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# One-Pot Synthesis of Pyrazine-2-carbaldehyde Containing 1,2,3-Triazoles: *In vitro* Antibacterial Activity

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In pursuit of enhanced antibacterial agents, a series of 3-(4-(aryl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehydes was synthesised (**4a-k**) through the utilisation of 3-aminopyrazine-2-carbaldehyde, alkyne and triflyl azide *via* an *in situ* synthesised 3-azidopyrazine-2-carbaldehyde, followed by an assessment of their *in vitro* antibacterial activity. The investigation of antibacterial efficacy was conducted against three Gram-positive bacterial strains *viz*. *Bacillus subtilis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, employing the standard broth microdilution methodology. Among the compounds evaluated, compounds **4f** and **4k** demonstrated significant antibacterial efficacy, with minimum inhibitory concentration (MIC) values ranging from 3.12 ± 0.39 to 12.5 ± 0.87 µg/mL against the examined Gram-positive bacterial strains. Ultimately, further structural optimization of these potent compounds may lead to their development as promising candidates for future therapeutic applications.

**Keywords: Pyrazine-2-carbaldehyde, 1,2,3-Triazoles, Synthesis, Antibacterial activity.**

## INTRODUCTION

The growing resistance of pathogenic microorganisms to existing antibiotic therapies poses a significant challenge for the public health organisations globally [1,2]. Bacteria are minuscule, single-celled entities; mostly are innocuous to humans, while specific strains confer advantageous effects [3]. A diverse array of bacteria possesses pathogenic qualities, potentially resulting in significant infectious diseases [4]. The oversight of microbial infections instigated by resistant pathogens represents a considerable challenge within the realm of public health [5]. This has led to a significant need for the development of innovative and more effective antimicrobial agents that demonstrate a wide range of inhibitory activity, effectiveness and reduced toxicity. A robust approach to the development of new antimicrobial agents requires the investigation of innovative mechanisms of action and structural alterations to improve target selectivity and efficacy [6,7].

Nitrogen-containing heterocyclic compounds play a crucial role in the fields of medicine and agrochemicals [8]. Among the various heterocyclic systems in organic chemistry, the five-membered compounds that include 1,2,3-triazoles and their derivatives hold significant importance due to their diverse applications in medical, pharmacological, biochemical and material research [9-20]. A number of compounds based on 1,2,3-triazole have been synthesised for the purpose of antibacterial applications [21]. Fig. 1 depicts a selection of commercially available pharmaceuticals, such as tazobactam and cefatrizine, which incorporate 1,2,3-triazole and are acknowledged for their efficacy as potent antibiotics [22]. In a similar vein, a multitude of biological studies have explored the therapeutic significance of pyrazine-containing substances in relation to human health and disease [23-26]. In 2019, the WHO model list of essential medicines featured two pyrazine-based compounds, pyrazinamide and sulfametopyrazine, which are FDA-approved antibacterial agents, as illustrated in Fig. 1 [27].

Considering the significant contributions of 1,2,3-triazoles and pyrazine in the advancement of various antibacterial agents, the application of molecular hybridisation techniques [28] to obtain highly effective biologically active substances and the ongoing investigations into the synthesis and biological assessment of new heterocyclic compounds [29,30]. In this study, we aimed to synthesise a series of novel 3-(4-(aryl)-1*H*-1,2,3-

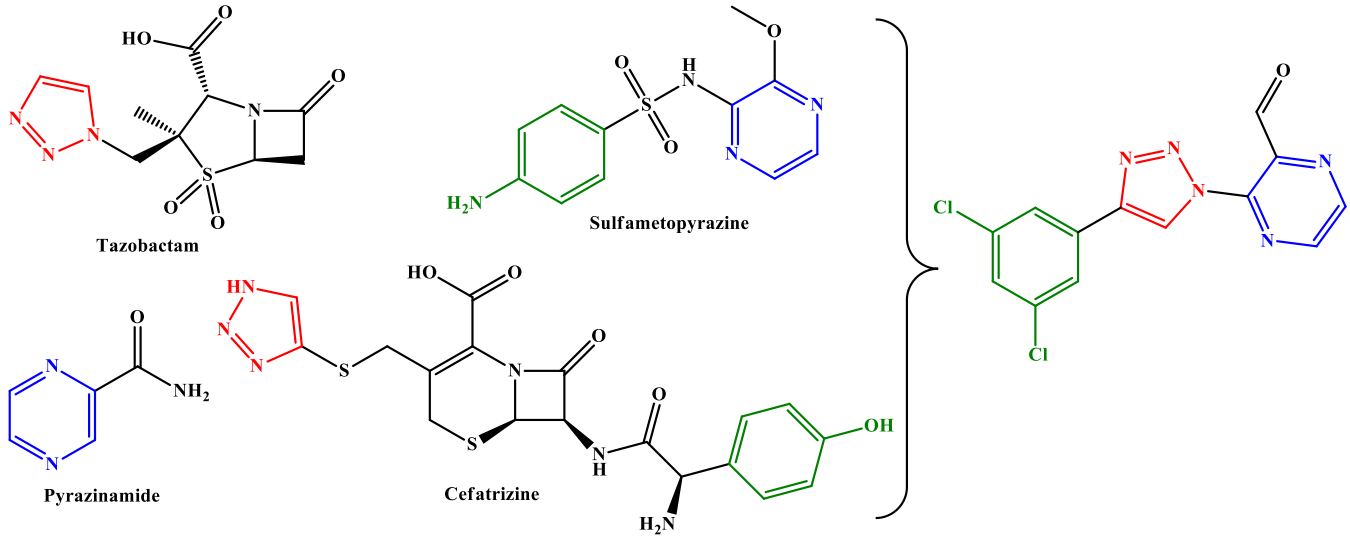



Fig. 1. Chemical structure of some FDA approved antibacterial drugs containing 1,2,3-triazoles and pyrazine moiety

triazol-1-yl)pyrazine-2-carbaldehyde (**4a-k**) in a one-pot reaction using a cost-effective Cu-catalysed 1,3-dipolar cycloaddition through an *in situ* generated azide.

## EXPERIMENTAL

All the reactants were purchased from the Aldrich Chemicals Company. All the reagents and solvents were purchased from SD Fine Chemicals Limited and used without further purification. Thin-layer chromatography (TLC) was performed using Merck silica gel $60F_{254}$ precoated plates (0.25 mm) and silica gel (particle size 60-120 mesh) was used for column chromatography. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker (operating at 400 MHz for $^1$H and 100 MHz for $^{13}$C). Mass spectra were recorded on a Jeol JMC-300 spectrometer (ESI, 70 eV). Elemental analyses were performed on Carlo Erba 106 and Perkin-Elmer model 240 analyzers. Melting points were determined using a Cintex apparatus and are uncorrected.

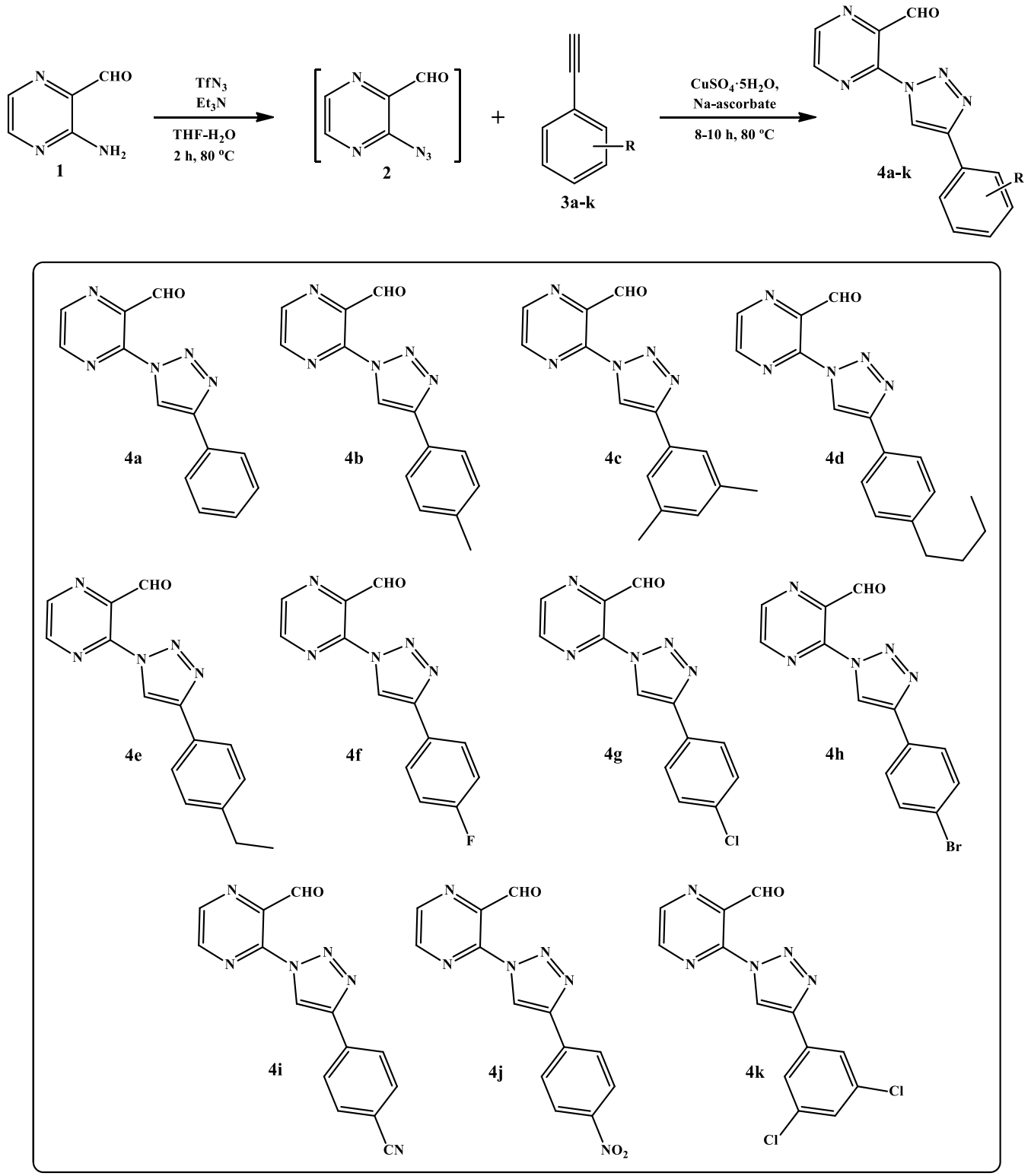
**General synthesis of 3-(4-(aryl)-1*H*-1,2,3-triazol-1-yl)-pyrazine-2-carbaldehyde (4a-k):** To a mixture of 3-amino-pyrazine-2-carbaldehyde (0.4 g, 3.2 mmol), alkyne (3.0 mmol) and triflyl azide (3.2 mmol) in a solvent mixture of THF and $H_2O$ (10 mL). To this solution, incorporate TEA, $CuSO_4 \cdot 5H_2O$ at a concentration of 10 mmol% and sodium ascorbate also at 10 mmol%. The reaction mixture underwent stirring for a duration of 3 h at ambient temperature, subsequently being subjected to heating at 60 ºC for a period ranging from 10 to 12 h. Upon concluding the reaction through TLC, the reaction mixture was meticulously transferred into a 20 mL of ice water. The resultant solid underwent a washing process with water and was subsequently dried under vacuum for 1 h (**Scheme-I**). The crude product obtained was then subjected to purification *via* column chromatography utilizing a hexane/ethyl acetate gradient, yielding the pure desired 1,2,3-triazoles in good yields.

**3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4a):** Dirty white solid; yield: 78%; m.p.: 81-83 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.63 (s, 1H, Alde-H), 8.96 (s, 1H, tri-H), 8.72 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.45 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.56 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.36-7.31 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 188.70, 152.24, 147.20, 145.23, 143.01, 139.20, 134.08, 129.34 (2C), 128.03, 126.80, 124.76 (2C); ESI-MS: 252 $[M+H]^+$; Elemental analysis of $C_{13}H_9N_5O$; calcd. (found) %: C, 62.15 (62.17); H, 3.61 (3.58); N, 27.87 (27.84).

**3-(4-(*p*-Tolyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4b):** Pale yellow solid; yield: 74%; m.p.: 86-88 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.63 (s, 1H, Alde-H), 8.94 (s, 1H, tri-H), 8.73 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.46 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.57 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.36 (d, *J* = 8.0 Hz, 2H, Ar-H), 2.23 (s, 3H, Ar-$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.68, 152.24, 147.08, 145.34, 143.36, 139.36, 136.19, 130.80, 129.10 (2C), 128.22, 126.25 (2C), 21.22; ESI-MS: 266 $[M+H]^+$; Elemental analysis of $C_{14}H_{11}N_5O$; calcd. (found) %: C, 63.39 (63.38); H, 4.18 (4.16); N, 26.40 (26.37).

**3-(4-(3,5-Dimethylphenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4c):** Dirty white solid; yield: 71%; m.p.: 107-109 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.65 (s, 1H, Alde-H), 8.96 (s, 1H, tri-H), 8.75 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.46 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.53 (s, 2H, Ar-H), 7.07 (s, 1H), 2.06 (s, 6H, Ar-$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.78, 152.21, 147.45, 145.22, 143.02, 139.50, 135.32 (2C), 128.75, 127.14, 126.51, 123.64 (2C), 20.48 (2C); ESI-MS: 280 $[M+H]^+$; Elemental analysis of $C_{15}H_{13}N_5O$; calcd. (found) %: C, 64.51 (64.48); H, 4.69 (4.68); N, 25.07 (25.05).

**3-(4-(4-Butylphenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4d):** Pale yellow solid; yield: 72%; m.p.: 113-115 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.62 (s, 1H, Alde-H), 8.94 (s, 1H, tri-H), 8.73 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.45 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.63 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.18 (d, *J* = 8.0 Hz, 2H, Ar-H), 2.50 (t, *J* = 4.0Hz, 2H, -$CH_2$-), 1.73-1.68 (m, 2H, -$CH_2$-), 1.36-1.32 (m, 2H, -$CH_2$-), 0.94 (t, *J* = 4.0 Hz, 3H, -$CH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.43, 152.32, 147.15, 145.24, 143.30, 141.09, 139.21, 132.86, 128.44, 127.15 (2C), 125.23 (2C),




**Scheme-I:** Synthesis of 3-(4-(aryl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (**4a-k**) and their isolated yields

36.65, 30.63, 20.46, 13.81; ESI-MS: 308 $[M+H]^+$; Elemental analysis of $C_{17}H_{17}N_5O$; calcd. (found) %: C, 66.43 (66.41); H, 5.58 (5.60); N, 22.79 (22.77).

**3-(4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4e):** Pale yellow solid; yield: 70%; m.p.: 105-107 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): δ 10.65 (s, 1H, Alde-H), 8.96 (s, 1H, tri-H), 8.74 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.46 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.71 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.00 (d, *J* = 8.0 Hz, 2H, Ar-H), 3.84 (s, 3H, $-OCH_3$); $^{13}$C NMR (100 MHz, $CDCl_3$): 187.43, 159.50, 152.32, 147.15, 145.24, 143.51, 139.21, 128.71, 125.23 (2C), 124.27, 114.44 (2C), 55.71; ESI-MS: 282 $[M+H]^+$; Elemental anal-

ysis of $C_{14}H_{11}N_5O_2$; calcd. (found) %: C, 59.78 (59.76); H, 3.94 (3.91); N, 24.90 (24.88).

**3-(4-(4-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4f):** Pale yellow solid; yield: 54%; m.p.: 98-100 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.63 (s, 1H, Alde-H), 8.95 (s, 1H, tri-H), 8.75 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.45 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.15 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.89 (d, *J* = 8.0 Hz, 2H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 188.63, 163.75, 161.64, 152.24, 147.86, 145.51, 143.38, 139.54, 129.68, 129.61, 128.64, 126.50, 115.46, 115.25; ESI-MS: 270 $[M+H]^+$; Elemental analysis of $C_{13}H_8FN_5O$; calcd. (found) %: C, 57.99 (57.96); H, 3.00 (2.98); N, 26.01 (25.97).

**3-(4-(4-Chlorophenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4g):** White solid; yield: 54%; m.p.: 92-94 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.64 (s, 1H, Alde-H), 8.96 (s, 1H, tri-H), 8.75 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.46 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.80 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.51 (d, *J* = 8.0 Hz, 2H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.78, 152.75, 147.86, 145.28, 143.44, 139.65, 134.37, 130.28, 129.34 (2C), 128.50, 126.28 (2C); ESI-MS: 286 $[M+H]^+$. Elemental analysis of $C_{13}H_8ClN_5O$; calcd. (found) %: C, 54.65 (54.63); H, 2.82 (2.80); N, 24.51 (24.47).

**4-(4-Bromophenyl)-1-(1-methyl-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole (4h):** Pale red solid; yield: 54%; m.p.: 117-119 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.64 (s, 1H, Alde-H), 8.95 (s, 1H, tri-H), 8.76 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.45 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.68 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.48 (d, *J* = 8.0 Hz, 2H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.15, 152.01, 147.07, 145.45, 143.33, 139.89, 132.37 (2C), 128.47, 127.37, 126.48 (2C), 123.35; ESI-MS: 330 $[M+H]^+$; Elemental analysis of $C_{13}H_8BrN_5O$; calcd. (found) %: C, 47.30 (47.28); H, 2.44 (2.41); N, 21.21 (21.18).

**4-(1-(3-Formylpyrazin-2-yl)-1*H*-1,2,3-triazol-4-yl)-benzonitrile (4i):** Pale green solid; yield: 54%; m.p.: 102-104 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.66 (s, 1H, Alde-H), 8.98 (s, 1H, tri-H), 8.76 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.47 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.98 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.53 (d, *J* = 8.0 Hz, 2H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.15, 152.01, 147.07, 145.45, 143.33, 139.89, 132.48, 130.14 (2C), 128.47, 125.27 (2C), 119.12, 113.07.; ESI-MS: 277 $[M+H]^+$. Elemental analysis of $C_{14}H_8N_6O$; calcd. (found) %: C, 60.87 (60.85); H, 2.92 (2.89); N, 30.42 (30.39).

**3-(4-(4-Nitrophenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (4j):** White solid; yield: 54%; m.p.: 121-123 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.69 (s, 1H, Alde-H), 8.99 (s, 1H, tri-H), 8.79 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.48 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.31 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.98 (d, *J* = 8.0 Hz, 2H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.15, 152.01, 147.07, 146.40, 145.45, 143.33, 139.89, 134.60, 128.47, 126.82 (2C), 124.45 (2C); ESI-MS: 297 $[M+H]^+$; Elemental analysis of $C_{13}H_8N_6O_3$; calcd. (found) %: C, 52.71 (52.68); H, 2.72 (2.70); N, 28.37 (28.34).

**3-(4-(3,5-Dichlorophenyl)-1*H*-1,2,3-triazol-1-yl)pyrazine- 2-carbaldehyde (4k):** Yellow solid; yield: 54%; m.p.: 125–127 ºC; $^1$H NMR (400 MHz, $CDCl_3$, δ ppm): 10.66 (s, 1H, Alde-H), 8.97 (s, 1H, tri-H), 8.76 (d, *J* = 8.0 Hz, 1H, pyrazine), 8.45 (d, *J* = 8.0 Hz, 1H, pyrazine), 7.72 (s, 2H, Ar-H), 7.45 (s, 1H, Ar-H); $^{13}$C NMR (100 MHz, $CDCl_3$, δ ppm): 187.15, 152.01, 147.07, 145.45, 143.33, 139.89, 134.40 (2C), 132.64, 127.38, 124.62, 124.39 (2C); ESI-MS: 320 [M+H; Elemental analysis of $C_{13}H_7Cl_2N_5O$; calcd. (found) %: C, 48.77 (48.75); H, 2.20 (2.17); N, 21.88 (21.84).

**Antibacterial activity:** To assess the antibacterial efficacy of synthesized derivatives **4a-k** against *Bacillus subtilis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, a broth microdilution method was employed. Bacterial cultures were prepared by inoculating nutrient broth with fresh colonies and incubating them at 37 ºC for 24 h to reach a concentration of approximately $1 \times 10^8$ CFU/mL. Each compound was dissolved in a solvent to prepare a stock solution, which was then serially diluted in a 96-well microtiter plate containing nutrient broth. Following the addition of the bacterial culture and a positive control (dicloxacillin), the plate was incubated at 37 ºC for 24 h. The antibacterial activity was evaluated by observing the turbidity in the wells, with the Minimum Inhibitory Concentration (MIC) being defined as the lowest compound concentration exhibiting no visible growth.

## RESULTS AND DISCUSSION

**Scheme-I** delineates the methodology employed in the synthesis of the intended final compounds. The commercially available 3-aminopyrazine-2-carbaldehyde (**1**) undergoes a reaction with $TfN_3$ and various aryl alkynes (**3**) through a one-pot Cu-catalysed [3+2] cycloaddition process, facilitated by the *in situ* generation of 3-azidopyrazine-2-carbaldehyde (**2**). The structures of all newly synthesized pyrazine-based 1,2,3-triazole derivatives (**4a-k**) were confirmed using $^1$H NMR, $^{13}$C NMR and mass spectrometric techniques.

All the spectral and analytical data of the synthesised compounds were in full agreement with the proposed structures and also discussed for a representative compound **4e**. $^1$H NMR reveals significant signals at δ 10.65 (s, 1H, aldehyde), δ 8.96 (s, 1H, tri-substituted), δ 8.74 (d, *J* = 8.0 Hz, 1H) and δ 8.46 (d, *J* = 8.0 Hz, 1H) corresponding to pyrazine protons, alongside δ 7.71 (d, 2H) and δ 7.00 (d, 2H) for the 4-methoxybenzene protons, while δ 3.84 (s, 3H) confirms the methoxy group. The $^{13}$C NMR spectrum shows signals at δ 187.43 (1C, aldehyde), δ 159.50 (1C, methoxy carbon), 125.23 (2C) and 114.44 (2C) for 4-methoxybenzene, with an additional signal at δ 55.71 (1C) for the methoxy carbon, substantiating the expected carbon environments. An ESI-Mass spectrum peak at *m/z* 282 for the [M+H] ion, coupled with elemental analysis confirms the molecular formula $C_{14}H_{11}N_5O_2$ for compound **4e**.

**Antibacterial activity:** The synthesised derivatives **4a-k** underwent assessment for their antibacterial efficacy against *B. subtilis*, *S. aureus* and *S. epidermidis* through the established broth microdilution method. The positive control employed was dicloxacillin. Table-1 presents the findings regarding the minimum inhibitory concentrations (MICs) of all newly synthesised compounds, measured in µg/mL.

Table-1 clearly shows that the majority of synthesised compounds were shown good to moderate activity with MIC

TABLE-1
*In vitro* ANTIBACTERIAL ACTIVITY DATA OF COMPOUNDS **(4a-k)**

| Compound | R | MIC (μg/mL)[a] | | |
|---|---|---|---|---|
| | | *B. subtilis* | *S. aureus* | *S. epidermidis* |
| **4a** | H | – | – | – |
| **4b** | 4-Me | 50 ± 1.89 | 50 ± 1.69 | – |
| **4c** | 3,5-diMe | 50 ± 1.71 | 50 ± 1.84 | – |
| **4d** | 4-$C_4H_9$ | 50 ± 1.21 | 50 ± 1.66 | 50 ± 1.32 |
| **4e** | 4-OMe | 25 ± 1.21 | 25 ± 1.08 | 25 ± 1.37 |
| **4f** | 4-F | 3.12 ± 0.78 | 6.25 ± 0.62 | 12.5 ± 1.09 |
| **4g** | 4-Cl | 6.25 ± 0.77 | 12.5 ± 0.83 | 25 ± 1.12 |
| **4h** | 4-Br | 12.5 ± 1.35 | 25 ± 1.02 | 50 ± 1.37 |
| **4i** | 4-CN | 12.5 ± 1.16 | 25 ± 1.67 | 25 ± 0.92 |
| **4j** | 4-$NO_2$ | 25 ± 1.24 | 25 ± 1.08 | 25 ± 1.31 |
| **4k** | 3,5-diCl | 3.12 ± 0.44 | 3.12 ± 0.39 | 12.5 ± 0.87 |
| Standard | Dicloxacillin | 1.56 ± 0.42 | 1.56 ± 0.33 | 6.25 ± 0.41 |

[a]MIC: *i.e.*, the lowest concentration of the test compound to inhibit the growth of bacteria.
Values are expressed as mean ± SD, "–" indicates concentration > 50 mg $mL^{-1}$.

values ranging from 3.12 ± 0.39 to 12.5 ± 0.87 μg/mL. Among all, compound **4k**, which has 3,5-dichlorophenyl groups attached to the 1,2,3-triazole ring, shows more potent activity against two tested bacterial strains *B. subtilis* (MIC = 3.12 ± 0.44 μg/mL) and *S. aureus* (MIC = 3.12 ± 0.39 vg/mL) and *S. epidermidis* (MIC = 12.5 ± 0.87 μg/mL) compared with standard dicloxacillin (MIC = 1.56 ± 0.42, 1.56 ± 0.33 and 6.25 ± 0.41 (μg/mL). Similarly, compound (**4f**) which has a 4-fluorophenyl group on the 1,2,3-triazole ring, shows good activity against tested bacterial strains *B. subtilis* (MIC = 3.12 ± 0.78 μg/mL), *S. aureus* (MIC = 6.25 ± 0.62 μg/mL) and *S. epidermidis* (MIC = 12.5 ± 0.87 μg/mL). Compound which containing 4-chlorophenyl group on 1,2,3-triazole ring (**4g**) shows good activity against *B. subtilis* (MIC = 6.25 ± 0.77 μg/mL) and moderate activity against *S. aureus* (MIC = 12.5 ± 0.83 μg/mL). The remaining compounds exhibited moderate to poor antibacterial activity against the tested bacterial strains. Notably, those containing electron-withdrawing substituents on the 1,2,3-triazole ring displayed improved antibacterial efficacy, emphasizing the significant impact of electronic effects on their biological performance. This observation suggests that the electronic nature of substituents plays a crucial role in enhancing the antimicrobial properties of these compounds.

## Conclusion

A series of new 3-(4-(aryl)-1*H*-1,2,3-triazol-1-yl)pyrazine-2-carbaldehyde (**4a-k**) were synthesised employing a one-pot Cu-catalysed cycloaddition *via* an *in situ* produced 3-azidopyrazine-2-carbaldehyde (**2**) and various aryl terminal alkynes. All newly synthesised derivatives were confirmed by $^1$H NMR, $^{13}$C NMR and mass analysis. Antibacterial activity *in vitro* against three Gram-positive bacterial strains of *B. subtilis*, *S. aureus* and *S. epidermidis*. Among all newly synthesised derivative compounds, those containing 3,5-dichlorophenyl (**4k**) and 4-fluorophenyl (**4f**) show good activity compared to the remaining compounds. The current study's findings may be considered for the design of a new class of very effective pharmacological compounds against Gram-positive infections.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

## DECLARATION OF AI-ASSISTED TECHNOLOGIES

During the preparation of this manuscript, the authors used an AI-assisted tool(s) to improve the language. The authors reviewed and edited the content and take full responsibility for the published work.

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