Synthesis, Characterization, and Biological Evaluation of Substituted 4-Methyl-5-nitro-2-(1-Phenyl-1H-[1, 2, 3] Triazol-4-ylmethoxy) Pyridine Derivatives

***Lavanya Rumandla, **G. Satyanarayana Goud**

*Assistant Professor, Department of Chemistry, NM Government Degree College, Jogipet, Telangana

**Assistant Professor, Department of Chemistry, Dr. BRR Government Degree College, Jadcherla, Telangana

INTRODUCTION:

Among nitrogen-containing five-membered heterocyclic compounds, **1,2,3-triazole** is one of the most important scaffolds because of its diverse applications in medicinal chemistry, chemical biology, organic synthesis, supramolecular chemistry, and various industrial fields [1]. The presence of the 1,2,3-triazole moiety in numerous biologically active compounds has attracted considerable attention owing to its excellent pharmacological properties and synthetic versatility.

Pyridine and its derivatives are widely distributed in nature and play indispensable roles in heterocyclic chemistry as well as medicinal chemistry. Pyridine-based ring systems constitute an important class of pharmacophores and have contributed significantly to the discovery and development of numerous therapeutic agents. Owing to their favorable physicochemical properties and diverse biological activities, pyridine derivatives are extensively employed in drug discovery. Furthermore, the pyridine scaffold readily accommodates a variety of substituents at different positions, facilitating the design and optimization of clinical candidates with improved pharmacokinetic profiles and enhanced biological potency.

In recent decades, pyridine derivatives have received considerable attention because of their broad spectrum of biological activities, including antiviral [2], anticancer [3], antifungal [4], anti-inflammatory [5], antimicrobial [6], and antitubercular [7] activities. These findings demonstrate the immense therapeutic potential of pyridine-containing compounds and encourage the continued development of novel pyridine-based molecules.

A survey of the literature reveals that numerous pyridine analogues exhibit potent activity against a wide range of pathogenic microorganisms. However, the emergence of antimicrobial drug resistance and the occurrence of undesirable side effects remain major challenges in the development of effective therapeutic agents. Consequently, the remarkable pharmacological profile of pyridine derivatives continues to stimulate the search for novel analogues with improved efficacy and safety.

The molecular hybridization approach, which involves the incorporation of two or more biologically active pharmacophores into a single molecular framework, has emerged as an effective strategy in medicinal chemistry for the development of compounds with enhanced biological activity and improved pharmacological properties. Since both **1,2,3-triazole** and **pyridine** moieties possess significant biological potential, their combination within a single molecular architecture is expected to produce compounds with enhanced therapeutic efficacy and structural diversity.

Based on these considerations, the present study focuses on the synthesis of a series of novel **4-methyl-5-nitro-2-(1-phenyl-1H-**[1,2,3]**triazol-4-ylmethoxy)pyridine derivatives**. The synthesized compounds were characterized using infrared (IR) spectroscopy, electrospray ionization mass spectrometry (ESI-MS), proton nuclear magnetic resonance

(^1H NMR), and carbon-13 nuclear magnetic resonance (^13C NMR) spectroscopy. Furthermore, the newly synthesized derivatives were evaluated for their cytotoxic and antimicrobial activities to investigate their potential as promising therapeutic agents.

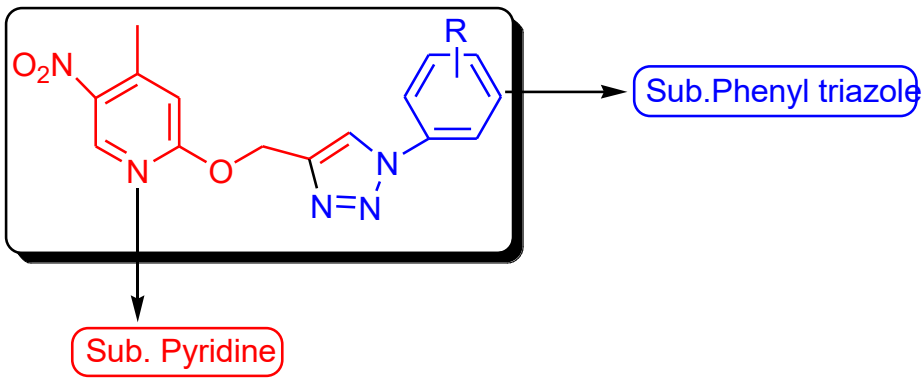
1.1 Methods and materials, Synthesis:

A concise review of the literature reveals several efficient synthetic approaches for the preparation of 1,2,3-triazole-linked heterocyclic derivatives with promising biological activities.

Qidong Tang et al. [8] designed, synthesized, and evaluated a series of novel pyrrolo[2,3-b]pyridine derivatives containing a 1,2,3-triazole moiety for their c-Met kinase inhibitory and antiproliferative activities against four human cancer cell lines (HT-29, A549, MCF-7, and PC-3) in vitro. Most of the synthesized compounds exhibited moderate to excellent biological activity. Among them, the most potent derivative demonstrated a c-Met kinase inhibitory activity with an IC_{50} value of 1.67 nM. Structure–activity relationship (SAR) studies revealed that the incorporation of electron-withdrawing substituents, such as X = CF3, R1 = F, and R2 = 4-F, on the molecular framework significantly enhanced the inhibitory activity by appropriately modulating the electron density around the five-atom linker

1.2 PRESENT WORK

To enhance the antibacterial potential of hybrid molecules containing multiple biologically active heterocyclic scaffolds, such as **pyridine** and **1,2,3-triazole**, we designed and synthesized a new series of pyridine–triazole hybrid derivatives. This work forms part of our ongoing research aimed at the development of novel pyridine- and triazole-based compounds with improved biological activity. In the present study, a series of novel **pyridine–triazole derivatives (a–l)** were synthesized and characterized. The synthesized compounds were subsequently evaluated for their antimicrobial activity against three representative Gram-positive bacterial strains using the disc diffusion method, and their inhibitory activities were investigated to assess their potential as promising antimicrobial agents



The wide range of biological applications and growing significance of Phenyl triazole-containing frameworks lead us to design an efficient and straight forward approach for synthesizing hybrid molecules with substituted phenyl triazoles and substituted Pyridineframeworks.

1.3 GENERAL EXPERIMENTAL METHODS

Merck was utilized straight out of the container without any additional purification, and TCI provided all of the chemicals, including the organic reagents and solvents. Using spectrometers set to run at 500 and 125 MHz (Bruker Avance II 400 MHz device), 1H and 13C NMR spectra were acquired in CDCl3. Singlet (s), doublet (d), doublet of doublet (dd), triplet (t), and multiplets (m) are the spin multiplicities. The coupling constant values are displayed in hertz. Parts per million (ppm) is the unit of measurement for chemical shift values. Distilled hexane and ethyl acetate were used as solvents in the chromatography process, which used a silica gel column with a mesh size range of 60–

120. The QSTAR XL GCMS and the Shimadzu FT-IR-8400s mass spectrometer were used to record the mass and infrared spectra, respectively. Melting points were measured in an exposed glass capillary tube using Dbk-Prog melting point equipment; the results were displayed without correction.

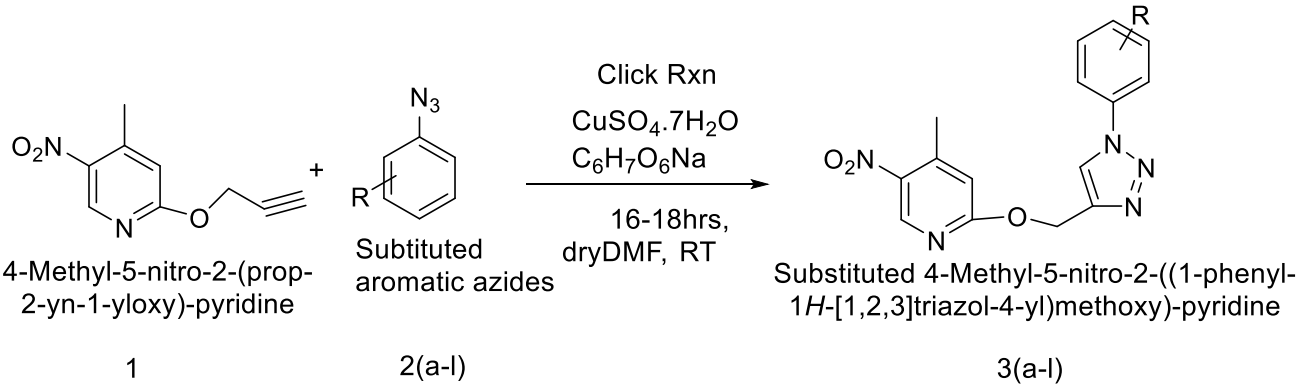
Experimental Procedure for the Synthesis of Substituted 4-Methyl-5-nitro-2-((1-phenyl-1H-[1,2,3]triazol-4-yl)methoxy)-pyridine 3(a-l):

The synthesis of substituted 4-methyl-5-nitro-2-((1-phenyl-1H-[1,2,3]triazol-4-yl)methoxy)pyridine derivatives (3a–l) was accomplished through a copper(I)-catalyzed azide–alkyne cycloaddition (CuAAC) "click" reaction. 4-Methyl-5-nitro-2-(prop-2-yn-1-yloxy)pyridine (1) was reacted with appropriately substituted azidobenzenes (2a–l) in the presence of CuSO4·7H2O and sodium ascorbate $C_6H_7O_6Na$ in dry DMF at ambient temperature. Under these click reaction conditions, the desired substituted 4-methyl-5-nitro-2-((1-phenyl-1H-[1,2,3]triazol-4-yl)methoxy)pyridine derivatives (3a–l) were obtained in good yields ranging from 80–86%.

The structures of the synthesized compounds were confirmed by IR, 1H NMR, 13C NMR, and ESI-MS spectral analyses. In the IR spectra, characteristic absorption bands were observed at 1533 cm^{-1} for the 1,2,3-triazole ring, 1453 cm^{-1} for the pyridine ring, and 1503 cm^{-1} for the aromatic benzene ring. The C–O–C stretching vibration of the ether linkage was also observed in the expected region, confirming the formation of the methoxy bridge.

In the 1H NMR spectra, the methyl (CH_3) protons appeared as a singlet at δ 2.45 ppm, while the methylene (CH_2) protons resonated as a singlet at δ 5.39 ppm. The characteristic proton of the 1,2,3-triazole ring appeared as a singlet at δ 8.82 ppm, whereas the pyridine N–CH proton was observed as a singlet at δ 9.28 ppm.

The 13C NMR spectra further supported the proposed structures. The carbon atom attached to the pyridine nitrogen resonated at δ 159.91 ppm, the triazole-linked carbon appeared at δ 154.80 ppm, and the aromatic carbon directly bonded to the triazole ring was observed at δ 136.46 ppm. These spectral data are in good agreement with the proposed structures of the synthesized pyridine–triazole derivatives.



Scheme-2

R=a=H, b=o-OCH_3, c=p-Br, d=p-NO_2, e=o-OH, f=p-OH, g=P-Cl, h=o-Me, i=p-Me,

j=p-OCH_3, k=p-CN, l=p-CF_3.

1.4 EXPERIMENTAL-TABLE-1:

S.No	Compound	M.P. (^{O}C)	M.F. (M.Wt.)	Time(h)	Yield (%)
1	4-methyl-5-nitro-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)pyridine (**3a**)	142-144	Mol. Formula: $C_{15}H_{13}N_5O_3$ (311)	8.5	83
2	2-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (**3b**)	152-154	Mol. Formula: $C_{16}H_{15}N_5O_4$ (341)	8.5	87
3	2-((1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (**3c**)	144-146	Mol. Formula: $C_{15}H_{12}BrN_5O_3$ (389)	9.5	82
4	4-methyl-5-nitro-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)pyridine (**3d**)	142-144	Mol. Formula: $C_{15}H_{12}N_6O_5$ (356)	10.5	84
5	2-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)phenol (**3e**)	148-150	Mol. Formula: $C_{15}H_{13}N_5O_4$ (327)	10	82
6	4-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)phenol (**3f**)	146-148	Mol. Formula: $C_{15}H_{13}N_5O_4$ (327)	9.5	88
7	2-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (**3g**)	150-152	Mol. Formula: $C_{15}H_{12}ClN_5O_3$ (345)	8.5	88
8	2-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (**3h**)	146-148	Mol. Formula: $C_{15}H_{12}BrN_5O_3$ (389)	9.5	84
9	4-methyl-5-nitro-2-((1-(p-tolyl)-1H-1,2,3-triazol-4-yl)methoxy)pyridine (**3i**)	154-156	Mol. Formula: $C_{16}H_{15}N_5O_3$ (325)	11.5	82
10	2-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (**3j**)	152-154	Mol. Formula: $C_{16}H_{15}N_5O_4$ (341)	9.5	84
11	4-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)benzonitrile (**3k**)	146-148	Mol. Formula: $C_{16}H_{12}N_6O_3$ (336)	10.5	82
12	4-methyl-5-nitro-2-((1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)methoxy)pyridine (**3l**)	156-158	Mol. Formula: $C_{16}H_{12}F_3N_5O_3$ (379)	11.5	85

1.5 ACTIVITY:

Cytotoxic Activity:

The % growth inhibitory activities of the synthesized compounds sub. 4-Methyl-5-nitro-2-(1-phenyl-1H-[1,2,3]triazol-4-ylmethoxy)-pyridine**(3a-l)** against MCF-7, HeLa, and PC-3 Cell lines

General Procedure:

The anticancer activity of all the synthesized derivatives containing substituted4-methyl-5-nitro-2-((1-phenyl-1H-1,2,3-triazol-4-yl) methoxy) pyridine **(3a-l)** nucleus was evaluated against three tumour cell lines (MCF-7, PC3 and Hela) by employing MTT assay. The in vitro screening for the anti-cancer activity of all the synthesized compounds was done in two steps. Initially, all the compounds were tested at two concentrations (5μM and 10μM) against the

above three cell lines and summarized in Table.1 to sort out the best compounds based on their percentage of cancer cell growth inhibition when they are incubated for 48 hrs. The initial screening study revealed that **3a-l** out of the total **3b, 3c, 3k,** and **3l** compounds exhibited significant anticancer activity with a range of 70-85% of cancer cell growth inhibition than the rest of the compounds.

Later, the selected compounds based on their anti-cancer activity were tested further with a greater number of concentrations so as to determine the IC_{50} value of the compounds which is a parameter used for the evaluation and comparison of the potency of the compounds with the standard drug used in this study. The IC_{50} values of the selected compounds were presented in **Table.2** and found to be in the range of 3.28±0.03μM, 4.08±0.06 μM, and 3.51±0.05 μM against MCF-7, PC-3 and HeLa cancer cell lines respectively. Whereas the IC_{50} value of the standard drug, doxorubicin was found to be 2.70±0.04μM (MCF-7), 3.81±0.03μM (PC-3), and 3.13±0.08 μM (HeLa). These results show that the selected compounds are more sensitive towards MCF-7 cancer cell lines than PC-3 and HeLa cancer cell lines.

CELL CULTURE

MC-7, PC-3 and HeLa were cultured in RPMI-1640 medium supplemented with 10% FBS, MCF-7 cells were maintained in MEM medium supplemented with 10% FBS. All the cell lines were cultured at humidified atmosphere containing 5% CO2 at 37◦C. The stock solutions of the synthesized derivatives were prepared in DMSO and added at desired concentrations to the cell culture. DMSO concentration did not exceed 1:1,000 in the final culture.

MTT ASSAY

Cytotoxic activities of the phenanthridine derivatives were evaluated by MTT assay. The stock solutions of synthesized derivatives were diluted with culture medium. The cells were seeded in 96-well plates at a density 5 × 10^4 cells per well and incubated until confluency 90–95%, then each well was treated with 100 μL medium containing the desired concentrations of synthesized derivatives and incubated for 48 h. 20 μL

MTT working solution (5 mg/mL) was then added to each well and incubated for another 4 h. At the end of incubation, the medium was carefully removed, and 200 μL DMSO was added. The optical density at 490 nm and 630 nm were then measured with a microplate reader (MODEL). The percentage of cell growth inhibition was calculated with the following equation:

% inhibition = [1– (Sample group OD490 – Samplegroup OD630)/ (Control group OD490-Control group OD630)] × 100%.

The IC_{50} values were calculated with Graphpad prism software, and standard deviations of the IC_{50} values were obtained from at least 3 independent experiments.

S.No	Entry Code	MCF-7		PC-3		HeLa	
		5μM	10μM	5μM	10μM	5μM	10μM
1	3a	69	74	57	68	65	72
2	**3b**	**90**	**86**	**82**	**91**	**84**	**87**
3	**3c**	**88**	**85**	**80**	**89**	**83**	**84**
4	3d	74	81	66	71	72	71
5	3e	61	68	52	62	61	68
6	3f	71	68	62	63	62	68
7	3g	72	76	60	62	63	71
8	3h	62	70	62	62	61	63
9	3i	62	65	55	61	64	68

10	3j	71	77	71	70	71	74
11	**3k**	**91**	**93**	**83**	**92**	**86**	**96**
12	**3l**	**90**	**87**	**81**	**91**	**87**	**91**
13	**Doxorubicin**	**94**	**98**	**85**	**94**	**89**	**98**
14	**Control**	**10**	**10**	**10**	**10**	**10**	**10**

Note: a.Values are average of three determinations and deviation of data results is 10-20 %

b. All compounds were dissolved in DMSO for testing.

c. MCF-7 Breast cancer cell lines

d. PC-3 Prostate Cancer cell lines

e. HeLa Cervical Cancer cell lines

As per the above preliminary screening studies, synthesized compounds **3b, 3c, 3k, and 3l** were found to have inhibited the growth of cancer cells effectively when compared with the other compounds. This compounds % growth inhibition was above 70% at the tested concentrations of 5µM& 10µM.Hence, those compounds with the best % growth inhibitory activity were selected, and they were further evaluated under the same conditions to determine the IC_{50} value at several concentrations such as 2, 4, 8, 16 and 32 µM.

Table-2: IC_{50} values of selected compounds with the standard drug doxorubicin:

		IC_{50} (µM±SEM)		
S.No	Entry No	MCF-7	PC-3	HeLa
1	**3b**	**3.62±0.03**	**3.30±0.09**	**3.41±0.06**
2	**3c**	**3.34±0.05**	**3.27±0.07**	**3.24±0.08**
3	3d	7.92±0.04	5.43±0.06	6.16±0.09
4	3e	7.39±0.05	9.62±0.14	7.07±0.11
5	3f	6.73±0.08	9.51±0.12	6.86±0.14
6	3g	4.77±0.03	4.13±0.06	4.68±0.05
7	3h	**3.28±0.05**	**4.08±0.03**	**3.51±0.02**
8	3i	**3.48±0.03**	**3.79±0.11**	**3.60±0.12**
9	**Doxorubicin**	**2.70±0.04**	**3.81±0.03**	**3.13±0.08**

1.6 ANTI-MICROBIAL ACTIVITY:

Antibacterial Activity of Compounds 3 (a-l):

By using the disc diffusion method, the antibacterial activity of all the newly synthesized compounds **3(a-l)** was evaluated against three representative Gram-positive bacteria (Bacillus Subtilis (MTCC 441), Bacillus Sphaericus (MTCC 11), and Staphylococcus Aureus (MTCC 96), as well as three representative Gram-negative bacteria (Pseudomonas Aeruginosa (MTCC 741), Klobsinella Aerogenes (MTCC 39), and ChromobacteriumViolaceum (MTCC 2656). Standard inoculums (1-2×107 c.f.u/mL 0.5 Mc Farland standards) were applied to the surface of sterile agar plates for the antibacterial test, and a sterile glass spreader was utilized to ensure uniform dispersion of the inoculums. The discs, which had a diameter of 6.26 mm, were made using Whatman No. 1 filter paper and dried at 140 °C for one hour. Nutrient agar medium was added to the sterile discs that had previously been soaked in a known concentration of the test chemicals. After being inverted, the plates were incubated at 37 °C for 24 hours. Table 3 presents the findings of measuring and comparing the mean inhibition zones with the standard medication Streptomycin.

Nearly all of the compounds **3(a-l)** are active and exhibit moderate to good antibacterial activity, according to the analysis of antibacterial screening data. Those with good activity were **3b, 3c, 3k, and 3 l (Table 3).** The activity of the other chemicals ranged from excellent to moderate.

Table 3. Antibacterial Activity of Compounds 37(a-l)

Mean zone inhibition (MZI)[a] in 100 μg/Ml						
Compound	***B. subtilis***	***B. sphaericus***	***S. aureus***	***P. aeruginosa***	***K. aerogenes***	***C. violaceum***
3a	19	16	20	14	15	18
3b	**31**	**24**	**31**	**18**	**28**	**23**
3c	**30**	**22**	**30**	**18**	**27**	**22**
3d	14	14	11	16	18	16
3e	16	12	16	12	12	13
3f	21	11	10	11	12	10
3g	14	13	20	12	18	13
3h	16	11	12	12	14	13
3i	12	12	12	12	18	16
3j	23	19	16	13	16	13
3k	**33**	**22**	**28**	**16**	**27**	**23**
3l	**32**	**23**	**29**	**17**	**27**	**23**
Streptomycin	**34**	**24**	**31**	**19**	**29**	**24**

[a]Values are mean (n = 3).

Antifungal Activity of Compounds 3(a-l):

Using the disc diffusion technique, compounds **3(a-l)** were further tested for their antifungal activity against Aspergillus fumigatus (HIC 6094), Trichophyton rubrum (IFO 9185), Trichophyton mentagrophytes (IFO 40996), and Candida albicans (ATCC 10231) in dimethyl sulfoxide (DMSO). The compounds examined for mean inhibition zone (MZI) values are listed in **Table 4**. Amphotericin B was employed as the reference medication, and the MZI results were measured and compared with controls.

The test compounds exhibited noteworthy action, according to the antifungal screening findings. Of the substances that were tested, compound It's noteworthy to note that compounds **3b, 3c, 3k, and 3l** shown strong antifungal activity against C. albicans, surpassing that of the conventional medication.

Table 4. Antifungal Activity of Compounds 37(a-l)

Compound	Mean zone inhibition (MZI)[a] in 100 μg/mL			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagrophytes*
3a	16	17	14	16
3b	**24**	**27**	**26**	**24**
3c	**23**	**26**	**25**	**23**
3d	18	17	21	18
3e	16	18	16	17
3f	15	16	14	18
3g	14	16	12	14
3h	19	21	19	17
3i	18	16	12	20
3j	16	13	16	18
3k	**24**	**26**	**24**	**23**
3l	**25**	**27**	**23**	**25**
Amphotericin B	**25**	**28**	**24**	**26**

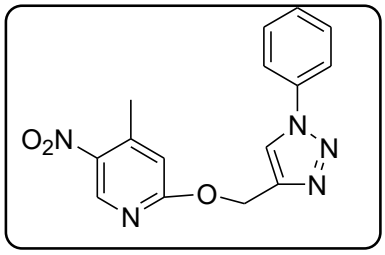
CONCLUSION

In conclusion, a series of novel **4-methyl-5-nitro-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)pyridine derivatives (3a–l)** were successfully synthesized via a click reaction and characterized by **IR, ^{1}H NMR, ^{13}C NMR, and ESI-MS** spectral analyses. The synthesized compounds were further evaluated for their **cytotoxic**, **antibacterial**, and **antifungal** activities.

Among the synthesized derivatives, compounds **3b**, **3c**, **3k**, and **3l** exhibited promising biological activity comparable to the reference standards. The enhanced inhibitory activity of these compounds may be attributed to the presence of **o-methoxy**, **p-bromo**, **p-cyano (nitrile)**, and **3-fluoro** substituents on the phenyl ring attached to the triazole moiety, respectively. These findings suggest that appropriate substitution on the phenyl ring of the triazole scaffold plays a crucial role in modulating the biological activity of the synthesized pyridine–triazole derivatives. Therefore, these compounds may serve as promising lead molecules for the development of new cytotoxic and antimicrobial agents.

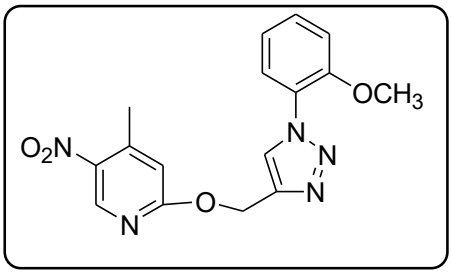
1.7 SPECTRAL DATA

Analytical data of 4-methyl-5-nitro-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)pyridine (3a)



Colour	Pale yellow solid
Yield	83%
Mol. Formula	$C_{15}H_{13}N_5O_3$
M.P	142-144°C
IR Data ν, cm^{-1}(KBr)	3380, 3160, 2929, 1657, 1603, 1294, 1039, 878, 754
^{1}H NMR-400 MHz (DMSO-d6)	9.28 (S, 1H), 8.82 (S, 1H), 7.89 (d, 2H, d=7.2Hz), 7.59 (t, 2H, J=7.6Hz), 7.51 (t, 1H, J=6.2Hz), 6.44 (s, 1H), 5.39 (S, 2H), 2.45 (s, 3H).
^{13}C NMR	159.91, 145.80, 142.95, 142.42, 136.46, 131.76, 129.93, 128.83, 122.12, 120.10, 119.07, 20.72
ESI-MS: m/z	311
Elemental Analysis	CAL: C, 77.87; H, 4.21; N, 22.50; O, 15.42 EXP: C, 74.50; H, 4.32; N,14.52; O, 8.64

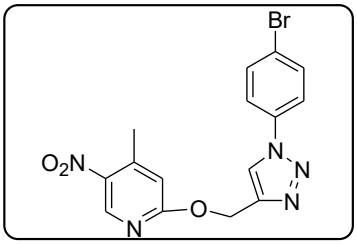
Analytical data of 4-methyl-5-nitro-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)pyridine (3b)



Colour	Pale yellow solid
Yield	87%
Mol. Formula	$C_{16}H_{15}N_5O_4$
M.P	152-154°C
IR Data ν, cm^{-1}(KBr	3148, 2991, 2792, 1999, 1532, 1728, 1643, 815, 682.
^{1}H NMR 400-MHz, DMSO-d6	8.95 (s, 1H), 8.30 (s, 1H), 7.74 (s, 1H), 7.43 (t, 1H, J=5.6Hz), 7.09 (d, 2H, J=6.4Hz), 6.38 (s, 1H), 5.34 (s, 2H), 3.89 (s, 3H), 2.52(s, 3H).
^{13}C NMR	159.88, 151.57.145.74, 142.33, 141.40, 131.66, 130.85, 125.92, 125.76, 125.46, 120.87, 119.0, 133.01, 56.12, 20.67
m/z	341
Elemental Analysis	CAL: C, 76.30; H, 4.43; N, 20.52; O, 18.75

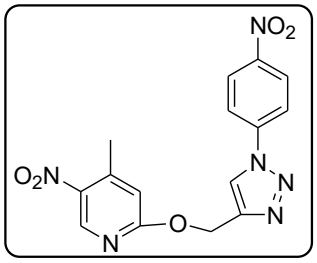
	EXP: C, 66.58, H, 3.99; Br, 13.56; N, 14.08

Analytical data of 2-((1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (3c)



Colour	White solid
Yield	82 %
Mol. Formula	$C_{15}H_{12}BrN_5O_3$
M.P	144-146°C
IR-Data ν, cm^{-1}(KBr	3151, 2955, 2794, 2001, 1546, 1732, 1644, 816, 689.
^{1}H NMR (400-MHz, DMSO-d6)	9.28 (s, 1H), 8.84 (s, 1H), 7.88 (d, 2H, J=6.3Hz), 7.80 (d, 2H, J=7.2Hz), 6.43 (s, 1H), 5.39 (s, 2H), 2.45 (s, 3H).
^{13}C NMR	159.85, 145.75, 143.15, 142.41, 135.63, 132.78, 131.72, 122.11, 121.89, 121.44, 119.05, 20.68.
m/z	389
Elemental Analysis	CAL:C, 76.17; H, 3.10; N, 8.95; O, 12.30 EXP: C, 75.20; H, 3.21; N, 8.52; O, 10.02

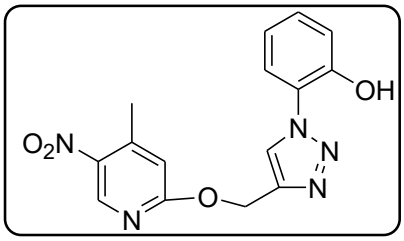
Analytical data of4-methyl-5-nitro-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)pyridine (3d)



Colour	Yellow solid
Yield	84%
Mol. Formula	$C_{15}H_{12}N_6O_5$
M.P	142-144° C
IR Data ν, cm^{-1}(KBr	3192, 2996, 2798, 2098, 1959, 1745, 1608, 821, 671.

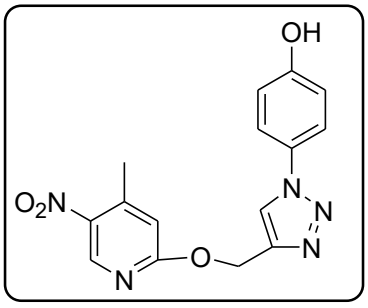
^{1}H NMR (400 MHz, DMSO-d6)	9.32 (s, 1H), 9.02 (s, 1H), 8.45 (d, 2H, J=6.7Hz), 8.23 (d, 2H, J=6.8 Hz), 6.45 (s, 1H), 5.42 (s, 2H), 2.50 (s, 3H).
^{13}C NMR	159.85, 146.78, 145.80, 143.66, 142.45, 140.66, 131.78, 125.58, 122.53, 120.65, 119.07, 20.69.
m/z	356
Elemental Analysis	CAL: C, 70.57; H, 3.39; N, 13.59; O, 8.45 EXP: C, 71.98; H, 3.32; Cl, 12.02; N, 8.21

Analytical data of 2-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)phenol (3e)



Colour	Yellow solid
Yield	82%
Mol. Formula	$C_{15}H_{13}N_5O_4$
M.P	148-150°C
IR-Data ν, cm^{-1}(KBr)	3425, 3187, 2986, 2791, 2081, 1962, 1598, 816, 666.
^{1}HNMR-400 MHz, DMSO-d6)	9.27 (s, 1H), 8.50 (s, 1H), 7.58 (d, 1H, J=6.3Hz), 7.34 (t, 1H, J=6.7 Hz), 7.14 (d, 1H, J=6.1 Hz), 6.97 (t, 1H, J=6.3 Hz), 6.43 (s, 1H), 5.38 (s, 2H), 2.20 (s, 3H).
^{13}C NMR	158.84, 145.77, 144.78, 142.87, 140.40, 136.66, 130.78, 123.82, 121.53, 119.45, 118.07, 19.69.
m/z	327
Elemental Analysis	CAL: C, 75.05; H, 4.00; N, 14.40; O, 16.55 EXP: C, 73.02; H, 4.12; N, 12.59; O, 12.01

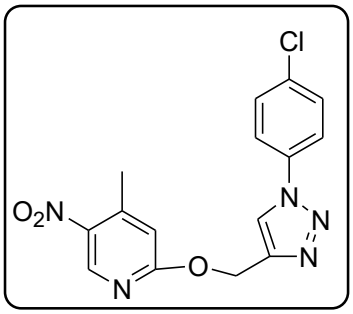
Analytical data of 4-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)phenol (3f)



Colour	Pale yellow solid,
Yield	88%

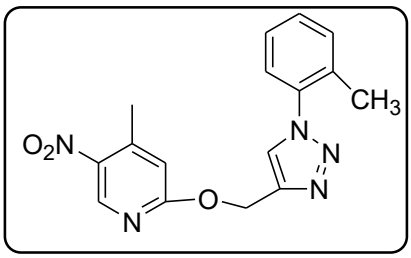
Mol. Formula	$C_{15}H_{13}N_5O_4$
M.P	146-148°C
IR Data ν, cm^{-1}(KBr)	3432, 3191, 2989, 2782, 2076, 1961, 1572, 812, 663.
^{1}H NMR (400-MHz, DMSO-d6)	9.92 (s, 1H), 9.25 (s, 1H), 8.61 (s, 1H), 7.64 (d, 2H, J=6.6 Hz), 6.92 (d, 2H, J=6.3 Hz), 6.43 (s, 1H), 5.36 (s, 2H), 2.50 (s, 3H).
^{13}C NMR	159.86, 157.81, 145.71, 142.36, 131.69, 128.57, 121.93, 119.02, 116.01, 20.68.
m/z	327
Elemental Analysis	CAL: C, 75.05; H, 4.00; N, 10.40; O, 09.55 EXP: C, 72.11; H, 3.78; N, 9.64; O, 09.72

Analytical data of 2-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (3g)



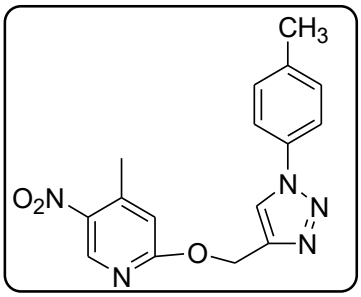
Colour	Yellow solid,
Yield	88%
Mol. Formula	$C_{15}H_{12}ClN_5O_3$
M.P	150-152°C
IR Data ν, cm^{-1}(KBr)	3195, 2992, 2783, 2077, 1963, 1575, 816, 666.
^{1}H NMR (400-MHz, DMSO-d6)	9.28 (s, 1H), 8.83 (s, 1H), 7.94 (d, 2H, J=6.2 Hz), 7.67 (d, 2H, J=6.1 Hz), 6.43 (s, 1H), 5.39 (s, 2H), 2.50 (s, 3H).
^{13}C NMR	159.85, 145.75, 143.12, 142.40, 135.23, 133.04, 131.72, 129.86, 122.17, 121.76, 119.05, 20.68.
m/z	345
Elemental Analysis	CAL:C, 72.11; H, 3.50; N, 10.26; O, 11.88 EXP: C, 71.95; H, 2.58; N, 11.56; O, 9.89

Analytical data of 2-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (3h)



Colour	White solid
Yield	84%
Mol. Formula	$C_{15}H_{12}BrN_5O_3$
M.P	146-148°C
IR Data ν, cm^{-1}(KBr)	3192, 2991, 2762, 2072, 1965, 1572, 814, 658.
^{1}H NMR (400-MHz, DMSO-d6)	9.27 (s, 1H), 8.49 (s, 1H), 7.47 (dd, 4H, J=6.1 Hz), 6.44 (s, 1H), 5.39 (s, 2H), 2.50 (s, 3H), 2.12(s, 3H)
^{13}C NMR	158.84, 144.71,141.79, 140.38, 136.40, 133.19, 131.69, 130.19, 128.21, 120.91, 118.91, 118.02, 19.66, 18.54.
m/z	389
Elemental Analysis	CAL:C, 69.17; H, 3.10; N, 14.95; O, 12.30 EXP: C, 67.56; H, 3.01; N, 12.68; O, 10.96

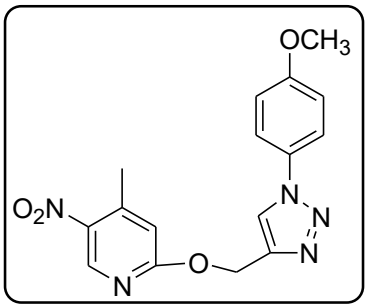
Analytical data of4-methyl-5-nitro-2-((1-(p-tolyl)-1H-1,2,3-triazol-4-yl)methoxy) pyridine (3i)



Colour	Yellow solid,
Yield	82%
Mol. Formula	$C_{16}H_{15}N_5O_3$
M.P	154-156°C
IR Data ν, cm^{-1}(KBr)	3192, 2991, 2762, 2072, 1965, 1572, 814, 658.
^{1}H NMR (400-MHz, DMSO-d6)	9.27 (s, 1H), 8.75 (s, 1H), 7.76 (d, 2H, J=6.1 Hz), 7.39 (d, 2H, J=6.2 Hz), 6.43 (s, 1H), 5.38 (s, 2H), 2.45 (s, 3H), 2.37(s, 3H)
^{13}C NMR	159.84, 145.71,142.79, 142.38, 138.40, 134.19, 131.69, 134.19, 130.21, 121.91, 119.91, 119.02, 20.66, 20.54.

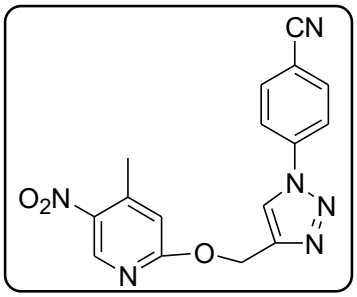
m/z	325
Elemental Analysis	C, 59.07; H, 4.65; N, 21.53; O, 14.75 EXP: C, 72.95; H, 3.67; N, 12.98; O, 13.46.

Analytical data of 2-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-5-nitropyridine (3j)



Colour	Pale yellow solid,
Yield	84%
Mol. Formula	$C_{16}H_{15}N_5O_4$
M.P	152-154°C
IR Data ν, cm^{-1} (KBr)	3131, 2997, 2767, 1972, 1765, 1552, 801, 671.
^{1}H NMR (400-MHz, DMSO-d6):	9.27 (s, 1H), 8.70 (s, 1H), 7.79 (d, 2H, J=621 Hz), 7.13 (d, 2H, J=6.43 Hz), 6.43 (s, 1H), 5.37 (s, 2H), 3.82 (s, 3H), 2.50(s, 3H)
^{13}C NMR	154.84, 144.71,141.79, 140.38, 137.40, 135.19, 131.69, 126.19, 122.21, 121.91, 120.91, 119.02, 38.66, 18.54.
m/z	341
Elemental Analysis	CAL:C, 76.30; H, 3.43; N,10.52; O, 13.75 EXP: C, 72.98; H,6.56; N, 12.87; O, 12.55

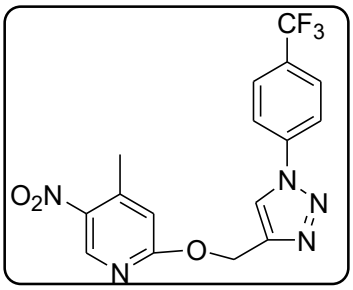
Analytical data of 4-(4-(((4-methyl-5-nitropyridin-2-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)benzonitrile (3k)



Colour	Pale yellow solid,
Yield	82%
Mol. Formula	$C_{16}H_{12}N_6O_3$

M.P	146-148°C
IR-Data ν, cm^{-1} (KBr)	3142, 2991, 2762, 1971, 1762, 1548, 799, 663.
^{1}H NMR (400-MHz, DMSO-d6):	9.29 (s, 1H), 8.96 (s, 1H), 8.13 (m, 2H), 6.44 (s, 1H), 5.41 (s, 1H),2.50(s, 3H)
^{13}C NMR	155.84, 145.71,143.79, 141.38, 136.40, 134.19, 132.69, 125.19, 122.27, 121.96, 120.95, 119.72, 38.65, 18.92.
m/z	336
Elemental Analysis	CAL: C, 57.14; H, 3.60; N, 24.99; O, 14.27 EXP: C, 72.98; H,8.56; N, 12.87; O, 12.55

Analytical data of 4-methyl-5-nitro-2-((1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)methoxy)pyridine (3l)



Colour	Pale yellow solid
Yield	85%
Mol. Formula	$C_{16}H_{12}F_3N_5O_3$
M.P	156-158°C
IR Data ν, cm^{-1} (KBr)	3162, 2998, 2772, 1976, 1768, 1558, 792, 661.
^{1}H NMR (400-MHz, DMSO-d6):	9.30 (s, 1H), 8.96 (s, 1H), 8.16 (d, 2H), 7.99 (s, 1H), 7.31 (s, 1H), 5.236 (s, 1H), 2.50(s, 3H)
^{13}C NMR	163.84, 151.71,145.79, 143.38, 138.40, 124.19, 128.69, 126.19, 122.27, 121.56, 120.21, 119.72, 39.65, 16.92.
m/z	379
Elemental Analysis	CAL: C, 77.67; H, 3.19; N, 12.46; O, 13.65 EXP: C, 70.65; H,3.56; N, 09.87; O, 10.23.

1.8 REFERENCES

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