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Synthesis and antimycobacterial evaluation of new 1-substituted benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole Derivatives

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ABSTRACT

A new series of 1-substituted benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole derivatives, 5a-k have been synthesized. The structure of the newly synthesized compounds was determined by spectral analysis. The title compounds were screened for their preliminary antitubercular activity against Mycobacterium tuberculosis H37Ra active and dormant (MTB, ATCC 25177) and antimicrobial activity against standard Gram-negative bacteria, Escherichia coli (NCIM 2576), Pseudomonas flurescence (NCIM 2059) and Gram-positive bacteria, Staphylococcus aureus (NCIM 2602), Bacillus subtilis (NCIM 2162). Most of the synthesized compounds reported moderate activity against M. tuberculosis H37Ra and Bacillus subtilis strains.

Keywords:1,2,3-Triazole,Pyrazole,Antitubercular Activity, Antibacterial Activity

I. INTRODUCTION

Mycobacterium tuberculosis (MTB) was one of the top 10 causes of death worldwide and was responsible for more deaths than HIV and malaria [1]. Due to emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens in the last decades, a need for new classes of antimicrobial agents is warranted. The increase in antibiotic resistance due to multiple factors has encouraged the search for new compounds which are active against multi-drug resistant pathogens.

The synthesis of motifs containing more than one heterocycle ring has received much attention in recent years. Triazole and its derivatives are important class of bioactive molecules. Among other heterocyclic derivatives, triazole compounds were reported as most promising candidates towards anti-TB activity [2-8]. They also exhibit significant pharmacological activities such as anti-microbial [9,10], anti-convulsant [11], anti-proliferative [12], anti-cancer [13], anti-malarial [14] β-lactamase inhibitors [15], fungicidal [16], insecticidal [17] and anti-viral activity [18].

Pyrazole and its derivatives are important structure in medicinal chemistry that could provide a rich spectrum of biological activities [19-28]. The structural diversity and biological importance of triazole and tpyrazole have made them attractive targets for synthesis. 1,2,3-Triazole and pyrazole rings present in the same molecule could be convenient models for investigation of their biological activity. Keeping in mind the biological significance of triazole and pyrazole derivatives, we report herein the synthesis 1-substituted benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole derivatives, **5a-k** as antimycobacterial agents.

II. METHODS AND MATERIAL

All the reactions were monitored by thin-layer chromatography (TLC). TLC was performed on Merck 60 F-254 silica gel plates with visualization by UV light. Melting points were determined in capillary tubes in silicon oil bath using a Veego melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on BRUKER AVANCE II 500 NMR spectrometer (Bruker Instruments Inc., Billerica, MA,

USA) at either 500-MHz (^{1}H NMR) and 126-MHz (^{13}C NMR) spectrometer instruments. Chemical shifts are reported from internal tetramethylsilane standard and are given in δ units. Column chromatography was performed on silica gel (100–200 mesh) supplied by Acme Chemical Co. (Mumbai, Maharashtra, India).

General procedure for synthesis of 4-ethynyl-1,3-diphenyl-1H-pyrazole (3a)

To a ice cold solution of diethyl (1-diazo-2-oxopropyl)phosphonate (13 mmol) and K_2CO_3 (20 mmol) in dry methanol (20 mL), solution of 1,3-diphenyl-1H-pyrazole-4-carbaldehyde (**2a**) [29] (10 mmol) in methanol (20 mL) was added and reaction mixture was stirred at room temperature for 24 hours. After completion of the reaction (TLC), solvent was distilled under vacuum and residue was dissolved in water (50 mL) and reaction mass was extracted by ethyl acetate (3 x 25 mL). Organic layer was washed with brine, dried over sodium sulphate and evaporated on rotary evaporator. The crude product was purified by column chromatography using Ethyl acetate:hexane (2:8) as eluent gave 4-ethynyl-1,3-diphenyl-1H-pyrazole (**3a**), Yield 1.02 gm, 42 %).

General procedure for the synthesis of 1-benzyl-4-(1,3-diphenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole (5a)

A reaction mixture of 4-ethynyl-1,3-diphenyl-1H-pyrazole, **3a** (0.244 g, 1 mmole), benzylazide, **4a** (0.14 gm, 1 mmole), copper sulphate (0.040 gm, 0.25 mmole) and sodium ascorbate (0.050 gm, 0.22 mmole) in DMF:Water (6 mL, 3:1) was stirred overnight. After completion of reaction (TLC), the reaction mixture was quenched in water and extracted by ethyl acetate (3 x 15 mL). Organic layer was dried over sodium sulphate and evaporated on rotary evaporator. The crude product was purified by column chromatography (Ethyl acetate:hexane) furnished target compound 1-benzyl-4-(1,3-diphenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole (**5a**). Compounds **5b-k** was synthesized by similar procedure.

4-(1,3-diphenyl-1H-pyrazol-4-yl)-1-(4-methylbenzyl)-1H-1,2,3-triazole, **5a**: ^{1}H NMR (500 MHz, DMSO) δ 8.46 (s, 1H), 8.06-8.08 (m, 4H), 7.89-7.91 (m, 5H), 7.42-7.44 (m, 2H), 7.30-7.31 (m, 2H), 7.12-7.14 (m, 2H), 5.64 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 150.96, 147.07, 140.41, 133.99, 130.43, 130.36, 129.90, 129.88, 126.91, 126.88, 126.48, 125.87, 121.38, 115.99, 115.53, 113.63, 113.22, 52.93, 21.49; LCMS: 392.2 $(M+H)^+$.

1-benzyl-4-(3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.79 – 7.74 (m, 2H), 7.50 – 7.44 (m, 6H), 7.37 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.25 – 7.20 (m, 3H), 5.52 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.54, 140.38, 139.64, 134.65, 131.97, 131.65, 130.09, 129.55, 129.15, 128.82, 127.91, 127.19, 126.89, 122.59, 120.58, 119.07, 112.54, 54.20; LCMS: 456.1 $(M+H)^+$.

4-(3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-fluorobenzyl)-1H-1,2,3-triazole, **5c:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.77 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.52 – 7.44 (m, 6H), 7.37 – 7.29 (m, 1H), 7.28 – 7.20 (m, 4H), 7.07 (t, *J* = 8.6 Hz, 2H), 5.49 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.87, 161.89, 149.55, 140.54, 139.63, 131.98, 131.68, 130.52, 130.50, 130.12, 129.83, 129.76, 129.56, 127.18, 126.93, 122.65, 120.34, 119.09, 116.24, 116.07, 112.45, 53.44; LCMS: 474.1 $(M+H)^+$.

4-(3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methylbenzyl)-1H-1,2,3-triazole, **5d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.70 – 7.65 (m, 2H), 7.43 – 7.36 (m, 6H), 7.25 – 7.21 (m, 1H), 7.12 – 7.08 (m, 3H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.39 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.53, 140.26, 139.65, 138.79, 131.97, 131.62, 130.08, 129.80, 129.55, 128.00, 127.16, 126.87, 122.55, 120.53, 119.06, 112.58, 54.01, 21.21; LCMS: 470.1 $(M+H)^+$.

1-benzyl-4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.77 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.58 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.47 (dd, *J* = 8.4, 7.6 Hz, 2H), 7.36 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.23 (dd, *J* = 7.0, 2.4 Hz, 2H), 7.19 (s, 1H), 7.03 (t, *J* = 8.7 Hz, 2H), 5.51 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.89, 161.92, 149.78, 140.53, 139.69, 134.68, 130.37, 130.30, 129.54, 129.13, 129.10, 128.79, 127.89, 126.98, 126.80, 120.43, 119.04, 115.56, 115.39, 112.53, 54.17; LCMS: 396.4 $(M+H)^+$.

1-(4-fluorobenzyl)-4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5f**: ^{1}H NMR (500 MHz,

$CDCl_3$) δ 8.42 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.47 (t, *J* = 7.9 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.23 (dd, *J* = 8.5, 5.2 Hz, 2H), 7.19 (s, 1H), 7.06 (t, *J* = 8.6 Hz, 4H), 5.48 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.92, 163.85, 161.95, 161.88, 149.77, 140.68, 139.66, 130.55, 130.52, 130.40, 130.33, 129.81, 129.75, 129.55, 129.13, 129.10, 126.98, 126.84, 120.19, 119.05, 116.22, 116.05, 115.58, 115.41, 112.44, 53.42; LCMS: 414.1 $(M+H)^+$.

1-(4-chlorobenzyl)-4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.51 (dd, *J* = 8.1, 5.6 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.26 (t, *J* = 7.8 Hz, 3H), 7.16 – 7.06 (m, 3H), 6.99 (t, *J* = 8.6 Hz, 2H), 5.40 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.93, 161.96, 149.78, 140.72, 139.65, 134.86, 133.17, 130.40, 130.34, 129.55, 129.33, 129.21, 129.11, 129.09, 127.01, 126.85, 120.26, 119.05, 115.61, 115.44, 112.36, 53.42; LCMS: 430.1 $(M+H)^+$.

4-(3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methylbenzyl)-1H-1,2,3-triazole, **5h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.76 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.58 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.46 (dd, *J* = 8.4, 7.6 Hz, 2H), 7.32 – 7.28 (m, 1H), 7.16 (t, *J* = 4.0 Hz, 3H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.03 (t, *J* = 8.8 Hz, 2H), 5.45 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.88, 161.91, 149.78, 140.41, 139.69, 138.75, 131.64, 130.37, 130.31, 129.76, 129.53, 129.14, 129.11, 127.96, 126.95, 126.77, 120.37, 119.07, 119.02, 115.53, 115.36, 112.59, 53.98, 21.16; LCMS: 410.2 $(M+H)^+$.

1-benzyl-4-(3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.77 (dd, *J* = 4.8, 3.8 Hz, 2H), 7.54 – 7.50 (m, 2H), 7.45 (dd, *J* = 8.5, 7.5 Hz, 2H), 7.38 – 7.32 (m, 3H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.24 – 7.19 (m, 3H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.49 (s, 2H), 3.82 (s, 3H) ; LCMS: 408.2 $(M+H)^+$.

1-(4-fluorobenzyl)-4-(3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.72 – 7.68 (m, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.39 (dd, *J* = 8.5, 7.6 Hz, 2H), 7.25 – 7.20 (m, 1H), 7.17 – 7.10 (m, 3H), 6.97 (t, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.38 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.75, 160.77, 158.78, 149.48, 139.92, 138.73, 129.61, 129.59, 128.78, 128.74, 128.67, 128.45, 125.63, 125.56, 124.40, 119.17, 117.93, 115.10, 114.93, 112.86, 111.35, 54.27, 52.30; LCMS: 426.1 $(M+H)^+$.

4-(3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methylbenzyl)-1H-1,2,3-triazole, **5k**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.77 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.46 (dd, *J* = 8.5, 7.5 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.21 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.45 (s, 2H), 3.83 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.78, 150.51, 140.74, 139.81, 138.57, 131.78, 129.80, 129.71, 129.48, 127.87, 126.70, 126.55, 125.50, 120.35, 118.95, 113.90, 112.53, 55.31, 53.91, 21.16; LCMS: 422.2 $(M+H)^+$.

Antitubercular Activity

All the synthesized compounds were screened for their *in vitro* activity against dormant and active *M. tuberculosis* H37Ra (ATCC 25177) at 3 μg/mL. Activity against MTB was determined through the XTT reduction menadione assay (XRMA) reading absorbance at 470 nm as per the protocol described in literature [30-34]. Percentage inhibition was calculated using the following formula:

% inhibition = [(control–CMP) / (control–blank)] x 100

Where 'control' is the activity of mycobacteria without compounds, 'CMP' is the activity of mycobacteria in the presence of compounds and 'blank' is the activity of the culture medium without mycobacteria.

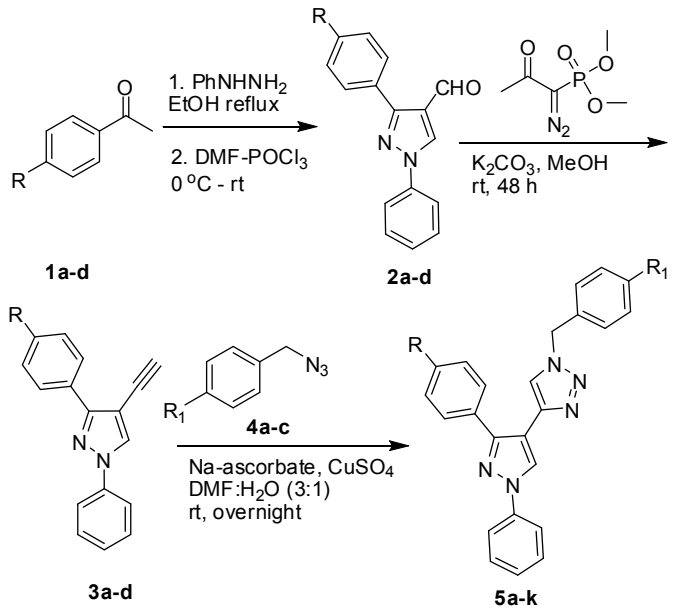
Antibacterial activity

All bacterial cultures were first grown in Luria Burtony media at 37 ºC at 180 rpm. Once the culture reaches 1 O.D., it is used for anti-bacterial assay. Bacterial strains *Escherichia coli* (NCIM 2576), *Pseudomonas flurescence*(NCIM 2059) as Gram-negative and *Staphylococcus aureus* (NCIM 2602), *Bacillus subtilis* (NCIM 2162) as Gram-positive were obtained from NCIM (NCL, Pune) and were grown in Luria Burtony medium from Hi Media, India. The assay was performed in 96 well plates after 8 hours and 12 hours for Gram negative and Gram positive bacteria, respectively. 0.1 % of 1 O.D. culture at 620 nm was used for screening

inoculated culture was added into each well of 96 well plate containing the compounds to be tested. Optical density for each plate was measured at 620 nm after 8 hours for Gram-negative bacteria and after 12 hours for Gram- positive bacteria.[34,35]

III. RESULTS AND DISCUSSION

A series of 1-benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole derivatives, **5a-k** were synthesized according to Scheme 1. Substituted acetophenone **1a-d** on condensation reaction with phenyl hydrazine in ethanol gave corresponding phenyl hydrazone derivative, which on Vilsmeyer-Hack formylation reaction with dimethyl formaide and phosphorus oxychloride gave 1-phenyl-3-substituted phenyl-1H-pyrazole-4-carbaldehyde, **2a-d.** Aldehyde **2a-d** on reaction with diethyl (1-diazo-2-oxopropyl)phosphonate and K_2CO_3 in methanol (Ohira-Bestman reaction) gave 4-ethynyl-1-phenyl-3-substituted phenyl-1H-pyrazole, **3a-d**. Alkyne **3a-d** on click reaction with substituted benzyl azide, **4a-c** furnished target compounds 1-benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole, **5a-k**. The physical constant and yields are predicted in **Table 1**



Scheme 1. Synthetic route of 1-benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole derivatives, **5a-k**

Comp.	R	R_1	MP (°C)	Yield[a] (%)
5a	H	CH3	140-142	68
5b	Br	H	138-140	65
5c	Br	4-F	136-138	60
5d	Br	4-CH_3	154-156	70
5e	F	H	140-141	58
5f	F	4-F	142-144	59
5g	F	Cl	169-171	52
5h	CH3	F	152-153	67
5i	OMe	H	102-103	60
5j	OMe	4-F	118-120	66
5k	OMe	4- CH_3	120-121	66

[a]Yield after column purification

The structure of 1-benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole compounds, **5a-k** was confirmed by NMR and mass. As a representative analysis of compound 4-(3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)-1-(4-methylbenzyl)-1H-1,2,3-triazole, **5i** the ^{1}H NMR spectrum of compound **5i** displayed three singlets in aliphatic region at δ 2.34 (CH_3), 3.83 (OCH_3) and 5.49 (Ar-CH_2-triazole). Two doublets at δ 6.88 and 7.52 were attributed to methoxy substituted phenyl ring, while multiplate at δ 7.27-7.31 and two double doublets δ 7.46 and 7.77 corresponds to protons of N-phenyl ring. Two doublets appeared at δ 7.12 and 7.16 corresponds to the protons of methyl substituted phenyl ring. Triazole and pyrazole protons were resonated as singlet at δ 7.21 and 8.43 respectively. The ^{13}C NMR spectrum of compound **51** showed three signals of aliphatic carbons at δ 21.16 (Ar-CH_3), 53.91 (Ar-CH_2-N) and 55.31 (Ar-OCH_3). Aromatic, triazole and pyrazole carbons showed signals from δ 112.53 to 159.72. Structure of compound **5i** was further confirmed by MS, molecular ion peak at *m*/*z* 422.20 $(M+H)^+$. Structures of all the derivatives were ascertained similarly.

Biological evaluation

The antitubercular activity for each synthesized compound was determined by measuring inhibition of growth against avirulent strain of *M. tuberculosis* H37Ra, dormant and active (MTB, ATCC 25177) in liquid medium. In a preliminary screening, the antimycobacterial activity of these compounds was assessed at 3 μg/mL concentration using first-line

antitubercular drug rifampicin as reference standard. *In vitro* activity studies against MTB were performed using the XRMA [30-34]. The antibacterial activity of synthesized compounds was determined against the standard Gram-negative bacteria, *E. coli* (NCIM 2576), *P. flurescence* (NCIM 2059) and Gram-positive bacteria, *S. aureus* (NCIM 2602), *B. subtilis* (NCIM 2162). Ampicillin served as positive control for antibacterial activity [34,35]. The *in vitro* preliminary screening values (% inhibition) against microorganism tested are summarized in **Table 2**.

Table 2. Antibacterial screening of compounds **5a-k** (% growth inhibition) at 3 µg/mL

Comp.	*S. aureus*	*B. subtilis*	*E. coli*	*P. flurescence*	*Dormant* H37Ra	Active H37Ra
5a	4.36	1.45	-	8.92	32.67	33.45
5b	13.95	41.42	-	5.81	34.1	47.5
5c	7.26	44.3	-	7.05	34.81	39.37
5d	19.27	27.59	-	-	37.07	46.53
5e	25.91	45.79	-	-	36.6	47.8
5f	-	50.36	-	7.13	26.72	30.88
5g	11.26	33.48	-	4.63	38.17	45.91
5h	24.68	-	-	-	36.86	51.14
5i	14.2	36.82	-	7.51	29.57	53
5j	10.86	25.71	-	3.1	43.49	44.32
5k	16.51	25.71	-	-	36.38	41.2
Amp	93.8	93.5	92.25	92.15		
Rifam[b]					96.4	97.88

a - indicates not active;
b - Rifampicin[b] 0.5 µg/mL concentration.

The *in vitro* antimycobacterial activity against *M. tuberculosis* H37Ra (dormant and active) *E. coli*, *P. flurescence*, *S. aureus* and *B. subtilis* revealed that most of the compounds reported moderate activity at 3 µg/mL against *M tuberculosis* and Gram positive bacterial strains. The preliminary structure activity relationship study revealed that replacement of hydrogen atom of phenyl ring A and B (**Figure 1**) by substituent groups like Br, F, OMe and CH_3 affects the activity.

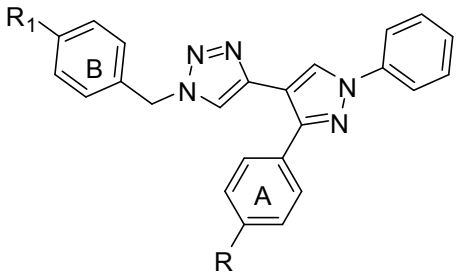


Figure 1. Compounds **5a-k**

Compound 5a (R = H, R_1 = CH_3) showed moderate activity against *M. tuberculosis* H37Ra dormant and active strains where as inactive against Gram +ve and Gram –ve bacterial strains. Among the compounds, **5b-d** with bromo substituted phenyl ring A and substituted phenyl ring B, compound **5b** (R_1= H) showed good activity against *M. tuberculosis* H37Ra active and *B. subtilis* and moderate activity against *M. tuberculosis* H37Ra dormant strain. Whereas, compound **5c** (R_1= F) showed good activity against *B. subtilis* and moderate activity against *M. tuberculosis* H37Ra dormant and active strains. Compound **5d** (R_1= CH_3) reported good activity against *M. tuberculosis* H37Ra active strain and moderate activity against *M. tuberculosis* H37Ra dormant and *B. subtilis* strains. Among the compounds, **5e-h** with 4-fluoro substituted phenyl ring A and substituted phenyl ring B, compound **5e** (R_1= H) showed good activity against *M. tuberculosis* H37Ra active and *B. subtilis* and moderate activity against *M. tuberculosis* H37Ra dormant and *S. aureus* strains. Compound **5f** (R_1= F) reported good activity against *B. subtilis* and moderate activity against both mycobacterial strains. Compound **5g** (R_1= Cl) showed good activity against *M. tuberculosis* H37Ra active strain and moderate activity against *M. tuberculosis* H37Ra dormant and *B. subtilis* strains. Compound **5h** reported good activity against *M. tuberculosis* H37Ra active strain and moderate activity against *M. tuberculosis* H37Ra dormant and *S. aureus* strains. Among the compounds, **5i-k** with 4-methoxy substituted phenyl ring A and substituted phenyl ring B, all compounds were reported good activity against *M. tuberculosis* H37Ra active strain. Compounds **5i** and **5k** showed moderate activity against *M. tuberculosis* H37Ra dormant and *B. subtilis* strains. Compound **5j** also reported good activity against *M. tuberculosis* H37Ra dormant strain and moderate activity against *B. Subtilis.*

Thus, it is concluded that compounds with R^1 = H, CH_3 and Cl, group showed good antibacterial activity against *M. tuberculosis* H37Ra active strain. compound with R = OMe and R^1 = H reported good activity against both *M. tuberculosis* H37Ra strains. It was worth to mention that all the synthesized compounds are less active against Gram –ve bacterial strains.

IV. CONCLUSION

In the present study, we have detailed the synthesis and primary biological screening of 1-substituted benzyl-4-(1-phenyl-3-substituted phenyl-1H-pyrazol-4-yl)-1H-1,2,3-triazole derivatives, **5a-k**. It can be concluded that, most of the synthesized compounds with Br, F and OMe substituted phenyl ring at 3-position of pyrazole and unsubstituted, 4-CH_3 and 4-Cl substituted benzyl ring at 1-position of 1,2,3-triazole showed good antitubercular activity against *M. tuberculosis* H37Ra active strain. Most of the synthesized compounds exhibited moderate to good antibacterial activity against *M. tuberculosis* H37Ra dormant *B. subtilis* strains. Thus, these results warrant the need for synthesis of similar libraries with other substituents to ascertain the trend described in this work.

V. Acknowledgments

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