Hybrid Approach for Synthesis and Antimicrobial Activity of Heterocyclic Compounds

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Keywords: Anti fungal, antibacterial, microbial strains, spectroscopic techniques.

Abstract. We have synthesized novel series of *N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)arylaniline and their derivatives. The structures of synthesized compounds were well characterized by spectroscopic techniques. Antimicrobial activity of the newly synthesized derivatives was evaluated against gram positive (*S. aureus* and *S. pyogenes*), gram negative bacteria (*E. coli* and *P. aeruginosa*), and strains of fungi (*C. albicans*, *A. niger* and *A. clavatus*). Among the screened derivatives **5c**, **5f**, **5i**, **5l** and **5t** demonstrated superior antimicrobial activity against microbial strains.

Introduction

Nitrogen-rich heterocycles, particularly pyrazole 1,3,4-oxadiazole and pyridine, represent an exclusive class of diversified frameworks exhibiting a broad spectrum of biological functions. Some microbial species are responsible for dangerous diseases such as food poisoning, typhoid and due to this; it is the global concern for public health. All these species are fully resisted against old fashionable antimicrobial drugs. For this reason new discovery of antimicrobials are important for the medicinal chemists. Heterocycles comprising nitrogen especially five member rings have captured huge interest due to their availability in many natural products and as vital part of synthetic bioactive molecules [1]. In this framework, pyridine, pyrazole and 1,3,4-oxadiazole templates featuring one, two nitrogen's and an oxygen atom [2] is recognized as a member of fortunate structural class particularly from medicinal point of view [3]. Commercially available drugs (Fig. 1) celecoxibe, zibotentan and sulphapyridine sequentially contain pyrazole [4], 1,3,4-oxadiazole [5] and pyridine heterocycles. Among the important heterocyclic scaffolds of biological and pharmacological interest, the pyrazole ring is able with diverse medicinal activities [6-12].

1,3,4-oxadiazoles scaffold is a group of heterocyclic compounds as they have attracted significant concern in medicinal chemistry. 1,3,4-oxadiazoles displayed a significant biological activity such as, antimicrobial [13], anti-HIV [14], antitumor [15], anticonvulsant [16], anti tubercular [17], antihypertensive. The pyridine core is leading in several natural products and significant important in the medicinal chemistry. A large number of biological activities are related with pyridines derivatives such as, anticancer [18], anti-ulcer [19], antitubercular and antimicrobial [20] activities etc.

Molecular hybridization is a significant tool for discovery of novel chemical entities. In the past some decades much attention has been given to the plan and synthesis of new types of pharmacologically diverse structural hybrid molecules [21]. Encouraged by the above-mentioned explanation, we have focused onto construct some novel antimicrobial derivatives containing pyrazole, 1,3,4-oxadiazole and pyridine scaffolds screened for antimicrobial activity. Previously our research group has worked on the synthesis of pyrazole and their derivatives as potential antimicrobials [22-24]. In furtherance to this, *N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)arylanilines (**5a-t**) have been synthesized and screened for their antimicrobial activity against standard strains of bacteria and fungi [25]. All final

compounds were categorised by different spectroscopic methods such as, infrared spectroscopy, ^1H and ^{13}C nuclear magnetic resonance and mass.

Figure 1. Chemical structures of clinically used antimicrobial agents.

Results and Discussion

Chemistry

All reactions except those in aqueous media were carried out by standard techniques for the keeping out of wetness. Melting points were determined on an electro thermal melting point apparatus and were reported uncorrected. TLC on silica gel plates (Merck, 60, F₂₅₄) was used for purity checking and reaction monitoring. Column chromatography on silica gel (Merck, 70-230 mesh and 230-400 mesh ASTH for flash chromatography) was applied when necessary to isolate and purify the reaction products. Elemental analysis (% C, H, N) was carried out by a Perkin-Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Perkin-Elmer FT-IR spectrophotometers in KBr. ^1H NMR and ^{13}C NMR spectra were recorded on Varian Gemini 500 MHz in DMSO-*d*₆ as a solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were scanned on a Shimadzu LC-MS 2010 spectrometer. Anhydrous reactions were carried out in oven-dried glassware in nitrogen atmosphere.

Synthetic tactics adopted to get the final compounds are depicted in Scheme 1. Here, compound **5** is a part of synthesis of new chemical moieties in the form of antimicrobials. In scheme 1, the key Schiff base *N'*-((1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)methylene)isonicotinohydrazide (**3**) was used as a starting material for the synthesis of final compounds (**5a-t**). Compound (**3**) was synthesized through simple condensation by 1-phenyl-3-(*p*-tolyl)-1*H*-pyrazole-4-carbaldehyde (**1**) and double amount of Isoniazide in 1,4-dioxane used as solvent. Compound (**1**) is Vilsmeier-Haack synthesis product; it provides intermediate for the synthesis of some novel substituted heterocyclic moieties. Compound (**3**) was cyclised by acetic anhydride and yielded 1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**4**). Further in final step compound (**4**) and different substituted aromatic anilines derivatives were condensed and convert in final products (**5a-t**).

Novel compounds (**5a-t**) were categorized by different spectroscopic methods such as, IR, ^1H NMR, ^{13}C NMR, and mass. In compound **5l**, group $>\text{C}=\text{N}-$ and $>\text{C}=\text{C}<$ stretching vibrations appeared at 1597 and 1537 cm^{-1} . Nitro group of aniline showed stretching vibrations at 1504 cm^{-1} . C-CH₃ group which was attached to 1,3,4-oxadiazole ring showed stretching vibrations at 1355 cm^{-1} . The absorption band at 1292 and 1224 cm^{-1} is due to stretching vibration of $>\text{C}=\text{N}-$ and C-O-C oxadiazole ring. In ^1H NMR characterization C₂-H and C₆-H protons of pyridine ring showed doublet at 8.82 ppm. In pyridine ring two protons C₃-H and C₅-H appeared at 8.12 ppm as doublet. Singlet signal of pyrazole ring was given by C₅-H at 7.96 ppm. All other aromatic 13 protons showed multiple in range of 6.95-8.15 ppm. At 5.85 ppm singlet signals appeared by one

proton of oxadiazole ring. Remaining six protons showed two singlet signals at 2.39 and 2.28 ppm out of six three protons are of $-\text{CH}_3$ ring and another three from $-\text{CH}_3-\text{C}=\text{N}$. Looking to the ^{13}C NMR spectra, the chemical shifts of the final compound **5l** has carbons that varied from $\delta = 158.3$ -21.5 ppm. Signal of C_2 and C_5 in 1,3,4-oxadiazole ring appeared at 158.0 at and 78.3 ppm. In pyridine ring C_2 , C_3 and C_5 showed peak at 149.2, 138.2 and 124.7 ppm. In pyrazole ring system C_3 , C_4 and C_5 signals appeared at 149.5, 123.8 and 117.8 ppm. One carbon of $-\text{CH}=\text{N}-$ displayed peak at 156.3 ppm. Furthermore, the mass spectrum of (**5a-t**) appeared a molecular ion peak corresponding to molecular formula (**5a-t**) onward of other fragment peaks, which supported the proposed structure of final compounds. Detail discussion of experimental data is given in supporting section.

Scheme 1. Synthetic pathway of targeted compounds (**5a-t**).

Preparation of *N'*-((1-phenyl-3-(p-tolyl)-1*H*-pyrazol-4-yl)methylene)isonicotinohydrazide (3) and preparation of 1-(2-(1-phenyl-3-(p-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone. (4)

Synthesis of compound (**3**) and (**4**) were achieved by reported method [26].

Preparation of *N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)arylaniline. (5)

A mixture of compound 1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethanone (**4**) (0.01 mol) and substituted aniline derivatives (0.02 mol) were taken in 30 mL ethanol (95%) and refluxed at 120°C for the period of 12 h. The mixture was concentrated under vacuum and poured into ice cold water. The solid products was separated and recrystallised in ethanol (95%). The completion of the reaction and the purity of compounds (**3**), (**4**) and (**5**) were checked on TLC [Aluminium sheet-silica gel 60, F₂₄₅ (E. Merck)] using hexane-ethyl acetate (8:2 v/v) as an irrigator and were developed in iodine chamber.

Table 1. Physical constant of derivatives (**5a-t**).

Sr. no	Substitution	M.P. (°C)	Yield (%)	Colour
5a	C ₆ H ₄ -H	177-180°C	63	Creemish yellow
5b	C ₆ H ₄ -2-F	145-148°C	70	Off white
5c	C ₆ H ₄ -4-F	135-138°C	79	Yellowish white
5d	C ₆ H ₄ -2-CH ₃	120-122°C	64	Light yellow
5e	C ₆ H ₄ -3-CH ₃	156-158°C	66	Yellow
5f	C ₆ H ₄ -4-CH ₃	202-204°C	71	Dark yellow
5g	C ₆ H ₄ -2-OCH ₃	158-159°C	64	Off white
5h	C ₆ H ₄ -3-OCH ₃	185-187°C	69	Creemish
5i	C ₆ H ₄ -4-OCH ₃	110-112°C	67	Buff
5j	C ₆ H ₄ -2-NO ₂	112-114°C	56	Yellow
5k	C ₆ H ₄ -3-NO ₂	165-167°C	59	Dark yellow
5l	C ₆ H ₄ -4-NO ₂	126-129°C	60	Orange
5m	C ₆ H ₄ -2-Cl	140-142°C	62	White
5n	C ₆ H ₄ -3-Cl	196-198°C	66	Off white
5o	C ₆ H ₄ -4-Cl	204-206°C	68	Brown
5p	C ₆ H ₄ -2-Br	196-199°C	70	Yellow
5q	C ₆ H ₄ -3-Br	177-179°C	72	Brown
5r	C ₆ H ₄ -4-Br	188-190°C	75	Reddish brown
5s	C ₆ H ₃ -4-Br-2-CH ₃	162-164°C	65	Off white
5t	C ₆ H ₃ -3-Cl-4-F	171-173°C	63	Pale yellow

Characterization of *N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: **5a**

IR (KBr, cm⁻¹): 1588, 1543 (>C=N-, >C=C< stretching), 1372 (-C-H stretching, -C-CH₃), 1295 (>C=N- stretching, Ar-NH₂), 1230 (C-O-C stretching, oxadiazole ring); ¹H NMR (DMSO-*d*₆, 400 MHz): δ = 8.96 (d, 2H, *J* = 8.1 Hz, C₂-H and C₆-H pyridine ring), 8.0 (d, 2H, *J* = 7.8 Hz, C₃-H and C₅-H pyridine ring), 7.96 (s, 1H, C₅-H pyrazole ring), 6.94-7.75 (m, 14H, Ar-H), 5.70 (s, 1H, C₅-H oxadiazole ring), 2.40 (s, 3H, -CH₃), 2.20 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 157.5 (1C, C₅ oxadiazole ring), 156.1 (1C, -CH=N-), 152.8 (1C, C₁ C₅H₅-N=), 149.0 (1C, C₃ pyrazole ring), 149.9 (2C, C₂ and C₆ pyridine ring), 139.4 (1C, C₁ aromatic ring), 138.5 (1C, C₄ pyridine ring), 131.4 (1C, C₁ C₆H₄-CH₃), 130.8 (3C, C₃ and C₅ C₅H₅-N=, C₁ C₆H₄-CH₃), 129.6 (2C, C₃ and C₅ C₆H₄-CH₃), 129.1 (2C, C₃ and C₅ aromatic ring), 127.0 (1C, C₄-C₅H₅-N=), 126.9 (1C, C₄ aromatic ring), 125.2 (2C, C₂ and C₆ C₆H₄-CH₃), 124.4 (2C, C₃ and C₅ pyridine ring), 123.5 (1C, C₅ pyrazole ring), 122.9 (2C, C₂ and C₆ C₅H₅-N=), 119.3 (2C, C₂ and C₆ aromatic ring), 117.7 (1C, C₄ pyrazole ring), 78.2 (1C, C₂ oxadiazole ring), 29.6 (1C, C₅ aromatic ring), 21.5 (1C, C₆H₄-CH₃), 21.1 (1C, =CH-CH₃); LCMS (ESI): *m/z* 499.2 (36.1%) [M⁺]; Anal. calcd. for C₃₁H₂₆N₆O: C, 74.68; H, 5.26; N, 16.86; Found: C, 74.72; H, 5.33; N, 16.93%.

Characterization of 2-fluoro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5b

IR (KBr, cm^{-1}): 1582, 1546 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1374 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1293 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1233 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring), 1075 ($\text{C}-\text{F}$ stretching); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.92 (d, 2H, J = 8.3 Hz C_2-H and C_6-H pyridine ring), 8.02 (d, 2H, J = 7.2 Hz, C_3-H and C_5-H pyridine ring), 7.93 (s, 1H, C_5-H pyrazole ring), 7.28-7.79 (m, 13H, $\text{Ar}-\text{H}$), 5.72 (s, 1H, C_5-H oxadiazole ring), 2.41 (s, 3H, $-\text{CH}_3$), 2.22 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 157.5 (1C, C_5 oxadiazole ring), 156.4 (1C, $-\text{CH}=\text{N}-$), 153.0 (1C, $\text{JC}-\text{F}$ 236.7 c/sec , $\text{C}_2\text{C}_5\text{H}_4-\text{N}=\text{}$), 149.5 (2C, C_2 and C_6 pyridine ring), 149.1 (1C, C_3 pyrazole ring), 139.3 (1C, C_1 aromatic ring), 138.6 (1C, C_4 pyridine ring), 136.5 (1C, $\text{C}_1\text{C}_5\text{H}_5-\text{N}=\text{}$), 131.8 (1C, $\text{C}_4\text{C}_6\text{H}_4-\text{CH}_3$), 130.5 (1C, $\text{C}_1\text{C}_6\text{H}_4-\text{CH}_3$), 129.9 (2C, C_3 and $\text{C}_5\text{C}_6\text{H}_4-\text{CH}_3$), 129.1 (2C, C_3 and C_5 aromatic ring), 128.4 (1C, $\text{C}_4\text{C}_5\text{H}_4-\text{N}=\text{}$), 126.7 (1C, C_4 aromatic ring), 125.3 (2C, C_2 and $\text{C}_6\text{C}_6\text{H}_4-\text{CH}_3$), 125.7 (1C, $\text{C}_5\text{C}_5\text{H}_5-\text{N}=\text{}$), 124.8 (2C, C_3 and C_5 pyridine ring), 123.7 (1C, $\text{C}_6\text{C}_5\text{H}_5-\text{N}=\text{}$), 123.4 (1C, C_5 pyrazole ring), 119.7 (2C, C_2 and C_6 aromatic ring), 118.0 (1C, $\text{C}_3\text{C}_5\text{H}_5-\text{N}=\text{}$), 117.8 (1C, C_4 pyrazole ring), 78.6 (1C, C_2 oxadiazole ring), 21.8 (1C, $\text{C}_6\text{H}_4-\text{CH}_3$), 21.5 (1C, $=\text{CH}-\text{CH}_3$); LCMS (ESI): m/z 517.2 (36.1%) [M^+]; Anal. calcd. for $\text{C}_{31}\text{H}_{25}\text{FN}_6\text{O}$: C, 72.08; H, 4.88; N, 16.27; Found: C, 72.15; H, 4.92; N, 16.30%.

Characterization of 4-fluoro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5c

IR (KBr, cm^{-1}): 1587, 1540 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1379 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1296 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1238 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring), 1050 ($\text{C}-\text{F}$ stretching); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.93 (d, 2H, J = 8.3 Hz C_2-H and C_6-H pyridine ring), 8.03 (d, 2H, J = 7.3 Hz C_3-H and C_5-H pyridine ring), 7.99 (s, 1H, C_5-H pyrazole ring), 7.30-7.85 (m, 13H, $\text{Ar}-\text{H}$), 5.78 (s, 1H, C_5-H oxadiazole ring), 2.44 (s, 3H, $-\text{CH}_3$), 2.25 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 161.4 (1C, $\text{JC}-\text{F}$ 233.3 c/sec , $\text{C}_4\text{C}_5\text{H}_4-\text{N}=\text{}$), 157.4 (1C, C_5 oxadiazole ring), 156.5 (1C, $-\text{CH}=\text{N}-$), 149.6 (2C, C_2 and C_6 pyridine ring), 149.2 (1C, C_3 pyrazole ring), 147.5 (1C, $\text{C}_1\text{C}_5\text{H}_4-\text{N}=\text{}$), 139.5 (1C, C_1 aromatic ring), 138.0 (1C, C_4 pyridine ring), 131.3, 130.4 (1C, $\text{C}_1\text{C}_6\text{H}_4-\text{CH}_3$), 129.8 (2C, C_3 and $\text{C}_5\text{C}_6\text{H}_4-\text{CH}_3$), 129.7 (2C, C_3 and C_5 aromatic ring), 126.4 (1C, C_4 aromatic ring), 125.4 (2C, C_2 and $\text{C}_6\text{C}_6\text{H}_4-\text{CH}_3$), 124.4 (2C, C_3 and C_5 pyridine ring), 123.9 (2C, C_6 and $\text{C}_2\text{C}_5\text{H}_4-\text{N}=\text{}$), 123.7 (1C, C_5 pyrazole ring), 119.7 (2C, C_2 and C_6 aromatic ring), 117.5 (1C, C_4 pyrazole ring), 116.2 (2C, C_5 and $\text{C}_3\text{C}_5\text{H}_4-\text{N}=\text{}$), 78.1 (1C, C_2 oxadiazole ring), 21.4 (1C, $\text{C}_6\text{H}_4-\text{CH}_3$), 21.6 (1C, $=\text{CH}-\text{CH}_3$); LCMS (ESI): m/z 517.2 (36.1%) [M^+]; Anal. calcd. for $\text{C}_{31}\text{H}_{25}\text{FN}_6\text{O}$: C, 72.08; H, 4.88; N, 16.27; Found: C, 72.12; H, 4.94; N, 16.33%.

Characterization of 2-methyl-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5d

IR (KBr, cm^{-1}): 1590, 1545 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1373 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1291 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1232 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.90 (d, 2H, J = 8.0 Hz C_2-H and C_6-H pyridine ring), 8.04 (d, 2H, J = 7.5 Hz C_3-H and C_5-H pyridine ring), 7.99 (s, 1H, C_5-H pyrazole ring), 7.00-7.70 (m, 13H, $\text{Ar}-\text{H}$), 5.79 (s, 1H, C_5-H oxadiazole ring), 2.42 (s, 6H, $-\text{CH}_3$), 2.23 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 157.4 (1C, C_5 oxadiazole ring), 156.3 (1C, $-\text{CH}=\text{N}-$), 149.8 (2C, C_2 and C_6 pyridine ring), 149.2 (1C, C_3 pyrazole ring), 139.1 (1C, C_1 aromatic ring), 138.7 (1C, C_4 pyridine ring), 136.7 (1C, $\text{C}_2\text{C}_5\text{H}_4-\text{N}=\text{}$), 131.7 (1C, $\text{C}_4\text{C}_6\text{H}_4-\text{CH}_3$), 130.9 (1C, $\text{C}_3\text{C}_5\text{H}_4-\text{N}=\text{}$), 130.6 (1C, $\text{C}_1\text{C}_6\text{H}_4-\text{CH}_3$), 129.7 (2C, C_3 and $\text{C}_5\text{C}_6\text{H}_4-\text{CH}_3$), 129.4 (2C, C_3 and C_5 aromatic ring), 128.1 (1C, $\text{C}_1\text{C}_5\text{H}_4-\text{N}=\text{}$), 127.7 (1C, $\text{C}_4\text{C}_5\text{H}_4-\text{N}=\text{}$), 127.6 (1C, $\text{C}_5\text{C}_5\text{H}_4-\text{N}=\text{}$), 126.8 (1C, C_4 aromatic ring), 125.3 (2C, C_2 and $\text{C}_6\text{C}_5\text{H}_4-\text{N}=\text{}$), 124.5 (2C, C_3 and C_5 pyridine ring), 123.8 (1C, C_5 pyrazole ring), 120.6 (1C, $\text{C}_4\text{C}_5\text{H}_4-\text{N}=\text{}$), 119.4 (2C, C_2 and C_6 aromatic ring), 117.4 (1C, C_4 pyrazole ring), 78.5 (1C, C_2 oxadiazole ring), 21.4 (1C, $\text{C}_6\text{H}_4-\text{CH}_3$), 21.7 (1C, $=\text{CH}-\text{CH}_3$), 18.6 (1C, $\text{CH}_3-\text{C}_5\text{H}_4-\text{N}=\text{}$); LCMS (ESI): m/z 513.2 (37.2%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}$: C, 74.98; H, 5.51; N, 16.39; Found: C, 75.03; H, 5.55; N, 16.42%.

Characterization of 3-methyl-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5e

IR (KBr, cm^{-1}): 1584, 1541 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1365 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1285 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1229 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.91 (d, 2H, J = 8.1 Hz C_2-H and C_6-H pyridine ring), 8.07 (d, 2H, J = 7.6 Hz C_3-H and C_5-H pyridine ring), 8.01 (s, 1H, C_5-H pyrazole ring), 6.75-7.70 (m, 13H, $\text{Ar}-\text{H}$), 5.80 (s, 1H, C_5-H oxadiazole ring), 2.41 (s, 6H, $-\text{CH}_3$), 2.24 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 157.8 (1C, C_5 oxadiazole ring), 156.8 (1C, $-\text{CH}=\text{N}-$), 152.7 (1C, C_1 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 149.7 (1C, C_3 pyrazole ring), 149.6 (2C, C_2 and C_6 pyridine ring), 139.8 (2C, 1C aromatic ring and 1C C_3 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 138.9 (1C, C_4 pyridine ring), 131.4 (1C, C_4 $\text{C}_6\text{H}_4-\text{CH}_3$), 130.9 (1C, C_1 $\text{C}_6\text{H}_4-\text{CH}_3$), 129.1 (1C, C_5 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 129.6 (2C, C_3 and C_5 aromatic ring), 129.6 (2C, C_3 and C_5 $\text{C}_6\text{H}_4-\text{CH}_3$), 125.7 (2C, C_2 and C_6 $\text{C}_6\text{H}_4-\text{CH}_3$), 124.6 (2C, C_3 and C_5 pyridine ring), 123.1 (1C, C_4 $\text{C}_6\text{H}_4-\text{CH}_3$), 123.0 (1C, C_5 pyrazole ring), 121.9 (1C, C_2 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 119.5 (2C, C_2 and C_6 aromatic ring), 119.7 (1C, C_5 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 117.8 (1C, C_4 pyrazole ring), 78.2 (1C, C_2 oxadiazole ring), 21.8 (2C, $\text{CH}_3-\text{C}_5\text{H}_4-\text{N}=\text{}$ and $\text{C}_6\text{H}_4-\text{CH}_3$), 21.7 (1C, $=\text{CH}-\text{CH}_3$); LCMS (ESI): m/z 513.2 (37.2%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}$: C, 74.98; H, 5.51; N, 16.39; Found: C, 74.92; H, 5.55; N, 16.43%.

Characterization of 4-methyl-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5f

IR (KBr, cm^{-1}): 1586, 1538 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1369 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1294 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1235 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.89 (d, 2H, J = 8.8 Hz C_2-H and C_6-H pyridine ring), 8.06 (d, 2H, J = 7.8 Hz C_3-H and C_5-H pyridine ring), 8.00 (s, 1H, C_5-H pyrazole ring), 7.25-7.72 (m, 13H, $\text{Ar}-\text{H}$), 5.81 (s, 1H, C_5-H oxadiazole ring), 2.41 (s, 6H, $-\text{CH}_3$), 2.22 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 157.4 (1C, C_5 oxadiazole ring), 156.2 (1C, $-\text{CH}=\text{N}-$), 149.6 (2C, C_2 and C_6 pyridine ring), 149.3 (1C, C_3 pyrazole ring), 149.1 (1C, C_1 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 139.3 (1C, C_1 aromatic ring), 138.1 (1C, C_4 pyridine ring), 136.4 (1C, C_4 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 131.7 (1C, C_4 $\text{C}_6\text{H}_4-\text{CH}_3$), 130.9 (1C, C_1 $\text{C}_6\text{H}_4-\text{CH}_3$), 130.3 (2C, C_3 and C_5 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 129.7 (2C, C_3 and C_5 $\text{C}_6\text{H}_4-\text{CH}_3$), 129.8 (2C, C_3 and C_5 aromatic ring), 126.7 (1C, C_1 aromatic ring), 125.8 (2C, C_2 and C_6 $\text{C}_6\text{H}_4-\text{CH}_3$), 125.2 (2C, C_2 and C_6 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 124.5 (2C, C_3 and C_5 pyridine ring), 123.6 (1C, C_5 pyrazole ring), 119.7 (2C, C_2 and C_6 aromatic ring), 117.3 (1C, C_4 pyrazole ring), 78.0 (1C, C_2 oxadiazole ring), 21.4 (2C, $\text{CH}_3-\text{C}_5\text{H}_4-\text{N}=\text{}$ and $\text{C}_6\text{H}_4-\text{CH}_3$), 21.6 (1C, $=\text{CH}-\text{CH}_3$); LCMS (ESI): m/z 513.2 (37.2%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}$: C, 74.98; H, 5.51; N, 16.39; Found: C, 75.06; H, 5.56; N, 16.41%.

Characterization of 2-methoxy-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5g

IR (KBr, cm^{-1}): 2830 ($\text{C}-\text{H}$ stretching, $-\text{OCH}_3$), 1580, 1542 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1371 ($-\text{C}-\text{H}$ stretching, $-\text{C}-\text{CH}_3$), 1290 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1232 ($\text{C}-\text{O}-\text{C}$ stretching, oxadiazole ring); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ = 8.88 (d, 2H, J = 8.7 Hz C_2-H and C_6-H pyridine ring), 8.02 (s, 1H, C_5-H pyrazole ring), 8.08 (d, 2H, J = 7.5 Hz C_3-H and C_5-H pyridine ring), 6.70-7.67 (m, 13H, $\text{Ar}-\text{H}$), 5.82 (s, 1H, C_5-H oxadiazole ring), 3.89 (s, 3H, $-\text{OCH}_3$), 2.39 (s, 3H, $-\text{CH}_3$), 2.24 (s, 3H, $-\text{CH}_3-\text{C}=\text{N}$); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 157.8 (1C, C_5 oxadiazole ring), 156.0 (1C, $-\text{CH}=\text{N}-$), 152.1 (1C, C_2 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 149.4 (1C, C_3 pyrazole ring), 149.2 (2C, C_2 and C_6 pyridine ring), 139.1 (1C, C_1 aromatic ring), 138.0 (1C, C_4 pyridine ring), 135.6 (1C, C_1 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 131.2 (1C, C_4 $\text{C}_6\text{H}_4-\text{CH}_3$), 130.4 (1C, C_1 $\text{C}_6\text{H}_4-\text{CH}_3$), 129.8 (2C, C_3 and C_5 aromatic ring), 129.6 (2C, C_3 and C_5 $\text{C}_6\text{H}_4-\text{CH}_3$), 126.5 (1C, C_4 aromatic ring), 125.4 (2C, C_2 and C_6 $\text{C}_6\text{H}_4-\text{CH}_3$), 124.5 (2C, C_3 and C_5 pyridine ring), 124.2 (1C, C_4 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 123.7 (1C, C_5 pyrazole ring), 122.0 (1C, C_5 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 119.3 (2C, C_2 and C_6 aromatic ring), 117.4 (1C, C_4 pyrazole ring), 115.6 (1C, C_3 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 115.1 (1C, C_3 $\text{C}_5\text{H}_4-\text{N}=\text{}$), 78.5 (1C, C_2 oxadiazole ring), 55.4 (1C, $-\text{OCH}_3$), 21.4 (1C, $\text{C}_6\text{H}_4-\text{CH}_3$), 21.0 (1C, $=\text{CH}-\text{CH}_3$); LCMS (ESI): m/z 528.2 (100.0%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}_2$: C, 72.71; H, 5.34; N, 15.90; Found: C, 72.75; H, 5.39; N, 15.95%.

Characterization of 3-methoxy-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5h

IR (KBr, cm^{-1}): 2825 (C-H stretching, $-\text{OCH}_3$), 1587, 1543 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1368 (C-H stretching, $-\text{C}-\text{CH}_3$), 1288 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1237 (C-O-C stretching, oxadiazole ring); ^1H NMR (DMSO- d_6 , 400 MHz): δ = 8.90 (d, 2H, J = 8.4 Hz $\text{C}_2\text{-H}$ and $\text{C}_6\text{-H}$ pyridine ring), 8.10 (d, 2H, J = 7.7 Hz $\text{C}_3\text{-H}$ and $\text{C}_5\text{-H}$ pyridine ring), 8.01 (s, 1H, $\text{C}_5\text{-H}$ pyrazole ring), 6.60-7.60 (m, 13H, Ar-H), 5.83 (s, 1H, $\text{C}_5\text{-H}$ oxadiazole ring), 3.88 (s, 3H, $-\text{OCH}_3$), 2.39 (s, 3H, $-\text{CH}_3$), 2.26 (s, 3H, $-\text{CH}_3\text{-C}=\text{N}$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 161.4 (1C, C_3 $\text{C}_6\text{H}_4\text{-CH}_3$), 157.5 (1C, C_5 oxadiazole ring), 156.1 (1C, $-\text{CH}=\text{N}-$), 150.6 (1C, C_1 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 149.3 (1C, C_3 pyrazole ring), 149.0 (2C, C_2 and C_6 pyridine ring), 139.5 (1C, C_1 aromatic ring), 138.1 (1C, C_4 aromatic ring), 131.7 (1C, C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 131.3 (1C, C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 130.3 (1C, C_1 $\text{C}_6\text{H}_4\text{-CH}_3$), 129.7 (2C, C_3 and C_5 aromatic ring), 129.3 (2C, C_3 and C_5 $\text{C}_6\text{H}_4\text{-CH}_3$), 126.5 (1C, C_4 aromatic ring), 125.3 (2C, C_2 and C_6 $\text{C}_6\text{H}_4\text{-CH}_3$), 124.7 (2C, C_3 and C_5 pyridine ring), 123.7 (1C, C_5 pyrazole ring), 119.5 (2C, C_2 and C_6 aromatic ring), 117.6 (1C, C_4 pyrazole ring), 114.9 (1C, C_1 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 108.5 (1C, C_2 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 106.7 (1C, C_4 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 78.3 (1C, C_2 oxadiazole ring), 55.3 (1C, $-\text{OCH}_3$), 21.4 (1C, $\text{C}_6\text{H}_4\text{-CH}_3$), 21.0 (1C, $=\text{CH-CH}_3$); LCMS (ESI): m/z 528.2 (100.0%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}_2$: C, 72.71; H, 5.34; N, 15.90; Found: C, 72.76; H, 5.40; N, 15.95%.

Characterization of 4-methoxy-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5i

IR (KBr, cm^{-1}): 2820 (C-H stretching, $-\text{OCH}_3$), 1581, 1536 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1364 (C-H stretching, $-\text{C}-\text{CH}_3$), 1283 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1235 (C-O-C stretching, oxadiazole ring); ^1H NMR (DMSO- d_6 , 400 MHz): δ = 8.87 (d, 2H, J = 8.3 Hz $\text{C}_2\text{-H}$ and $\text{C}_6\text{-H}$ pyridine ring), 8.07 (d, 2H, J = 7.7 Hz $\text{C}_3\text{-H}$ and $\text{C}_5\text{-H}$ pyridine ring), 8.03 (s, 1H, $\text{C}_5\text{-H}$ pyrazole ring), 7.10-7.67 (m, 13H, Ar-H), 5.86 (s, 1H, $\text{C}_5\text{-H}$ oxadiazole ring), 3.90 (s, 3H, $-\text{OCH}_3$), 2.37 (s, 3H, $-\text{CH}_3$), 2.27 (s, 3H, $-\text{CH}_3\text{-C}=\text{N}$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 159.2 (1C, C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 157.6 (1C, C_5 oxadiazole ring), 156.1 (1C, $-\text{CH}=\text{N}-$), 149.8 (1C, C_3 pyrazole ring), 149.3 (2C, C_2 and C_6 pyridine ring), 144.3 (1C, C_1 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 139.1 (1C, C_1 aromatic ring), 138.7 (1C, C_4 pyridine ring), 131.3 (1C, C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 130.4 (1C, C_1 $\text{C}_6\text{H}_4\text{-CH}_3$), 129.1 (2C, C_3 and C_5 aromatic ring), 129.1 (2C, C_3 and C_5 $\text{C}_6\text{H}_4\text{-CH}_3$), 126.7 (1C, C_4 aromatic ring), 125.8 (2C, C_2 and C_6 $\text{C}_6\text{H}_4\text{-CH}_3$), 124.6 (2C, C_3 and C_5 pyridine ring), 123.2 (1C, C_5 pyrazole ring), 122.7 (2C, C_2 and C_6 $\text{C}_6\text{H}_4\text{-CH}_3$), 119.5 (2C, C_2 and C_6 aromatic ring), 117.5 (1C, C_4 pyrazole ring), 115.7 (2C, C_3 and C_5 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 78.1 (1C, C_2 oxadiazole ring), 55.1 (1C, $-\text{OCH}_3$), 21.4 (1C, $\text{C}_6\text{H}_4\text{-CH}_3$), 21.3 (1C, $=\text{CH-CH}_3$); LCMS (ESI): m/z 528.2 (100.0%) [M^+]; Anal. calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_6\text{O}_2$: C, 72.71; H, 5.34; N, 15.90; Found: C, 72.75; H, 5.42; N, 15.96%.

Characterization of 2-nitro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5j

IR (KBr, cm^{-1}): 1585, 1540 ($>\text{C}=\text{N}-$, $>\text{C}=\text{C}<$ stretching), 1510 ($-\text{N}=\text{O}$ stretching, $\text{Ar}-\text{NO}_2$), 1370 (C-H stretching, $-\text{C}-\text{CH}_3$), 1298 ($>\text{C}=\text{N}-$ stretching, $\text{Ar}-\text{NH}_2$), 1232 (C-O-C stretching, oxadiazole ring); ^1H NMR (DMSO- d_6 , 400 MHz): δ = 8.85 (d, 2H, J = 8.3 Hz $\text{C}_2\text{-H}$ and $\text{C}_6\text{-H}$ pyridine ring), 8.04 (d, 2H, J = 7.3 Hz $\text{C}_3\text{-H}$ and $\text{C}_5\text{-H}$ pyridine ring), 7.99 (s, 1H, $\text{C}_5\text{-H}$ pyrazole ring), 7.60-8.07 (m, 13H, Ar-H), 5.88 (s, 1H, $\text{C}_5\text{-H}$ oxadiazole ring), 2.35 (s, 3H, $-\text{CH}_3$), 2.25 (s, 3H, $-\text{CH}_3\text{-C}=\text{N}$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 157.4 (1C, C_5 oxadiazole ring), 156.1 (1C, $-\text{CH}=\text{N}-$), 149.5 (1C, C_3 pyrazole ring), 149.3 (2C, C_2 and C_6 pyridine ring), 145.7 (1C, C_2 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 142.3 (1C, C_2 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 139.1 (1C, C_1 aromatic ring), 138.2 (1C, C_4 pyridine ring), 131.4 (1C, C_4 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 131.1 (1C, C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 130.5 (2C, C_6 $\text{C}_5\text{H}_4\text{-N}=\text{}$ and C_4 $\text{C}_6\text{H}_4\text{-CH}_3$), 129.7 (2C, C_3 and C_5 $\text{C}_6\text{H}_4\text{-CH}_3$), 129.4 (2C, C_3 and C_5 aromatic ring), 128.6 (1C, C_4 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 126.7 (1C, C_4 aromatic ring), 125.7 (2C, C_2 and C_6 $\text{C}_6\text{H}_4\text{-CH}_3$), 125.6 (1C, C_3 $\text{C}_5\text{H}_4\text{-N}=\text{}$), 124.6 (2C, C_3 and C_5 pyridine ring), 123.8 (1C, C_5 pyrazole ring), 119.7 (2C, C_2 and C_6 aromatic ring), 117.2 (1C, C_4 pyrazole ring), 78.5 (1C, C_2 oxadiazole ring), 21.4 (1C, $\text{C}_6\text{H}_4\text{-CH}_3$), 21.0 (1C, $=\text{CH-CH}_3$);

LCMS (ESI): m/z 544.2 (36.5%) [M^+]; Anal. calcd. for $C_{31}H_{25}N_7O_3$: C, 68.50; H, 4.64; N, 18.04; Found: C, 68.55; H, 4.69; N, 18.10%.

Characterization of 3-nitro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5k

IR (KBr, cm^{-1}): 1590, 1532 ($>C=N-$, $>C=C<$ stretching), 1500 ($-N=O$ stretching, Ar- NO_2), 1365 ($-C-H$ stretching, $-C-CH_3$), 1295 ($>C=N-$ stretching, Ar- NH_2), 1228 (C-O-C stretching, oxadiazole ring); 1H NMR (DMSO- d_6 , 400 MHz): δ = 8.84 (d, 2H, J = 8.3 Hz C₂-H and C₆-H pyridine ring), 8.09 (d, 2H, J = 7.3 Hz C₃-H and C₅-H pyridine ring), 7.97 (s, 1H, C₅-H pyrazole ring), 7.35-7.80 (m, 13H, Ar-H), 5.89 (s, 1H, C₅-H oxadiazole ring), 2.34 (s, 3H, $-CH_3$), 2.26 (s, 3H, $-CH_3-C=N$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 157.4 (1C, C₅ oxadiazole ring), 156.2 (1C, $-CH=N-$), 149.4 (2C, C₃ pyrazole ring and C₁ C₅H₄-N=), 149.2 (1C, C₃ C₅H₄-N=), 149.0 (2C, C₂ and C₆ pyridine ring), 139.1 (1C, C₁ aromatic ring), 138.0 (1C, C₄ pyridine ring), 132.7 (1C, C₅ C₅H₄-N=), 131.2 (1C, C₄ C₆H₄-CH₃), 130.8 (1C, C₁ C₆H₄-CH₃), 129.4 (2C, C₃ and C₅ aromatic ring), 129.0 (2C, C₃ and C₅ C₆H₄-CH₃), 128.6 (1C, C₆ C₅H₄-N=), 126.7 (1C, C₄ aromatic ring), 125.1 (2C, C₂ and C₆ C₆H₄-CH₃), 124.8 (2C, C₃ and C₅ pyridine ring), 123.0 (1C, C₅ pyrazole ring), 122.7 (1C, C₄ C₅H₄-N=), 119.5 (2C, C₂ and C₆ aromatic ring), 118.3 (1C, C₂ C₅H₄-N=), 117.7 (1C, C₄ pyrazole ring), 78.9 (1C, C₂ oxadiazole ring), 21.5 (1C, C₆H₄-CH₃), 21.3 (1C, $=CH-CH_3$); LCMS (ESI): m/z 544.2 (36.5%) [M^+]; Anal. calcd. for $C_{31}H_{25}N_7O_3$: C, 68.50; H, 4.64; N, 18.04; Found: C, 68.56; H, 4.69; N, 18.10%.

Characterization of 4-nitro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5l

IR (KBr, cm^{-1}): 1597, 1537 ($>C=N-$, $>C=C<$ stretching), 1504 ($-N=O$ stretching, Ar- NO_2), 1355 ($-C-H$ stretching, $-C-CH_3$), 1292 ($>C=N-$ stretching, Ar- NH_2), 1224 (C-O-C stretching, oxadiazole ring); 1H NMR (DMSO- d_6 , 400 MHz): δ = 8.82 (d, 2H, J = 8.0 Hz C₂-H and C₆-H pyridine ring), 8.12 (d, 2H, J = 7.0 Hz C₃-H and C₅-H pyridine ring), 7.96 (s, 1H, C₅-H pyrazole ring), 6.95-8.15 (m, 13H, Ar-H), 5.85 (s, 1H, C₅-H oxadiazole ring), 2.39 (s, 3H, $-CH_3$), 2.28 (s, 3H, $-CH_3-C=N$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 158.3 (1C, C₁ C₅H₄-N=), 157.0 (1C, C₅ oxadiazole ring), 156.3 (1C, $-CH=N-$), 149.5 (1C, C₃ pyrazole ring), 149.2 (2C, C₂ and C₆ pyridine ring), 146.2 (1C, C₄ C₅H₄-N=), 139.1 (1C, C₁ aromatic ring), 138.2 (1C, C₄ pyridine ring), 131.0 (1C, C₄ C₆H₄-CH₃), 130.5 (1C, C₁ C₆H₄-CH₃), 129.4 (2C, C₃ and C₅ C₆H₄-CH₃), 129.0 (2C, C₃ and C₅ aromatic ring), 128.6 (1C, C₆ C₅H₄-N=), 126.2 (1C, C₄ aromatic ring), 125.5 (2C, C₂ and C₆ C₆H₄-CH₃), 125.2 (2C, C₃ C₅H₄-N= and C₅ C₅H₄-N=), 124.7 (2C, C₃ and C₅ pyridine ring), 123.4 (2C, C₂ C₅H₄-N= and C₆ C₅H₄-N=), 123.8 (1C, C₅ pyrazole ring), 119.4 (2C, C₂ and C₆ aromatic ring), 117.8 (1C, C₄ pyrazole ring), 78.3 (1C, C₂ oxadiazole ring), 21.9 (1C, C₆H₄-CH₃), 21.5 (1C, $=CH-CH_3$); LCMS (ESI): m/z 544.2 (36.5%) [M^+]; Anal. calcd. for $C_{31}H_{25}N_7O_3$: C, 68.50; H, 4.64; N, 18.04; Found: C, 68.55; H, 4.72; N, 18.13%.

Characterization of 2-chloro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5m

IR (KBr, cm^{-1}): 1594, 1539 ($>C=N-$, $>C=C<$ stretching), 1353 ($-C-H$ stretching, $-C-CH_3$), 1289 ($>C=N-$ stretching, Ar- NH_2), 1220 (C-O-C stretching, oxadiazole ring), 760 (C-Cl stretching); 1H NMR (DMSO- d_6 , 400 MHz): δ = 8.83 (d, 2H, J = 8.4 Hz C₂-H and C₆-H pyridine ring), 8.08 (d, 2H, J = 7.4 Hz C₃-H and C₅-H pyridine ring), 7.94 (s, 1H, C₅-H pyrazole ring), 7.30-7.70 (m, 13H, Ar-H), 5.89 (s, 1H, C₅-H oxadiazole ring), 2.43 (s, 3H, $-CH_3$), 2.29 (s, 3H, $-CH_3-C=N$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 157.3 (1C, C₅ oxadiazole ring), 156.0 (1C, $-CH=N-$), 149.2 (1C, C₃ pyrazole ring), 149.0 (2C, C₂ and C₆ pyridine ring), 139.8 (1C, C₁ C₅H₄-N=), 139.2 (1C, C₁ aromatic ring), 138.6 (1C, C₄ pyridine ring), 131.4 (1C, C₄ C₆H₄-CH₃), 130.8 (1C, C₁ C₆H₄-CH₃), 130.1 (1C, C₃ C₅H₄-N=), 129.9 (2C, C₃ and C₅ aromatic ring), 129.5 (2C, C₃ and C₅ C₆H₄-CH₃), 128.4 (1C, C₄ C₅H₄-N=), 128.3 (1C, C₅ C₅H₄-N=), 127.5 (1C, C₂ C₅H₄-N=), 126.7 (1C, C₄ aromatic ring), 125.5 (2C, C₂ and C₆ C₆H₄-CH₃), 124.9 (2C, C₃ and C₅ pyridine ring), 123.8 (1C, C₅ pyrazole ring), 119.4 (2C, C₂ and C₆ aromatic ring), 118.7 (1C, C₆ C₅H₄-N=), 117.7 (1C, C₅ pyrazole ring),

78.6 (1C, C₂ oxadiazole ring), 21.8 (1C, C₆H₄-CH₃), 21.3 (1C, =CH-CH₃); LCMS (ESI): m/z 534.2 (38.5%) [M⁺]; Anal. calcd. for C₃₁H₂₅ClN₆O: C, 69.85; H, 4.73; N, 15.77; Found: C, 69.89; H, 4.77; N, 15.79%.

Characterization of 3-chloro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5n

IR (KBr, cm⁻¹): 1587, 1535 (>C=N-, >C=C< stretching), 1350 (-C-H stretching, -C-CH₃), 1282 (>C=N- stretching, Ar-NH₂), 1225 (C-O-C stretching, oxadiazole ring), 740 (C-Cl stretching); ¹H NMR (DMSO-d₆, 400 MHz): δ = 8.85 (d, 2H, *J* = 8.3 Hz C₂-H and C₆-H pyridine ring), 8.11 (d, 2H, *J* = 7.4 Hz C₃-H and C₅-H pyridine ring), 7.95 (s, 1H, C₅-H pyrazole ring), 6.90-7.62 (m, 13H, Ar-H), 5.93 (s, 1H, C₅-H oxadiazole ring), 2.44 (s, 3H, -CH₃), 2.30 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-d₆): δ = 157.8 (1C, C₅ oxadiazole ring), 156.1 (1C, -CH=N-), 150.4 (1C, C₁ C₅H₄-N=), 149.4 (2C, C₂ and C₆ pyridine ring), 149.1 (1C, C₃ pyrazole ring), 139.3 (1C, C₁ C₅H₄-N=), 138.0 (1C, C₄ pyridine ring), 134.7 (1C, C₃ C₅H₄-N=), 131.9 (1C, C₅ C₅H₄-N=), 131.0 (1C, C₄ C₆H₄-CH₃), 130.4 (1C, C₁ C₆H₄-CH₃), 129.8 (2C, C₃ and C₅ aromatic ring), 129.2 (2C, C₃ and C₅ C₆H₄-CH₃), 127.9 (1C, C₄ C₅H₄-N=), 126.7 (1C, C₄ aromatic ring), 125.1 (2C, C₂ and C₆ C₆H₄-CH₃), 124.0 (2C, C₃ and C₅ pyridine ring), 123.7 (1C, C₅ pyrazole ring), 122.4 (1C, C₂ C₆H₄-CH₃), 120.7 (1C, C₆ C₆H₄-CH₃), 119.5 (2C, C₂ and C₆ aromatic ring), 117.1 (1C, C₄ pyrazole ring), 78.2 (1C, C₂ oxadiazole ring), 21.8 (1C, C₆H₄-CH₃), 21.7 (1C, =CH-CH₃); LCMS (ESI): m/z 534.2 (38.5%) [M⁺]; Anal. calcd. for C₃₁H₂₅ClN₆O: C, 69.85; H, 4.73; N, 15.77; Found: C, 69.90; H, 4.77; N, 15.82%.

Characterization of 4-chloro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5o

IR (KBr, cm⁻¹): 1582, 1537 (>C=N-, >C=C< stretching), 1356 (-C-H stretching, -C-CH₃), 1288 (>C=N- stretching, Ar-NH₂), 1228 (C-O-C stretching, oxadiazole ring), 752 (C-Cl stretching); ¹H NMR (DMSO-d₆, 400 MHz): δ = 8.80 (d, 2H, *J* = 8.3 Hz C₂-H and C₆-H pyridine ring), 8.13 (d, 2H, *J* = 7.0 Hz C₃-H and C₅-H pyridine ring), 7.96 (s, 1H, C₅-H pyrazole ring), 7.10-7.63 (m, 13H, Ar-H), 5.91 (s, 1H, C₅-H oxadiazole ring), 2.44 (s, 3H, -CH₃), 2.31 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-d₆): δ = 157.1 (1C, C₅ oxadiazole ring), 156.4 (1C, -CH=N-), 150.2 (1C, C₁ C₅H₄-N=), 149.8 (2C, C₂ and C₆ pyridine ring), 149.2 (1C, C₃ pyrazole ring), 139.1 (1C, C₁ aromatic ring), 138.7 (1C, C₄ pyridine ring), 132.4 (1C, C₄ C₅H₄-N=), 131.7 (1C, C₄ C₆H₄-CH₃), 130.8 (2C, C₅ and C₃ C₅H₄-N=), 130.2 (1C, C₁ C₆H₄-CH₃), 129.7 (2C, C₃ and C₅ C₆H₄-CH₃), 129.4 (2C, C₃ and C₅ aromatic ring), 126.7 (1C, C₄ aromatic ring), 125.2 (2C, C₂ and C₆ C₆H₄-CH₃), 124.8 (2C, C₃ and C₅ pyridine ring), 123.7 (1C, C₅ pyrazole ring), 122.8 (2C, C₂ and C₆ C₆H₄-CH₃), 119.5 (2C, C₂ and C₆ aromatic ring), 117.8 (1C, C₅ pyrazole ring), 78.0 (1C, C₂ oxadiazole ring), 21.9 (1C, C₆H₄-CH₃), 21.7 (1C, =CH-CH₃); LCMS (ESI): m/z 534.2 (38.5%) [M⁺]; Anal. calcd. for C₃₁H₂₅ClN₆O: C, 69.85; H, 4.73; N, 15.77; Found: C, 69.89; H, 4.78; N, 15.83%.

Characterization of 2-bromo-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5p

IR (KBr, cm⁻¹): 1588, 1531 (>C=N-, >C=C< stretching), 1356 (-C-H stretching, -C-CH₃), 1290 (>C=N- stretching, Ar-NH₂), 1226 (C-O-C stretching, oxadiazole ring), 540 (C-Br stretching); ¹H NMR (DMSO-d₆, 400 MHz): δ = 8.81 (d, 2H, *J* = 8.8 Hz C₂-H and C₆-H pyridine ring), 8.10 (d, 2H, *J* = 7.8 Hz C₃-H and C₅-H pyridine ring), 7.98 (s, 1H, C₅-H pyrazole ring), 7.20-7.75 (m, 13H, Ar-H), 5.90 (s, 1H, C₅-H oxadiazole ring), 2.45 (s, 3H, -CH₃), 2.32 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-d₆): δ = 157.0 (1C, C₅ oxadiazole ring), 156.9 (1C, -CH=N-), 149.5 (2C, C₂ and C₆ pyridine ring), 149.3 (1C, C₃ pyrazole ring), 146.7 (1C, C₁ C₅H₄-N=), 139.1 (1C, C₁ aromatic ring), 138.7 (1C, C₄ pyridine ring), 132.7 (1C, C₃ C₅H₄-N=), 131.0 (1C, C₄ C₆H₄-CH₃), 130.8 (1C, C₄ C₆H₄-CH₃), 129.8 (1C, C₅ C₅H₄-N=), 129.4 (2C, C₃ and C₅ aromatic ring), 129.2 (2C, C₃ and C₅ C₆H₄-CH₃), 126.8 (1C, C₄ C₅H₄-N=), 126.2 (1C, C₄ aromatic ring), 125.0 (2C, C₂ and C₆ C₆H₄-CH₃), 124.7 (2C, C₃ and C₅ pyridine ring), 123.8 (1C, C₅ pyrazole ring), 119.2 (2C, C₂ and C₆ aromatic ring), 119.0 (1C, C₆ C₅H₄-N=), 118.7 (1C, C₂ C₅H₄-N=), 117.8 (1C, C₄ pyrazole ring),

78.4 (1C, C₂ oxadiazole ring), 21.8 (1C, C₆H₄-CH₃), 21.7 (1C, =CH-CH₃); LCMS (ESI): m/z 576.1 (96.3%) [M⁺]; Anal. calcd. for C₃₁H₂₅BrN₆O: C, 64.48; H, 4.36; N, 14.55; Found: C, 64.52; H, 4.41; N, 14.59%.

Characterization of 3-bromo-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5q

IR (KBr, cm⁻¹): 1597, 1533 (>C=N-, >C=C< stretching), 1359 (-C-H stretching, -C-CH₃), 1293 (>C=N- stretching, Ar-NH₂), 1229 (C-O-C stretching, oxadiazole ring), 565 (C-Br stretching); ¹H NMR (DMSO-*d*₆, 400 MHz): δ = 8.79 (d, 2H, *J* = 8.8 Hz C₂-H and C₆-H pyridine ring), 8.14 (d, 2H, *J* = 7.8 Hz C₃-H and C₅-H pyridine ring), 8.03 (s, 1H, C₅-H pyrazole ring), 7.00-7.72 (m, 13H, Ar-H), 5.89 (s, 1H, C₅-H oxadiazole ring), 2.46 (s, 3H, -CH₃), 2.30 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 157.8 (1C, C₅ oxadiazole ring), 156.2 (1C, -CH=N-), 149.2 (2C, C₂ and C₆ pyridine ring), 149.1 (1C, C₃ pyrazole ring), 139.4 (1C, C₁ aromatic ring), 138.4 (1C, C₄ pyridine ring), 131.4 (1C, C₄ C₆H₄-CH₃), 130.8 (1C, C₅ C₅H₄-N=), 130.1 (1C, C₁ C₆H₄-CH₃), 129.3 (2C, C₃ and C₅ aromatic ring), 129.2 (2C, C₃ and C₅ C₆H₄-CH₃), 126.7 (1C, C₄ aromatic ring), 125.9 (2C, C₂ and C₆ C₆H₄-CH₃), 125.1 (1C, C₄ C₅H₄-N=), 124.5 (2C, C₃ and C₅ pyridine ring), 123.4 (2C, C₅ pyrazole ring and C₃ C₅H₄-N=), 123.2 (1C, C₂ C₅H₄-N=), 121.7 (1C, C₆ C₅H₄-N=), 119.2 (2C, C₂ and C₆ aromatic ring), 117.3 (1C, C₄ pyrazole ring), 78.5 (1C, C₂ oxadiazole ring), 21.9 (1C, C₆H₄-CH₃), 21.5 (1C, =CH-CH₃); LCMS (ESI): m/z 576.1 (96.3%) [M⁺]; Anal. calcd. for C₃₁H₂₅BrN₆O: C, 64.48; H, 4.36; N, 14.55; Found: C, 64.54; H, 4.39; N, 14.60%.

Characterization of 4-bromo-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5r

IR (KBr, cm⁻¹): 1594, 1536 (>C=N-, >C=C< stretching), 1353 (-C-H stretching, -C-CH₃), 1290 (>C=N- stretching, Ar-NH₂), 1232 (C-O-C stretching, oxadiazole ring), 550 (C-Br stretching); ¹H NMR (DMSO-*d*₆, 400 MHz): δ = 8.78 (d, 2H, *J* = 8.9 Hz C₂-H and C₆-H pyridine ring), 8.12 (d, 2H, *J* = 7.2 Hz C₃-H and C₅-H pyridine ring), 8.04 (s, 1H, C₅-H pyrazole ring), 7.25-7.78 (m, 13H, Ar-H), 5.87 (s, 1H, C₅-H oxadiazole ring), 2.44 (s, 3H, -CH₃), 2.32 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 157.6 (1C, C₅ oxadiazole ring), 156.1 (1C, -CH=N-), 151.5 (1C, C₁ C₅H₄-N=), 149.8 (2C, C₂ and C₆ pyridine ring), 149.4 (1C, C₃ pyrazole ring), 139.3 (1C, C₁ aromatic ring), 138.7 (1C, C₄ pyridine ring), 132.0 (2C, C₃ and C₅ C₅H₄-N=), 131.0 (1C, C₄ C₆H₄-CH₃), 130.7 (1C, C₁ C₆H₄-CH₃), 129.4 (2C, C₃ and C₅ C₆H₄-CH₃), 129.2 (2C, C₃ and C₅ aromatic ring), 126.1 (1C, C₄ aromatic ring), 125.3 (2C, C₃ and C₅ C₆H₄-CH₃), 124.7 (2C, C₃ and C₅ pyridine ring), 123.7 (1C, C₅ pyrazole ring), 122.7 (2C, C₂ and C₆ C₅H₄-N=), 121.4 (1C, C₄ C₅H₄-N=), 119.2 (2C, C₂ and C₆ aromatic ring), 117.1 (1C, C₄ pyrazole ring), 78.7 (1C, C₂ oxadiazole ring), 21.7 (1C, C₆H₄-CH₃), 21.1 (1C, =CH-CH₃); LCMS (ESI): m/z 576.1 (96.3%) [M⁺]; Anal. calcd. for C₃₁H₂₅BrN₆O: C, 64.48; H, 4.36; N, 14.55; Found: C, 64.50; H, 4.40; N, 14.61%.

Characterization of 4-bromo-2-methyl-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5s

IR (KBr, cm⁻¹): 1599, 1545 (>C=N-, >C=C< stretching), 1356 (-C-H stretching, -C-CH₃), 1294 (>C=N- stretching, Ar-NH₂), 1238 (C-O-C stretching, oxadiazole ring), 555 (C-Br stretching); ¹H NMR (DMSO-*d*₆, 400 MHz): δ = 8.79 (d, 2H, *J* = 8.2 Hz C₂-H and C₆-H pyridine ring), 8.15 (d, 2H, *J* = 7.4 Hz C₃-H and C₅-H pyridine ring), 8.07 (s, 1H, C₅-H pyrazole ring), 7.15-7.72 (m, 12H, Ar-H), 5.87 (s, 1H, C₅-H oxadiazole ring), 2.42 (s, 3H, -CH₃), 2.33 (s, 3H, -CH₃-C=N); ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 157.2 (1C, C₅ oxadiazole ring), 156.7 (1C, -CH=N-), 149.8 (1C, C₃ pyrazole ring), 149.5 (2C, C₂ and C₆ pyridine ring), 139.6 (1C, C₁ aromatic ring), 138.3 (1C, C₄ pyridine ring), 135.7 (1C, C₃ C₅H₃-N=), 132.0 (1C, C₂ C₅H₃-N=), 131.9 (1C, C₄ C₆H₄-CH₃), 130.0 (1C, C₁ C₆H₄-CH₃), 129.8 (1C, C₅ C₅H₃-N=), 129.4 (2C, C₃ and C₅ C₆H₄-CH₃), 129.1 (2C, C₃ and C₅ aromatic ring), 127.8 (1C, C₁ C₅H₃-N=), 126.4 (1C, C₄ aromatic ring), 125.2 (2C, C₂ and C₆ C₆H₄-CH₃), 124.8 (2C, C₃ and C₅ pyridine ring), 124.2 (1C, C₆ C₅H₃-N=), 123.8 (1C, C₅ pyrazole ring), 121.1 (1C, C₄ C₅H₃-N=), 119.0 (2C, C₂ and C₆ aromatic ring), 117.5 (1C, C₄ pyrazole ring), 78.2 (1C, C₂ oxadiazole ring), 21.5 (1C, C₆H₄-CH₃), 21.4 (1C, =CH-CH₃), 17.3 (1C, -CH₃); LCMS

(ESI): m/z 591.1 (35.7%) [M^+]; Anal. calcd. for $C_{32}H_{27}BrN_6O$: C, 64.98; H, 4.60; N, 14.21; Found: C, 65.05; H, 4.63; N, 14.26%.

3-chloro-4-fluoro-*N*-(1-(2-(1-phenyl-3-(*p*-tolyl)-1*H*-pyrazol-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)ethylidene)aniline: 5t

IR (KBr, cm^{-1}): 1595, 1544 ($>C=N-$, $>C=C<$ stretching), 1359 ($-C-H$ stretching, $-C-CH_3$), 1291 ($>C=N-$ stretching, $Ar-NH_2$), 1239 ($C-O-C$ stretching, oxadiazole ring), 1150 ($C-F$ stretching), 852 ($C-Cl$ stretching); 1H NMR (DMSO- d_6 , 400 MHz): δ = 8.81 (d, 2H, J = 8.9 Hz C_2-H and C_6-H pyridine ring), 8.14 (d, 2H, J = 7.9 Hz C_3-H and C_5-H pyridine ring), 8.08 (s, 1H, C_5-H pyrazole ring), 7.18-7.72 (m, 12H, $Ar-H$), 5.86 (s, 1H, C_5-H oxadiazole ring), 2.40 (s, 3H, $-CH_3$), 2.31 (s, 3H, $-CH_3-C=N$); ^{13}C NMR (100 MHz, DMSO- d_6): δ = 157.6 (1C, C_5 oxadiazole ring), 157.2 (1C, $JC-F$ 233.4 c/sec , $C_4C_5H_3-N=$), 156.3 (1C, $-CH=N-$), 149.7 (1C, C_3 pyrazole ring), 149.4 (2C, C_2 and C_6 pyridine ring), 146.4 (1C, $C_1C_5H_3-N=$), 139.5 (1C, C_1 aromatic ring), 138.4 (1C, C_4 pyridine ring), 133.4, 131.2 (1C, $C_4C_6H_4-CH_3$), 130.9 (1C, $C_1C_6H_4-CH_3$), 129.4 (2C, C_3 and $C_5C_6H_4-CH_3$), 129.2 (2C, C_3 and C_5 aromatic ring), 126.7 (1C, C_4 aromatic ring), 125.9 (2C, C_2 and $C_6C_6H_4-CH_3$), 124.9 (2C, C_3 and C_5 pyridine ring), 124.5 (1C, $C_2C_5H_3-N=$), 123.7 (1C, C_5 pyrazole ring), 122.8 (2C, C_3 and $C_6C_5H_3-N=$), 119.0 (2C, C_2 and C_6 aromatic ring), 118.9 (1C, $C_5C_5H_3-N=$), 117.5 (1C, C_4 pyrazole ring), 78.5 (1C, C_2 oxadiazole ring), 21.9 (1C, $C_6H_4-CH_3$), 21.7 (1C, $=CH-CH_3$); LCMS (ESI): m/z 552.2 (38.5%) [M^+]; Anal. calcd. for $C_{31}H_{24}ClFN_6O$: C, 67.57; H, 4.39; N, 15.25; Found: C, 67.63; H, 4.42; N, 15.32%.

Antimicrobial assay

Antimicrobial studies of newly synthesized derivatives **5a-t** were carried out against the representative group of Gram positive *S. aureus* (MTCC-96), *S. pyogenes* (MTCC-442) and Gram-negative *E. coli* (MTCC-443), *P. aeruginosa* (MTCC-1688) bacterial and fungal strains such as, *C. albicans* (MTCC-227), *A. niger* (MTCC-282) and *A. clavatus* (MTCC-1323). The results depicted in Table 2 exposed that most of the tested compounds displayed variable inhibitory effects. These all titled compounds (**5a-t**) were shown screening at different concentration of 1000, 500, 200, 100, 50, and 25 $\mu g/mL$ by broth dilution method [27-29]. In this method 2% DMSO used as a diluents and standard drugs to test upon standard microbial strains. At 1000 $\mu g/mL$ concentration synthesized compounds were diluted. The control tube containing no antibiotic was immediately subcultured [before inoculation] by spreading a loopful evenly over quarter of a plate of medium suitable for the growth of test organisms. At 37°C, for 24 h the culture tubes were then incubated and the development of bacteria was monitored visually and spectrophotometrically. 10 $\mu g/mL$ suspensions were more inoculated on a suitable media, after 24 and 48 h development of bacterial strains was noted. The lowest concentration (the highest dilution) required to arrest the growth of bacteria was regarded as MIC. DMSO and sterilized distilled water were used as negative control, while chloramphenicol antibiotic (1 U strength) was used as positive control. The recently synthesized derivatives **5a-t** was displayed for their antifungal activity against in six sets against *C. albicans* (MTCC-227), *A. niger* (MTCC-282) and *A. clavatus* (MTCC-1323) at various primary concentrations of 1000, 500 and 250 $\mu g\ ml^{-1}$. The primary screen active compounds were similarly diluted to obtain 200, 125, 100, 62.5, 50, 25 and 12.5 $\mu g\ ml^{-1}$ concentrations for secondary screening to test in a second set of dilution against all microorganisms, For antifungal activity griseofulvin used as a standard drug, which showed 500, 100 and 100 $\mu g\ ml^{-1}$ MIC against responsible fungal strains such as *C. albicans*, *A. niger* and *A. clavatus*. For development of fungi, in the present method, we have used Sabourauds dextrose broth at 28°C in aerobic condition for 48 h. Sterilized distilled water and DMSO and used as negative controls while 'griseofulvin' (1 U strength) was used as a positive control".

Antimicrobial studies

For antibacterial activity ampicillin used as a standard drug and results displayed in Table 2. Compounds **5c** and **5l** having (C_6H_4-4-F), ($C_6H_4-4-NO_2$) displayed excellent activity against *E. coli*. In case of gram negative bacteria *P. aeruginosa*, compounds **5c** (C_6H_4-4-F) and **5r** ($C_6H_4-4-NO_2$)

exhibited very good and good activity at MIC = 25 and 50 $\mu\text{g ml}^{-1}$. Compound **5t** ($\text{C}_6\text{H}_3\text{-3-Cl-4-F}$) had shown MIC = 12.5 $\mu\text{g ml}^{-1}$ which observed as the highest inhibition against *S. pyogenes*. Other compounds showed moderate activity against bacterial strains as shown in Table 2. For antifungal activity MIC was carried out on *C. albicans*, *A. niger* and *A. clavatus* by conventional broth dilution method. Griseofulvin was used as a standard drug for antifungal activity at different concentration of 1000, 500, 250, 100, 50, 25 and 12.5 $\mu\text{g/mL}$. Excellent and good activity possessed against *C. albicans* and *A. clavatus* by derivatives **5i** ($\text{C}_6\text{H}_4\text{-4-OCH}_3$) and **5f** ($\text{C}_6\text{H}_4\text{-4-CH}_3$). Other derivatives showed moderate antifungal activity against responsible fungal strains. The results of the antifungal studies are reported in Table 2. Data given in table shown that the presence of functional group at *para* position amended antibacterial activity as compared to *ortho* and *meta* substituted derivatives.

Table 2. Results of antimicrobial activity of compounds (**5a-t**).

Sr. no.	-Ar	Minimum inhibitory concentration (MIC) for bacteria ($\mu\text{g/mL}$)				Minimum inhibitory concentration (MIC) for fungi ($\mu\text{g/mL}$)		
		<i>E.c.</i>	<i>P.a.</i>	<i>S.a.</i>	<i>S.p.</i>	<i>C.a.</i>	<i>A.n.</i>	<i>A.c.</i>
5a	$\text{C}_6\text{H}_4\text{-H}$	100	125	250	100	1000	>1000	>1000
5b	$\text{C}_6\text{H}_4\text{-2-F}$	100	1000	1000	250	1000	1000	1000
5c	$\text{C}_6\text{H}_4\text{-4-F}$	12.5	25	1000	250	500	>1000	>1000
5d	$\text{C}_6\text{H}_4\text{-2-CH}_3$	100	125	200	100	250	500	100
5e	$\text{C}_6\text{H}_4\text{-3-CH}_3$	500	250	1000	500	500	>1000	>1000
5f	$\text{C}_6\text{H}_4\text{-4-CH}_3$	200	250	200	25	50	100	50
5g	$\text{C}_6\text{H}_4\text{-2-OCH}_3$	100	200	250	250	>1000	>1000	>1000
5h	$\text{C}_6\text{H}_4\text{-3-OCH}_3$	250	250	1000	200	500	100	100
5i	$\text{C}_6\text{H}_4\text{-4-OCH}_3$	200	200	250	125	50	1000	50
5j	$\text{C}_6\text{H}_4\text{-2-NO}_2$	250	250	500	200	>1000	250	1000
5k	$\text{C}_6\text{H}_4\text{-3-NO}_2$	125	125	250	250	250	500	500
5l	$\text{C}_6\text{H}_4\text{-4-NO}_2$	12.5	200	250	200	1000	100	1000
5m	$\text{C}_6\text{H}_4\text{-2-Cl}$	200	125	250	125	1000	1000	1000
5n	$\text{C}_6\text{H}_4\text{-3-Cl}$	125	125	250	100	500	1000	>1000
5o	$\text{C}_6\text{H}_4\text{-4-Cl}$	100	200	500	100	1000	25	12.5
5p	$\text{C}_6\text{H}_4\text{-2-Br}$	200	250	250	250	1000	1000	1000
5q	$\text{C}_6\text{H}_4\text{-3-Br}$	250	250	500	100	500	>1000	>1000
5r	$\text{C}_6\text{H}_4\text{-4-Br}$	100	50	250	250	>1000	>1000	>1000
5s	$\text{C}_6\text{H}_3\text{-4-Br-2-CH}_3$	125	200	500	200	>1000	>1000	>1000
5t	$\text{C}_6\text{H}_3\text{-3-Cl-4-F}$	100	500	500	12.5	250	>1000	>1000
Ampicillin		100	100	250	100	-	-	-
Griseofulvin		-	-	-	-	500	100	100

E. c.- *Escherichia coli* MTCC 443; *P. a.*- *Pseudomonas aeruginosa* MTCC 1688, *S. a.*- *Staphylococcus aureus* MTCC 96; *S. p.*- *Staphylococcus pyogenes* MTCC 442; *C. a.*- *Candida albicans* MTCC 227; *A. n.*- *Aspergillus niger* MTCC 282; *A. c.*- *Aspergillus clavatus* MTCC 1323

SAR studies

SAR studies exposed that the antimicrobial activity in heterocyclic class of pyrazole, 1,3,4-oxadiazole and pyridine scaffolds rely on the character of the peripheral substituent and their spatial relationship within this framework. Different electronic environment of the molecules was confirmed by the pattern of substitution. The electronic nature of the substituent escort to important variance in antimicrobial activity. The occurrence of chloro, fluoro and nitro substituents at *para* situation on aromatic ring arrangement has enlarged the antibacterial activity of compounds

compared to those of electron withdrawing groups. The presence of electron donating such as methyl and methoxy group on phenyl ring provides a positive effect on antifungal activity.

Conclusion

We have synthesized novel series of (**5a-t**) by conventional method with growth in product of reactions. The excellent properties of this new series of titled compounds of antimicrobial activity deserve further examination. The mode of action at molecular level explains the activity observed. The effectiveness and deeper insight in to titled compounds' SAR study committed to show additional physiochemical and biological parameters.

Acknowledgments

The authors are thankful to the University Grants Commission (UGC) New Delhi, and Department of Science and Technology (DST), New Delhi, for financial support under the NON-SAP and DST-FIST programs respectively. N. C. Desai is highly thankful to the UGC, New Delhi for providing a UGC-BSR one-time grant (2012).

Supporting Information

IR, ^1H and ^{13}C NMR and Mass spectra have been provided in supporting information.

Conflict of interest

There is no conflict of interest.

Supporting Information

1. IR of -4- NO_2 Compound 5l

2. ¹H NMR of -4-NO₂ Compound 5l

3. Mass of 4-NO₂ Compound 5l

4. ^{13}C NMR of 4-NO₂ Compound 5l

5. Mass of 4-CH₃ Compound 5f

6. ¹³C NMR of -4-CH₃ Compound 5f

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