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Research Article

# ONE-POT SYNTHESIS OF 2,4,5-TRIARYLIMIDAZOLES FROM KETO-OXIMES: CHARACTERIZATION AND EVALUATION OF ANTIMICROBIAL ACTIVITY

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**ABSTRACT**

**Background and Objective:** Imidazole scaffold is pervasive in pharmaceuticals and it possesses diverse type of biological activities, especially triarylimidazole derivatives are biologically prominent molecules which inspired the current investigation. The objective of the work is to synthesize 15 novel 2,4,5-triarylimidazole derivatives and evaluate their antimicrobial and antimycobacterial activity against selected bacterial and fungal strains.

**Methods:** The title compounds 2,4,5-triaryl-imidazole were synthesized from the corresponding aryl aldehydes and keto-oximes through the cyclization to N-hydroxyimidazoles and reduced thermally to the different imidazole derivatives. Agar disc diffusion method is employed for the antimicrobial and antimycobacterial studies.

**Results:** Fifteen novel 2,4,5-triarylimidazoles were synthesized in adequate yields and characterization of the molecules was done by detailed spectral analysis using advanced analytical support. Results disclosed that all the synthesized compounds were exhibiting antimicrobial properties. Compounds ***3h, 3g, 3b,*** and ***3m*** were stated to possess potent antimicrobial properties in the given bacterial and fungal strains.

**Conclusion:** The current investigation results support the antimicrobial and antimycobacterial activity of the synthesized 2,4,5-triarylimidazole derivatives. Further, research is necessary to explore the mechanism involved in the antimicrobial activity.

**Keywords:** Triarylimidazoles, Cyclization, Antibacterial, Antifungal, Antimycobacterial.

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## INTRODUCTION

Imidazole is renowned for its diversified pharmacological activities and synthetic utilities. Imidazole is five-membered heterocyclic molecules cherished with two nitrogen atoms bridged through a carbon [1]. Since it can act as both base and weak acid, it acts as an efficient nucleophile to generate diversified molecules. It is a planar molecule with two tautomeric forms [2]. The wide substitution capability and ability to annulate with different pharmacophores at various positions made imidazole a unique synthetic starter [3].

Numerous natural products have been reported in literature with imidazole moiety possessing a wide range of biochemical applications [4]. Imidazole cyclized with aromatic systems has been focused for the development of lead molecules for treating infections caused by tough microbes like mycobacterium [5]. Imidazole moiety is a backbone for some biomolecules such as adenine, guanine, histamine, histidine, cyanocobalamin, and biotin [6]. Due to its ubiquitous applications as antimicrobial [7,8], antifungal [9], antiparasitic [10], antidepressant [11], antioxidant [12], and anticancer [13] and reported to possess anti-inflammatory [14], analgesic [15,16], and antidiabetic [17] properties, the current investigation was carried out to design and synthesize few imidazole-based molecules for the antimicrobial properties. Since infections are the major challenges in the health-care system, developing and exploring new antimicrobial agents are always an important research area [18].

Several synthetic strategies have been proposed in literature either with catalysts like Yttrium(III) trifluoroacetate [19] and catalytic free conditions like microwave irradiation [20]. The current work illustrates the synthesis and antimicrobial activities of 2,4,5-triarylimidazoles (Scheme 1). Fifteen novel derivatives have been prepared and screened for *in vitro* antimicrobial studies on various Gram-positive and Gram-negative bacteria, fungal, and mycobacterial species.

## METHODS

All chemicals and solvents used in this work were synthetic grade purchased from Sigma-Aldrich and used without purification. Merck precoated aluminum TLC plates of silica gel 60 F254 were employed for the reaction monitoring and the spots visualized with iodine vapors and in UV chamber. Column chromatography was used for the purification and isolation of the pure compounds. Melting points were determined by Remi electronic melting point apparatus. IR spectra were recorded on Agilent FTIR by KBr pellet method. $^1$H NMR recorded on BRUKER DRX – 400 MHz. Chemical shift values (δ) articulated in ppm with reference to internal standard tetramethylsilane. The splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet. MASS recorded on BRUKER ESI-IT MS.

### General procedure for the synthesis of 2,4,5-triarylimidazole *(3a-o)*

To the mixture of keto-oximes (0.1 mmol), ammonium acetate (0.4 mmol), and aldehydes (1.1 mmol), glacial acetic acid (2.0 mL) was added with stirring. The mixture was refluxed for 8 h. After the workup with sodium bicarbonate, the crude product of N-hydroxyimidazoles (***2a-o***) was filtered and purified. Synthesized N-hydroxyimidazoles (***2a-o***) (0.1 mmol) were reduced with $TiCl_3$ (0.1 mmol) to corresponding 2,4,5-triarylimidazoles (***3a-o***).

### Antimicrobial activity

*Antibacterial and antifungal activity*

The bacterial and fungal strains were obtained from the Department of Microbiology, Osmania University. They were preserved at 4°C. Antibacterial activity of the compounds **(3a-o)** was studied against Gram-positive and Gram-negative bacterial and fungal strains *Staphylococcus aureus* (NCTC 7447), *Bacillus subtilis* (MTCC-619), *Escherichia coli* (NCTC 6571), *Streptococcus pneumonia*, *Aspergillus niger,* and *Candida albicans* (recultured), respectively, by disc diffusion

method and ampicillin (100 µg/ml) and nystatin (10 µg/ml) in DMSO were used as reference antibiotics. Agar media were taken in the pre-sterilized Petri dishes and the microorganisms were grown. A stock solution of 60 µg/ml for all the prepared compounds **(3a-o)** is made using DMSO. The disc (6 mm in diameter) was impregnated with 200 µg/ml, 100 µg/ml, and 50 µg/ml of each test solution, placed on the seeded agar medium and the Petri dishes were incubated at 37°C for 24 h. DMF alone was used as control at the equal aforementioned concentration. Zone of inhibition of each compound in mm was recorded and the results are furnished in Table 3.

*Antimycobacterial activity*

*Mycobacterium tuberculosis (MTB) H37Rv* (ATCC 27294) strains, which are susceptible to rifampicin and isoniazid were used for the study of antitubercular activity of the synthesized compounds. The bacterial strains were subcultured to have a fresh batch for the study, supplied with Muller-Hinton broth at 37°C for 2 weeks. Bacterial suspensions with 0.5 McFarland standard turbidity equivalents to 108 CFU were prepared by diluting it with normal saline solution. The mixture was vortexed for 30 s in a glass vessel and the particles were allowed to settle [21]. About 100 µL of the microbial suspension was used for the inoculation. The stock solutions of 100 µg/mL of synthesized compounds were prepared in DMSO. To determine the minimum inhibitory concentration of title compounds, serial dilution of compounds with varying strengths (50, 25, 12.5, 6.25, 3.12, 1.6, and 0.8 µg/mL) was prepared from the respective stock solutions.

Middlebrook 7H11 agar medium was used for growing the mycobacterium, supplemented with Oleic Albumin Dextrose Catalase, after sterilization under moist heat using autoclave at 121°C for 15 min. Then, medium was diluted with various strengths (50, 25, 12.5, 6.25, 3.12, 1.6, and 0.8 µg/mL) of synthesized (**3a-o**) compounds in appropriate volumes. Using aseptic technique, 5-ml of middle brook 7H11 agar medium was dispensed into each labeled quadrants of sterile Quad-plates and allowed to solidify under laminar airflow with lids slightly opened.

After solidification, bacterial suspension from the culture broth was inoculated aseptically through a loop (3 mm internal diameter) and incubated for 21 days at 37°C. The minimum inhibitory concentration (MIC) was determined by counting the colonies formed on the medium by comparing with the controls. DMSO and isoniazid were served as negative and positive controls, respectively [22-24].

## RESULTS AND DISCUSSION

A novel series of fifteen 2,4,5-triarylimidazoles were synthesized by a feasible method (Scheme 1) with adequate yields. The structure elucidation of all the compounds was made using advanced analytical methods such as mass and NMR. The structures of the synthesized compounds along with the percent yield and melting points are depicted in Table 1.

**4-(4-(4-fluorophenyl)-2-p-tolyl-1H-imidazol-5-yl)pyrimidine (Compound 3a)**

1H NMR(400 MHz, d6-DMSO): δ 2.25 (3H, s), 7.19 (2H, ddd, J = 8.1, 1.3, 0.5 Hz), 7.40–7.47 (3H, 7.42 (dd, J = 5.9, 0.5 Hz), 7.44 (ddd, J = 8.5, 1.6, 0.5 Hz)), 7.79–7.87 (4H, 7.84 (ddd, J = 8.1, 1.6, 0.4 Hz), 7.82 (ddd, J = 8.5, 1.6, 0.5 Hz)), 8.78 (1H, dd, J = 5.9, 1.6 Hz), 8.86 (1H, dd, J = 1.6, 0.5 Hz). MS for $C_{20}H_{15}FN_4$ $[M + H]^+$: m/z = 331.3.

**4-(4-(4-fluorophenyl)-2-(4-methoxyphenyl)-1H-imidazol-5-yl) pyrimidine (Compound 3b)**

1H NMR(400 MHz, d6-DMSO): δ 3.89 (3H, s), 7.21 (2H, ddd, J = 8.4, 1.3, 0.4 Hz), 7.31–7.38 (3H, 7.36 (dd, J = 6.8, 0.4 Hz), 7.34 (ddd, J = 8.4, 1.5, 0.5 Hz)), 7.78–7.90 (4H, 7.86 (ddd, J = 8.4, 1.7, 0.4 Hz), 7.81 (ddd, J = 8.4, 1.6, 0.5 Hz)), 8.76 (1H, dd, J = 6.8, 1.7 Hz), 8.83 (1H, dd, J = 1.7, 0.4 Hz). MS for $C_{20}H_{15}FN_4O$ $[M + H]^+$: m/z = 347.1

**4-(2-(4-chlorophenyl)-4-(4-fluorophenyl)-1H-imidazol-5-yl) pyrimidine (Compound 3c)**

1H NMR(400 MHz, d6-DMSO): δ 7.39–7.45 (3H, 7.42 (dd, J = 5.9, 0.4 Hz), 7.42 (ddd, J = 8.5, 1.5, 0.5 Hz)), 7.81 (2H, ddd, J = 8.4, 1.6, 0.4 Hz), 7.78–7.85 (4H, 7.81 (ddd, J = 8.4, 1.6, 0.4 Hz), 7.82 (ddd, J = 8.5, 1.6, 0.5 Hz)), 8.58 (1H, dd, J = 5.9, 1.6 Hz), 8.75 (1H, dd, J = 1.6, 0.4 Hz). MS for $C_{19}H_{12}ClFN_4$ $[M + H]^+$: m/z = 351.07.

**4-(2-ethyl-4-(4-fluorophenyl)-1H-imidazol-5-yl)pyrimidine (Compound 3d)**

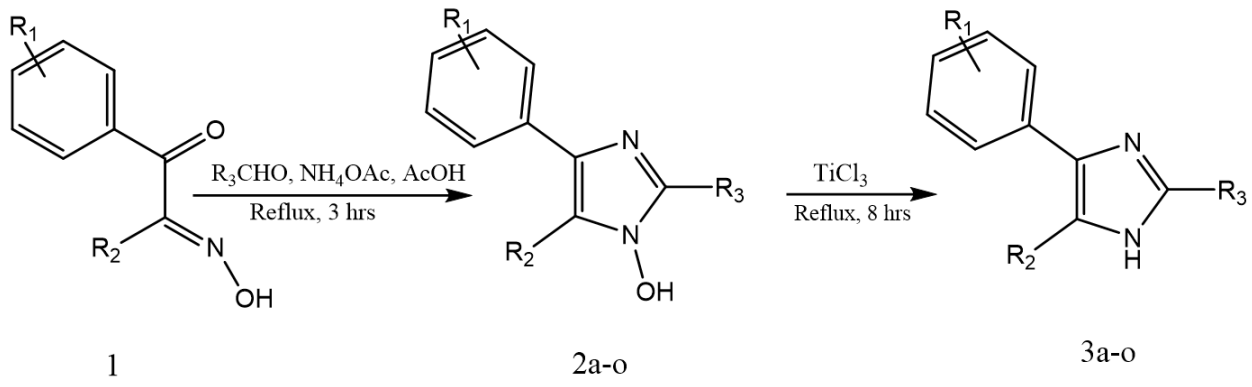
1H NMR(400 MHz, d6-DMSO): δ 1.35 (3H, t, J = 6.7 Hz), 3.11 (2H, q, J = 6.7 Hz), 7.29 (2H, ddd, J = 8.6, 1.5, 0.5 Hz), 7.35 (1H, dd, J = 6.0, 0.5 Hz), 7.66 (2H, ddd, J = 8.6, 1.6, 0.5 Hz), 8.72 (1H, dd, J = 6.0, 1.7 Hz), 8.82 (1H, dd, J = 1.7, 0.5 Hz). MS for $C_{15}H_{13}FN_4$ $[M + H]^+$: m/z = 269.2

**4-(2-tert-butyl-4-(4-fluorophenyl)-1H-imidazol-5-yl)pyrimidine (Compound 3e)**

1H NMR(400 MHz, d6-DMSO): δ 1.47 (9H, s), 7.29 (2H, ddd, J = 8.6, 1.5, 0.5 Hz), 7.35 (1H, dd, J = 6.0, 0.5 Hz), 7.66 (2H, ddd, J = 8.6, 1.6, 0.5 Hz), 8.72 (1H, dd, J = 6.0, 1.7 Hz), 8.82 (1H, dd, J = 1.7, 0.5 Hz). MS for $C_{17}H_{17}FN_4$ $[M + H]^+$: m/z = 297.25.

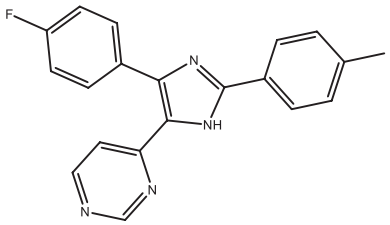
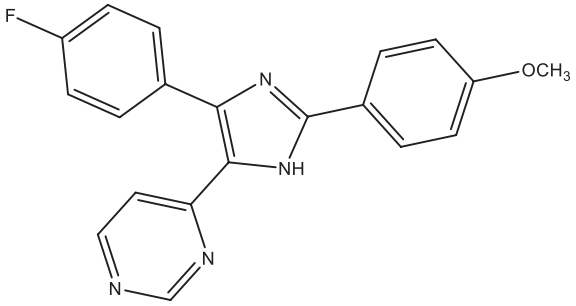
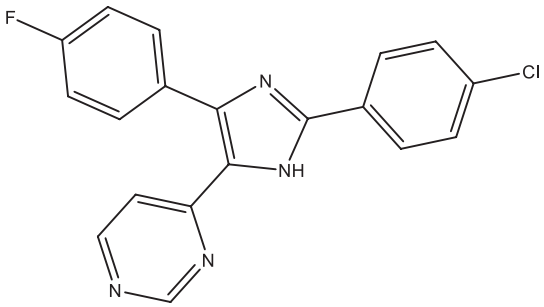
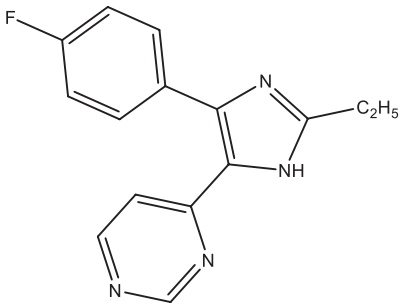
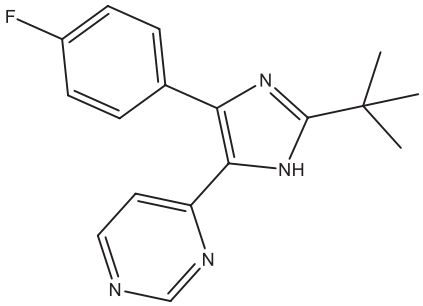
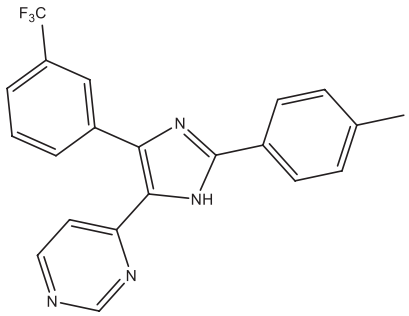
**4-(2-p-tolyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyrimidine (Compound 3f)**

1H NMR(400 MHz, d6-DMSO): δ 2.22 (3H, s), 7.19 (2H, ddd, J = 8.1, 1.4, 0.5 Hz), 7.46 (1H, dd, J = 5.8, 0.5 Hz), 7.51–7.65 (2H, 7.61 (ddd, J = 8.0, 7.7, 0.4 Hz), 7.54 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.73 (2H, ddd, J = 8.1, 1.6,



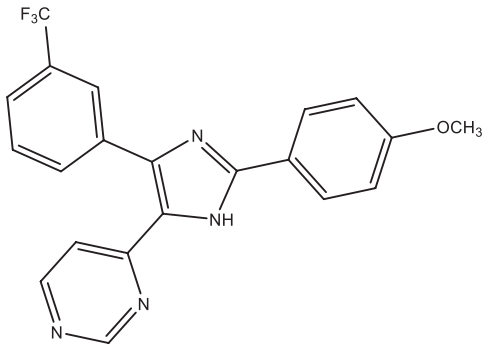
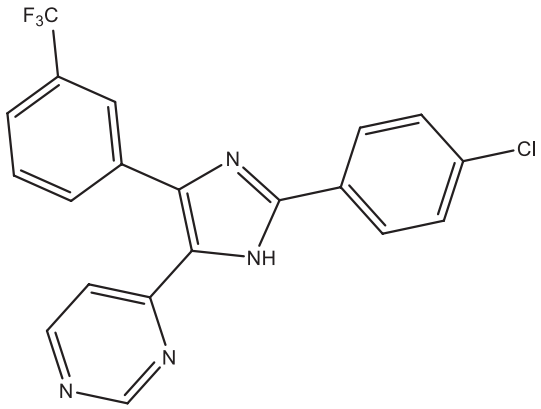
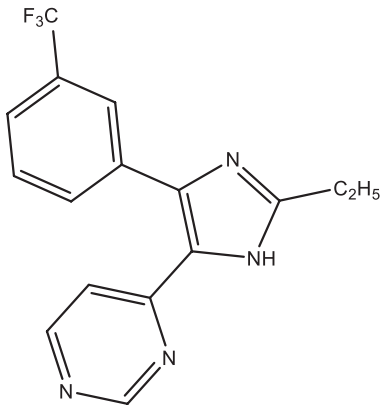
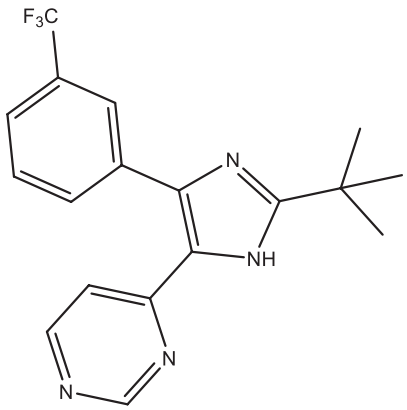

**Scheme 1: Synthesis of 2,4,5-triarylimidazoles (3a-o)**

**Table 1: Structures and physical data of synthesized compounds**

| S. No. | Compound | Structure | Yield (%) | M.P |
|---|---|---|---|---|
| 1 | **3a** |  | 44 | 164–165°C |
| 2 | **3b** |  | 56 | 167–168°C |
| 3 | **3c** |  | 40 | 179–180°C |
| 4 | **3d** |  | 21 | 151–153°C |
| 5 | **3e** |  | 34 | 149–150°C |
| 6 | **3f** |  | 49 | 163–165°C |

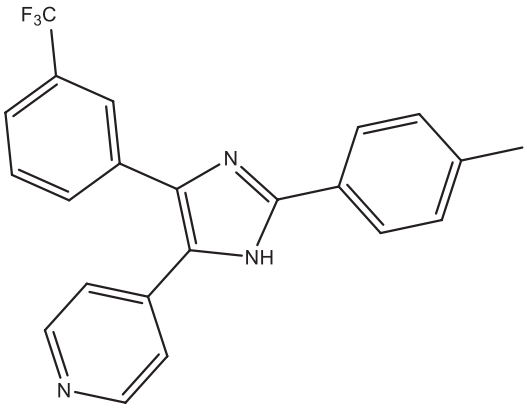
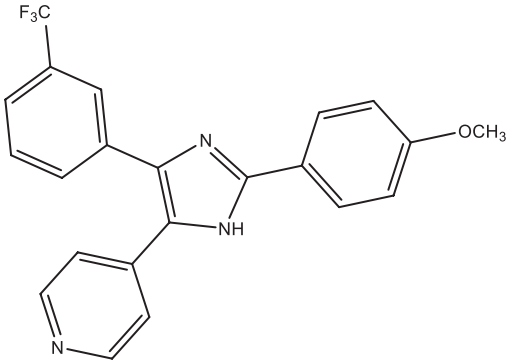
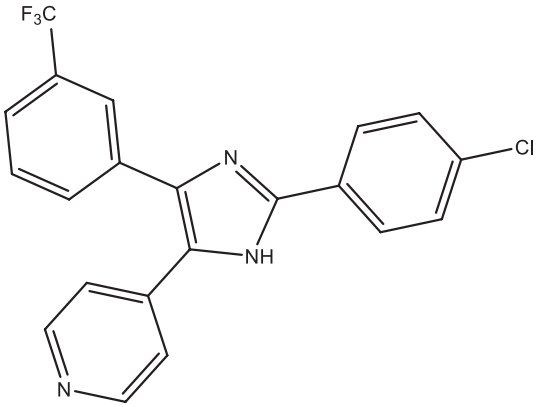
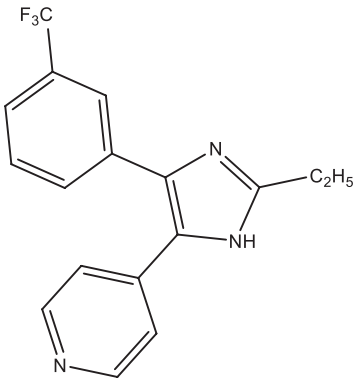
*(contd...)*

**Table 1:** ***(Continued)***

| S. No. | Compound | Structure | Yield (%) | M.P |
|---|---|---|---|---|
| 7 | **3g** |  | 51 | 169–170°C |
| 8 | **3h** |  | 37 | 173–175°C |
| 9 | **3i** |  | 17 | 167–168°C |
| 10 | **3j** |  | 29 | 165–166°C |

*(contd...)*

**Table 1:** ***(Continued)***

| S. No. | Compound | Structure | Yield (%) | M.P |
|---|---|---|---|---|
| 11 | **3k** |  | 50 | 153–154°C |
| 12 | **3l** |  | 63 | 159–160°C |
| 13 | **3m** |  | 45 | 167–168°C |
| 14 | **3n** |  | 26 | 145–146°C |

*(contd...)*

**Table 1:** ***(Continued)***

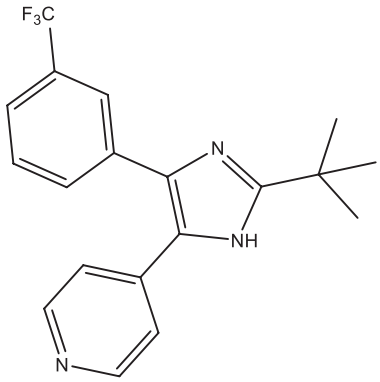
| S. No. | Compound | Structure | Yield (%) | M.P |
|---|---|---|---|---|
| 15 | **3o** |  | 25 | 147– |

**Table 2: Antibacterial activity of 2,4,5-triarylimidazoles**

| Compound | Zone of inhibition | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *E. coli* | | | *S. aureus* | | | *B. subtilis* | | | *S. pneumonia* | | |
| | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** |
| 3a | 8 | 11 | 14 | 7 | 12 | 14 | 11 | 13 | 16 | 8 | 9 | 13 |
| 3b | 11 | 16 | 20 | 10 | 14 | 18 | 16 | 17 | 20 | 10 | 12 | 14 |
| 3c | 12 | 15 | 18 | 11 | 13 | 17 | 16 | 19 | 22 | 11 | 13 | 19 |
| 3d | 7 | 10 | 14 | 6 | 11 | 13 | 11 | 12 | 14 | 7 | 9 | 13 |
| 3e | 11 | 16 | 20 | 10 | 15 | 19 | 17 | 18 | 21 | 10 | 15 | 18 |
| 3f | 6 | 8 | 13 | 8 | 9 | 11 | 11 | 13 | 15 | 6 | 12 | 15 |
| 3g | 12 | 16 | 19 | 10 | 14 | 18 | 18 | 19 | 20 | 11 | 15 | 17 |
| 3h | 14 | 18 | 21 | 12 | 16 | 20 | 18 | 22 | 25 | 11 | 16 | 21 |
| 3i | 10 | 15 | 19 | 11 | 15 | 17 | 13 | 16 | 20 | 9 | 13 | 15 |
| 3j | 6 | 9 | 13 | 5 | 7 | 12 | 10 | 15 | 19 | 5 | 9 | 12 |
| 3k | 5 | 8 | 16 | 5 | 8 | 13 | 9 | 13 | 18 | 7 | 10 | 13 |
| 3l | 9 | 12 | 15 | 8 | 10 | 15 | 11 | 18 | 20 | 8 | 11 | 14 |
| 3m | 12 | 14 | 18 | 12 | 15 | 16 | 15 | 17 | 19 | 10 | 13 | 17 |
| 3n | 6 | 10 | 14 | 8 | 10 | 14 | 10 | 15 | 20 | 5 | 9 | 12 |
| 3o | 5 | 9 | 10 | 9 | 12 | 15 | 8 | 13 | 18 | 7 | 10 | 13 |
| Ampicillin (100 µg/ml) | 20 | | | 19 | | | 23 | | | 21 | | |

*E. coli*: *Escherichia coli, S. pneumonia*: *Streptococcus pneumonia, S. aureus*: *Staphylococcus aureus, B. subtilis*: *Bacillus subtilis*

**Table 3: Antifungal activity of 2,4,5-triarylimidazoles**

| Compound | Zone of inhibition | | | | | |
|---|---|---|---|---|---|---|
| | *A. niger* | | | *C. albicans* | | |
| | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** | **50 µg/ml** | **100 µg/ml** | **200 µg/ml** |
| 3a | 9 | 13 | 16 | 10 | 15 | 17 |
| 3b | 10 | 16 | 20 | 11 | 15 | 20 |
| 3c | 11 | 14 | 21 | 13 | 15 | 20 |
| 3d | 9 | 11 | 13 | 8 | 10 | 13 |
| 3e | 11 | 14 | 21 | 12 | 15 | 19 |
| 3f | 9 | 12 | 15 | 10 | 13 | 15 |
| 3g | 11 | 15 | 20 | 14 | 17 | 21 |
| 3h | 13 | 16 | 23 | 13 | 17 | 23 |
| 3i | 9 | 12 | 15 | 10 | 12 | 15 |
| 3j | 10 | 12 | 15 | 8 | 13 | 15 |
| 3k | 8 | 10 | 14 | 9 | 14 | 17 |
| 3l | 9 | 12 | 15 | 11 | 14 | 20 |
| 3m | 11 | 13 | 19 | 11 | 14 | 19 |
| 3n | 8 | 10 | 13 | 8 | 10 | 13 |
| 3o | 9 | 12 | 14 | 8 | 12 | 16 |
| Nystatin | 26 | | | 24 | | |

*A. niger*: *Aspergillus niger*, *C. albicans*: *Candida albicans*

**Table 4: Antimycobacterial activity of 2,4,5-triarylimidazoles**

| Compound | MIC against MTB H37Rv (µg/mL) |
|---|---|
| 3a | 12.5 |
| 3b | 6.25 |
| 3c | 25 |
| 3d | 25 |
| 3e | 50 |
| 3f | 12.5 |
| 3g | 3.12 |
| 3h | 3.12 |
| 3i | 25 |
| 3j | 50 |
| 3k | 25 |
| 3l | 50 |
| 3m | 6.25 |
| 3n | 25 |
| 3o | 50 |
| Isoniazid | 0.36 |

MTB: *Mycobacterium tuberculosis*, MIC: Minimum inhibitory concentration

0.4 Hz), 7.83–7.91 (2H, 7.90 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.86 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.58 (1H, dd, J = 5.8, 1.6 Hz), 8.75 (1H, dd, J = 1.6, 0.5 Hz). MS for $C_{21}H_{15}F_3N_4$ [M + H]$^+$: m/z = 381.1.

**4-(2-(4-methoxyphenyl)-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)pyrimidine (Compound 3g)**

1H NMR(400 MHz, d6-DMSO): δ 3.92 (3H, s), 7.17 (2H, ddd, J = 8.5, 1.4, 0.4 Hz), 7.40 (1H, dd, J = 6.6, 0.4 Hz), 7.51–7.63 (2H, 7.59 (ddd, J = 8.0, 7.6, 0.4 Hz), 7.54 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.84–7.95 (4H, 7.89 (ddd, J = 1.8, 1.6, 0.4 Hz), 7.92 (ddd, J = 8.5, 1.7, 0.4 Hz), 7.88 (ddd, J = 7.6, 1.8, 1.5 Hz)), 8.73 (1H, dd, J = 1.7, 0.4 Hz), 8.78 (1H, dd, J = 6.6, 1.7 Hz). MS for $C_{21}H_{15}F_3N_4O$[M + H]$^+$: m/z = 397.2.

**4-(2-(4-chlorophenyl)-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)pyrimidine (Compound 3h)**

1H NMR(400 MHz, d6-DMSO): δ 7.46 (1H, dd, J = 5.1, 0.5 Hz), 7.51-7.66 (2H, 7.62 (ddd, J = 8.0, 7.7, 0.4 Hz), 7.54 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.71 (2H, ddd, J = 8.4, 1.6, 0.4 Hz), 7.80 (2H, ddd, J = 8.4, 1.6, 0.4 Hz), 7.85–7.93 (2H, 7.92 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.88 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.59 (1H, dd, J = 5.1, 1.6 Hz), 8.77 (1H, dd, J = 1.6, 0.5 Hz). MS for $C_{20}H_{12}ClF_3N_4$ [M + H]$^+$: m/z = 401.05.

**4-(2-ethyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyrimidine (Compound 3i)**

1H NMR(400 MHz, d6-DMSO): δ 1.30 (3H, t, J = 5.9 Hz), 2.60 (2H, q, J = 5.9 Hz), 7.22 (2H, ddd, J = 8.1, 1.7, 0.4 Hz), 7.46 (1H, dd, J = 5.8, 0.5 Hz), 7.51–7.65 (2H, 7.61 (ddd, J = 8.0, 7.7, 0.4 Hz), 7.54 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.73 (2H, ddd, J = 8.1, 1.6, 0.4 Hz), 7.83–7.91 (2H, 7.90 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.86 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.75 (1H, dd, J = 1.6, 0.5 Hz), 8.80 (1H, dd, J = 5.8, 1.6 Hz). MS for $C_{16}H_{13}F_3N_4$ [M + H]$^+$: m/z = 319.1.

**4-(2-tert-butyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyrimidine (Compound 3j)**

1H NMR(400 MHz, d6-DMSO): δ 1.39 (9H, s), 7.25 (2H, ddd, J = 8.4, 1.8, 0.5 Hz), 7.46 (1H, dd, J = 5.8, 0.5 Hz), 7.51–7.66 (2H, 7.61 (ddd, J = 8.0, 7.7, 0.4 Hz), 7.54 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.74 (2H, ddd, J = 8.4, 1.6, 0.4 Hz), 7.83–7.91 (2H, 7.90 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.86 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.59 (1H, dd, J = 5.8, 1.6 Hz), 8.76 (1H, dd, J = 1.6, 0.5 Hz). MS for $C_{18}H_{17}F_3N_4$ [M + H]$^+$: m/z = 347.2.

**4-(2-p-tolyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyridine (Compound 3k)**

1H NMR(400 MHz, d6-DMSO): δ 2.25 (3H, s), 7.18 (2H, ddd, J = 8.2, 1.6, 0.5 Hz), 7.49 (1H, ddd, J = 8.0, 1.6, 1.5 Hz), 7.59 (1H, ddd, J = 8.0, 7.7, 0.4 Hz), 7.67 (2H, ddd, J = 8.2, 1.8, 0.4 Hz), 7.80–7.87 (2H, 7.85 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.83 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.23 (2H, ddd, J = 6.6, 1.8, 0.5 Hz), 8.48 (2H, ddd, J = 6.6, 2.0, 0.5 Hz). MS for $C_{22}H_{16}F_3N_3$ [M + H]$^+$: m/z = 380.1.

**4-(2-(4-methoxyphenyl)-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)pyridine (Compound 3l)**

1H NMR(400 MHz, d6-DMSO): δ 3.90 (3H, s), 7.20 (2H, ddd, J = 8.6, 1.4, 0.4 Hz), 7.46–7.61 (2H, 7.57 (ddd, J = 8.0, 7.6, 0.4 Hz), 7.50 (ddd, J = 8.0, 1.6, 1.5 Hz)), 7.74–7.85 (4H, 7.84 (ddd, J = 1.8, 1.6, 0.4 Hz), 7.81 (ddd, J = 7.6, 1.8, 1.5 Hz), 7.77 (ddd, J = 8.6, 1.7, 0.4 Hz)), 7.91 (2H, ddd, J = 6.6, 1.9, 0.5 Hz), 8.47 (2H, ddd, J = 6.6, 2.0, 0.5 Hz). MS for $C_{22}H_{16}F_3N_3O$[M + H]$^+$: m/z = 396.1.

**4-(2-(4-chlorophenyl)-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)pyridine (Compound 3m)**

1H NMR(400 MHz, d6-DMSO): δ 7.50 (1H, ddd, J = 8.0, 1.6, 1.5 Hz), 7.56–7.70 (3H, 7.67 (ddd, J = 8.3, 1.6, 0.4 Hz), 7.60 (ddd, J = 8.0, 7.7, 0.4 Hz)), 7.75 (2H, ddd, J = 8.3, 1.6, 0.4 Hz), 7.82–7.88 (2H, 7.86 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.85 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.09 (2H, ddd, J = 6.6, 1.8, 0.5 Hz), 8.50 (2H, ddd, J = 6.6, 2.0, 0.5 Hz). MS for $C_{21}H_{13}ClF_3N_3$ [M + H]$^+$: m/z = 400.05.

**4-(2-ethyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyridine (Compound 3n)**

1H NMR(400 MHz, d6-DMSO): δ 1.29 (3H, t, J = 6.1 Hz), 2.63 (2H, q, J = 6.1 Hz), 7.41 (2H, ddd, J = 8.4, 1.6, 0.5 Hz), 7.49 (1H, ddd, J = 8.0, 1.6, 1.5 Hz), 7.59 (1H, ddd, J = 8.0, 7.7, 0.4 Hz), 7.67 (2H, ddd, J = 8.4, 1.8, 0.4 Hz), 7.80–7.87 (2H, 7.85 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.83 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.23 (2H, ddd, J = 6.6, 1.8, 0.5 Hz), 8.48 (2H, ddd, J = 6.6, 2.0, 0.5 Hz). MS for $C_{17}H_{14}F_3N_3$ [M + H]$^+$: m/z = 318.2.

**4-(2-tert-butyl-4-(3-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) pyridine (Compound 3o)**

1H NMR(400 MHz, d6-DMSO): δ 1.38 (9H, s), 7.23 (2H, ddd, J = 8.4, 1.4, 0.5 Hz), 7.49 (1H, ddd, J = 8.0, 1.6, 1.5 Hz), 7.59 (1H, ddd, J = 8.0, 7.7, 0.4 Hz), 7.67 (2H, ddd, J = 8.4, 1.8, 0.4 Hz), 7.80–7.87 (2H, 7.85 (ddd, J = 1.7, 1.6, 0.4 Hz), 7.83 (ddd, J = 7.7, 1.7, 1.5 Hz)), 8.23 (2H, ddd, J = 6.6, 1.8, 0.5 Hz), 8.48 (2H, ddd, J = 6.6, 2.0, 0.5 Hz). MS for $C_{19}H_{18}F_3N_3$ [M + H]$^+$: m/z = 346.15.

**Antimicrobial activity**

Antibacterial activity of the compounds (3a-o) was screened against Gram-positive and Gram-negative bacterial and fungal strains *S. aureus* (NCTC 7447), *B. subtilis* (MTCC-619), *E. coli* (NCTC 6571), *S. pneumonia*, *A. niger,* and *C. albicans* (recultured), respectively, by disc diffusion method, and ampicillin (100 µg/ml) and nystatin (10 µg/ml) in DMSO were used as reference standards (Tables 2 and 3).

From the above data, it is coherent that ***3h*** is the highly active among all the synthesized compounds, as it displayed better inhibition against all the bacterial and fungal species followed by compound ***3g, 3b,*** and ***3m***. Among all the species, *B. subtilis* displayed better sensitivity toward the prepared molecules.

**Antimycobacterial activity**

All the 15 compounds **(*3a-o*)** were screened for antitubercular activity against MTB H37Rv (ATCC 27294) which are susceptible to isoniazid at various concentrations (100, 50, 25, 12.5, 6.25, 3.12, 1.6, and 0.8 µg/mL) using the middle brook 7H11 medium. The antitubercular activity was expressed as MIC (the minimum concentration of the test sample (Table 4) that can inhibit the complete growth on the culture) and is compared with the standard drugs isoniazid.

The results indicated that few of the synthesized compounds exhibited comparatively good antitubercular activity against isoniazid sensitive MTB H 37Rv (ATCC 27294) strain. The results are depicted in Table 5. From the results, it is evident that the compounds ***3h*** and ***3g*** (MIC – 3.12 µg/mL) have excellent antitubercular activity followed by compounds ***3b*** and ***3m*** (MIC – 6.25 µg/mL) showed significant antitubercular activity against MTB H 37Rv (ATCC 27294) strain.

## SUMMARY AND CONCLUSION

The present study concerns the synthesis, antibacterial, antifungal, and antimycobacterial activities of 15 novel 2,4,5-triarylimidazole derivatives. All the titled compounds have been synthesized through a feasible method by cyclization of N-hydroxyimidazole and keto-oximes and structure elucidation followed by antimicrobial screening on various Gram-positive and Gram-negative bacteria, fungal, and mycobacterium. Since imidazole derivatives are acclaimed to possess antimicrobial properties, above data support the antimicrobial potency of the synthesized 2,4,5-triarylimidazole derivatives. Among the 15 compounds, ***3h, 3g, 3b,*** and ***3m*** exhibited comparatively higher activities than the other. Further, research is necessary to explore the mechanism involved in the antimicrobial activity.

## AUTHORS' CONTRIBUTIONS

All authors contribute equally to this manuscript.

## CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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