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RAPID COMMUNICATION

One-pot three-component condensation for the synthesis of 2,4,6-triarylpyridines and evaluation of their antimicrobial activity

D ASHOK[a,*], M RAM REDDY[a], RAVINDER DHARAVATH[a], NALAPARAJU NAGARAJU[a], KATTA RAMAKRISHNA[a], SRINIVAS GUNDU[a] and M SARASIJA[b]

[a]Green and Medicinal chemistry Laboratory, Department of Chemistry, Osmania University, Hyderabad, Telangana 500 007, India
[b]Department of Chemistry, Satavahana University, Karimnagar, Telangana 505 001, India
E-mail: ashokdou@gmail.com

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Abstract. A new series of 2,4,6-triarylpyridines are synthesised through one-pot three-component condensation of triazole pyrazolyl aldehydes and acetophenones with ammonium acetate in moderate to good yields. The structures of the synthesised compounds are confirmed by spectral methods *viz.* IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis. All these scaffolds are evaluated for their *in vitro* antimicrobial activity and found to exhibit promising antimicrobial potency.

Keywords. 2,4,6-triarylpyridine; aldehyde; ammonium acetate; sealed-tube; antimicrobial.

1. Introduction

The development of a new generation of antimicrobial drugs for the treatment of pathogenic diseases is needed due to dramatically increased multidrug resistance of various microorganisms against currently available antibiotics in the market.[1] Moreover, the diseases produced by the microorganisms lead to a tremendous loss in the economy and also threatens the living world.[2, 3]

In our day to day life, the study of nitrogen-containing heterocycles became an interesting topic for being the most abundant in nature and having various biological as well as industrial applications. 1,2,3-triazole, a five-membered heterocycle containing three nitrogen atoms has gained an enormous interest due to various biological applications such as anticancer,[4] anti-inflammatory,[5] anti-acetylcholinesterase,[6] anti-proliferative,[7] antiviral[8] and antimicrobial[9] agents. Also, 1,2,3-triazoles have great significance in medicinal chemistry as they act as pharmacophores and linkers between two or more scaffolds of interest in molecular hybridization approaches.[10] Drugs like TSAO[11] (anti-HIV agent), Cefatrizine[12] (antibiotic agent) and Tazobactum[13] (an antibacterial agent) are available in the market that contains 1,2,3-triazole moiety (Figure 1). Furthermore, the researchers are also focusing on the synthesis of pyrazole compounds, a five-membered heterocycle containing two nitrogen atoms. The great interest on pyrazoles is because of various pharmaceutical and biological applications including antimicrobial,[14] anticancer,[15] anti-inflammatory,[16] antiviral,[17] antibacterial[18] and antitubercular[19] activities. In recent years, several drugs are developed from the pyrazole derivatives such as Celecoxib[20] and Rimonabant[21] that are available in the market (Figure 1).

Pyridines are biologically significant nuclei found in many natural products such as vitamins (niacin and vitamin B_6), coenzymes (NAD) and alkaloids (trigonelline).[22] Pyridine scaffold is present in many drugs and pesticides due to special features *viz.,* stability, basic in nature, water-solubility, small molecular size and the ability of hydrogen bond forming. These also act as bioisosteres of amides, amines and heterocyclic rings containing nitrogen atoms.[23] Furthermore, the pyridine and its derivatives have various biological activities including antimicrobial,[24] anticancer,[25]

*For correspondence

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antitubercular,[26] antimalarial[27] and anti-inflammatory.[28] Some of the drugs like Sulfapyridine,[29] Salazosulfapyridine[30] and Mepyramine[31] contain the pyridine ring as active pharmacophore are available in the market (Figure 1).

From the literature survey, it is clear that the pyridine and its derivatives can be synthesised from various methods.[32] However many of these synthetic procedures suffer some disadvantages including multistep reactions, long reaction times, high usage of catalysts, low yield, the formation of a mixture of products and formation of by-products.[33] Nowadays these 2,4,6-triaryl substituted pyridines are also synthesised through the one-pot three-component condensation of aromatic aldehyde, ketones and ammonium acetate.[33–35] This procedure involves a reduction of time, cost and energy because in this method the intermediates are not isolated.

Based on the biological significance of 1,2,3-triazole, pyrazole, pyridine and advantage of multicomponent reactions, we designed and synthesised a series of new 2,4,6-triaryl substituted pyridine derivatives and evaluated the *in vitro* antimicrobial activity.

2. Experimental

2.1 *Materials*

All the chemicals and solvents were purchased from Sigma Aldrich and other commercial suppliers. Progress of the reaction was monitored by thin-layer

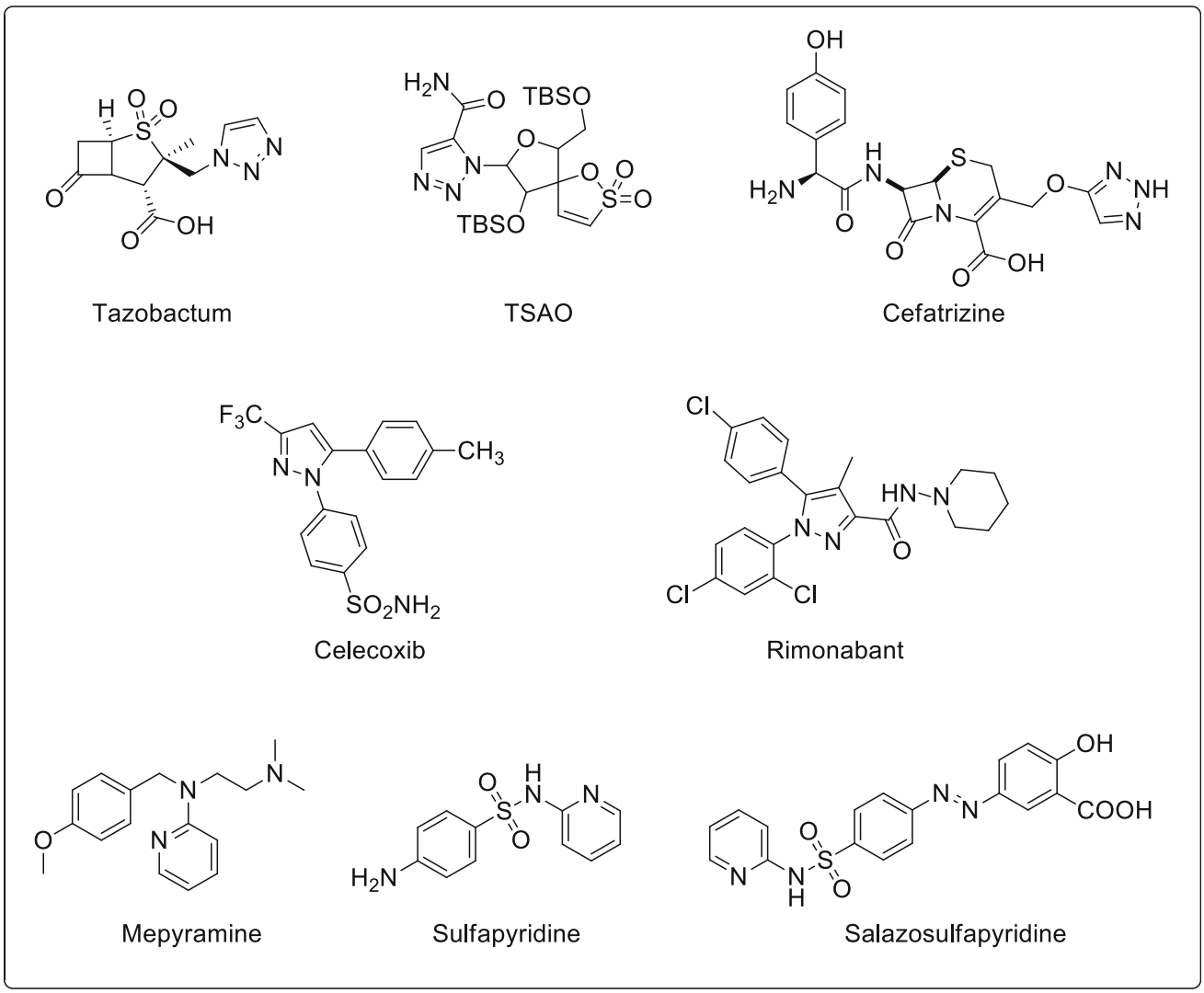


Figure 1. Some of the triazole, pyrazole and pyridine based drugs available in the market.

chromatography (TLC) on silica gel plates (60 F_{254}), visualizing with ultraviolet light. Column chromatography was performed on silica gel (60–120 mesh) using distilled hexane, ethyl acetate. ^{1}H NMR and ^{13}C NMR spectra were determined on Bruker AVANCE-400 spectrometer using $CDCl_3$ solvent at 400 and 100 MHz, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet). Coupling constants (J) are given in hertz. Infrared spectra were recorded on a Shimadzu FT-IR-8400s spectrometer. Melting points were determined using Stuart SMP3 melting point apparatus and are uncorrected.

2.2 *Synthesis*

General procedure for synthesis of 4-(3-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-aryl-1*H*-pyrazol-4-yl)-2,6-diarylpyridines 3(a-l) A mixture of triazolo pyrazolyl aldehydes **1(a-f)** (1 mmol), acetophenones **2(a,b)** (2 mmol) and NH_4OAc (0.308 g, 4 mmol) in DMF (10 mL) in a sealed-tube was heated at 100 °C for 6 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into crushed ice and the solid obtained was filtered, washed with excess water and dried. The crude product was purified by column chromatography using hexane and ethyl acetate (3:2, v/v) as eluent to afford the desired product.

2,6-Bis(4-methoxyphenyl)-4-(3-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3a) White solid; Yield: 80%; M.p.: 98–100 °C; IR (KBr, cm^{-1}): 2931, 1671, 1601, 1245, 832; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, Pyrazole-H), 8.10 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.88 (s, 2H, Ar-H), 7.85 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.52 (t, *J* = 8.2 Hz, 2H, Ar-H), 7.44–7.34 (m, 4H), 7.03 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.00 (t, *J* = 8.7 Hz, 4H, Ar-H), 3.87 (s, 6H, OCH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.42, 156.63, 142.73, 141.10, 139.62, 138.50, 133.11, 132.38, 129.59, 129.49, 129.35, 129.24, 128.32, 127.08, 126.59, 122.92, 119.16, 116.59, 114.69, 114.02, 55.37, 9.78; MS (ESI): 591 $[M+H]^+$.

2,6-Bis(3,4-dimethoxyphenyl)-4-(3-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3b) White solid; Yield: 66%; M.p.: 114–116 °C; IR (KBr, cm^{-1}): 2966, 1741, 1600, 1215; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H, Pyrazole-H), 7.76 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.72–7.70 (m, 3H, Ar-H), 7.59 (s, 2H, Ar-H), 7.46–7.09 (m, 6H, Ar-H), 7.09–7.07 (m, 3H, Ar-H), 6.88 (d, *J* = 8.0 Hz, 2H, Ar-H), 3.94 (s, 6H, OCH_3), 3.90 (s, 6H, OCH_3), 2.65 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.29, 153.12, 148.93, 144.11, 140.05, 139.41, 131.80, 130.37, 129.36, 126.97, 126.59, 126.00, 123.18, 122.04, 118.44, 114.65, 110.28, 110.09, 56.05, 55.64, 10.34; MS (ESI): 651 $[M+H]^+$.

4-(3-(1-(4-Bromophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)2,6-bis(4-methoxyphenyl)pyridine (3c) White solid; Yield: 78%; M.p.: 107–109 °C; IR (KBr, cm^{-1}): 2966, 1741, 1601, 1237, 830; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H, Pyrazole-H), 8.10 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.87 (s, 2H, Ar-H), 7.84 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.68 (d, *J* = 8.7 Hz, 4H), 7.52 (t, *J* = 8.2 Hz, 2H, Ar-H), 7.39–7.35 (m, 3H, Ar-H), 7.00 (d, *J* = 8.7 Hz, 4H, Ar-H), 3.86 (s, 6H, OCH_3), 2.39 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.44, 156.64, 142.37, 141.01, 139.56, 139.05, 135.32, 132.84, 132.78, 132.32, 129.62, 128.32, 127.16, 126.69, 126.56, 123.65, 123.01, 119.16, 116.66, 114.02, 55.38, 9.95; MS (ESI): 670 $[M+2]^+$.

4-(3-(1-(4-Bromophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)-2,6-bis(3,4-dimethoxyphenyl)pyridine (3d) White solid; Yield: 74%; M.p.: 118–120 °C; IR (KBr, cm^{-1}): 2967, 1741, 1597, 1214, 809; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H, Pyrazole-H), 7.98 (s, 2H, Ar-H), 7.86–7.84 (m, 4H, Ar-H), 7.70–7.67 (m, 4H, Ar-H), 7.53 (t, *J* = 8.5 Hz, 2H, Ar-H), 7.39–7.37 (m, 3H, Ar-H), 6.97 (d, *J* = 8.2 Hz, 2H, Ar-H), 4.02 (s, 6H, OCH_3), 3.95 (s, 6H, OCH_3), 2.43 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.55, 149.92, 149.09, 142.42, 141.00, 139.53, 139.10, 135.30, 133.01, 132.86, 132.59, 129.64, 127.21, 126.75, 126.51, 123.68, 122.93, 119.55, 119.15, 117.02, 111.03, 110.16, 56.03, 55.91, 10.03; MS (ESI): 730 $[M+2]^+$.

4-(3-(1-(4-Chlorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)-2,6-bis(4-methoxyphenyl)pyridine (3e) White solid; Yield: 80%; M.p:. 106–108 °C; IR (KBr, cm^{-1}): 2927, 1735, 1601, 1244, 831; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, Pyrazole-H), 8.09 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.87 (s, 2H, Ar-H), 7.84 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.54–7.49 (m, 4H, Ar-H), 7.44 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.36 (t, *J* = 7.2 Hz, 1H, Ar-H), 6.99 (d, *J* = 8.8 Hz, 4H, Ar-H), 3.86 (s, 6H, OCH_3), 2.38 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.45, 156.60, 142.37, 141.03, 139.57, 139.03, 135.64, 134.83, 132.91, 132.31, 129.84, 129.61, 128.31, 127.13, 126.33, 122.98, 119.14, 118.48, 116.65, 114.02, 55.36, 9.92; MS (ESI): 625 $[M+H]^+$.

4-(3-(1-(4-Chlorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)-2,6-bis(3,4-dimethoxyphenyl)pyridine (3f) White solid; Yield: 75%; M.p.: 90–92 °C; IR (KBr, cm^{-1}): 2966, 1741, 1601, 1237, 830; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H, Pyrazole-H), 7.99 (s, 2H, Ar-H), 7.86–7.84 (m, 3H, Ar-H), 7.69 (dd, *J* = 2.0 Hz, 8.2 Hz, 2H, Ar-H), 7.59–7.51 (m, 5H, Ar-H), 7.44 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.38 (t, *J* = 7.2 Hz, 1H, Ar-H), 6.98 (d, *J* = 8.7 Hz, 2H, Ar-H), 4.02 (s, 6H, OCH_3), 3.95 (s, 6H, OCH_3), 2.43 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.58, 149.99, 149.17, 142.49, 141.00, 139.57,

139.06, 135.68, 134.83, 133.02, 132.67, 129.86, 129.63, 127.20, 126.70, 126.28, 122.98, 119.56, 119.17, 117.03, 111.14, 110.28, 56.00, 55.97, 9.95; MS (ESI): 685 $[M+H]^+$.

4-(3-(1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-Pyrazol-4-yl)-2,6-bis(4-methoxyphenyl)pyridine (3g) White solid; Yield: 77%; M.p.: 148–150 °C; IR (KBr, cm^{-1}): 2966, 1741, 1600, 1239, 837; ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, Pyrazole-H), 8.11 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.88 (s, 2H, Ar-H), 7.85 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.53 (t, *J* = 7.7 Hz, 2H, Ar-H), 7.49–7.46 (m, 2H, Ar-H), 7.38 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.24 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.00 (d, *J* = 8.7 Hz, 4H, Ar-H), 3.87 (s, 6H, OCH_3), 2.37 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.19 (d, *J* = 259.7 Hz), 156.66, 155.12, 154.10, 152.56, 139.59, 138.81, 133.04, 130.17 (d, *J* = 2.2 Hz), 129.63, 128.34, 127.18, 127.16 (d, *J* = 8.8 Hz), 126.66, 123.01, 119.18, 116.71, 116.67 (d, *J* = 23.5 Hz), 114.04, 106.13, 55.38, 9.84; MS (ESI): 609 $[M+H]^+$.

2,6-Bis(3,4-dimethoxyphenyl)-4-(3-(1-(4-florophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3h) White solid; Yield: 72%; M.p.: 104–106 °C; IR (KBr, cm^{-1}): 2967, 1741, 1598, 1220, 810; ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H, Pyrazole-H), 7.99 (s, 2H, Ar-H), 7.86–7.84 (m, 4H, Ar-H), 7.69 (dd, *J* = 2.0 Hz, 8.5 Hz, 2H, Ar-H), 7.52 (t, *J* = 7.5 Hz, 2H, Ar-H), 7.48–7.45 (m, 2H, Ar-H), 7.37 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.25 (d, *J* = 7.2 Hz, 2H, Ar-H), 6.97 (d, *J* = 8.5 Hz, 2H, Ar-H), 4.02 (s, 6H, OCH_3), 3.94 (s, 6H, OCH_3), 2.41 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.95 (d, *J* = 250.9 Hz), 156.53, 149.93, 149.12, 142.52, 141.02, 139.55, 138.88, 133.18, 132.64, 132.41 (d, *J* = 2.9 Hz), 129.62, 127.17, 127.08 (d, *J* = 8.8 Hz), 126.71, 122.90, 119.54, 119.13, 117.00, 116.69 (d, *J* = 22.7 Hz), 111.08, 110.19, 55.98, 55.95, 9.88; MS (ESI): 669 $[M+H]^+$.

2,6-Bis(4-methoxyphenyl)-4-(3-(5-methyl-1-(*ρ*-tolyl)-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3i) White solid; Yield: 77%; M.p.: 122–124 °C; IR (KBr, cm^{-1}): 2967, 1741, 1601, 1237, 807; ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, Pyrazole-H), 8.10 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.88 (s, 2H, Ar-H), 7.85 (d, *J* = 7.5 Hz, 2H, Ar-H), 7.52 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.38–7.34 (m, 5H, Ar-H), 7.00 (d, *J* = 8.7 Hz, 4H, Ar-H), 3.86 (s, 6H, OCH_3), 2.44 (s, 3H, CH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.43, 156.64, 142.72, 141.16, 139.76, 139.63, 138.64, 132.94, 132.40, 130.56, 130.12, 129.58, 129.35, 128.33, 127.08, 126.59, 125.00, 119.16, 116.58, 114.02, 55.36, 21.24, 9.84; MS (ESI): 605 $[M+H]^+$.

2,6-Bis(3,4-dimethoxyphenyl)-4-(3-(5-methyl-1-(*ρ*-tolyl)-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3j) White solid; Yield: 74%; M.p.: 108–110 °C; IR (KBr, cm^{-1}): 2928, 1741, 1597, 1253, 807; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (s, 1H, Pyrazole-H), 7.98 (s, 2H, Ar-H), 7.86 (d, *J* = 7.7 Hz, 2H, Ar-H), 7.83–7.82 (m, 2H, Ar-H), 7.69 (dd, *J* = 1.7 Hz, 8.2 Hz, 2H, Ar-H), 7.52 (t, *J* = 7.5 Hz, 2H, Ar-H), 7.38–7.35 (m, 5H, Ar-H), 6.97 (d, *J* = 8.5 Hz, 2H, Ar-H), 4.01 (s, 6H, OCH_3), 3.94 (s, 6H, OCH_3), 2.45 (s, 3H, CH_3), 2.39 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.55, 149.94, 149.14, 142.77, 141.08, 139.79, 139.61, 138.67, 133.87, 133.06, 132.68, 130.13, 129.61, 127.12, 126.62, 124.93, 122.86, 119.56, 119.16, 116.92, 111.12, 110.23, 55.98, 55.96, 21.24, 9.88; MS (ESI): 665 $[M+H]^+$.

2,6-Bis(4-methoxyphenyl)-4-(3-(1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3k) White solid; Yield: 75%; M.p.: 94–96 °C; IR (KBr, cm^{-1}): 2967, 1741, 1601, 1237, 832; ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, Pyrazole-H), 8.10 (d, *J* = 8.7 Hz, 4H, Ar-H), 7.88 (s, 2H, Ar-H), 7.85 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.51 (t, *J* = 8.2 Hz, 2H, Ar-H), 7.40–7.34 (m, 3H, Ar-H), 7.03 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.00 (d, *J* = 8.7 Hz, 4H, Ar-H), 3.87 (s, 3H, OCH_3), 3.86 (s, 6H, OCH_3), 2.33 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.40, 160.36, 156.62, 142.71, 141.10, 139.59, 138.50, 133.12, 132.36, 129.61, 129.22, 128.33, 127.10, 126.60, 122.90, 119.14, 116.58, 114.68, 114.03, 113.99, 55.70, 55.42, 9.84; MS (ESI): 621 $[M+H]^+$.

2,6-Bis(3,4-dimethoxyphenyl)-4-(3-(1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-1-phenyl-1*H*-pyrazol-4-yl)pyridine (3l) White solid; Yield: 70%; M.p.: 150–152 °C; IR (KBr, cm^{-1}): 2928, 1741, 1597, 1253, 807; ^1H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, 1H, Pyrazole-H), 7.98 (s, 2H, Ar-H), 7.86–7.83 (m, 4H, Ar-H), 7.69 (dd, *J* = 2.0 Hz, 8.5 Hz, 2H, Ar-H), 7.52 (t, *J* = 8.2 Hz, 2H, Ar-H), 7.39–7.37 (m, 3H, Ar-H), 7.04 (d, *J* = 8.7 Hz, 2H, Ar-H), 6.98 (d, *J* = 8.2 Hz, 2H, Ar-H), 4.02 (s, 6H, OCH_3), 3.94 (s, 6H, OCH_3), 3.88 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.37, 156.53, 149.91, 149.11, 142.80, 141.08, 139.59, 138.54, 133.23, 132.67, 129.61, 129.21, 127.12, 126.62, 126.53, 122.84, 119.55, 119.14, 116.93, 114.69, 111.08, 110.18, 55.98, 55.96, 55.65, 9.82; MS (ESI): 681 $[M+H]^+$.

2.3 *Antimicrobial activity*

2.3a *Antibacterial assay*: The test organisms were cultured on Muller Hinton Agar (MHA) slants, incubated at 37 ± 0.5 °C for 24 h and the synthesized compounds were evaluated for antibacterial activity against these freshly prepared strains of test organisms by agar diffusion method. The broth cultures were diluted with sterilized saline to bring the final size of inoculum approximately to 10^5–10^6 CFU/mL. The compounds were diluted in acetone, DMSO, and diethyl ether for biological assays. Among the three solvents, diethyl ether turned out to be a better solvent than the remaining two solvents. The bacterial culture was placed in the media and incubated at 37 °C for 24 h along with the

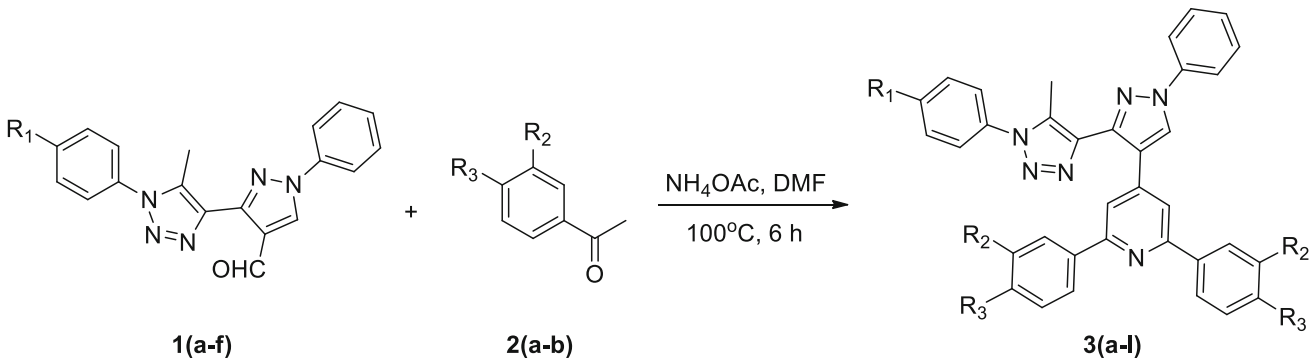
diluted compounds introduced through discs dipped and placed over the nutrient media. The disc of Streptomycin was also incorporated into the medium for comparison. Growth inhibition of bacterial strains in the presence of tested compounds and standards was measured with the help of the standard scale.

2.3b *Antifungal Assay*: The test organisms were cultured on Potato Dextrose Agar (PDA) incubated at 27 ± 0.2 °C for 24–48 h and the antifungal activity of synthesized compounds were evaluated by poison plate technique. The broth cultures were diluted with sterilized saline to bring the final size of inoculum approximately to 10^5–10^6 CFU/mL. The compounds were diluted in acetone, DMSO, and diethyl ether for biological assays. Among the three solvents, diethyl turned out to be a better solvent than the remaining two solvents. The culture strains of fungi were maintained on potato dextrose agar and spores were transferred to the PDA medium and the plates were then incubated at 27 ± 0.2 °C for 24–48 h. Growth inhibition of fungal strains in the presence of test material and a standard, Nystatin, was measured with the help of standard scale.

3. Results and Discussion

3.1 *Chemistry*

The synthetic route adopted for the synthesis of the titled compounds is depicted in Scheme 1. To obtain the title compounds **3(a-l)**, initially the triazolo pyrazolyl aldehydes **1(a-f)** were synthesized according to the literature protocol.[36] Compounds **1(a-f)** on reaction with substituted acetophenones **2(a,b)** and ammonium acetate in DMF solvent gave the title compounds. To improve the yields and to develop an



3a: R_1 = H; R_2 = H; R_3 = OCH_3
3b: R_1 = H; R_2 = OCH_3; R_3 = OCH_3
3c: R_1 = Br; R_2 = H; R_3 = OCH_3
3d: R_1 = Br; R_2 = OCH_3; R_3 = OCH_3
3e: R_1 = Cl; R_2 = H; R_3 = OCH_3
3f: R_1 = Cl; R_2 = OCH_3; R_3 = OCH_3
3g: R_1 = F; R_2 = H; R_3 = OCH_3
3h: R_1 = F; R_2 = OCH_3; R_3 = OCH_3
3i: R_1 = CH_3; R_2 = H; R_3 = OCH_3
3j: R_1 = CH_3; R_2 = OCH_3; R_3 = OCH_3
3k: R_1 = OCH_3; R_2 = H; R_3 = OCH_3
3l: R_1 = OCH_3; R_2 = OCH_3; R_3 = OCH_3

Scheme 1. Synthetic route for the preparation of title compounds.

Table 1. Optimisation of reaction conditions to synthesis the compound **3a**.

S. No.	Solvent	Temperature (°C)	Time (h)	Yield (%)
1	Acetonitrile	80	6	60
2	Methanol	65	6	65
3	Ethanol	80	6	69
4	Toluene	110	6	68
5	DMF	100	6	80
6	DMF	120	6	78
7	DMF	150	8	77

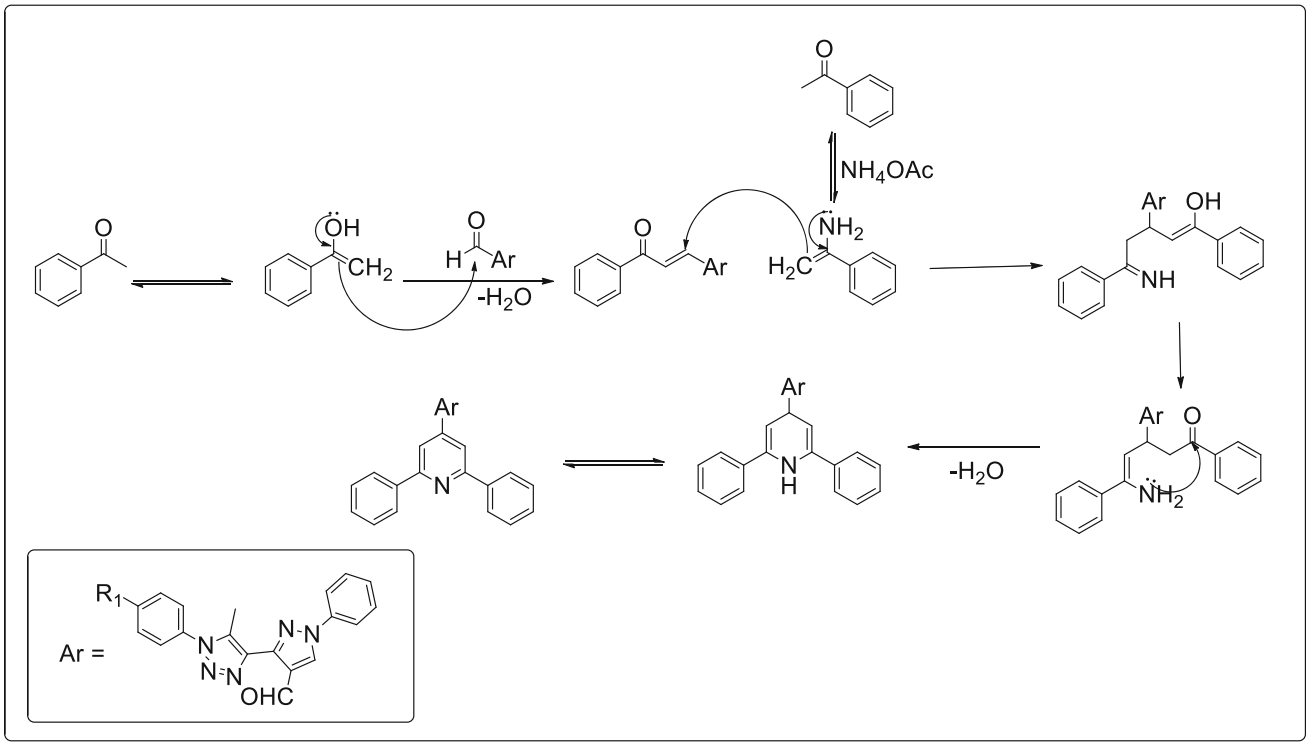


Figure 2. Plausible mechanism for the title compounds.

Table 2. Antibacterial and antifungal activities of compounds **3(a-1).**

Zone of inhibition (mm) after 24 h

	Gram-positive bacteria				Gram-negative bacteria				Fungal strains	
	S. aureus		*B. subtills*		*P. putida*		*E. coli*		*A. niger*	*A. flavus*
Compound	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	10 µg/mL	20 µg/mL	50 µg/mL	50 µg/mL
3a	5	11	7	13	6.5	10.5	6	10	8	7
3b	6	13	8	12	6.5	11	6.5	12	9	8.5
3c	6	12	8	13	6	12	7	13	8	9
3d	8	15	9	16	7.5	15	9	16	15	13
3e	7	14	8	14	7	13	7.5	14	11	10
3f	10	16.5	11	18	9.5	18	11	19	15.8	14
3g	8.5	15.5	9	16.5	8	16	9	17	15	15
3h	12.5	17.5	13.5	18	11	20.5	13	20	17	17.5
3i	7	14	8	15	6.5	14	8	15	12	10
3j	9	15.5	9.5	16	8.5	17	10	17	16	14.5
3k	11	16.5	12	18.5	10.5	19	12	20.5	16.5	16
3l	12	18	14	19	11	20	13	21	18	17
Streptomycin	9	16	10	17	9	17	10	18	-	-
Nystatin	-	-	-	-	-	-	-	-	16	15

efficient synthetic protocol, a preliminary study of the effect of solvents and temperature on synthesis of title compounds has been carried out by synthesizing compound **3a** using different solvents as shown in Table 1.

From the optimisation study (Table 1) it is clear that all the solvents gave moderate to good yields. Among them, DMF was found to be the better solvent to carry out the reaction. Furthermore, there is no greater increment in the yield, when the temperature and

reaction time was increased. Based on the preliminary optimisation study results, synthesised the desired compounds **3(a-l)** by carrying the reaction in DMF solvent at 100 °C for 6 h. The plausible mechanism for the formation for title compounds is depicted in Figure 2.

3.2 *Antimicrobial activity*

All the synthesised compounds **3(a-l)** were evaluated for their *in vitro* antimicrobial activity using Agar-well diffusion method by measuring the zone of inhibition in mm. Antibacterial activity was evaluated against two Gram-positive bacterial strains *viz., Staphylococcus aureus* and *Bacillus subtills* and two Gram-negative bacterial strains *viz., Pseudomonas putida* and *Escherichia coli* at two different concentrations (10 µg/mL and 20 µg/mL). Streptomycin was used as a standard drug and the results were depicted in Table 2. Furthermore, the compounds were screened for their *in vitro* antifungal activity against two fungal strains *viz. Aspergillus Niger* and *Aspergillus Flavus* at 50 µg/mL concentration, by using Nystatin as a standard drug and the results were depicted in Table 2.

From Table 2, it can be envisaged that most of the title compounds displayed moderate to good activity. Among all the synthesised scaffolds, compounds **3l**, **3h**, **3k** and **3f** exhibited higher zone of inhibition and the compounds **3j**, **3g** and **3d** displayed equipotent zone of inhibition with the standard drug against bacterial strains. Furthermore, the compounds **3l**, **3h** and **3k** shown higher zone of inhibition and the compounds **3j**, **3g**, **3f** and **3d** shown moderate zone of inhibition against the tested fungal strains.

4. Conclusions

In conclusion, we synthesised a series of new 4-(3-(5-methyl-1-aryl-1*H*-1,2,3-triazol-4-yl)-1-aryl-1*H*-pyrazol-4-yl)-2,6-diarylpyridine derivatives through the one-pot three-component condensation method. The higher yields, reduced reaction time, minimal purification, simplicity in procedure and low cost are the advantages of the reported method. Furthermore, the compounds **3l**, **3h**, **3k** and **3f** exhibited promising antibacterial activity and the compounds **3l**, **3h** and **3k** displayed good antifungal activity against the tested microorganisms.

Supplementary Information (SI)

Figures S1-S24 are available at www.ias.ac.in/chemsci.

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