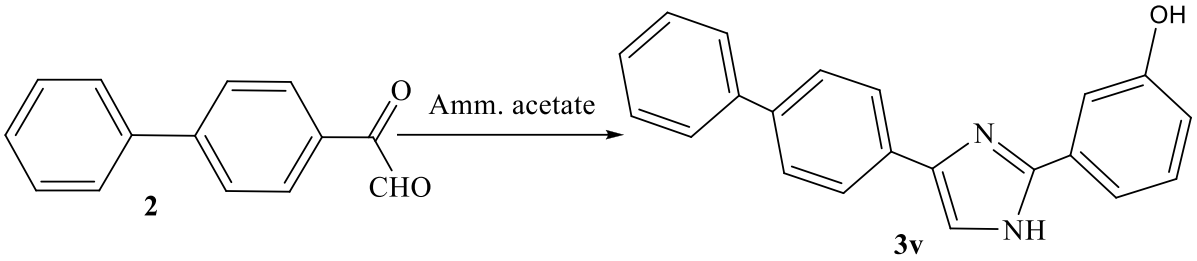
2 3ii

Synthesis of 4-(biphenyl-4-yl)-2-(3-chlorophenyl)-1H-imidazole (3iv):



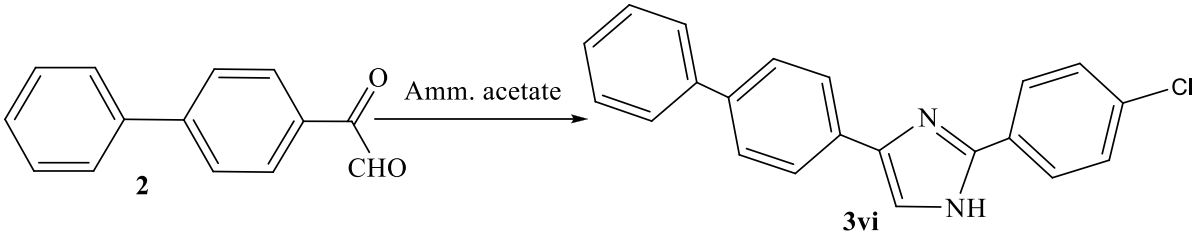
2 3iv

Synthesis of 3-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3v):



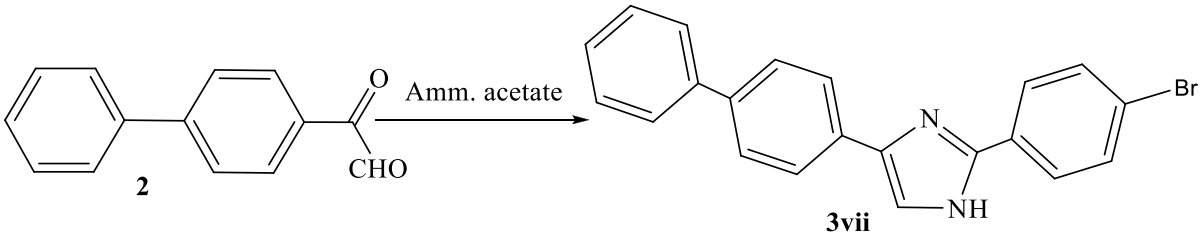
2 3v

Synthesis of 4-(biphenyl-4-yl)-2-(4-chlorophenyl)-1H-imidazole (3vi):



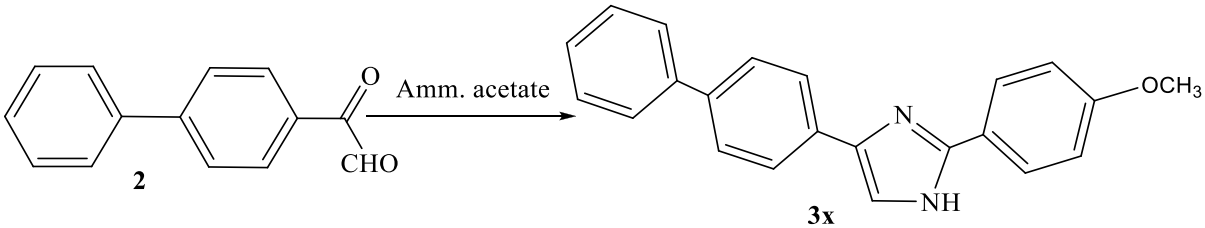
2 3vi

Synthesis of 4-(biphenyl-4-yl)-2-(4-bromophenyl)-1H-imidazole (3vii):



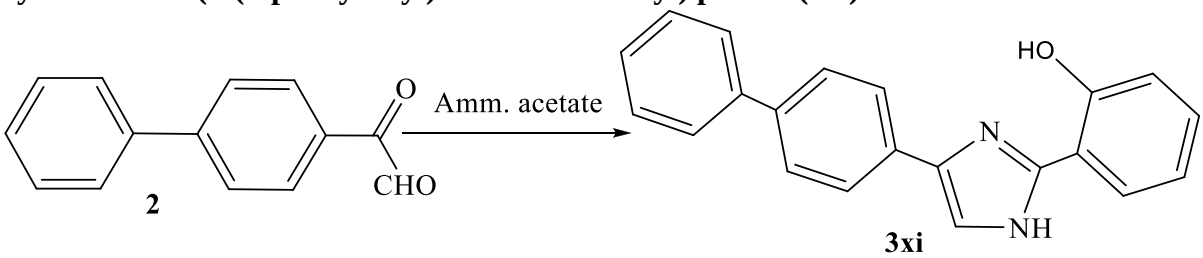
2 3vii

Synthesis of 4-(biphenyl-4-yl)-2-(4-methoxyphenyl)-1H-imidazole (3x):



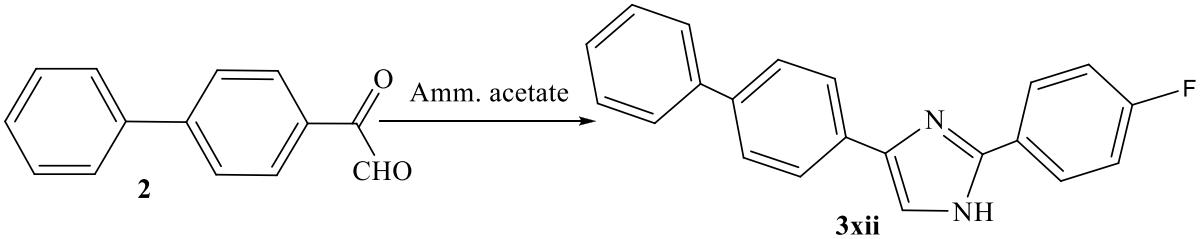
2 3x

Synthesis of 3-(4-(biphenyl-4-yl)-1H-imidazol-2-yl) phenol (3xi):



2 3xi

Synthesis of 4-(biphenyl-4-yl)-2-(4-fluorophenyl)-1H-imidazole (3xii):



2 3xii

Synthetic Series-3:

Compounds **(4i-xii)** synthesis of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1-phenyl-1H-imidazoles were prepared from Scheme 3.

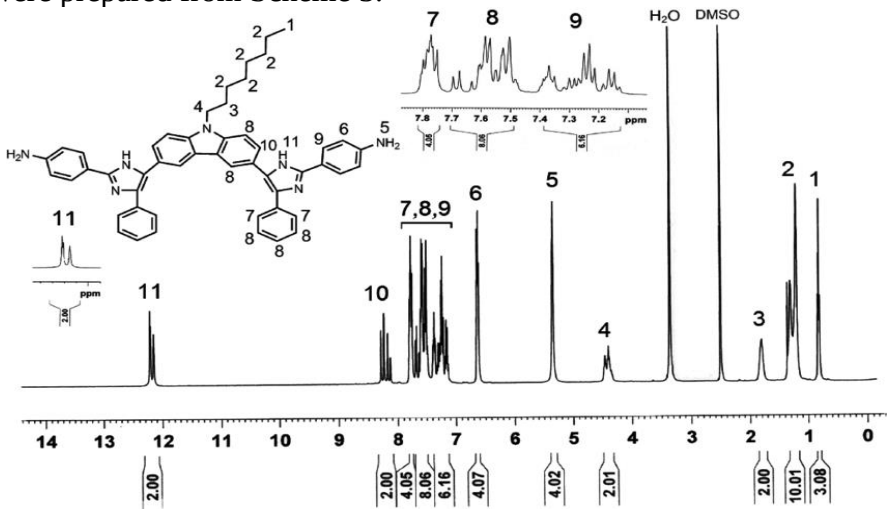


Fig.8: Structural investigation of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1-phenyl-1H-imidazoles by ^{1}H-NMR

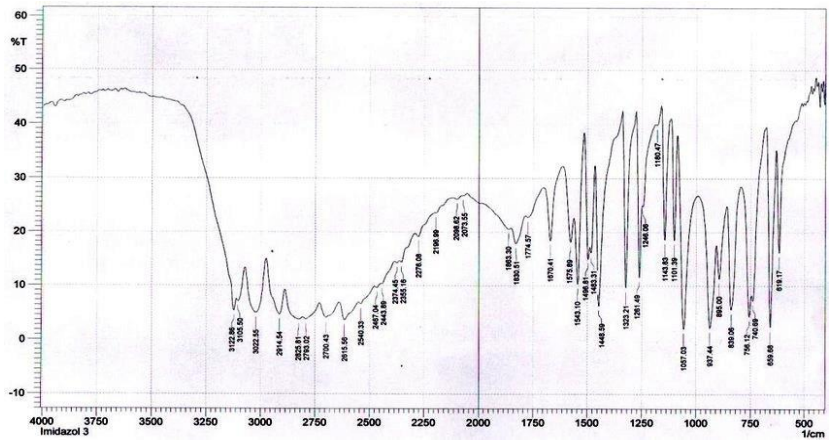
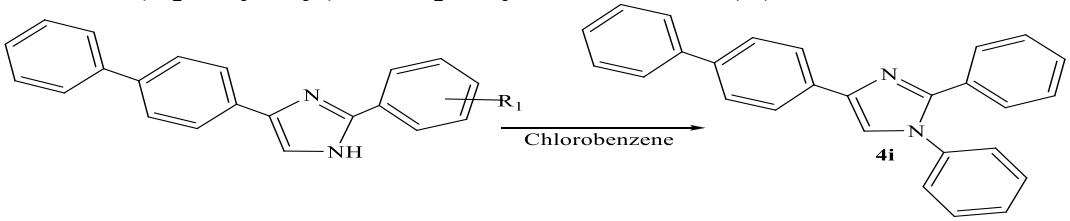
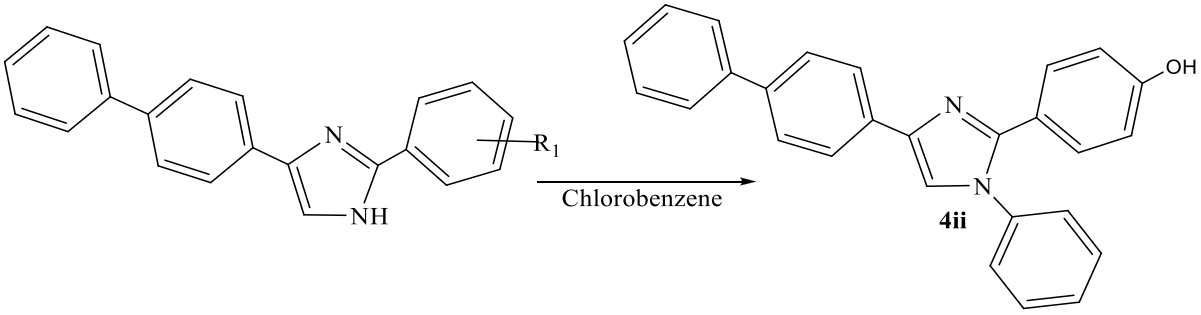


Fig.9: Structural investigation of 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1-phenyl-1H-imidazoles by ^{1}H by FTIR

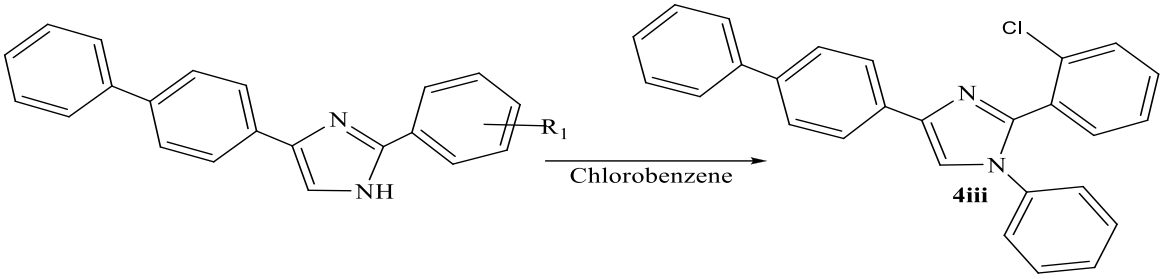
Synthesis of 4-(biphenyl-4-yl)-1, 2-diphenyl-1H-imidazole (4i):



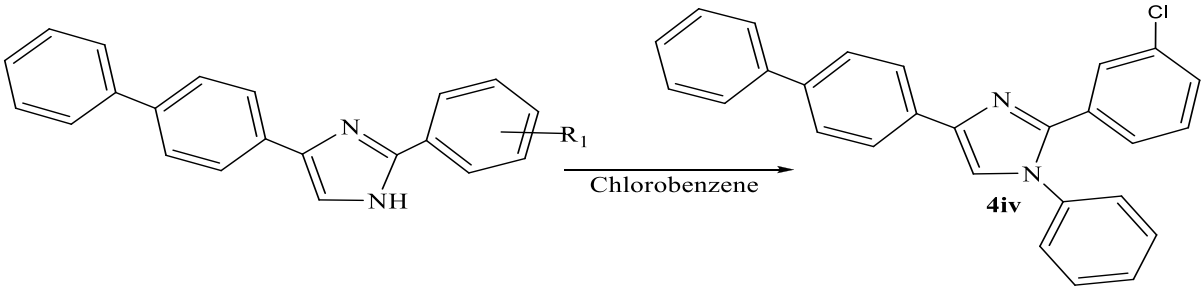
Synthesis of 4-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl) phenol (4ii):



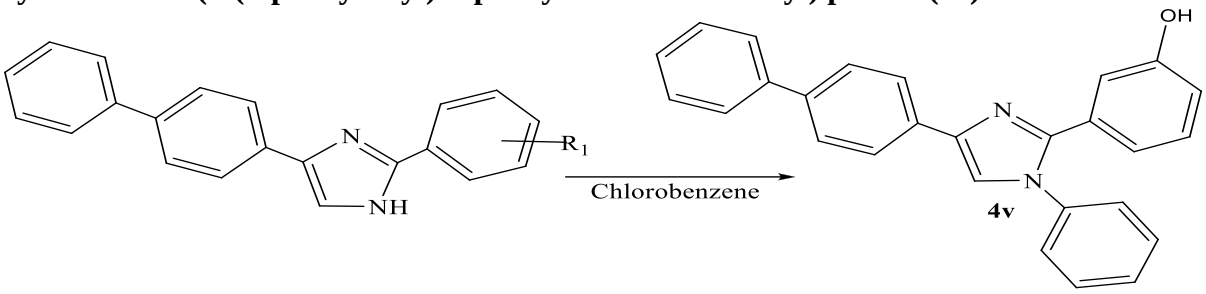
Synthesis of 4-(biphenyl-4-yl)-2-(2-chlorophenyl)-1-phenyl-1H-imidazole (4iii):



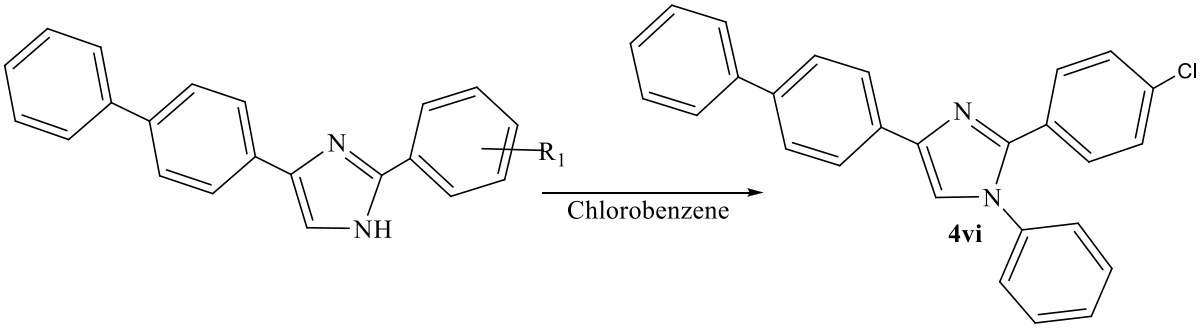
Synthesis of 4-(biphenyl-4-yl)-2-(3-chlorophenyl)-1-phenyl-1H-imidazole (4iv):



Synthesis of 3-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl) phenol (4v):

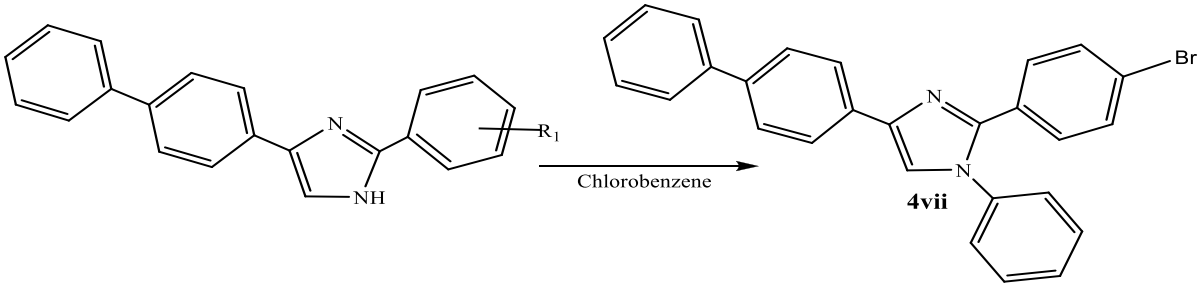


Synthesis of 4-(biphenyl-4-yl)-2-(4-chlorophenyl)-1H-imidazole (4vi):

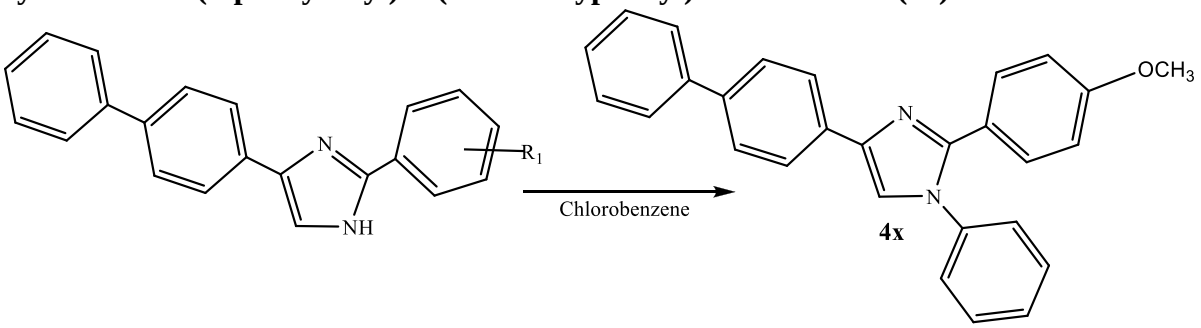


Yield: 68%, Mp: 192-193°C, R_f = 0.41. IR (KBr, cm^{-1}): 3102(C-H, Ar-H), 2961(C-H, CH_2), 1623 (C=N), 1484(C=C), 715(C-Cl). ^{1}H-NMR (DMSO-d_6, δ, ppm): 7.97-6.31 (H, m, Ar-H), 8.79(1H, s, CH, imidazole). ESI-MS (m/z): 406 (M^+). Anal.calcd. for $C_{27}H_{19}ClN_2$: C, 65.31; H, 4.68; N, 13.61. Found: C, 65.41; H, 4.75; N, 13.65.

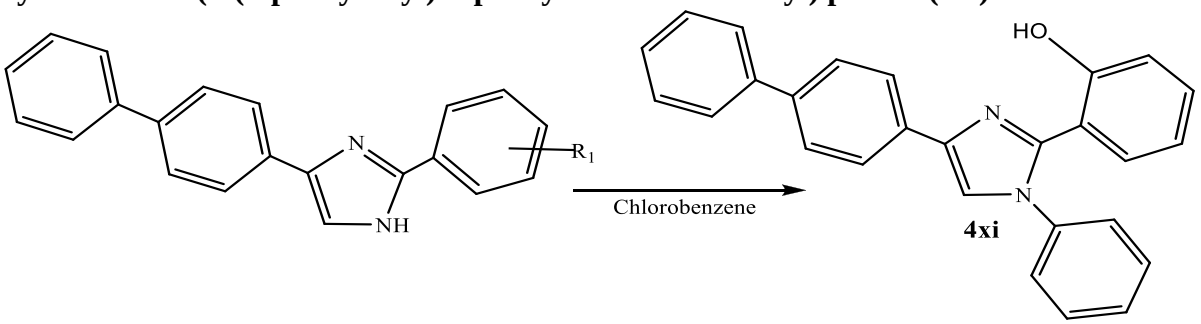
Synthesis of 4-(biphenyl-4-yl)-2-(4-bromophenyl)-1-phenyl-1H-imidazole (4vii):



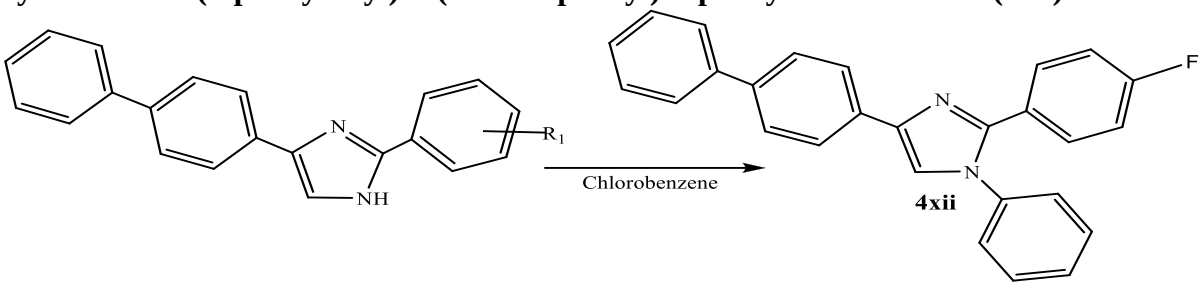
Synthesis of 4-(biphenyl-4-yl)-2-(4-methoxyphenyl)-1H-imidazole (4x):



Synthesis of 2-(4-(biphenyl-4-yl)-1-phenyl-1H-imidazol-2-yl) phenol (4xi):



Synthesis of 4-(biphenyl-4-yl)-2-(4-fluorophenyl)-1-phenyl-1H-imidazole (4xii):



BIOLOGICAL EVALUATION:

Synthetic Series-1:

Antibacterial activity of newly synthesized compounds (**2a-j** & **3a-j)** was screened against bacterial strains viz. *Escherichia coli (E. coli*, MTCC 2961*), Staphylococcus aureus (S. aureus*, MTCC 3160*), Bacillus subtilis (B. subtilis*, MTCC 121*), Klebsiella pneumoniae (K. pneumoniae*, MTCC 3040*) and Micrococcus luteus (M. luteus*, MTCC 7527*)*. The anti-fungal activity was screened against fungal strains viz. *Candida albicans (C. albicans*, MTCC 227*), Aspergillus niger (A. niger*, MTCC 277*) and Aspergillus flavus (A. flavus*, MTCC 418*)*.

Evaluation of Anti-microbial Screening:

Table.1: Compounds code, Substituted (-R), log P and molar refractivity of title compounds (**2a-j**) and (**3a-j**).

Compd.	Subs. (-R)	C log P	Molar Refractivity
2a	H	4.93	99.71
2b	4-Cl	3.85	112.80
2c	2-OH	4.41	112.80
2d	4-OH	6.35	109.50
2e	4-NO_2	5.21	99.69
2f	4-OCH_3	6.65	115.09
2g	4-$N(CH_3)_2$	5.93	109.36
2h	3,4-$(OCH_3)_2$	5.93	109.36
2i	4-OCH_3 3-OH	4.07	113.06
2j	4-OC_2H_5 3-OH	4.77	113.06
3a	H	6.68	105.57
3b	4-Cl	6.58	118.66
3c	2-OH	6.28	118.66
3d	4-OH	8.14	115.46
3e	4-NO_2	7.00	105.56
3f	4-OCH_3	8.44	120.95
3g	4-$N(CH_3)_2$	7.68	115.22
3h	3,4-$(OCH_3)_2$	7.68	115.22
3i	4-OCH_3 3-OH	6.54	118.92
3j	4-OC_2H_5 3-OH	6.54	118.92

Antibacterial Activity:

Table.2. Antibacterial activity measure as zone of inhibition of title compounds **(2a-j)** and **(3a-j)**

Compd.	**E. coli (MTCC-1687)**		**S. aureus (MTCC-2940)**		**B. subtilis (MTCC- 441)**		**M. luteus (MTCC 7527)**		**K. pneumonia (MTCC 3040)**	
	50µg/ml ±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml ±SD	100µg/ml ±SD
2a	7.10 ± 1.31	14.01± 2.01	Nt	nt	8.32±0 .58	9.20±1. 32	10.31 ± 1.58	9.31 ± 1.1`	11.30±0. 51	12.31±1.1 5
2b	14.17±1 .76	22.00± 1.25	15.61± 1.51	17.67± 1.53	16.21± 1.2	18.20± 1.32	15.50 ± 1.32	18.17 ± 1.44	19.40±1. 21	14.14±2.4 1
2c	13.17±3 .26	17.17± 0.76	9.03±1 .42	11.50± 1.50	13.53± 1.3	15.75± 1.32	nt	nt	11.31±1. 32	18.31±1.0 4
2d	18.33±1 .54	15.33± 1.12	14.17± 1.21	20.83± 1.04	18.02± 1.1	17.17± 0.76	12.17 ± 1.26	13.67 ± 1.1`	11.11±1. 16	20.65±1.1 2
2e	15.04±1 .32	17.83± 2.04	14.17± 1.12	15.00± 1.73	15.61± 1.5	15.67± 1.12	14.61 ± 1.53	16.67 ± 0.58	14.26±1. 31	14.62±0.5 3
2f	19.33±2 .04	20.33± 1.52	14.67± 1.54	25.33± 1.53	16.6±1 .73	13.20± 1.72	nt	nt	11.61±1. 53	19.31±1.1 2

2g	16.00±1.73	21.33±1.53	17.30±1.35	14.33±1.53	15.61±1.5	18.67 ±1.53	17.12 ±1.00	19.21 ±1.01	15.01±1.11	18.34±1.07
2h	14.17±1.04	16.50±1.31	Nt	nt	14.61±1.5	14.31 ±1.15	12.33 ±1.53	13.67 ±0.53	12.31±1.13	14.61±0.58
2i	13.1±1.24	21.33±1.51	12.17±1.26	16.33±0.58	15.31±1.1	12.33 ±1.53	10.33 ±1.15	16.32 ±1.21	11.33±1.15	16.12±1.21
2j	12.17±1.44	11.33±1.15	12.17±0.76	13.17±1.04	11.17±1.8	12.62 ±1.53	15.33 ±1.53	14.67 ±1.15	15.13±1.51	15.62±1.11
3a	11.61±1.53	11.03±1.10	13.67±2.08	15.67±1.53	10.50±1.3	12.32 ±1.53	9.67 ±1.15	11.21 ±2.01	11.65±1.12	14.01±2.03
3b	11.87±1.01	15.53±1.87	Nt	nt	12.33±1.5	14.67 ±1.51	nt	nt	15.17±0.76	14.51 ±0.82
3c	11.51±0.51	17.67±1.13	15.67±1.53	15.61±1.53	14.33±1.5	17.83 ±1.26	15.00 ±1.00	15.67 ±1.53	nt	nt
3d	24.21±1.32	26.61±1.15	20.17±2.76	24.31±1.53	19.35 ± 1.31	23.17±1.44	26.00 ±1.00	21.83 ±1.26	22.12±1.00	20.91±1.21
3e	14.01±1.12	15.20±0.82	14.51±1.31	16.61±1.51	13.31±1.5	19.61±1.32	13.15 ±0.71	14.51 ±0.81	14.71±0.71	15.21±0.23
3f	21.13±1.17	22.02±1.27	19.72±1.71	25.31±1.52	21.81±1.1	25.11±1.31	20.32 ±1.43	21.81 ±1.13	23.21±1.01	20.13±1.35
3g	13.31±2.01	15.51±1.50	14.61±1.23	11.31±1.53	15.12±1.4	19.12±1.33	15.61±1.51	16.31±1.10	14.21±1.51	15.31±1.17
3h	12.21±1.16	16.32±0.82	13.50±2.31	12.61±1.51	15.31±1.5	14.30±1.35	nt	nt	13.16 ±0.71	14.5 ±0.87
3i	15.10±0.52	14.61±1.12	Nt	nt	17.31±1.5	15.31±1.21	15.21±1.21	13.61±1.51	14.01 ±1.13	16.67±1.55
3j	15.31±2.13	11.30±1.52	13.61±1.53	15.31±1.31	17.12±1.2	16.10±1.53	15.61±1.32	16.31±1.52	nt	nt
Cipro.	28.70±1.26	30.13±2.34	29.33±1.53	30.83±1.76	28.67±1.5	30.81±1.61	28.33±1.53	31.17±2.21	28.87 ±1.71	30.11±1.57

Measure zone of inhibition in millimeter,SD = standard deviation, Compd.; Compunds, Cipro; Ciprofloxacin. Nt means not tested compounds.

Table.3. Antibacterial activity as percentage inhibition of title compounds **(2a-j)** and **(3a-j)**.

Compd	E. coli **(**MTCC-1687)		S. aureus **(**MTCC-2940)		B. subtilis **(**MTCC- 441)		M. luteus (MTCC 7527)		K. pneumonia (MTCC 3040)	
	50µg/ml ±SD[b]	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml ±SD	100µg/ml±SD	50µg/ml ±SD	100µg/ml±SD	50µg/ml ±SD	100µg/ml ±SD
2a	nt	nt	Nt	nt	44.83±3.26	65.19±3.48	66.41±1.74	40.01±4.71	44.10±4.65	38.51±3.91
2b	62.39±4.39	68.73±6.48	60.13±5.41	55.47±4.53	55.22±1.71	55.36±7.29	56.96±7.41	55.47±6.21	60.32±4.32	60.71±5.41
2c	41.12±3.28	58.56±1.79	51.70±2.89	36.16±3.23	45.72±5.95	46.10±1.22	nt	nt	44.12±3.22	54.21±2.72
2d	50.10±1.90	57.21±5.61	44.64±3.03	46.79±1.66	51.20±2.51	47.81±4.91	47.86±2.13	48.85±1.66	44.10±2.90	49.21±4.61
2e	56.39±1.26	59.83±6.26	49.48±3.06	52.21±3.66	46.51±4.42	52.67±2.79	54.94±6.62	55.66±2.32	57.39±3.26	50.83±4.24
2f	55.05±3	51.04±	58.10±	50.12±	68.05±	60.76±	nt	nt	53.05±3.	51.04±5.7

	.52	3.79	5.61	1.61	1.61	7.17			55	1
2g	48.01±6.16	59.32±7.67	46.69±5.78	47.94±2.44	55.50±2.11	53.36±2.90	56.43±6.73	57.66±2.21	46.07±6.16	59.31±6.67
2h	42.78±4.33	41.22±2.83	Nt	nt	48.59±2.01	44.96±1.47	65.93±3.87	48.78±2.50	48.78±4.32	40.25±2.83
2i	nt	nt	53.94±1.76	53.54±3.37	52.03±1.53	56.86±7.73	67.66±4.60	57.44±4.44	59.85±3.12	60.84±7.36
2j	42.03±6.24	39.69±5.04	39.00±2.91	37.44±2.28	40.49±4.23	36.70±2.89	47.25±7.20	57.29±2.72	50.03±5.21	40.69±5.08
3a	52.47±3.82	47.72±3.79	40.46±5.22	61.14±5.10	32.08±4.62	36.51±4.88	34.29±5.66	39.26±4.46	Nt	nt
3b	45.10±4.77	47.52±4.70	Nt	nt	45.86±3.05	48.29±6.97	43.11±4.94	49.58±1.65	48.67±4.77	46.59±3.72
3c	56.26±3.98	51.42±6.82	57.22±2.93	55.11±7.34	48.5 ±7.78	nt	nt	60.82±1.84	58.26±3.98	65.45±5.82
3d	76.23±3.51	72.51±3.04	68.05±2.87	85.12±4.81	67.64±5.66	76.72±1.83	70.67±3.87	88.25±1.53	67.64±3.51	71.54±1.04
3e	32.61±4.24	54.55±4.96	48.17±1.07	62.16±3.33	24.83±3.26	25.19±3.48	29.48±2.74	39.05±3.34	28.60±4.64	43.55±3.96
3f	70.13±4.39	70.71±6.41	67.18±5.41	74.97±5.51	64.69±1.31	70.16±6.21	76.96±1.41	69.69±6.21	70.79±4.31	70.63±4.41
3g	40.12±3.71	49.59±4.73	40.35±4.88	47.01±6.92	44.81±3.06	47.21±6.97	nt	nt	49.10±4.77	50.59±3.70
3h	53.26±1.98	51.41±6.81	51.22±3.93	54.11±7.36	48.52±6.78	48.82±4.61	53.12±5.65	55.82±6.84	57.26±3.98	51.45±5.82
3i	37.07±3.16	56.31±4.61	nt	nt	51.50±4.11	50.31±2.90	55.43±6.73	57.66±1.21	nt	nt
3j	nt	nt	29.17±2.01	33.16±3.33	26.83±3.21	29.11±3.41	29.48±2.74	31.05±4.34	32.60±4.64	47.51±5.92
Cipro.	100.00±2.31	100.00 ±1.53	100.00 ±2.43	100.00 ±1.57	100.00 ±1.12	100.00 ±4.32	100.00±1.71	100.00 ±5.31	100.00±5.18	100.00±1.53

Measure zone of inhibition in percentage inhibition, SD = standard deviation, Compd.=Compunds, Cipro=Ciprofloxacin.

Antifungal Activity:

Table 4. Anti-fungal activity as as zone of inhibition of title compounds **(2a-j)** and **(3a-j)**.

Compd.	C. albicans (MTCC-3617)		A. niger (MTCC-281)		A. flavus (MTCC 418)	
	50µg/ml±SD[b]	100µg/ml±SD[b]	50µg/ml±SD[b]	100µg/ml±SD[b]	50µg/ml±SD[b]	100µg/ml±SD[b]
2a	nt	Nt	13.61±1.53	11.16±1.10	9.35±1.61	11.01±1.32

2b	13.31±2.30	17.15±2.43	12.33±2.15	16.38±1.51	nt	Nt
2c	12.33 ± 1.53	16.23±3.17	19.17±1.21	12.67±1.15	14.11±1.26	15.61±1.10
2d	19.01 ± 2.01	13.03±1.70	16.70±1.12	18.33±2.08	16.31±1.42	16.31±2.08
2e	15.34 ± 1.51	17.21±1.21	Nt	nt	15.01±1.04	18.61±1.53
2f	20.61 ± 1.04	24.21±1.14	21.67±1.08	21.31±1.31	23.67±2.08	13.33±2.53
2g	15.63 ± 2.08	15.24±1.21	15.32±1.01	16.24±1.72	14.21±2.01	11.05±2.71
2h	nt	Nt	16.67±2.58	16.35±2.08	13.67±1.51	16.31±2.01
2i	14.83 ± 1.61	21.32±2.28	15.41±2.31	13.61±1.53	nt	nt
2j	16.13 ± 1.04	15.31±1.53	15.01±1.07	17.31±1.53	18.21±1.22	20.31±1.53
3a	11.63 ± 3.53	17.20±1.21	13.33±2.51	16.43±1.12	11.31±1.54	17.01±1.32
3b	nt	Nt	16.61±1.15	15.81±1.04	15.61±1.47	16.81±1.01
3c	15.67 ± 1.53	18.31±1.54	15.67±1.52	19.23±1.08	16.54±1.23	19.13±2.01
3d	24.12 ± 2.12	25.66±1.21	25.7±1.56	28.19±1.61	26.67±1.53	28.81±1.63
3e	11.61 ± 1.52	19.17±2.26	17.67±1.52	16.33±1.01	nt	nt
3f	22.21 ± 1.63	26.73±1.08	25.50±1.12	21.67±1.57	27.50±1.32	23.61±1.53
3g	nt	Nt	16.00±1.00	14.31±1.54	15.03±1.42	16.32±1.53
3h	14.67 ± 1.63	22.04 ± 1.55	13.33±1.53	16.01±1.06	11.33±1.33	18.56±1.21
3i	14.31 ± 1.34	14.09 ± 4.65	14.61±1.53	18.83±1.23	14.67±1.51	16.83±1.04
3j	16.67 ± 2.51	15.31 ± 2.53	16.60±1.53	15.31±2.08	nt	nt
Fluco.	31.23 ± 1.14	31.81 ± 1.72	30.17±1.32	31.23±1.21	28.56±2.51	31.15±2.13

Zone of inhibition measure in millimeter, SD = standard deviation, Fluco = Fluconazole, nt means not tested compounds.

Table 5. Antifungal activity of the synthesized compounds **(2a-j)** and **(3a-j)** as percentage inhibition.

Compd.	C. albicans (MTCC-3617)		A. niger (MTCC-281)		A. flavus (MTCC 418)	
	50 µg/ml ± SD[b]	100 µg/ml ± SD[b]	50 µg/ml ± SD[b]	100 µg/ml ± SD[b]	50 µg/ml ± SD[b]	100 µg/ml ± SDb
2a	nt	Nt	26.31 ± 1.81	41.21 ± 4.38	24.7` ± `.81	42.26 ± 1.31
2b	47.10 ± 4.31	45.56 ± 1.41	46.16 ± 3.31	48.16 ± 2.83	nt	nt
2c	35.92 ± 3.78	46.58 ± 3.16	57.23 ± 2.41	50.82 ± 1.01	48.2` ± `.43	67.1` ± 1.01
2d	46.21 ± 5.48	56.25 ± 1.29	50.`8 ± 3.07	56.25 ± 3.92	51.48 ± 3.07	51.46 ± 4.92

2e	49.74 ± 3.25	49.27 ± 1.54	nt	Nt	52.81 ± 3.02	45.21 ± 2.79
2f	69.05 ± 2.88	65.11 ± 4.00	51.39 ± 1.61	65.21 ± 1.93	51.91 ± 3.68	51.30 ± 3.93
2g	56.21 ± 3.45	54.20 ± 0.30	48.31 ± 1.31	47.13 ± 4.21	67.31 ± 4.38	49.13 ± 4.21
2h	nt	Nt	55.84 ± 2.12	45.13 ± 2.81	41.82 ± 1.12	51.11 ± 3.88
2i	67.09 ± 4.01	64.52 ± 4.30	60.13± 5.59	56.12 ± 1.69	nt	nt
2j	35.25 ± 1.94	48.61 ± 6.49	40.31 ± 2.96	43.21 ± 5.34	53.30 ± 1.96	52.29 ± 1.31
3a	46.19 ± 3.14	35.45 ± 2.80	43.6` ± 5.18	42.23± 2.41	31.61 ± 7.18	41.19 ± 2.44
3b	nt	Nt	45.22 ± 2.11	48.71 ± 1.31	42.29 ± 4.11	51.71 ± 2.36
3c	55.31 ± 2.48	55.27 ± 2.63	53.42 ± 1.48	56.21 ± 2.91	43.42 ± 2.48	58.21 ± 3.93
3d	70.21 ± 1.21	73.37 ± 2.61	69.02 ± 2.02	76.19 ± 3.79	61.01 ± 4.02	78.13 ± 1.71
3e	40.12 ± 3.13	41.82 ± 1.62	47.84 ± 1.12	41.11 ± 1.88	nt	nt
3f	68.01 ± 2.07	70.04 ± 2.30	71.01 ± 4.59	70.21 ± 1.61	69.01 ± 1.51	74.33 ± 2.62
3g	nt	Nt	61.30 ± 3.96	40.29 ± 3.31	65.65 ± 2.91	57.29 ± 5.33
3h	47.94 ± 1.11	46.16 ± 3.81	50.61 ± 4.18	41.18 ± 4.44	47.61 ± 7.11	45.15 ± 1.41
3i	48.41 ± 4.25	50.31 ± 1.68	41.23 ± 2.14	50.71 ± 2.36	51.21 ± 2.12	59.71 ± 2.35
3j	58.23 ± 2.41	57.21 ± 1.63	65.41 ± 1.41	51.29 ± 3.32	nt	nt
Fluco.	100.00 ± 2.35	100.00 ± 2.12	100.00 ± 2.34	100.00 ± 3.43	100.00 ± 2.34	100.00 ± 3.43

Zone of inhibition represented in percentage inhibition, SD = standard deviation, Fluco- Fluconazole, nt means not tested compound

Synthetic Series-2 (Scheme 2):

The inhibition of microbial growth under standardized condition may be utilized for demonstrating the therapeutic efficacy of any subtle change in the antibiotic molecule. Which may not be detected by chemical method will be revealed by a reduction in the anti-microbial activity and hence microbiological assays are very useful for resolving doubts regarding possible loss of potency of antibiotics and their preparations of the antibiotic having a known activity. The in-vitro antibacterial and antifungal activities of the synthesized compounds were carried out by microdilution susceptibility test using cup-plate technique. Antibacterial activity of newly synthesized compounds (**3i-xii**)was screened against bacterial strains viz. *Escherichia coli (E. coli*, MTCC 2961*), Staphylococcus aureus (S. aureus,* MTCC 3160*), Bacillussubtilis (B. subtilis,*MTCC 121*), Klebsiella pneumoniae (K. pneumoniae,*MTCC 3040*) and Micrococcus luteus (M. luteus,*MTCC 7527*)*. The anti-fungal activity was screened against fungal strains viz.*Candida albicans (C. albicans*, MTCC 227*), Aspergillus niger (A.niger*, MTCC 277*) and Aspergillus flavus (A. flavus,* MTCC 418*).*

Evaluation of Anti-microbial Screening:

Table.6. Compounds code, Substituted (-R_1), log P and molar refractivity of title compounds (**3i-xii**).

Compd.	Subs. (-R)	C log P	Molar Refractivity
3i	H	3.91	89.81
3ii	4-OH	5.83	113.70
3iii	2-Cl	4.45	112.80
3iv	3-Cl	6.31	114.63
3v	3-OH	5.95	107.79

3vi	4-Cl	5.27	113.01
3vii	4-Br	5.91	109.35
3viii	4-$N(CH_3)_2$	6.03	112.13
3ix	3-OCH_3	5.73	113.17
3x	4-OCH_3	6.73	113.51
3xi	2-OH	6.21	112.67
3xii	4-F	5.58	109.63

Anti-bacterial activity

Experimental Procedure:

Table.7. Antibacterial activity measure by zone of inhibition of title compounds(**3i-xii**).

Compd.	*E. coli* **(**MTCC-1687)		*S. aureus* **(**MTCC-2940)		*B. subtilis* **(**MTCC- 441)		*M. luteus* (MTCC 7527)		*K.pneumonia* (MTCC 3040)	
	50 µg/ml ± SD[b]	100 µg/ml ± SD	50 µg/ml ± SD	100 µg/ml ± SD	50 µg/ml ± SD	100 µg/ml ± SD	50 µg/ml ± SD	100 µg/ml±SD	50 µg/ml ± SD	100 µg/ml±SD
3i	8.11 ± 2.35	14.01 ± 2.01	nt	nt	8.32 ± 0.58	9.20 ± 1.32	10.31 ± 1.58	9.31 ± 1.1`	11.30 ± 0.51	12.31 ± 1.15
3ii	14.13 ± 1.71	16.78 ± 1.21	15.61 ± 1.51	17.21 ± 2.51	13.21 ± 1.31	14.21 ± 1.32	14.47 ± 1.32	17.17 ± 1.44	15.41 ± 1.31	18.51 ± 1.37
3iii	12.17 ± 3.26	13.58 ± 1.27	nt	nt	13.51 ± 1.37	15.72 ± 2.32	nt	nt	12.31 ± 1.31	17.31 ± 1.13
3iv	20.31 ± 1.51	23.53 ± 1.23	14.18 ± 1.32	16.87 ± 1.17	19.17 ± 1.16	21.97 ± 0.67	15.21 ± 1.23	16.54 ± 1.18	18.13 ± 1.15	20.53 ± 2.13
3v	15.13 ± 1.33	17.37 ± 1.04	13.17 ± 1.12	14.65 ± 1.71	14.64 ± 1.52	15.61 ± 1.12	13.61 ± 1.53	15.67 ± 0.58	14.22 ± 1.36	14.61 ± 1.13
3vi	14.17 ± 1.12	16.31 ± 1.51	14.61 ± 1.45	15.23 ± 2.53	16.6 ± 1.73	15.21 ± 1.25	11.67 ± 1.53	18.31 ± 1.12	nt	nt
3vii	16.23 ± 2.35	15.31 ± 1.53	nt	nt	15.47 ± 1.23	17.68 ± 1.51	17.21 ± 1.00	18.21 ± 1.01	15.01 ± 1.17	17.12 ± 1.11
3viii	16.15 ± 1.13	17.36 ± 2.31	15.61 ± 1.45	16.23 ± 2.51	14.61 ± 1.53	15.31 ± 1.11	15.17 ± 1.39	17.61 ± 0.21	14.37 ± 1.13	16.89 ± 0.55
3ix	14.15 ± 1.11	16.36 ± 1.33	15.17 ± 1.21	16.33 ± 1.11	13.23 ± 1.13	14.83 ± 1.53	15.93 ± 1.15	17.31 ± 1.27	14.31 ± 1.13	15.17 ± 1.25
3x	18.15 ± 1.41	21.61 ± 1.03	15.11 ± 0.5	17.21± 1.23	17.01 ± 1.31	19.61 ± 1.41	15.16 ± 1.51	14.61 ± 2.13	17.81 ± 1.32	20.61 ± 1.16
3xi	nt	nt	13.61 ± 1.05	15.61 ± 1.33	11.51 ± 1.72	13.12 ± 1.51	9.61 ± 1.15	11.67 ± 2.36	nt	nt
3xii	11.68 ± 1.15	15.51 ± 1.67	11.23 ± 2.07	14.61 ± 1.57	12.33 ± 1.32	14.61 ± 1.51	nt	nt	15.11 ± 1.05	14.58 ± 2.11

Cipro.	27.51 ± 1.21	29.11 ± 1.17	29.31 ± 1.41	30.37 ± 1.71	28.45 ± 1.51	29.81 ± 1.61	28.33 ± 1.53	30.17 ± 1.11	29.41 ± 1.41	30.17 ± 1.35

Measure zone of inhibition in millimeter, SD; Standard Deviation, Compd.; Compunds, Cipro; Ciprofloxacin, nt; means not tested compounds.

Table.8. Antibacterial activity as percentage inhibition of title compounds (**3i-xii**).

Compd	*E. coli* (MTCC-1687)		*S. aureus* (MTCC-2940)		*B. subtilis* (MTCC- 441)		*M. luteus* (MTCC 7527)		*K. pneumonia* (MTCC 3040)	
	50µg/ml ±SD	100 µg/ ml±SD	50 µg/ ml± SD	100 µg/ ml± SD	50 µg/ ml ± SD	100 µg/ ml± SD	50 µg/ ml± SD	100 µg/ ml± SD	50 µg/ ml± SD	100 µg/ ml±SD
3i	40.83±2.21	51.31± 3.41	nt	nt	44.81 ± 3.26	65.19 ± 3.45	61.41 ± 2.72	38.51 ± 5.71	43.15 ± 4.01	39.61 ± 3.46
3ii	61.32±4.31	65.52 ± 5.43	60.27 ± 5.46	54.67 ± 3.53	51.23 ± 1.74	54.36 ± 6.21	57.83 ± 5.42	56.41 ± 6.27	62.31 ± 4.27	59.61 ± 4.41
3iii	68.27±4.21	64.71 ± 5.31	nt	nt	59.71 ± 4.94	66.11 ± 1.23	nt	nt	57.29 ± 3.21	64.31 ± 3.82
3iv	67.11±2.91	57.25 ± 3.62	48.62 ± 3.27	44.81 ± 2.61	64.27 ± 2.51	50.31 ± 3.91	65.81 ± 3.15	61.72 ± 1.63	58.11 ± 2.75	51.26 ± 5.61
3v	45.13±5.21	40.61 ± 5.14	39.01 ± 1.91	38.43 ± 2.21	41.41 ± 4.21	35.77 ± 2.81	47.26 ± 5.20	55.39 ± 2.71	51.05 ± 4.31	40.63 ± 5.21
3vi	55.41±3.41	48.62 ± 3.75	40.41 ± 5.61	61.18 ± 4.10	32.01 ± 4.62	37.51 ± 4.58	36.21 ± 5.63	40.21 ± 4.41	nt	nt
3vii	40.10±4.77	48.52 ± 3.70	nt	nt	45.86 ± 3.01	48.29 ± 6.91	57.11 ± 4.94	53.51 ± 1.65	44.63 ± 4.77	51.51 ± 3.71
3viii	61.78±4.33	57.22 ± 2.83	48.52 ± 2.01	45.96 ± 1.47	53.52 ± 2.01	47.96 ± 1.47	61.31 ± 3.82	57.71 ± 2.50	50.62 ± 4.32	45.21 ± 2.35
3ix	59.31±1.21	56.81 ± 5.26	53.94 ± 2.73	50.61 ± 3.37	51.03 ± 2.53	56.86 ± 7.73	64.66 ± 4.60	57.44 ± 4.44	58.85 ± 3.12	60.84 ± 7.36
3x	60.31±1.21	58.81 ± 5.26	48.48 ± 2.06	51.21 ± 3.66	65.51 ± 4.42	63.67 ± 2.79	59.94 ± 5.62	55.61 ± 1.32	69.39 ± 3.26	64.83 ± 4.24
3xi	nt	nt	58.10 ± 5.61	50.12 ± 1.61	68.05 ± 1.61	60.76 ± 7.17	53.05 ± 3.55	51.04 ± 5.71	nt	nt
3xii	48.01±6.11	58.32 ± 6.51	50.61 ± 5.78	47.94 ± 3.44	52.47 ± 2.11	54.16 ± 2.90	nt	nt	48.17 ± 5.13	58.31 ± 5.61
Cipro.	100.00± 1.41	100.00 ± 1.52	100.00 ± 1.65	100.00 ± 2.37	100.00 ± 1.15	100.00 ± 3.45	100.00 ± 1.63	100.00 ± 4.21	100.00 ± 5.89	100.00 ± 2.41

Measure zone of inhibition in percentage inhibition, SD; Standard Deviation, Compd.; Compunds, Cipro; Ciprofloxacin, nt; means not tested compounds

Antifungal Activity:

Experimental Procedure:

Table.9. Antifungal activity as zone of inhibition of title compounds (**3i-xii).**

Compd.	*C. albicans* (MTCC-3617)		*A. niger* (MTCC-281)		*A. flavus* (MTCC 418)	
	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD
3i	15.67±1.53	18.31±1.54	15.67±1.52	19.23±1.08	16.54±1.23	19.13±2.01
3ii	17.12±2.41	19.63±1.21	19.71±1.56	20.19±1.61	19.67±1.53	21.81±1.64
3iii	11.61±1.52	19.17±2.26	17.67±1.52	16.33±1.01	nt	nt
3iv	16.21±1.63	18.7±1.08	19.50±1.12	22.67±1.57	21.50±1.32	23.61±1.53

3v	nt	Nt	16.00±1.00	14.31±1.54	15.03±1.42	16.32±1.53
3vi	20.61±1.04	24.21±1.14	21.67±1.08	21.31±1.31	23.67±2.08	13.33±2.53
3vii	14.67±1.63	22.04±1.55	13.33±1.53	16.01±1.06	11.33±1.33	18.56±1.21
3viii	17.31±1.34	19.09±4.65	14.61±1.53	18.83±1.23	21.67±1.51	22.39±1.04
3ix	16.67±2.51	15.31±2.53	16.60±1.53	15.31±2.08	nt	nt
3x	17.13±1.04	19.31±1.53	16.01±1.07	19.36±1.53	18.21±1.22	20.31±1.53
3xi	19.63±3.53	22.20±1.21	13.33±2.51	16.43±1.12	11.31±1.54	17.01±1.32
3xii	nt	Nt	16.61±1.15	15.81±1.04	15.61±1.47	16.81±1.01
Fluco.	31.23±1.14	31.81±1.72	30.17±1.32	31.23±1.21	28.56±2.51	31.15±2.13

Zone of inhibition measure in millimeter, SD; Standard Deviation,Fluco; Fluconazole, nt; means not tested compounds.

Table.10. Antifungal activity as percentage inhibition of the synthetic compounds (**3i-xii**).

Compd.	*C. albicans* (MTCC-3617)		*A. niger* (MTCC-281)		*A. flavus* (MTCC 418)	
	50µg/ml±SD	100µg/ml±SD	50 µg/ml ± SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD
3i	55.31±2.48	55.27±2.63	53.42±1.48	56.21±2.91	43.42±2.48	58.21±3.93
3ii	54.21±1.23	58.37±2.61	63.02±2.02	66.19±3.79	57.01±3.02	60.13±1.61
3iii	40.12±3.13	41.82±1.62	47.84±1.12	41.11±1.88	nt	nt
3iv	55.01±2.07	59.04±2.30	61.01±4.59	63.21±1.61	69.01±1.51	72.33±2.62
3v	nt	Nt	61.30±3.96	40.29±3.31	65.65±2.91	57.29±5.33
3vi	47.94±1.11	46.16±3.81	50.61±4.18	41.18±4.44	47.61±7.11	45.15±1.41
3vii	48.41±4.25	50.31±1.68	41.23±2.14	50.71±2.36	51.21±2.12	56.71±2.35
3viii	57.19±3.14	63.45±2.80	59.67±5.18	62.23±2.41	60.31±7.18	63.19±2.44
3ix	53.19±1.17	57.19±1.67	49.22±2.11	52.71±1.31	54.29±4.11	58.71±2.36
3x	59.23±2.41	61.27±1.63	65.41±1.41	51.29±3.32	61.23±3.17	63.71±1.31
3xi	67.09±4.01	64.52±4.30	60.13±5.59	56.12±1.69	nt	nt
3xii	nt	Nt	45.22±2.11	48.71±1.31	42.29±4.11	51.71±2.36
Fluco.	100.00±2.35	100.00±2.12	100.00±2.34	100.00±3.43	100.00±2.34	100.00±3.43

Zone of inhibition represented in percentage inhibition, SD; Standard deviation,Fluco; Fluconazole, nt; means not tested compounds.

Synthetic Series-3 (Scheme 3):

The inhibition of microbial growth under standardized condition may be utilized for demonstrating the therapeutic efficacy of any subtle change in the antibiotic molecule. Which may not be detected by chemical method will be revealed by a reduction in the anti-microbial activity and hence microbiological assays are very useful for resolving doubts regarding possible loss of potency of antibiotics and their preparations of the antibiotic having a known activity. The in-vitro antibacterial and antifungal activities of the synthesized compounds were carried out by microdilution susceptibility test using cup-plate technique. Antibacterial activity of newly synthesized compounds (**4i-xii**)was screened against bacterial strains viz. *Escherichia coli (E. coli,* MTCC 2961*), Staphylococcus aureus (S. aureus,* MTCC 3160*), Bacillussubtilis (B. subtilis,*MTCC 121*), Klebsiella pneumoniae (K. pneumoniae,*MTCC 3040*) and Micrococcus luteus (M. luteus,*MTCC 7527*)*. The anti-fungal activity was screened against fungal strains viz.*Candida albicans (C. albicans,* MTCC 227*), Aspergillus niger (A.niger,* MTCC 277*) and Aspergillus flavus (A. flavus,* MTCC 418*).*

Evaluation of Anti-microbial Screening:

Table.11. Compounds code, Substituted (-R_1), log P and molar refractivity of title compounds (**4i-xii**).

Compd.	Subs. (-R)	C log P	Molar Refractivity
4i	H	3.87	88.91
4ii	4-OH	5.67	112.01
4iii	2-Cl	4.41	113.73
4iv	3-Cl	5.98	114.01
4v	3-OH	6.13	106.89
4vi	4-Cl	5.93	113.27
4vii	4-Br	5.71	110.31
4viii	4-$N(CH_3)_2$	5.21	112.25
4ix	3-OCH_3	5.71	113.11
4x	4-OCH_3	6.72	113.81
4xi	2-OH	5.32	112.37
4xii	4-F	5.62	111.29

Anti-bacterial Activity:

Table 12. Antibacterial activity measure by zone of inhibition of title compounds (**4i-xii**).

Compd.	*E. coli* (MTCC-1687)		*S. aureus* (MTCC-2940)		*B. subtilis* (MTCC- 441)		*M. luteus* (MTCC 7527)		*K. pneumonia* (MTCC 3040)	
	50µg/ml ±SD[b]	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/m ±SD	100µg/ml±SD	50µg/ml±SD	100 µg/ml±SD	50 µg/ml ± SD	100 µg/ml±SD
4i	9.15±1.11	11.17±1.15	nt	nt	10.31±1.13	11.12±1.41	8.11±.51	9.41±1.05	nt	nt
4ii	19.15±1.32	21.11±1.03	15.21±1.41	17.31±1.11	18.21±1.41	21.51±1.05	nt	nt	21.11±1.01	23.11±1.15
4iii	12.11±1.17	13.01±1.21	nt	nt	11.11±1.31	13.01±1.43	nt	nt	13.11±1.71	15.03±1.11
4iv	23.18±1.11	25.15±1.21	15.61±1.41	16.13±1.32	24.1±1.61	25.11±1.23	17.61±1.42	18.11±1.17	21.15±1.19	23.37±1.11
4v	18.12±1.31	19.13±1.11	14.11±1.15	16.13±1.51	17.32±1.41	19.12±1.11	18.31±1.12	19.41±1.03	17.21±1.17	18.31±1.15
4vi	14.31±1.21	16.13±1.11	nt	nt	18.13±.12	19.21±2.13	14.11±1.25	15.17±1.12	18.31±1.11	19.05±1.15
4vii	15.21±1.31	16.01±1.12	nt	nt	12.41±1.21	14.01±1.01	nt	Nt	15.13±1.11	16.03±2.13
4viii	nt	nt	13.11±1.31	15.21±1.21	14.71±1.35	15.41±2.01	nt	Nt	14.31±1.14	15.43±1.03
4ix	14.11±1.12	15.31±1.05	11.12±1.61	13.21±1.17	nt	nt	15.01±1.11	17.51±1.43	13.11±1.15	14.11±1.31

4x	21.17±1.32	23.41±1.12	18.11±1.03	19.11±1.31	22.05±1.27	24.21±1.61	nt	Nt	25.01±1.31	26.72±1.15
4xi	nt	nt	13.7±1.82	14.51±1.29	11.03±1.11	12.57±1.41	10.21±1.12	11.51±1.31	nt	nt
4xii	17.13±1.11	19.41±1.41	15.21±1.21	18.3±1.13	16.31±1.05	17.11±1.31	nt	Nt	18.16±1.57	20.13±1.43
Cipro.	27.17±1.05	28.13±1.19	29.17±1.51	30.71±1.11	27.41±.31	29.01±1.51	28.31±.33	29.11±1.11	29.51±1.21	30.11±1.03

Measure zone of inhibition in millimeter, SD; Standard Deviation, Compd.; Compunds, Cipro; Ciprofloxacin, nt; means not tested compounds.

Table.13. Antibacterial activity as percentage inhibition of title compounds (**4i-xii**).

Compd	*E. coli* (MTCC-1687)		*S. aureus* (MTCC-2940)		*B. subtilis* (MTCC- 441)		*M. luteus* (MTCC 7527)		*K. pneumonia* (MTCC 3040)	
	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD
4i	41.11±3.25	48.52±4.61	nt	nt	43.75±3.21	51.21±5.31	38.21±3.75	44.11±1.51	nt	nt
4ii	57.31±3.21	54.23±3.41	55.21±5.41	48.21±3.51	56.21±2.53	53.27±1.35	nt	Nt	63.11±5.21	59.03±2.34
4iii	47.21±3.15	52.11±2.61	nt	nt	45.71±4.51	51.15±1.21	nt	Nt	46.31±4.37	52.17±2.14
4iv	67.31±2.31	60.51±3.67	40.37±4.52	38.15±2.37	65.17±5.23	58.64±4.61	46.21±5.23	52.37±3.71	69.32±3.47	62.41±5.34
4v	56.11±4.23	48.31±2.17	38.72±1.81	36.41±2.61	41.41±4.21	35.77±2.81	53.21±3.25	50.47±4.27	51.37±4.21	49.31±3.41
4vi	52.16±2.15	56.21±3.21	nt	nt	60.21±3.52	57.36±4.01	50.11±3.16	53.21±1.65	58.15±2.71	52.34±1.31
4vii	48.16±1.32	49.12±3.11	nt	nt	43.81±3.15	45.21±4.32	nt	Nt	47.61±4.71	49.83±1.75
4viii	nt	nt	44.51±3.14	45.17±1.41	51.67±2.01	48.03±1.41	nt	Nt	50.89±4.31	48.67±2.31
4ix	57.11±3.27	58.21±4.21	46.35±2.11	47.71±3.31	nt	nt	51.13±3.52	53.41±2.41	48.61±3.57	49.31±1.53
4x	64.51±1.61	59.21±4.21	42.13±1.31	40.21±3.61	62.31±3.41	57.12±2.51	nt	Nt	76.13±1.21	65.81±3.25
4xi	nt	nt	46.88±2.63	47.15±1.31	42.51±1.21	44.11±5.15	39.12±1.51	41.31±3.64	nt	nt
4xii	51.21±2.13	48.31±3.57	45.31±2.47	41.91±5.48	50.41±4.16	53.15±3.67	nt	Nt	52.15±5.17	58.67±1.32
Cipro.	100.00±1.41	100.00±1.52	100.00±1.65	100.00±2.37	100.00±1.15	100.00±3.45	100.00± 1.63	100.00±4.21	100.00± 5.89	100.00±2.41

Measure zone of inhibition in percentage inhibition, SD; Standard Deviation, Compd.; Compunds, Cipro; Ciprofloxacin, nt; means not tested compounds

Antifungal Activity:

Table.14. Antifungal activity as zone of inhibition of title compounds (**4i-xii**)**.**

Compd.	*C. albicans* (MTCC-3617)		*A. niger* (MTCC-281)		*A. flavus* (MTCC 418)	
	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD
4i	12.15±1.51	13.31±1.21	15.23±1.41	16.05±1.63	13.51±1.6	14.13±1.18

4ii	18.17±1.42	20.15±1.27	19.03±1.51	21.31±1.42	7 17.61±1.03	21.01±1.61
4iii	11.13±1.21	15.14±1.53	16.21±1.34	18.31±2.13	nt	nt
4iv	21.32±1.11	25.41±1.15	21.61±1.05	23.17±1.35	20.71±1.21	24.32±1.51
4v	17.21±1.31	18.91±1.11	16.71±2.13	18.31±1.51	17.03±1.41	19.31±1.57
4vi	nt	Nt	18.11±1.13	20.61±1.43	20.13±1.52	22.05±1.42
4vii	14.61±1.23	20.13±1.42	13.45±1.51	17.12±1.23	nt	nt
4viii	nt	Nt	14.62±1.54	18.71±1.41	21.05±1.11	22.31±2.17
4ix	17.61±1.21	15.11±1.31	16.11±2.11	17.31±1.37	nt	nt
4x	25.11±1.21	27.32 ± 1.51	22.15 ± 1.67	23.45 ± 1.47	20.67 ± 1.21	23.67±1.87
4xi	nt	Nt	14.31 ± 1.31	16.87 ± 1.17	nt	nt
4xii	19.12±2.51	20.21 ± 1.45	17.62 ± 1.11	18.47 ± 2.41	16.78 ± 1.41	18.67±1.31
Fluco.	31.23±1.14	31.81 ± 1.72	30.17 ± 1.32	31.23 ± 1.21	28.56 ± 2.51	31.15±2.13

Zone of inhibition measure in millimeter, SD; Standard Deviation, Fluco; Fluconazole, nt; means not tested compounds.

Table.15. Antifungal activity as percentage inhibition of the synthetic compounds (**4i-xii**).

Compd.	*C. albicans* (MTCC-3617)		*A. niger* (MTCC-281)		*A. flavus* (MTCC 418)	
	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD	50µg/ml±SD	100µg/ml±SD
4i	41.12±1.32	43.21±1.11	50.41±1.05	53.27±1.87	43.21±1.21	48.17±2.11
4ii	55.67±1.21	58.71±1.92	62.11±1.51	65.11±1.32	60.43±1.62	61.11±1.32
4iii	37.11±2.53	41.37±1.21	51.42±1.17	57.12±1.51	Nt	nt
4iv	70.12±1.15	76.13±3.41	69.21±4.13	73.12±3.41	72.41±3.12	73.11±1.42
4v	58.32±1.12	64.21±2.35	61.51±1.62	63.25±2.31	67.23±2.11	68.21±4.11
4vi	nt	Nt	63.12±2.53	66.31±1.46	70.11±1.32	71.31±2.43
4vii	47.17±2.31	61.61±1.63	43.51±2.17	58.31±2.89	Nt	nt
4viii	nt	Nt	48.32±3.12	63.27±1.41	64.31±4.11	69.27±1.31
4ix	55.45±1.11	48.31±1.62	53.61±2.17	54.01±1.35	Nt	nt
4x	72.41±2.45	79.25±1.53	65.23±1.45	66.21±2.43	68.98±2.75	69.05±1.25
4xi	nt	Nt	48.17±4.23	61.11±1.62	Nt	nt
4xii	64.12±3.11	66.31±1.25	59.21±2.17	60.75±1.35	57.21±4.17	59.41±2.31
Fluco.	100.00±2.31	100.00±2.17	100.00±2.42	100.00±2.49	100.00±2.35	100.00±3.52

Zone of inhibition represented in percentage inhibition, SD; Standard deviation,Fluco; Fluconazole, nt; means not tested compounds.

CONCLUSION

A new series of imidazole derivatives were synthesized and their assigned structure confirmed by IR, NMR and MS spectroscopy. Pharmacological evaluation of synthetic compounds showed that

some compounds exhibited potent antibacterial and anti-fungal activities. On the basis of the obtained results of pharmacological studies of synthesized compounds it is concluded that imidazole derivatives having chloro group in the phenyl ring at the meta position showed synergistic effect on pharmacological activities like antibacterial and anti-fungal activity. All the newly synthesized compounds were assayed *in-vitro* for their antibacterial activity against *Escherichia coli (E. coli*, MTCC 2961*), Staphylococcus aureus (S. aureus*, MTCC 3160*), Bacillus subtilis (B. subtilis*, MTCC 121*), Klebsiella pneumoniae (K. pneumoniae, MTCC 3040) and Micrococcus luteus (M. luteus*, MTCC 7527*)* and Ciprofloxacin was used as the reference drug for comparing tested compounds. All the newly synthesized compounds were assayed *in-vitro* for their antifungal activity against fungal strains viz.*Candida albicans (C. albicans*, MTCC 227*), Aspergillus niger (A. niger*, MTCC 277*) and Aspergillus flavus (A. flavus*, MTCC 418*)* and Fluconazole was used as the reference drug for comparing tested compounds.A number of compounds 4-(4-chlorophenyl)-2-(substituted) phenyl-1*H*-imidazole **(2a-j)** and 4-(4-chlorophenyl)-1,2-(substituted phenyl)-1 phenyl-1*H*-imidazol **(3a-j)** have been successfully synthesized. The pharmacological study was performed to evaluate the effects of substituent on the antibacterial and antifungal activities. The biological activity result revealed that all the newly synthesized compounds 4-(4-chlorophenyl)-1,2-(substituted phenyl)-1-phenyl-1*H*-imidazol **(3a-j)** exhibited better antibacterial activity as compared to antifungal activity in compare to reference drug. The results of anti-bacterial screening further revealed that among all the compounds screening, the compound (**3d**) and (**3f**) have displayed significant anti-bacterial activity against *E. coli*, S. aureus and *K. pneumoniae* while compounds (**3e**), (**3g**) and (**3h**) as well as compounds (**2d**) and (**2f**) showed moderate anti-bacterial activity in compare to standard drug ciprofloxacin. The results of anti-fungal screening showed that the compound (**2d**) and (**2f**) showed notable anti-fungal activity against *A. niger*and *A. flavus*. The compound (**3d**), (**3f**), (**3g**) and (**3i**) showed moderate activity against *C. albicans* and *A. flavus*. A number of compounds **3i-xii** [4-(biphenyl-4-yl)-2-(substituted phenyl)-*1H*-imidazole] have been successfully synthesized. The pharmacological study was performed to evaluate the effects of substituent on the antibacterial and antifungal activities. The biological activity result revealed that all the newly synthetic compounds **3i-xii** [4-(biphenyl-4-yl)-2-(substituted phenyl)-*1H*-imidazole] exhibited better antibacterial activity as compared to antifungal activity in compare to reference drug. The results of anti-bacterial screening further revealed that among all the compounds, the compound (**3iv**) and (**3x**) were observed significant anti-bacterial activity against *E. coli, B. subtilis* and *K. pneumoniae* while compounds (**3ii**), (**3viii**) and (**3ix**) as well as compounds (**3xi**) and (**3vii**) showed moderate anti-bacterial activity in compare to standard drug ciprofloxacin. The results of anti-fungal screening showed that the compound (**3ii**) and (**3viii**) showed good anti-fungal activity against *A. niger* and *A. flavus* and compound (**3xi**) showed notable activity against *C. albicans*. The compound (**3vii**) and (**3ix**) were shown moderate activity against *C. albicans* and *A. niger*. All the tested compounds were found mild to moderately active, while compounds **3d, 3f, 3iv, 3x, 4vi** and **4x** were found to have more active in compare to others. Whereas compound **(3d)** [Synthesis of 4-(4-(4-chlorophenyl)-1-phenyl-1H-imidazol-2-yl) phenol] was observed the significant growth inhibition against the *Escherichia coli* microorganism and *Aspergillus flavus*.The outcomes of this research work may be found useful in the further drug design and development by researchers working on the above mentioned areas and could serve as novel template for development of potential and selective agents in future.

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