WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 8, 1366-1377. Research Article ISSN 2277– 7105

SYNTHETIC STUDY ON SOME IMIDAZOLE ANALOGUES AND THEIR ANTIMICROBIAL ACTIVITY

Nandini K.[1], N. K. Hemanth Kumar[2] and Y. B. Basavaraju[1*]

[1]Department of Studies in Chemistry, Masanasagangotri, University of Mysore, Mysuru-570 006.

[2]Department of Studies in Botany, Masanasagangotri, University of Mysore, Mysuru-570 006.

Article Received on
30 May 2020,

Revised on 20 June 2020,
Accepted on 10 July 2020,

DOI: 10.20959/wjpr20208-18017

***Corresponding Author**
Y. B. Basavaraju
Department of Studies in Chemistry,
Masanasagangotri,
University of Mysore,
Mysuru-570 006.

ABSTRACT

In the present research work, some imidazole analogues were synthesized. The structures of newly synthesized compounds were confirmed by spectral data and their antimicrobial activity was tested using Streptomycin and Fluconazole as a standard drug. The compounds 5b and 5g were found to be the most potent analogues of the series.

KEYWORDS: Ammonium acetate, antibacterial activity, antifungal activity, benzil, lactic acid and imidazole.

INTRODUCTION

Nitrogen containing five membered heterocyclic imidazole nucleus shows various biological properties. This ring system is present in important biological building blocks, such as histidine and the related hormone histamine. Imidazole can serve as a base and as a weak acid. Imidazole drugs have broadened scope in remedying various dispositions in clinical medicines. Many drugs contain an imidazole ring, such as antifungal drugs.[1-3] Moreover 2-substituted imidazolines are synthetically important due to their use as a synthetic intermediates,[4] catalysts,[5] chiral auxiliaries,[6] chiral catalysts[7] in various synthetic reactions.

It is also called an important synthon for the preparation of biologically active compounds.[8] In recent years, the high therapeutic properties of the imidazole related drugs have been attracting the attention of medicinal chemists to synthesize a large number of novel

chemotherapeutic agents. Medicinal properties of imidazole containing compounds include anticancer,[9-11] antimicrobial,[12, 13] analgesic,[14] anti-HIV,[15,16] antihistaminic,[17] antioxidant activity[18-21] and anthelmintic agents.[22] Encouraged by these observations and in continuation of our research work to discover some biologically active heterocyclic compounds, we were synthesized a new series of heterocyclic imidazoles by facile and routine methods.

EXPERIMENTAL

MATERIALS AND METHODS

To synthesize the analogues the required reagents and solvents were purchased from Alfa aiser, Merck and sigma Aldrich chemical of AR grade and used as provided. Thin layer chromatography (TLC) analysis was performed with alumina sheets precoated with silica gel and the column chromatography was performed by using SiO_2, 60-120 mesh (Merck). ^1H NMR and ^{13}C NMR spectra were obtained by bruker spectrometer in the appropriate solvent (DMSO-d_6, $CDCl_3$) with TMS as an internal reference. Melting points were obtained on a reichert thermopan melting point apparatus, equipped with a microscope and are uncorrected. The mass spectra were recorded on LCMS-Agilent 1100 series mode. Elemental analysis was performed on Leco CHNS-932 analyser.

Synthesis

General procedure for the preparation of imidazole derivatives 3(a,b)

Take 100 mL round bottom flask with a magnetic stirrer bar, add a mixture of bezil **1** (2 mmol) and substituted benzaldehyde **2(a,b)** (2 mmol) and ammonium acetate (2.5 mmol) was dissolved in 1 mL lactic acid and the content was heated to reflux on hot plate for 1-2 hrs with stirring. After reflux the mixture was cooled to room temperature and the precipitate was removed by filteration, water (100 mL) was added to filtrate and collected by filtration with suction. Filtrate was neutralized with Ammonium Hydroxide and second crop of solid was collected. The two crop of solid was combined and recrystallized from water-ethanol affords imidazole derivatives **3(a,b)**. The yield and melting point of purified analogues was reported as below. Progress of the reaction was monitored by TLC using hexane: ethyl acetate (8:2 ratios) mixture as mobile phase.

2,4,5-Triphenyl-1H-imidazole (3a)

The white solid, m.p.: 271-27 ^0C, Yield-70%. IR (KBr)γ_{max} (cm^{-1}): 3412 (N-H), 3025 (Ar-H), 1624 (C=N), 1345 (C-N) and 1072 (C-F); ^1H NMR (DMSO-d_6 400MHz) δppm: 12.79 (s,

1H, NH of pyrazole), 7.38-8.12 (m, 15H, Ar-H); ^{13}C NMR ($CDCl_3$-100MHz) δ ppm: 177.3, 138.1, 134.5, 130.8, 129.2, 129.0, 128.4, 127.6; MS (ESI) m/z: 296.15 (M^+). Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; found: C, 84.14; H, 5.41%.

2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazole (3b)

The light yellow solid, m.p.: 247-249 ^{0}C, Yield-68%. IR (KBr)γ_{max} (cm^{-1}): 3417 (N-H), 3032 (Ar-H), 1631 (C=N) and 1342 (C-N); ^{1}H NMR (DMSO-d_6 400MHz): 12.83 (s, 1H, NH of pyrazole), 7.23-7.79 (m, 14H, Ar-H); ^{13}C NMR ($CDCl_3$-100MHz) δ ppm: 176.8, 162.6, 137.9, 130.1, 129.2, 129.0, 128.7, 128.5, 127.3, 115.8; MS (ESI) m/z: 314.13 (M^+). Anal. Calcd. for $C_{21}H_{15}FN_2$: C, 80.24; H, 4.81; found: C, 79.98; H, 4.85%.

General procedure for the preparation of chloroacetyl imidazole derivatives 4(a,b)

Chloroacetyl imidazole derivatives **4(a,b)** were obtained by dissolving imidazole derivatives **3(a,b)** (0.01mole) in 30ml of dry benzene taken in a beaker and stirred well. In another beaker containing 30mL of dry benzene with chloroacetyl chloride (0.01mole) was added drop wise to the beaker containing imidazole derivative. The stirring continued vigorously until the reaction mixture is so thick (4-5hrs). Excess of solvent and chloroacetyl chloride was removed by distillation under reduced pressure and the residue was washed with aqueous sodium bicarbonate (5%w/v, 30mL) and subsequently with cold water (50mL). . Finally the product obtained was recrystallised by using ethanol as solvent.

2-Chloro-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (4a)

The white solid, m.p.: 225-227 ^{0}C, Yield-72%. IR (KBr) γ_{max} (cm^{-1}): 3097 (Ar-H), 1663 (C=O), 1636 (C=N), 1583 (C=C), 1331 (C-N) and 767 (C-Cl); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.38-8.25 (m, 15H, Ar-H), 4.40 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 160.4, 143.5, 138.0, 137.6, 132.8, 130.5, 131.0, 129.2, 129.0, 128.5, 127.3, 47.4; MS (ESI) m/z: 372.16 (M^+). Anal. Calcd. for $C_{23}H_{17}ClN_2O$: C, 74.09; H, 4.60; found: C, 74.01; H, 4.77%.

2-Chloro-1-(2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)ethanone (4b)

The brown solid, m.p.: 197-199 ^{0}C, Yield-67%. IR (KBr) γ_{max} (cm^{-1}): 3102 (Ar-H), 1668 (C=O), 1629 (C=N), 1580 (C=C), 1336 (C-N), 1221 (C-F) and 771 (C-Cl); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.25-7.84 (m, 14H, Ar-H), 4.47 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 162.7, 160.5, 143.6, 138.3, 137.7, 133.2, 129.2, 128.9, 128.6, 128.4,

127.3, 126.1, 115.7, 47.1; MS (ESI) m/z: 390.17 (M^+). Anal. Calcd. for $C_{23}H_{16}ClFN_2O$: C, 70.68; H, 4.13; found: C, 70.55; H, 4.19%.

General procedure for the preparation of imidazole analogues 5(a-j)

The analogues of imidazole **5(a-j)** were obtained by the reaction of **4(a,b)** (0.004mole) with different heterocyclic compounds (**R_1 in scheme-1**) in ethyl acetate (30mL) in presence of triethylamine (0.005mole). The reaction mixture was refluxed for about 3-4hrs, after the completion of the reaction, reaction mass was cooled to room temperature and distilled off. The resultant residue is treated with water (30mL) with stirring. The separated solid was filtered, washed with water and dried**.**

2-(Piperazin-1-yl)-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (5a)

The brown solid, m.p.: 232-234 ^{0}C, Yield-79%. IR (KBr) γ_{max} (cm^{-1}): 3335 (N-H), 3163 (Ar-H), 1694 (C=O), 1647 (C=N) and 1342 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.40-8.19 (m, 15H, Ar-H), 3.49 (s, 2H, CH_2), 2.63 (t, 4H, J= 3.6 Hz, CH_2 of piparazine), 2.34 (t, 4H, J= 4.4 Hz, CH_2 of piparazine), 1.92 (s, 1H, N-H of piperazine); ^{13}C NMR ($CDCl_3$-100MHz) δppm:168.4, 142.3, 140.8, 139.5, 138.2, 136.4, 136.0, 132.1, 128.3, 128.0, 126.9, 126.7, 58.2, 56.4, 45.9; MS (ESI) m/z: 422.15 (M^+). Anal. Calcd. for $C_{27}H_{26}N_4O$: C, 76.75; H, 6.20; found: C, 76.71; H, 6.17%.

2-Morpholino-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (5b)

The light brown solid, m.p.: 217-219 ^{0}C, Yield-81%.IR (KBr) γ_{max} (cm^{-1}): 3052 (Ar-H), 1680 (C=O), 1635 (C=N) and 1345 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.43-8.32 (m, 15H, Ar-H), 3.63 (t, 4H, J= 4.4 Hz, CH_2 of morpholine), 3.46 (s, 2H, CH_2), 2.49 (t, 4H, J= 4.8 Hz, CH_2 of morpholine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 168.2, 143.5, 137.9, 137.5, 132.8, 131.3, 19.1, 129.0, 128.6, 127.3, 66.2, 58.5, 54.9; MS (ESI) m/z: 423.06 (M^+). Anal. Calcd. for $C_{27}H_{25}N_3O_2$: C, 76.57; H, 5.95; found: C, 76.54; H, 6.04%.

2-(Piperidin-1-yl)-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (5c)

The brown solid, m.p.: 210-212 ^{0}C, Yield-74%. IR (KBr) γ_{max} (cm^{-1}): 3135 (Ar-H), 1686 (C=O), 1623 (C=N) and 1349 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.38-8.24 (m, 15H, Ar-H), 3.43 (s, 2H, CH_2), 2.47 (t, 4H, J= 4.4 Hz, CH_2 of piperidine), 1.56 (t, 4H, J= 4.0 Hz, CH_2 of piperidine), 1.54 (q, 2H, J= 5.5 Hz, CH_2 of piperidine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 168.1, 143.8, 138.1, 137.4, 133.1, 131.0, 130.5, 129.4, 129.2, 128.5, 127.7,

58.6, 55.9, 25.0, 24.3; MS (ESI) m/z: 421.12 (M^+). Anal. Calcd. for $C_{28}H_{27}N_3O$: C, 79.78; H, 6.46; found: C, 76.74; H, 6.51%.

2-Thiomorpholino-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (5d)

The yellow solid, m.p.: 262-264 ^{0}C, Yield-70%. IR (KBr) γ_{max} (cm^{-1}): 3122 (Ar-H), 1695 (C=O), 1637 (C=N) and 1351 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.36-8.05 (m, 15H, Ar-H), 3.45 (s, 2H, CH_2), 2.71 (t, 4H, J= 4.2 Hz, CH_2 of thiomorpholine), 2.52 (t, 4H, J= 3.8 Hz, CH_2 of thiomorpholine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 168.4, 143.6, 138.0, 137.7, 132.8, 131.4, 130.3, 129.2, 129.1, 128.7, 127.4, 59.5, 58.2, 27.3; MS (ESI) m/z: 439.18 (M^+). Anal. Calcd. for $C_{27}H_{25}N_3OS$: C, 73.77; H, 5.73; found: C, 73.71; H, 5.80%.

2-(Pyrrolidin-1-yl)-1-(2,4,5-triphenyl-1H-imidazol-1-yl)ethanone (5e):

The reddish brown solid, m.p.: 249-251 ^{0}C, Yield-70%.IR (KBr) γ_{max} (cm^{-1}): 3126 (Ar-H), 1691 (C=O), 1641 (C=N) and 1332 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.34-8.21 (m, 15H, Ar-H), 3.48 (s, 2H, CH_2), 2.48 (t, 4H, J= 3.5 Hz, CH_2 of pyrrolidine), 1.66 (t, 4H, J= 3.0 Hz, CH_2 of pyrrolidine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 167.7, 143.4, 137.8, 137.3, 133.2, 131.7, 130.6, 129.5, 129.4, 128.9, 127.1, 58.5, 59.9, 23.3; MS (ESI) m/z: 407.22 (M^+). Anal. Calcd. for $C_{27}H_{25}N_3O$: C, 79.58; H, 6.18; found: C, 79.55; H, 6.22%.

1-(2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-(piperazin-1-yl)ethanone (5f)

The red solid, m.p.: 239-241 ^{0}C, Yield-79%.IR (KBr) γ_{max} (cm^{-1}): 3115 (Ar-H), 1687 (C=O), 1629 (C=N) and 1349 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.32-7.78 (m, 14H, Ar-H), 3.44 (s, 2H, CH_2), 2.64 (t, 4H, J= 4.0 Hz, CH_2 of piparazine), 2.33 (t, 4H, J= 4.4 Hz, CH_2 of piparazine), 1.90 (s, 1H, N-H of piperazine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 167.9, 162.7, 143.2, 137.7, 137.4, 133.5, 129.6, 129.4, 129.2, 128.6, 127.2, 126.3, 116.5, 58.7, 56.5, 45.3; MS (ESI) m/z: 440.19 (M^+). Anal. Calcd. for $C_{27}H_{25}FN_4O$: C, 73.62; H, 5.72; found: C, 73.57; H, 5.76%.

1-(2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-morpholinoethanone (5g):

The brown semi solid, Yield-76%.IR (KBr) γ_{max} (cm^{-1}): 3156 (Ar-H), 1662 (C=O), 1628 (C=N) and 1398 (C-N); ^{1}H NMR (DMSO-d_6 400MHz) δppm: 7.31 -7.77 (m, 14H, Ar-H), 3.64 (t, 4H, J= 3.6 Hz, CH_2 of morpholine), 3.49 (s, 2H, CH_2), 2.48 (t, 4H, J= 4.8 Hz, CH_2 of morpholine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 167.2, 162.2, 143.6, 137.9, 137.2, 133.3, 129.3, 128.5, 128.0, 127.2, 126.0, 116.0, 66.1, 58.9, 54.8; MS (ESI) m/z: 441.06 (M^+). Anal. Calcd. for $C_{27}H_{24}FN_3O_2$: C, 73.45; H, 5.48; found: C, 73.43; H, 5.52%.

1-(2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-(piperidin-1-yl)ethanone (5h):

The reddish brown solid, m.p.: 204-206 ^{0}C, Yield-82%. IR (KBr) γ_{max} (cm^{-1}): 3142 (Ar-H), 1671 (C=O), 1624 (C=N) and 1387 (C-N); ^{1}H NMR (DMSO-d$_6$ 400MHz) δppm: 7.26 -7.79 (m, 14H, Ar-H), 3.51 (s, 2H, CH_2), 2.43 (t, 4H, J= 4.2 Hz, CH_2 of piperidine), 1.57 (t, 2H, J= 3.8 Hz, CH_2 of piperidine), 1.50 (q, 4H, J= 4.0 Hz, CH_2 of piperidine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 167.5, 162.4, 143.8, 137.6, 137.3, 133.1, 129.5, 129.3, 128.5, 127.2, 126.4, 115.7, 58.6, 55.8, 25.3, 24.7; MS (ESI) m/z: 439.18 (M^+). Anal. Calcd. for $C_{28}H_{26}FN_3O$: C, 76.51; H, 5.96; found: C, 76.48; H, 6.02%.

1-(2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-thiomorpholinoethanone (5i):

The yellow semi solid, Yield-75%. IR (KBr) γ_{max} (cm^{-1}): 3145 (Ar-H), 1678 (C=O), 1627 (C=N) and 1362 (C-N); ^{1}H NMR (DMSO-d$_6$ 400MHz) δppm: 7.31-7-82 (m, 14H, Ar-H), 3.42 (s, 2H, CH_2), 2.70 (t, 4H, J= 4.0 Hz, CH_2 of thiomorpholine), 2.52 (t, 4H, J= 4.4 Hz, CH_2 of thiomorpholine); ^{13}C NMR ($CDCl_3$-100MHz) δppm: 168.5, 162.8, 143.5, 138.3, 137.6, 133.5, 129.3, 129.1, 128.8, 127.6, 126.3, 116.4, 59.7, 58.3, 27.5; MS (ESI) m/z: 457.14 (M^+). Anal. Calcd. for $C_{27}H_{24}FN_3OS$: C, 70.87; H, 5.29; found: C, 70.83; H, 5.32%.

1-(2-(4-Fluorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)-2-(pyrrolidin-1-yl)ethanone (5j):

The red solid, m.p.: 207-209 ^{0}C, Yield-69%. IR (KBr) γ_{max} (cm^{-1}): 3159 (Ar-H), 1683 (C=O), 1647 (C=N imidazole) and 1365 (C-N); ^{1}H NMR (DMSO-d$_6$ 400MHz) δppm: 7.27-7.78 (m, 14H, Ar-H), 3.49 (s, 2H, CH_2), 2.49 (t, 4H, J= 4.0 Hz, CH_2 of pyrrolidine), 1.65 (t, 4H, J= 3.8 Hz, CH_2 of pyrrolidine; ^{13}C NMR ($CDCl_3$-100MHz) δppm: 168.1, 162.5, 143.8, 138.4, 137.9, 133.2, 129.6, 129.4, 128.6, 127.4, 126.5, 116.2, 59.9, 58.6, 23.1; MS (ESI) m/z: 425.09 (M^+). Anal. Calcd. for $C_{27}H_{24}FN_3O$: C, 76.21; H, 5.69; found: C, 76.19; H, 5.73%.

ANTIMICROBIAL TESTING

Antibacterial studies

The antibacterial activities of some newly synthesized analogues **(5a-j)** were determined by the well plate method in Mueller–Hinton Agar.[23] It was carried out against 24 h old cultures of bacterial strains. In this work, Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa were used to investigate the activity. The test compounds were dissolved in dimethyl sulfoxide (DMSO) at concentration of 1 and 0.5 mg/mL. 20 mL of sterilized agar media was poured into each pre-sterilized petri dish. Excess of suspension was decanted and plates were dried by placing in an incubator at 37 ^{0}C for an hour. About 60 mL of 24 h old

culture suspension was poured and neatly swabbed with the pre-sterilized cotton swabs. Six millimetre diameter well was then punched carefully using a sterile cork borer and 30 mL of test solutions of different concentrations was added into each labelled well. The plates were incubated for 24 h at 37 ^{0}C. The inhibition zone that appeared after 24 h, around the well in each plate was measured as zone of inhibition in mm. Experiments were triplicates and standard deviation was calculated.

Antifungal studies

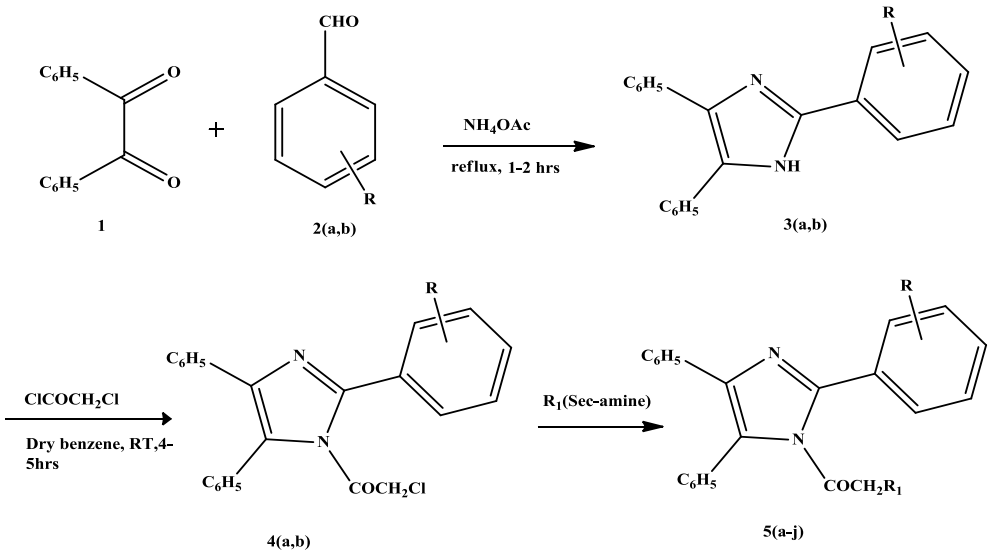
Antifungal studies of newly synthesized imidazole analogues **(5a-j)** were carried out against Aspergillus flavus, Chrysosporium keratinophilum, Candida albicans. Sabourands agar media were prepared by dissolving peptone (10 g), D-glucose (40 g) and agar (20 g) in distilled water (1000 mL) and adjusting the pH to 5.7. Normal saline was used to make a suspension of spore of fungal strains for lawning. A loopful of particular fungal strain was transferred to 3 mL saline to get a suspension of corresponding species.[24] 20 mL of agar media was poured into each petri dish. Excess of suspension was decanted and plates were dried by placing in an incubator at 37 ^{0}C for 1 h. Using sterile cork borer punched carefully, wells were made on these seeded agar plates and different concentrations of the test compounds in DMSO were added into each labeled well. A control was also prepared for the plates in the same way using solvent DMSO. The petri dishes were prepared in triplicate and maintained at 25 ^{0}C for 72 h. Antifungal activity was determined by measuring the diameter of inhibition zone. Activity of each compound was compared with fluconazole as standard and zones of inhibition were determined for all the synthesized compounds **(5a-j)**.

RESULTS AND DISCUSSION

CHEMISTRY

Herein, we report the synthesis of series of imidazole analogues viz., benzil and the synthetic route to the target compounds is outlined in **scheme 1**. 2,4,5-triphenyl-1H-imidazole **3a** and 2-(4- fluorophenyl)-4,5-diphenyl-1H-imidazole **3b,** are obtained by cyclisation of benzil **1** and benzaldehyde **2a** and 4-fluorobenzaldehyde **2b** in presence of ammonium acetate in lactic acid by refluxing for 5-6 hrs. Further treatment with chloroacetyl chloride obtains a set of cloroacetyl imidazole derivatives 1-(2-chloroethyl)-2,4,5-triphenyl-1H-imidazole **4a** and 1-(2-chloroethyl)-2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole **4b.** In the final step, compounds reacts with different secondary amines in presence of triethylamine accomplished the desired new series of imidazole analogues **(5a-j)**.

SCHEME: 1



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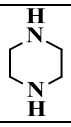
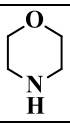
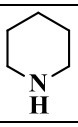
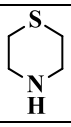
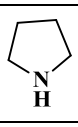
R_1					

ANTIMICROBIAL TESTING

Antibacterial studies

The antibacterial activity of newly synthesized imidazole analogues **(5a-j)** was determined by the well plate method. In this study, E. coli ATCC 25922 (Gram-negative), S. aureus ATCC 25923 (Gram-positive) and P. aeruginosa ATCC 27853 (Gram-negative) were selected due to their infectious nature. The test compounds were dissolved in dimethyl sulfoxide (DMSO) at concentrations of 1 and 0.5 mg/mL. The antibacterial screening revealed that some of the tested analogues showed good inhibition against various tested microbial strains (Table 1). The results indicated that among the tested analogues **5b, 5g** showed good activity against P. aeruginosa and E. coli at the concentrations of 1 and 0.5 mg/mL compared to standard drug streptomycin. Whereas, the analogues **5a, 5e, 5f, 5h, 5j** revealed moderate activity against all of the three tested bacterial strains at 1 mg/mL concentrations. The remaining compounds **5c, 5d, 5i** showed very least activity against all of the three tested bacterial strains.

Table 1: Inhibitory zone (diameter) mm of the synthesized compounds 5(a-j) against tested bacterial strains by the well plate method. Each value represents mean ± SD (n= 3).

Comp. No.	Escherichia coli		Staphylococcus aureus		Pseudomonas aeroginosa	
Conc. in mg/mL	1.0	0.5	1.0	0.5	1.0	0.5
Control	00	00	00	00	00	00
Streptomycin	18 ± 0.02	12 ± 0.02	16 ± 0.01	12 ± 0.02	17 ± 0.02	13 ± 0.01
5a	11 ± 0.01	9 ± 0.01	10 ± 0.02	8 ± 0.01	9 ± 0.02	10 ± 0.01
5b	15 ± 0.02	10 ± 0.02	9 ± 0.03	6 ± 0.02	12 ± 0.01	8 ± 0.02
5c	7 ± 0.01	5 ± 0.01	4 ± 0.02	4 ± 0.02	6 ± 0.02	5 ± 0.03
5d	3 ± 0.02	2 ± 0.02	2 ± 0.01	1 ± 0.01	4 ± 0.01	3 ± 0.02
5e	10 ± 0.01	7 ± 0.02	9± 0.01	8 ± 0.03	10 ± 0.01	7± 0.01
5f	13 ± 0.02	9 ± 0.02	11 ± 0.03	9 ± 0.02	10 ± 0.02	8 ± 0.01
5g	19 ± 0.01	11 ± 0.01	15 ± 0.01	10 ± 0.02	15 ± 0.02	11 ± 0.01
5h	9 ± 0.01	6 ± 0.02	9 ± 0.01	8 ± 0.02	11 ± 0.02	10 ± 0.03
5i	4 ± 0.02	3 ± 0.02	5 ± 0.01	3 ± 0.01	4 ± 0.02	3 ± 0.02
5j	10 ± 0.02	7 ± 0.01	10 ± 0.02	9 ± 0.01	8 ± 0.01	9 ± 0.01

Antifungal studies

Newly synthesized compounds **(5a-j)** were also screened for their antifungal activity against A. flavus MTCC 3306, C. Keratinophilum MTCC 2827 and C. albicans MTCC 3017, because of their infectious nature. The compounds were dissolved in DMSO and antifungal activity was determined by the well plate method at concentrations of 1 and 0.5 mg/mL.

The antifungal result data (Table 2) indicated that, the synthesized analogues showed a variable degree of inhibition against the tested fungi. As a result, the analogues **5b, 5g** showed good activity. Whereas, the analogues **5a, 5f, 5j** revealed moderate activity and the remaining analogues **5c, 5d, 5e, 5h, 5i** showed very least activity against A. flavus ,C. keratinophilum and C. albicans at the concentrations of 1 and 0.5 mg/mL compared to standard drug Fluconazole.

Table 2: Inhibitory zone (diameter) mm of the synthesized compounds 5(a-j) against tested fungal strains by the well plate method. Each value represents mean ± SD (n=3).

Comp. No.	Aspergillus flavus		Chrysosporium keratinophilum		Candida albicans	
Conc. in mg/mL	1.0	0.5	1.0	0.5	1.0	0.5
Control	00	00	00	00	00	00
Fluconazole	14 ± 0.01	12 ± 0.01	17 ± 0.02	16 ± 0.01	20 ± 0.01	18 ± 0.02
5a	9 ± 0.02	8± 0.01	10 ± 0.02	9 ± 0.01	13 ± 0.01	11 ± 0.01
5b	11 ± 0.01	9± 0.03	15 ± 0.01	13 ± 0.01	16 ± 0.02	15± 0.02
5c	3 ± 0.03	2 ± 0.02	3 ± 0.01	4 ± 0.01	3 ± 0.01	1 ± 0.02
5d	2 ± 0.02	1 ± 0.02	2 ± 0.02	2 ± 0.01	3 ± 0.01	2 ± 0.01
5e	5 ± 0.01	3 ± 0.02	4 ± 0.01	3 ± 0.02	6 ± 0.02	4 ± 0.02
5f	10 ± 0.02	8 ± 0.01	9 ± 0.01	10 ± 0.01	11 ± 0.02	10 ± 0.02
5g	13 ± 0.02	11 ± 0.02	16 ± 0.02	14 ± 0.02	18 ± 0.01	17 ± 0.01
5h	5 ± 0.02	4 ± 0.02	5 ± 0.03	4 ± 0.01	6 ± 0.041	4 ± 0.01
5i	4 ± 0.01	3 ± 0.02	2 ± 0.01	1 ± 0.01	4 ± 0.02	3 ± 0.02
5j	9 ± 0.01	7 ± 0.02	10 ± 0.01	8 ± 0.02	10 ± 0.02	9 ± 0.02

CONCLUSION

All the synthesised analogues **(5a-j)** were obtained in good yields by simple and efficient method in good yields, the synthesised analogues were characterised by spectral studies and evaluated their antimicrobial activities. In both antibacterial and antifungal activity the analogues **5b** and **5g** showed very good activity in the well plate method.

ACKNOWLEDGMENTS

University Grants Commission, New Delhi is gratefully acknowledged for proving grant under RGNF for SC. IOE, University of Mysore is acknowledged for providing spectral facilities. University of Mysore, Mysuru is acknowledged.

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