Journal of Advanced Scientific Research

Available online through https://sciensage.info

ISSN

0976-9595

Research Article

Synthesis and Antimicrobial Activity of Novel Imidazo[1,2-A]Pyridines Containing 1,2,3-Triazole

A. Nagaraj*, G. Amala, S. Raghaveer

Department of Chemistry, Telangana University, Nizamabad, India.

*Corresponding author: nagarajadki@gmail.com

Received: 15-11-2025; Accepted: 02-12-2025; Published: 31-12-2025

https://doi.org/10.55218/JASR.2025161203

ABSTRACT

A series of novel2(5-methyl-1-aryl-1H-1,2,3-triazol-4-yl)imidazo-[1,2-a]pyridine13(a-l) has been synthesized from 2-bromo-1-(5-methyl-1-aryl-1H-1,2,3-triazol-4-yl)-1-ethanone 12(a-c) and assayed for their bacterial activity against gram-positive bacteria, viz. B. subtilis, B. sphaericus, and S. aureus and gram-negative bacteria viz. P. aeruginosa, K. aerogenes and C. violaceum and fungal strains viz. C. albicans, A. fumigatus, T. rubrum and T. mentagrophytes. The compounds 13b, 13j, showed significant antibacterial activity, compounds 13c and 13g exhibited good inhibitory activity against all fungal strains, and the other compounds also showed moderate to good antimicrobial activity.

Keywords: Triazole, Imidazo-pyridine, Synthesis, Antimicrobial Activity.

INTRODUCTION

The derivatives of the pyridine ring are an exceptional class of heterocyclic compounds with varied biological and pharmacological activities.[1-5] Among them, imidazopyridine and its derivatives are a significant class of nitrogen-containing fused heterocyclic compoundshowed pharmacological activities [6-9].In general, they are $GABA_A$ receptor agonists[10] however, recently proton pump inhibitors [11], aromatase inhibitors [12], NSAIDs[13], antibacterial[14], anticancer [15], antiviral [16], antifungal [17], antitumor [18], antiulcer [19]. Furthermore, imidazolpyridine moieties are present in a number of commercially available medications, including the anti-anxiolytic [20] necopidem 1 and saripidem 2, acute heart failure [21]olprinone 3, insomnia drug [22] zolpidem 4, peptic ulcer drug[23] zolimidine 5, anxiolytic[22] alpidem 6, and antibiotic[24] rifaximin 7 (Fig 1).

Further, the 1,2,3-triazoles are renowned scaffolds that are simple to conjugate with additional heterocyclic groups. As a result, a variety of bioactive compounds with antibacterial [25,26] anticancer[27] and anti-hypercholesterolemic [28,29] actions have begun to target these triazole conjugated structural motifs as a common pharmacological target.

Owing to the immense importance and varied bioactivities exhibited byimidazo[1,2-a]pyridine, triazole and their derivatives, in continuation of our ongoing research on the synthesis of novel heterocyclic compounds, it was thought of interest to synthesize new heterocyclic compounds incorporating both imidazo[1,2-a]pyridine and triazole rings in one molecule with potential biological activity. In this article, we wish to report the synthesis of novel2(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)imidazo-[1,2-*a*]pyridine13(a-l) and evaluation of their *in vitro* antimicrobial activity.

MATERIALS AND METHOD

Commercial-grade reagents were used as supplied. Solvents, except analytical reagent grade, were dried and purified according to the literature when necessary. Reaction progress and purity of the compounds were checked by thin-layer chromatography (TLC) on pre-coated silica gel F_{254} plates from Merck and compounds were visualized either by exposure to UV light. Silica gel chromatographic columns (70–230 mesh) were used for separations. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded as KBr disks on a Perkin–Elmer FTIR spectrometer. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shifts are reported as δ ppm against TMS as an internal standard and coupling constants (J) are reported in Hz units. Mass spectra were recorded on a VG Micromass 7070H spectrometer.

General procedure for the synthesis of 1-arylazides 10(a-c)

To a cold solution of corresponding arylamine **8** (0.01 mol) in dilute hydrochloric acid (15 mL), sodium nitrite (1.1 mol) was added in small portions at 0 to 5°C and stirred for one hour to afford the diazonium chloride **9**, then a solution of sodium azide (1.2 mol in 10 mL water) was added in drop wise manner and stirring was continued for 30 min and the resulting solid was filtered and recrystallized from ethanol to give pure compound **10(a-c)** in good yields.

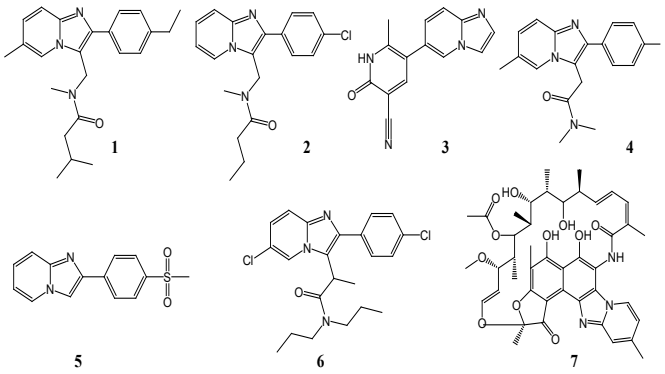

Figure 1: Imidazolpyridine moieties present in different commercially available medications

1-Azidobenzene (10a)

IR (KBr) ν_{max}: 3110 (C-H, ArH), 2167 (N_3), 1610 (C=C), 1277 (C-N) cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 7.10–7.20 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ120.4, 122.7, 128.4, 140.6; MS: *m/z* 119 (M^+).

1-Azido-4-fluorobenzene (10b)

IR (KBr) ν_{max}: 3067, 2120, 1607, 1272, 1031 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 6.80 (d, J = 8.2 Hz, 2H, ArH), 6.98 (d, J = 8.2 Hz, 2H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ114.7, 125.8, 139.9, 164.5; MS: *m/z* 137 (M^+).

1-Azido-4-chlorobenzene (10c)

IR (KBr) ν_{max}: 3071, 2117, 1609, 1268, 687 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 7.20–7.25 (m, 4H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ122.8, 125.7, 136.8, 140.5; MS: *m/z* 153 (M^+).

General procedure for the synthesis of 1-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-ethanone 11(a-c)

To a solution of corresponding compound **10(a-c)** (0.01 mol) in ethanol: water (1:1), acetylacetone (0.015 mol) and K_2CO_3 (0.02 mol) was added the resulting mixture was stirred in an oil bath at 80°C for 3 hours. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature and poured into ice-cold water. The product that precipitated out was filtered, washed successively with ice-cold water, and purified by column chromatography on silica gel (60-120 mesh) with ethyl acetate-petroleum ether mixture (40:60) as the eluting solvent to obtain the corresponding compounds **11(a-c)**.

1-(5-Methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1-ethanone (11a)

IR (KBr) ν_{max}: 3074, 1710, 1579, 1027 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.17 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 7.35-7.40 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ16.9, 29.1, 124.9, 128.1, 129.0, 130.5, 140.3, 144.7, 191.2; MS: *m/z* 202 (M^++1).

1-[1-(4-Fluorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-1-ethanone (11b)

IR (KBr) ν_{max}: 3069, 1698, 1581, 1302, 1033 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.15 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 7.50-7.55 (m, 4H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ16.3, 29.7, 118.9, 124.5, 128.2, 138.0, 143.3, 166.3, 190.7; MS: *m/z* 219 (M^+).

1-[1-(4-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-1-ethanone (11c)

IR (KBr) ν_{max}: 3071, 1701, 1578, 1307, 1031 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.19 (s, 3H, CH_3), 2.92 (s, 3H, CH_3), 7.32 (d, J = 8.4 Hz, 2H, ArH), 7.94 (d, J = 8.4 Hz, 2H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ16.2, 29.4, 125.3, 129.5, 131.8, 134.2, 140.5, 143.3, 191.1; MS: *m/z* 235 (M^+).

General procedure for the synthesis of 2-bromo-1-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-ethanone 12(a-c)

A mixture of corresponding compound 11(a-c) (0.01 mol) and *p*-toluenesulfonic acid (0.005 mol) in DCM (50 mL) was stirred at 0°C for 10 minutes; then, Br_2 (0.01 mol) in DCM (20 mL) was added dropwise in the reaction mixture. The reaction mixture was stirred for 12 hours at room temperature (TLC). After completion of the reaction, sodium bicarbonate solution was added to the reaction mixture and stirred for 10 min. The aqueous layer was extracted with DCM, and the combined organic layer was washed with water, dried with sodium sulfate, and distilled under vacuum to give the corresponding compound 12(a-c).

2-Bromo-1(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)1-ethanone (12a)

IR (KBr) ν_{max}: 3081, 1710, 1578, 1321, 1018, 682 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.72 (s, 3H, CH_3), 4.82 (s, 2H, CH_2), 7.45-7.55 (m, 5H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.7, 34.7, 125.1, 130.6, 131.0, 132.4, 136.6, 142.9, 182.5; MS: *m/z* 280 (M^+).

2-Bromo-1-[1-(4-fluorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-1-ethanone (12b)

IR (KBr) ν_{max}: 3107, 1700, 1571, 1340, 1017, 686 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.70 (s, 3H, CH_3), 4.86 (s, 2H, CH_2), 7.40-7.50 (m, 4H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.5, 34.8, 119.0, 127.1, 131.8, 138.9, 141.2, 162.6, 181.2; MS: *m/z* 298 (M^+).

2-Bromo-1-[1-(4-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-1-ethanone (12c)

IR (KBr) νmax: 3101, 1700, 1571, 1340, 1017, 686 cm-1; 1H-NMR (DMSO-d6,300 MHz): δ 2.69 (s, 3H, CH3), 4.79 (s, 2H, CH2), 7.41 (d, J = 8.6 Hz, 2H, ArH), 8.12 (d, J = 8.6 Hz, 2H, ArH); 13C-NMR (DMSO-d6,300 MHz): δ14.1, 33.4, 128.5, 130.3, 132.7, 136.1, 139.0, 143.1, 180.7; MS: m/z 314 (M+).

General procedure for the synthesis of 2(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)imidazo-[1,2-*a*]pyridine13(a-l)

A mixture of corresponding compound **12(a-c)** (0.01 mol) and 2-aminopyridine (0.015 mol) was refluxed in dry ethanol (15 mL). The reaction was monitored on TLC. After the completion of the reaction, the solvent was evaporated under vacuum, and the residue was dissolved in ethyl acetate. The organic layer was washed with sodium bicarbonate and water. The solvent was dried over sodium

sulfate and distilled under vacuum. The product was purified by crystallization in ethanol. The structure of all the synthesized compounds was confirmed by spectral analysis.

2-(5-Methyl-1-phenyl-1H-1,2,3-triazol-4-yl)imidazo[1,2-a] pyridine (13a)

IR (KBr) ν_{max}: 3089, 1610, 1499, 1428, 1342, 1287 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.76 (s, 3H, CH_3), 6.40-6.50 (m, 2H, ArH), 7.35-7.40 (m, 6H, ArH), 8.01 (d, J = 7.1 Hz, 1H, ArH), 8.32 (s, 1H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.7, 110.9, 118.7, 123.7, 124.8, 125.3, 126.2, 126.9, 128.6, 130.4, 131.2, 141.4, 143.1, 149.2; MS: *m/z* 276 (M^++1).

6-Chloro-2-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl) imidazo[1,2-a]pyridine (13b)

IR (KBr) ν_{max}: 3087, 1607, 1480, 1427, 1339, 1286, 687 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.71 (s, 3H, CH_3), 7.40-7.45 (m, 6H, ArH), 8.27 (s, 1H, ArH), 7.80-7.85 (m, 2H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.2, 120.9, 122.7, 123.1, 123.9, 124.0, 125.5, 126.2, 126.3, 127.2, 132.1, 142.8, 143.5, 151.8; MS: *m/z* 309 (M^+).

6-Bromo-2-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl) imidazo[1,2-a]pyridine (13c)

IR (KBr) ν_{max}: 3102, 1621, 1501, 1418, 1333, 1283, 689 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.74 (s, 3H, CH_3), 7.35-7.40 (m, 7H, ArH), 8.41 (s, 1H, ArH), 8.34 (s, 1H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ15.1, 110.8, 124.2, 125.5, 125.9, 126.7, 127.1, 128.0, 129.3, 130.5, 131.0, 143.9, 145.3, 152.4; MS: *m/z* 354 (M^+).

7-Methyl-2-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl) imidazo[1,2-a]pyridine (13d)

IR (KBr) ν_{max}: 3077, 1607, 1507, 1421, 1344, 1285 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.37 (s, 3H, CH_3), 2.72 (s, 3H, CH_3), 6.72 (d, J = 7.4 Hz, 1H, ArH), 7.45-7.50 (m, 6H, ArH), 8.44 (s, 1H, ArH), 7.88 (d, J = 7.4 Hz, 1H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.3, 21.9, 113.7, 114.7, 123.1, 123.9, 125.1, 125.7, 126.9, 127.2, 127.9, 130.2, 143.4, 144.3, 151.4; MS: *m/z* 290 (M^++1).

2-[1-(4-Fluorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl] imidazo[1,2-a]pyridine (13e)

IR (KBr) ν_{max}: 3068, 1601, 1497, 1431, 1340, 1289, 1031 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.70 (s, 3H, CH_3), 6.85-6.90 (m, 2H, ArH), 7.25-7.30 (m, 5H, ArH), 8.01 (d, J = 7.9 Hz, 1H, ArH), 8.39 (s, 1H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.4, 113.4, 114.8, 118.0, 125.0, 125.2, 126.6, 128.1, 130.2, 131.1, 142.2, 143.8, 149.0, 165.3; MS: *m/z* 293 (M^+).

6-Chloro-2[1-(4-fluorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]imidazo[1,2-a]pyridine (13f)

IR (KBr) ν_{max}: 3112, 1600, 1488, 1438, 1337, 1277, 1037, 684 cm^{-1}; ^{1}H-NMR (DMSO-d_6,300 MHz): δ 2.75 (s, 3H, CH_3), 7.30-7.40 (m, 6H, ArH), 7.93 (s, 1H, ArH), 8.35 (s, 1H, ArH); ^{13}C-NMR (DMSO-d_6,300 MHz): δ14.7, 114.5, 120.3, 122.1, 124.0, 125.0, 125.6, 127.1, 129.1, 130.7, 142.7, 144.1, 154.2, 166.8; MS: *m/z* 327 (M^+).

6-Bromo-2[1(4-fluorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]imidazo[1,2-a]pyridine (13g)

IR (KBr) ν_{max}: 3097, 1605, 1492, 1426, 1336, 1281, 1032, 688 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 2.68 (s, 3H, CH_3), 7.30-7.40 (m, 6H, ArH), 8.48 (s, 1H, ArH), 8.67 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ14.2, 111.2, 114.8, 123.0, 125.3, 126.7, 128.7, 130.7, 131.2, 133.4, 142.5, 145.1, 167.1; MS: *m/z* 372 (M^+).

2[1(4-Fluorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]-7-methylimidazo[1,2-a]pyridine (13h)

IR (KBr) ν_{max}: 3074, 1603, 1497, 1423, 1337, 1286, 1026 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 2.47 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 6.62 (d, J = 7.1 Hz, 1H, ArH), 7.35-7.40 (m, 5H, ArH), 8.00 (d, J = 7.1 Hz, 1H, ArH), 8.35 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ22.7, 14.3, 113.5, 114.9, 115.0, 123.9, 124.1, 125.1, 126.8, 130.8, 131.4, 142.0, 143.5, 151.0, 166.0; MS: *m/z* 308 (M^++1).

2-[1(4-chlorophenyl)5-methyl-1H-1,2,3-triazol-4-yl] imidazo[1,2-a]pyridine (13i)

IR (KBr) ν_{max}: 3081, 1608, 1500, 1417, 1341, 1283, 687 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 2.69 (s, 3H, CH_3), 6.60-6.70 (m, 2H, ArH), 7.35-7.40 (m, 3H, ArH), 8.00-810 (m, 3H, ArH), 8.44 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ13.7, 119.0, 120.7, 125.1, 125.9, 126.7, 127.8, 128.2, 129.5, 131.8, 132.7, 140.1, 141.3, 147.0; MS: *m/z* 309 (M^++1).

6-Chloro-2[1-(4-chlorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]imidazo[1,2-a]pyri- dine (13j)

IR (KBr) $_{max}$: 3089, 1611, 1503, 1419, 1342, 1286, 684 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 2.72 (s, 3H, CH_3), 7.40-7.45 (m, 3H, ArH), 7.60 (d, J = 8.9 Hz, 1H, ArH), 7.90-8.00 (m, 3H, ArH), 8.31 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ13.6, 120.9, 122.4, 123.6, 126.0, 126.7, 126.9, 126.9, 128.4, 132.2, 133.0, 141.3, 142.1, 153.1; MS: *m/z* 344 (M^+).

6-Bromo-2[1(4-chlorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]imidazo[1,2-a]pyri- dine (13k):

IR (KBr) ν_{max}: 3071, 1615, 1487, 1420, 1339, 1286, 689 cm^{-1}; ^{1}H NMR (DMSO-d_6,300 MHz): δ 2.71 (s, 3H, CH_3), 7.30-7.45 (m, 5H, ArH), 8.14 (d, J = 8.3 Hz, 2H, ArH), 8.37 (s, 1H, ArH), 8.55 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ13.5, 111.4, 125.4, 126.9, 127.5, 127.9, 128.0, 129.1, 128.1, 132.1, 133.8, 140.5, 144.3, 151.7; MS: *m/z* 388 (M^+).

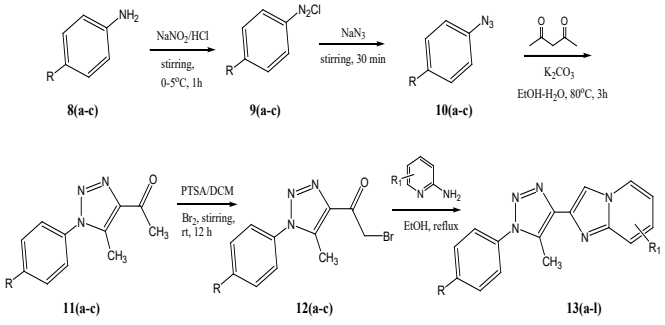

Figure 2: Synthetic route of title compounds 13(a-l)

Table 1: Synthetic route of title compounds 13(a-l)

Comp.	*R*	*R1*	*Comp.*	*R*	*R1*	*Comp.*	*R*	*R1*
13a	H	H	13e	F	H	13i	Cl	H
13b	H	6-Cl	13f	F	6-Cl	13j	Cl	6-Cl
13c	H	6-Br	13g	F	6-Br	13k	Cl	6-Br
13d	H	7-CH3	13h	F	7-CH3	13l	Cl	7-CH3

2[1-(4-Chlorophenyl)5-methyl-1H-1,2,3-triazol-4-yl]7-methylimidazo[1,2-a]pyri- dine (13l)

IR (KBr) ν_{max}: 3067, 1606, 1489, 1416, 1336, 1289, 688 cm^{-1}; ^1H NMR (DMSO-d_6,300 MHz): δ 2.73 (s, 3H, CH_3), 6.77 (d, J = 7.5 Hz, 1H, ArH), 7.35-7.40 (m, 3H, ArH), 7.90-8.00 (m, 3H, ArH); ^{13}C NMR (DMSO-d_6,300 MHz): δ13.1, 23.1, 113.4, 114.5, 124.1, 124.9, 126.2, 126.9, 127.0, 129.3, 130.2, 132.1, 140.7, 142.3, 148.9; MS: *m/z* 323 (M^+).

Antibacterial Assay

All the newly synthesized compounds **13(a-l)** were assayed for their antibacterial activity against Gram-positive bacteria, *viz*. *Bacillus subtilis* (MTCC 441), *B. sphaericus* (MTCC 11), and *Staphylococcus aureus* (MTCC 96), and Gram-negative bacteria *viz*. *Pseudomonas aeruginosa* (MTCC 741), *Klebsiella aerogenes* (MTCC 39), and *Chromobacterium violaceum* (MTCC 2625) by disc diffusion and broth dilution methods (Villanova 1982). For the antibacterial assay, standard inoculums (1-2 $\times 10^7$ c.f.u/mL 0.5 McFarland standards) were introduced onto the surface of sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculums. The discs measuring 6.26 mm in diameter were prepared from Whatman no.1 filter paper and sterilized by dry heat at 140℃ for 1 hour. The sterile discs previously soaked in a known concentration of the test compounds were placed in the nutrient agar medium. The plates were inverted and incubated for 24 hours at 37℃. The inhibition zones were measured and compared with the standard drug penicillin (Table 1). For the determination of MIC, bacteria were grown overnight in Luria Bertani (LB) broth at 37°C harvested by centrifugation, and then washed twice with sterile distilled water. Stock solutions of the series of compounds were prepared in DMSO. Each stock solution was diluted with standard method broth (Difco) to prepare serial two-fold dilutions in the range of 50–0.8 μg/mL. Ten microliters of the broth containing about 10^5c.f.u/ml of test bacteria were added to each well of a 96–well microtiter plate. Culture plates were incubated for 24 hours at 37°C and the growth was monitored visually and spectrometrically. The minimal inhibitory concentrations (MIC, μg/mL) were measured and compared with the standard drug penicillin (Table 1).

Antifungal Assay

Compounds 13(a-l) were also evaluated for their antifungal activity against *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185) and *T. mentagrophytes* (IFO 40996) in DMSO by disc diffusion and broth dilution methods (Villanova 1982). For the antifungal assay, Sabouraud's agar media was prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 mL) and adjusting the *p*H to 5.7. Normal saline was used to make a suspension of spore of the fungal strain for lining. A loopful of a particular fungal strain was transferred to 3 mL saline to get a suspension of the corresponding species. About 20 mL of agar media was poured into each petri-dish, excess of suspension was decanted and the plates were dried by placing in an incubator at 37°C for 1 hour. Using an agar punch well were made and each

Table 2: Antibacterial activity of compounds 13(a-l)

Compound	*Minimal inhibitory concentration in μg/mL (zone of inhibition in mm)*[a]					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
13a	30 (10)	28 (11)	35 (12)	30 (13)	26 (10)	24 (7)
13b	12 (16)	14 (19)	17 (15)	20 (18)	18 (19)	28 (9)
13c	24 (9)	35 (13)	20 (10)	30 (11)	35 (10)	13 (8)
13d	25 (11)	25 (14)	28 (9)	35 (10)	27 (10)	25 (11)
13e	12 (18)	14 (20)	30 (8)	30 (10)	28 (10)	30 (11)
13f	14 (20)	18 (17)	17 (28)	22 (15)	23 (15)	20 (18)
13g	30 (9)	30 (9)	35 (10)	10 (20)	14 (16)	10 (17)
13h	22 (10)	25 (8)	11 (19)	40 (9)	25 (10)	30 (10)
13i	25 (10)	20 (11)	30 (11)	25 (10)	35 (9)	25 (8)
13j	11(18)	14(20)	14(27)	17(18)	18(21)	20(16)
13k	10(19)	24(5)	22(10)	33(10)	27(9)	28(10)
13l	35(8)	30(8)	35(9)	40(10)	20(4)	30(9)
Penicillin	1.56 (25)	3.12 (28)	1.56 (40)	6.25 (25)	6.25 (30)	12.5 (25)

[a]The values in parentheses indicate the zone of inhibition.

well was labelled. A control was also prepared in triplicate and maintained at 37°C for 3 to 4 days. The *C. albicans* was grown for 48 hours at 28°C in YPD broth (1% yeast extract, 2% peptone and 2% dextrose), harvested by centrifugation and then washed twice with sterile distilled water. *A. fumigatus*, *T. rubrum* and *T. mentagrophytes* were plated in potato dextrose agar (PDA) (Difco) and incubated at 28°C for two weeks. Spores were washed three times with sterile distilled water and resuspended in distilled water to obtain an initial inoculum size of 10^5 spores/ml. Each test compound was dissolved in DMSO and diluted with potato dextrose broth (Difco) to prepare serial two-fold dilutions in the range 100 to 0.8 µg/mL. Ten microliters of the broth containing about 10^3 (for yeast) and 10^4 (for filamentous fungi) cells/mL of test fungi was added to each well of a 96-well microtiter plate. Culture plates were incubated for about 48–72 hours at 28°C. The inhibition zone and minimal inhibitory concentration (MIC) were determined and compared with the standard drug fluconazole (Table 2).

RESULTS AND DISCUSSION

Chemistry

The intermediate required for the synthesis of title compounds has been synthesized fromcorresponding arylazide10(a-c) on reaction with acetylacetone 2 in the presence of anhydrous potassium carbonate in ethanol under reflux at 80°C for 3 hours to yield corresponding 1-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-ethanone11(a-c) in 62 to 70% of yield. The bromination of corresponding compound 11 with bromine in dichloromethane in the presence of PTSA under stirring at room temperature for 12 hours, afforded corresponding 2-bromo-1-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-ethanone 12(a-c) in 45-55% of yield. The corresponding compound 12 on cyclo-condensation with 2-aminopyridine in ethanol under reflux temperature, afforded the corresponding 2(5-methyl-1-aryl-1H-1,2,3-triazol-4-yl)imidazo-[1,2-*a*]pyridine13(a-l) in 45 to 60% of yields (Table 1). The structure of the synthesized compound was confirmed by the interpretation of its IR, NMR and MS spectral analyses.

The IR spectrum of compound 11a, the absorption bands due to C=O and C=N appear at 1710 and 1579 cm^{-1}. In the ^{1}H-NMR spectra, the aromatic protons of phenyl groups appeared as a multiplet at δ 7.35-7.40 and the protons of methyl groups appeared as a singlet at δ 2.17 and 2.89 ppm. In it ^{13}C-NMR spectra, the signals of the triazole ring appeared at δ 128.1 and 140.3 ppm.The structure of was further confirmed by the mass spectrum, which showed a molecular ion peak at *m/z*202.

The IR spectra of compound 12a, the characteristic stretching frequency of the C=O and C-Br was observed at 1710 and 682 cm^{-1}. The ^{1}H NMR spectrum showed, phenyl ring signal at *d* 7.45-7.55 as multiplets for five, the signal at *d*2.72 as singlet, integrating three protons assigned for methyl group and at *d*4.82 integrating two protons assigned for methylene group. ^{13}C NMR spectrum exhibit the signal at *d* 136.6 and 132.4 for (C-5) and (C-4) carbons of triazole ring, the carbonyl carbon appeared at *d*182.5 (C=O) ppm.The structure of was further confirmed by the mass spectrum, which showed a molecular ion peak at *m/z*280.

The IR spectra of compound **13a**, the stretching frequency at 1499 (N=N), 1610 (C=C) of triazole ring C=N of imidazopyridine absorption bands appeared at 1428 cm^{-1}. Its ^{1}H NMR spectrum showed a signal at d6.40-6.50 and 7.35-7.40ppm as multiplets for two and six protons in each and a signal at *d* 8.01 ppm as doublet for one proton assigned to 4th position of pyridine ring the signal corresponding to the 3rd position of imidazole ring observed at *d* 8.32 ppmas a singlet, the methyl group protons appear *d*2.76 as singlet, integrating three protons. Its ^{13}C NMR spectrum exhibit the signal at *d*130.4 (C-5) and 149.2 (C-4) for triazole ring carbons. The imidazopyridine ring carbons appeared at *d*131.2 (C-2), 126.9 (C-3), 126.2 (C-4), 118.7 (C-5), 123.7 (C-6) and118.7 (C-7) ppm.The structure of was further confirmed by the mass spectrum, which showed a molecular ion peak at *m/z*276.

Table 3: Antifungal activity of compounds 13(a-j)

Compound	*Minimal inhibitory concentration in µg/mL (zone of inhibition in mm)*[a]			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagrophytes*
13a	30 (11)	40 (11)	30 (8)	30 (10)
13b	25 (13)	30 (14)	40 (9)	35 (10)
13c	20(18)	21(17)	22(18)	20(18)
13d	35 (11)	30 (10)	18 (19)	20 (18)
13e	30 (8)	30 (10)	35 (11)	30 (10)
13f	30 (7)	35 (11)	30 (9)	35 (9)
13g	19 (14)	22 (15)	25 (18)	18 (18)
13h	35 (13)	30 (10)	40 (14)	35 (13)
13i	15 (20)	20 (18)	25 (10)	20 (10)
13j	18(20)	20(18)	35(10)	28(11)
13k	28(9)	30(10)	35(10)	29(8)
13l	30(10)	27(7)	32(10)	40(13)
Fluconazole	16 (22)	18 (20)	20 (22)	16 (20)

aThe values in parentheses indicate the zone of inhibition.

Antibacterial Activity

The *in vitro* antibacterial activity of compounds 13(a-l) were evaluated against Gram +ve bacteria (*Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus*) and Gram -ve bacteria (*Pseudomonas aeruginosa*, *Klobsinella aerogenes*, and *Chromobacterium violaceum*) disc diffusion and broth dilution method [30]. Inhibition zones were measured, compared with the standard drug penicillin andthe minimal inhibitory concentrations (MIC, μg/ml) were measured and compared with the standard drug penicillin (Table 2). The investigation of antibacterial screening data revealed that all the tested compounds exhibited interesting biological activity, however, with a degree of variation. Antibacterial screening data revealed that all the tested compounds 13(a-l) are active and showed moderate to good antibacterial activity towards all the tested strains. Compounds containing 6-chloroon imidazopyridine (13b), chlorophenyl on triazole 6-chloro on imidazopyridine (13j) respectively exhibited potent inhibitory activity towards both Gram-positive and Gram-negative bacterial strains. Compounds containing fluorophenyl on triazole 6-chloro on imidazopyridine (13f) showed significant activity towards Gram-positive bacteria and considerable antibacterial activity. Compound containing 4-fluorophenyl ring on triazole ring (13e) showed significant activity towards *B. subtilis* and *B. sphaericus,* compound with 4-fluorophenyl on triazole and bromo on imidazopyridine showed good activity towards Gram-negative bacterial strains, compounds 13h and 13k also showed significant activity towards *S. aureus* and *B. subtilis* respectively.

Antifungal Activity

The *in vitro* antifungal activity of compounds 13(a-l) were evaluated against *Candida albicans*, *Aspergillus fumigatus*, *Trichophyton rubrum* and *Trichophyton mentagrophytes* by disc diffusion and broth dilution method [30]. The inhibition zone and minimal inhibitory concentration (MIC) were determined and compared with the standard drug fluconazole (Table 3). The investigation of antibacterial screening data revealed that all the tested compounds exhibited interesting biological activity, however, with a degree of variation.

The antifungal screening data reveal that, most of the newly synthesized compounds were active with moderate to good antifungal activity. The compounds containing 5-bromo on imidazopyridine (**13c**)and 4-fluorophenyl on triazole and 5-bromoon imidazopyridinering (**13c**) showed significant activity towards all the tested fungal strains. Compounds with 5-methyl group on imidazopyridine (**13d**) showed considerable antifungal activity against *T. rubrum* and *T. mentagrophytes*, similarly compounds with chlorosubstituent on both triazole and imidazopyridine ring (**13j**) showed good activity against *C. albicans* and *A. fumigatus*. The other compounds also showed moderate to good activity.

CONCLUSION

A series of novel2(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)imidazo-[1,2-*a*]pyridine**13(a-l)**has been synthesized from 2-bromo-1-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-ethanone **12(a-c)**and assayed for their antimicrobial activity against Gram-positive and Gram-negative bacteria and fungi. The compounds **13b**, **13j**, showed significant antibacterial activity, compounds **13c** and **13g**exhibited good inhibitory activity against all fungal strains, the other compounds also showed moderate to good antimicrobial activity.

ACKNOWLEDGEMENTS

The authors are thankful to the Director, Indian Institute of Chemical Technology, Hyderabad, India, for providing NMR and mass spectral data. Head, Department of Chemistry is gratefully acknowledged.

REFERENCES

1. Leeson P.D., Springthorpe B,*Nat Rev Drug Discov,* 2007;**6**:881–890.
2. Labarrios E.M., Delgado F., Tamariz J., Aguilar R, *Tetrahedron*, 2015;**71**:6961–6978.
3. Kerru N., Gummidi L., Maddila S., Gangu K.K., Jonnalagadda S.B. *Molecules*, 2020;**25**:1–42.
4. Ju Y., Varma R.S. *J Org Chem,* 2006;**71**:135–141.
5. Eftekhari-Sis B., Zirak M., Akbari A. *Chem Rev,* 2013;**113**:2958–3043.
6. Katritzky A., Ramsden C., Scriven E., Taylor R. *Elsevier; Amsterdam, The Netherlands:* 2008;**11**:409–499.
7. Enguehard-Gueiffier C., Gueiffier A. *Mini Rev Med Chem,* 2007;**7**:888–899.
8. Kishbaugh T.L.S. *Curr Top Med Chem,* 2016;**16**:3274–3302.
9. Abignente E. *Actual Chim Thér,* 1991;**18**:193–214.
10. Foster, A.C. Kemp, J.A. *Curr OpinPharmacol,* 2006; **6**:7–17.
11. Bamford, M. *Prog Med Chem,* 2009; **47**:75–162.
12. Dowsett, M.; Smithers, D.; Moore, J.; Trunet, P.F.; Coombes, R.C.; Powles, T.J.; Rubens, R.; Smith, I.E. *Eur J Cancer,* 1994; **30**:1453–1458.
13. Mikashima, H. Goto, K. *Yakugaku Zasshi,* 1982; **102**:99–103
14. Rival, Y. Grassy, G, Taudou, A, Ecalle, R. *Euro J MedChem,*1991; **26**:13.
15. Dam, J. Ismail, Z. Kurebwa, T. Gangat, N. Harmse, L. Marques, H. M.Lemmerer, A. Bode, M. L. de Koning, C. B. *Euro J Med Chem*,2017; **126**:353.
16. Gudmundsson, K. S. Williams, J. D. Drach, J. C. Townsend, L. B. *J Med Chem*,2003; **46**: 1449
17. Fisher M. H. Lusi, A. *ACS Pub*, 2002).
18. Goel, R. Luxami, V. Paul, K. *Current Topics in Medicinal Chemistry*2016; **16**:3590.
19. Kaminski, J. J. Doweyko, A. M. *J Med Chem*,1997; **40**: 427.
20. Boerner R., Moller H. *Psychopharmakotherapie*, 1997;**4**:145–148.
21. Yukiiri K., Mizushige K., Ueda T., Nishiyama Y., Aoyama T., Kohno M. *J Cardiovasc Pharmacol*, 2001;**37**:375–380.
22. Langer S., Arbilla S., Benavides J., Scatton B. *Adv BiochemPsychopharmacol,* 1990;**46**:61–72.
23. Almirante L., Polo L., Mugnaini A., Provinciali E., Rugarli P., Biancotti A., Gamba A., Murmann W. *J Med Chem*, 1965;**8**:305–312.
24. Koo H.L., DuPont H.L. *Curr Opin Gastroenterol*, 2010;**26**:17–25.
25. Lauria A, Delisi R, Mingoia F, Terenzi A, Martorana A, Barone G, Almerico A. M. *Eur J Org Chem,* 2014;**16**:3289–306.
26. Kuntala N, Telu J. R, Banothu V, Nallapati S. B, Anireddy J. S, Pal S. *Med Chem Comm,* 2015;**6**:1612.
27. Dofe V. S, Sarkate A. P, Lokwani D. K, Kathwate S. H, Gill C. H. *Res Chem Interm*, 2017;**43**:7331–45.
28. Jadhav R. P, Raundal H. N, Patil A. A, Bobade V. D. *J Saudi Chem Soc,* 2017;**21**:152.
29. Brik A, Alexandratos J, Lin Y. C, Elder J. H, Olson A. J, Wlodawer A, Wong C. H. *Chem Bio Chem.* 2005;**6**:1167–2119.
30. National Committee for Clinical Laboratory Standards (NCCLS), *Nat Comm Lab Stands*, Villanova, 1982, pp 242.

HOW TO CITE THIS ARTICLE: Nagaraj A, Amala G, Raghaveer S. Synthesis and Antimicrobial Activity of Novel Imidazo[1,2-A]Pyridines Containing 1,2,3-Triazole. *J Adv Sci Res*. 2025;16(12): 13-18 **DOI:** 10.55218/JASR.2025161203