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Synthesis, Characterization and Biological evaluation of some 1,2,3-Triazoles Containing Quinoline

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ABSTRACT

*A series of substituted 1,2,3-triazoles (**4a-n**) were synthesized from 4-azido-2,8-bistrifluoromethylquinoline (**2**). The 1,3-dipolar cycloaddition reaction of (**2**) with acetyl acetone gave 4-acetyl-1-(2,8-bistrifluoromethylquinolin-4-yl)-5-methyl-1H-1,2,3-triazole (**3**), which was then subjected to Claisen-Schmidt condensation with different aromatic aldehydes to afford 1-aryl-4-{1-[2,8-bistrifluoromethylquinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-ones (**4a-n**). The structures of newly synthesized compounds were characterized by analytical and spectral data. The synthesized 1,2,3-triazole derivatives were evaluated for qualitative (zone of inhibition) and quantitative antimicrobial activity (MIC). Preliminary pharmacological observations revealed that some of the derivatives shown promising in vitro antibacterial and antifungal activity.*

Keywords: 1,3–Dipolar cycloaddition, 4-Azido-2,8-bistrifluoromethylquinoline, Antimicrobial activity, Minimum inhibitory concentration, Zone of inhibition.

INTRODUCTION

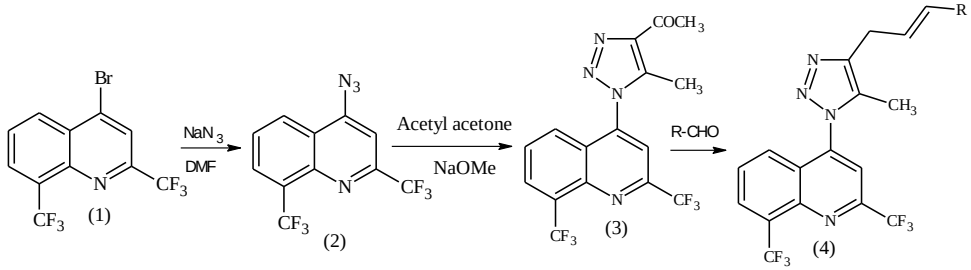
The enhanced prevalence of diseases caused by microorganisms has become a worldwide problem. The gradual development of resistance among pathogens to routinely used pesticides demands a renewed effort to seek antimicrobial agents effective against pathogenic microbes [1]. Further, the use of combinations of pesticides with different mode of activity can delay the process of resistance development among these pathogens. Fungicide mixtures may also display a synergistic interaction by which the amount of active ingredient used can be reduced. The control of routine disease caused by bacterial and fungal pathogens has become challenging due to rapid spread of these pathogens as well as lack of economical feasibility. In this context, development of new chemicals with dual activity against bacterial and fungal pathogens is required to overcome this problem. Functionalized 1,2,3-triazoles constitute one of the common fragments present in biologically active compounds [2] This has resulted in a wealth of synthetic methodology for their preparation and incorporation in more complex structures. The accentuated interest in these compounds continues to be expressed in the pharmaceutical community and biological properties of these

agents have been the subject of ongoing investigations [3]. The triazole scaffold has a wide range of therapeutic uses as it is ubiquitously found in drugs. The derivatives of 1,2,3-triazoles constitute an important family of heterocyclic compounds due to their chemotherapeutical values [4]. Some 1,2,3-triazoles are used as DNA cleaving agents and potassium channels activators [5]. Since many of them have remarkable antimicrobial [6,7], analgesic, anti-inflammatory [8], local anesthetic [9], antimalarial [10], antiviral [11] antiproliferatine [12], anticonvulsant [13], antineoplastic [14] and anticancer activity [15], their synthesis and transformations have been received particular interest for a long time. Fluorine incorporated compounds exhibit dramatically improved potency compared to their non-fluorinated analogues [16] since its incorporation alters the electronic, lipophilic and steric parameters and can critically increase the intrinsic activity, chemical and metabolic stability. In particular, introduction of CF_3 group in organic molecules immensely increased the pharmacological activity as well as lipophilicity [17]. Recently, we have reported the synthesis and antimicrobial studies of bioactive 1,2,3-triazoles attached to quinoline moiety with CF_3 group [3]. In continuation of our research on bioactive heterocycles and their biological evaluation, it was contemplated to synthesize some 1,2,3-triazoles containing bis - trifluoromethyl substituted quinoline moiety and to evaluate them for their *in vitro* antimicrobial activity.

MATERIALS AND METHODS

Melting points were determined by the open capillary method and are uncorrected. The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 4100 type A spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian 400 MHz NMR spectrometer/Perkin-Elmer EM 300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded on a MDS SCIEX/API4000 spectrophotometer. Elemental analysis was carried out using Flash EA 1112 Series, CHNSO Analyzer (Thermo). The progress of the reaction was monitored by thin layer chromatography (TLC) on pre-coated silica gel plates. All the reagents used are from Spectrochem and Aldrich. They were used directly without any purification.

The new derivatives of 1,2,3-triazoles (**4a-n**) were prepared by the method outlined in **Scheme 1**. The reaction of compound (**1**) with sodium azide in DMF to afford 4-azido-2,8-bistrifluoromethylquinoline (**2**). The reaction of 4-azido-2,8-bistrifluoromethylquinoline (**2**) with acetyl acetone in presence of sodium methoxide in methanol at 0 °C yielded 4-acetyl-1-(2,8-bistrifluoromethylquinolin-4-yl)-5-methyl-1*H*-1,2,3-triazole (**3**) which was then subjected to Claisen-Schmidt condensation with different aromatic aldehydes to afford 3-aryl-1-{1-[2,8-bistrifluoromethylquinolin-4-yl]-5-methyl-1*H*-1,2,3-triazol-4-yl}prop-2-en-1-ones (**4a-n**). The newly synthesized compounds were characterized by elemental analyses, IR, ^{1}H NMR and mass spectral data. The characterization data of compounds (**4a-n**) are given in table 1. The newly synthesized compounds were screened for their antibacterial and antifungal activities. The results of antimicrobial studies are summarized in table 2 and table 3.



R=-C_6H_5, 4-OCH_3-C_6H_4, 3-OCH_3-C_6H_4, 4-SCH_3-C_6H_4, 4-F-C_6H_4, 4-Cl-C_6H_4, 2-Cl-C_6H_4, 4-C_6H_5-C_6H_4, 3-pyridyl-C_6H_4, 4-OH-3-OCH_3-C_6H_3, 3,4-$(OCH_3)_2$-C_6H_3, 2-Cl-6-F-C_6H_3, 6-OCH_3-2-naphtyl, 2-NO_2-3,4-$(OCH_3)_2$-C_6H_2.

Scheme 1: Synthesis of 1,2,3-triazoles

RESULTS AND DISCUSSION

The single crystal X-ray crystallography of 4-acetyl-1-(2,8-bistrifluoromethylquinolin-4-yl)-5-methyl-1*H*-[1,2,3]triazole (**3**) was recorded [18] (fig 1). There are two independent molecules in the asymmetric unit of the compound (**3**). The triazole ring is not coplanar with the quinoline ring system; the dihedral angle between the two planes being 74.47 (12) and 63.97 (13)^0 in the two molecules. The crystal structure is characterized by intermolecular C—H….F, C—H….N and C—H….O hydrogen bonding. Weak intramolecular C—H….F interactions are observed. Bond distances within the aromatic rings are in agreement with those observed related structures. The packing of the molecules when viewed along the *a* axis is as shown in fig 2.

Crystal Data

$C_{16}H_{10}F_6N_4O$	*F*(000) = 1568
Mr = 388.28	*D*x = 1.534 Mg m−3
Monoclinic, *P*21/*n*	Melting point: 427 K
Hall symbol: -P 2yn	Mo *K*α radiation, λ = 0.71073 Å
a = 14.064 (2) Å	Cell parameters from 5923 reflections
b = 8.7275 (13) Å	θ = 1.5–25.0 °
c = 27.468 (4) Å	μ = 0.14 mm−1
β = 94.172 (2) °	*T* = 293 K
V = 3362.6 (9) Å3	Plate, colorless
Z = 8	0.20 × 0.20 × 0.15 mm

Data Collection

Bruker SMART CCD area-detector diffractometer	5923 independent reflections
Radiation source: fine-focus sealed tube	4754 reflections with *I* > 2σ(*I*)
Graphite	*R*int = 0.028
ω and φ scans	θmax = 25.0°, θmin = 1.5°
Absorption correction: ψ scan (*SADABS*; Bruker, 2001)	*h* = −16→16
*T*min = 0.972, *T*max = 0.979	*k* = −10→10
23473 measured reflections	*l* = −32→30

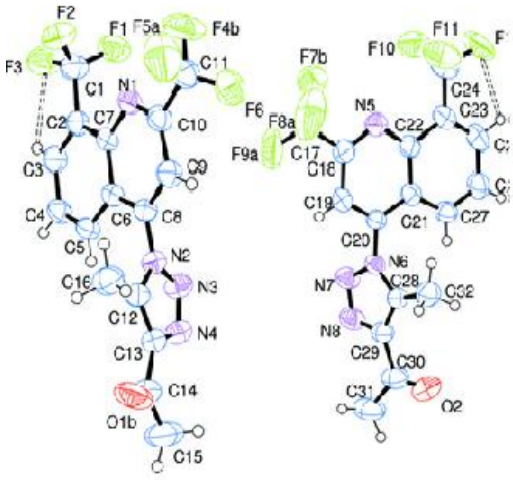


Fig 1: The molecular structure of 4-acetyl-1-(2,8-bistrifluoromethylquinolin-4-yl)-5-methyl-1,2,3-triazole (**3**).Displacement ellipsoids are drawn at the 50% probability level. Dashed lines indicate hydrogen bonds.

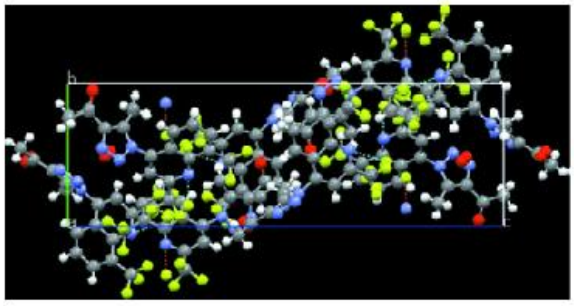


Fig 2: A view of the structure down the axis a.

Table 1. Characterization data of 1,2,3-triazoles, **4a-n**

Compd.	R_1/R_2	Mol. Formula	Mol. Wt.	M. P. (° C)	Yield (%)
4a	C_6H_5	$C_{23}H_{14}F_6N_4O$	476.37	180-182	60
4b	4-OCH_3-C_6H_4	$C_{24}H_{16}F_6N_4O_2$	506	218-220	65
4c	3-OCH_3-C_6H_4	$C_{24}H_{16}F_6N_4O_2$	506	186-188	64
4d	4-SCH_3-C_6H_4	$C_{24}H_{16}F_6N_4OS$	522.46	122-124	70
4e	4-OH-3-OCH_3-C_6H_3	$C_{24}H_{16}F_6N_4O_3$	522.39	280	66
4f	3,4-$(OCH_3)_2$-C_6H_3	$C_{25}H_{18}F_6N_4O_3$	536.42	142-144	80
4g	2-NO_2-3,4-$(OCH_3)_2$-C_6H_2	$C_{25}H_{17}F_6N_5O_5$	581.42	180	64
4h	4-F-C_6H_4	$C_{23}H_{13}F_7N_4O$	494.36	142-144	75
4i	2-Cl-C_6H_4	$C_{23}H_{13}ClF_6N_4O$	510	116-118	70
4j	4-Cl-C_6H_4	$C_{23}H_{13}ClF_6N_4O$	510	218-220	68
4k	2-Cl-6-F-C_6H_3	$C_{23}H_{12}ClF_7N_4O$	528.8	220	68
4l	4-C_6H_4-C_6H_4	$C_{29}H_{18}F_6N_4O$	522.46	146-148	72
4m	6-OCH_3-2-naphtyl	$C_{28}H_{18}F_6N_4O_2$	556.46	210-212	62
4n	3-pyridyl	$C_{22}H_{13}F_6N_5O$	477.36	104-106	60

Antimicrobial activity: The newly synthesized 1,2,3-triazoles (**4a-n**) were screened for their *in vitro* antibacterial and antifungal activity. For antibacterial studies micro-organisms employed were *Staphylococcus aureus*, *Escherichia coli*, Pseudomonas *aeruginosa* and *Klebsiella pneumoniae.* For antifungal screening, *Aspergillus flavus*, Aspergillus *fumigatus*, *Penicillium Marneffei* and *Trichophyton mentagrophytes* strains were used. Both microbial studies were assessed by Minimum Inhibitory Concentration (MIC) by serial dilution method [19]. For this, the compound whose MIC has to be determined was dissolved in serially diluted DMF. Then a standard drop of the culture prepared for the assay is added to each of the dilutions, and incubated for 16–18 h at 37 °C. MIC is the highest dilution of the compound, which shows clear fluid with no development of turbidity. The antimicrobial activity data are presented in table 2 and table 3. Ciprofloxacin and Cyclopiroxolamine were used as reference standards for antibacterial and antifungal activity respectively. In order to ensure that the solvent had no effect on bacterial growth, a negative control test also performed containing inoculated broth supplemented with only DMF at the same dilution used in our experiment and found inactive in culture media. Three replicates were made for each analysis. The MIC values were evaluated at concentration range, 0.024-50 µg mL^{-1}. The MIC was noted by seeing the lowest concentration of the drug at which there was no visible growth. The figures in the tables show the MIC values in µg mL^{-1}.

Table 2: Antibacterial activity data of 1,2,3-triazoles**, 4a-n**

Compd.	*S. aureus*	*E. coli*	*P. aeruginosa*	*K. pneumoniae*
4a	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)
4b	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4c	12.5 (10-15)	12.5 (11-16)	12.5 (16-20)	6.25 (16-20)
4d	12.5 (10-15)	12.5 (11-16)	12.5 (16-20)	6.25 (16-20)
4e	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4f	6.25 (16-20)	12.5 (16-20)	12.5 (16-20)	6.25 (16-20)
4g	25 (13-17)	25 (15-19)	25 (13-18)	25 (15-19)
4h	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)
4i	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)

4j	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)
4k	12.5 (11-15)	12.5 (11-16)	12.5 (11-15)	12.5 (11-15)
4l	6.25(16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4m	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)
4n	3.125 (20-25)	6.25 (16-20)	6.25(16-20)	6.25(16-20)
Ciprofloxacin	1.56 (22-30)	6.25 (30-40)	6.25 (25-33)	6.25 (23-27)

The variation in antimicrobial activity of the test compounds was explored by varying only one substituent, *viz*. 3-aryl-prop-2-en-1-one at the 4 position of the 1,2,3-triazole moiety. In this connection different electron donating or electron withdrawing groups attached to the phenyl ring as substituents are studied to explore the antimicrobial potency. Among the tested compounds, **4n** exhibited maximum antimicrobial activity against all the bacterial pathogens, which may be due to the presence 3-pyridyl moiety. On the other hand, The compounds containing one or more electron releasing group/s *viz*. 4-OMe (**4b**), 2-OH-3-OMe (**4e**), 3-OMe (**4c**), 3,4-$(OMe)_2$ (**4f**), 4-SCH_3 (**4d**) in the phenyl ring exhibited good to moderate activity. The compounds with 4-OMe and 2-OH-3-OMe groups shown maximum inhibition zone compared to 3-OMe, 3,4-$(OMe)_2$, 4-SCH_3 substituents and unsubstituted phenyl group. However, compounds with electron withdrawing 4-Cl (**4j**), 2-Cl-6-F (**4k**), 2-NO_2-3,4-$(OMe)_2$ (**4g**), 4-F (**4h**) and 2-Cl (**4i**) substituents showed moderate and marginal antimicrobial activity. The replacement of phenyl ring with a naphthyl ring containing electron releasing substituent (**4m**) also showed only marginal activity. On the other hand, replacement of phenyl ring with biphenyl ring (**4l**) resulted in dramatic increase in the activity.

Table 3: Antifungal activity data of [1,2,3]triazoles**, 4a-n**

Compd.	*A. flavus*	*A. fumigatus*	*P. marneffei*	*T. mentagrophytes*
4a	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)
4b	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4c	6.25 (16-20)	12.5 (11-15)	12.5 (11-15)	6.25 (16-20)
4d	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4e	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)	6.25 (16-20)
4f	6.25 (16-20)	12.5 (16-20)	12.5 (16-20)	6.25 (16-20)
4g	25 (13-18)	12.5 (11-15)	25 (13-17)	25 (15-19)
4h	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)
4i	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)
4j	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)
4k	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)	12.5 (11-15)
4l	6.25 (16-20)	12.5 (11-15)	12.5 (11-15)	6.25 (16-20)
4m	25 (13-17)	25 (13-17)	25 (13-17)	25 (13-17)
4n	6.25 (16-20)	12.5 (11-15)	12.5 (11-15)	6.25 (16-20)
Cyclopiroxolamine	3.125 (25-30)	6.25 (25-30)	6.25 (20-27)	3.125 (27-33)

Experimental

Procedure for the Synthesis of 4-Azido-2,8-bis-trifluoromethylquinoline (2) : 4-Bromo-2,8-bis-trifluoromethylquinoline (**1**) (10g, 0.029 mol) was treated with 2.08g (0.03 mol) of sodium azide in 5 volume of DMF. The reaction mixture was heated to 90 °C for 1 h. The progress of the reaction was monitored by TLC using hexane/ethyl acetate as mobile phase. After the completion of reaction, the reaction mixture was cooled to 20 °C and quenched to ice water. The precipitated yellow colored 4-azido-2,8-bis-trifluoromethylquinoline (**2**) was isolated by filtration. Recrystallisation of the crude product from methanol gave pure product as colorless micro crystals (yield 8.55g (85.48%), m.p. 63-65 °C). IR (KBr, $\gamma_{max,}$ cm^{-1}): 3020 (Ar-H), 2111 (N_3), 1575 (C=N), 1128 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.51 (s,

1H, quinolinyl-H), 7.69 (t, 1H, quinolinyl-H, *J*=7.8 Hz), 8.186 (d, 1H, quinolinyl-H, *J*=7.2 Hz), 8.33 (d, 1H, quinolinyl-H, *J*=7.2 Hz); Anal. Calcd. (%) for $C_{11}H_4F_6N_4$: C, 43.15; H ,1.32; N, 18.30; Found: C, 43.14; H, 1.30; N, 18.28.

Synthesis of 4-Acetyl-1-(2,8-bistrifluoromethylquinolin-4-yl)-5-methyl-1H-1,2,3-triazole (3) : A solution of 4-azido-2,8-bistrifluoromethylquinoline (**2**) (2.5g, 0.008 mol) in methanol (25 mL) was treated with acetyl acetone (0.9g, 0.009 mol) and the mixture was cooled to 0 °C. Sodium methoxide (0.009 mol) was added in lots under nitrogen atmosphere over a period of 30 minutes and the temperature was slowly increased to 25-26 °C. It was then stirred for 3 h. The progress of the reaction was monitored by TLC using ethyl acetate/hexane as mobile phase. The reaction mass was quenched to ice water, filtered and dried. The recrystallisation of the crude product from methanol gave yellow crystals of the title compound (yield 2.4g (76%), m. p. 152-154 °C). IR (KBr, $\gamma_{max,}$ cm^{-1}): 3030 (Ar-H), 1681 (C=O), 1578 (C=C), 999 (C-F); ^{1}H NMR (400 MHz, CD_3OD, δ ppm): 2.50 (s, 3H, CH_3), 2.75 (s, 3H, $COCH_3$), 7.80 (d, 1H, quinolinyl-H, *J*=8.4 Hz), 7.95 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 8.319 (s, 1H, quinolinyl-H), 8.42 (d, 1H, quinolinyl-H, *J*=8.4 Hz); ^{13}C NMR (100 MHz, CD_3OD, δ ppm): 8.44, 26.56, 116.39, 122.02, 124.73, 125.20, 127.18, 128.47, 128.77, 129.75, 130.65, 130.70, 140.31, 141.77, 143.19, 144.71, 148.34, 148.71, 193.95; DEPT (100 MHz, CD_3OD, δ ppm): 8.44, 26.56, 116.39, 127.19, 129.75, 130.65, 130.70; MS (m/z): 388 (M^+); Anal. Calcd. (%) for $C_{16}H_{10}F_6N_4O$: C, 49.49; H, 2.60; N, 14.43; Found: C, 49.47; H, 2.61; N, 14.44.

General Procedure For Synthesis of 3-Aryl-1-{-1-[2,8-bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-one (4a-n) : The 4-Acetyltrialzole (**3**) was treated with equimolar quantity of aromatic aldehydes in methanol (10 volume). The mixture was cooled to 10 °C, 10% sodium hydroxide (1 volume) was added and stirred for 8 h. The completion of the reaction was checked by TLC (Ethyl acetate/hexane). The reaction mass was cooled to 0 °C, filtered and washed with cold methanol to yield the title compound. The recrystallisation was done using methanol to get pure compound.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-phenyl prop-2-en-1-one (4a) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3045 (Ar-H), 1689 (C=O), 1595 (C=C), 1189 (C-F); ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 2.55 (s, 3H, CH_3), 7.06-7.12 (m, 3H, phenyl-H), 7.34 (d, 2H, phenyl-H, *J*=7.8 Hz), 7.39 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.52 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 7.65 (s, 1H, quinolinyl-H), 7.83 (d, 1H, CH=CH, *J*=15.6 Hz), 7.91 (d, 1H, CH=CH, *J*=15.6 Hz), 8.25 (d, 1H, quinolinyl-H, *J*=8.0 Hz). Anal. Calcd. (%) for $C_{23}H_{14}F_6N_4O$: C, 57.99; H, 2.96, N, 11.76; Found C, 57.98; H, 2.98; N, 11.77.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(4-ethoxy phenyl)prop-2-en-1-one (4b): IR (KBr, $\gamma_{max,}$ cm^{-1}): 3055 (Ar-H), 1692 (C=O), 1598 (C=C), 1185 (C-F); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.60 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 6.97 (d, 2H, 4-methoxyphenyl-H, *J*=8.0 Hz), 7.36 (d, 2H, 4-methoxyphenyl-H, *J*=8.0 Hz), 7.40 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.54 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 7.72 (s, 1H, quinolinyl-H), 7.85 (d, 1H, CH=CH, *J*=16 Hz), 7.99 (d, 1H, CH=CH, *J*=16 Hz), 8.33 (d, 1H, quinolinyl-H, *J*=8.0 Hz); MS (m/z): 507 (M+1). Anal. Calcd. (%) for $C_{24}H_{16}F_6N_4O_2$: C, 56.92; H, 3.18; N, 11.06; Found C, 56.93; H, 3.19; N, 11.07.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(3-methoxy phenyl)prop-2-en-1-one (4c) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3033 (Ar-H), 1690 (C=O), 1575 (C=C), 1095 (C-F); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.61 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 6.98-7.06 (m, 4H, 3-methoxyphenyl-H), 7.42 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.55 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 7.73 (s, 1H, quinolinyl-H), 7.89 (d, 1H, CH=CH, *J*=16 Hz), 7.99 (d, 1H, CH=CH, *J*=16 Hz), 8.35 (d, 1H, quinolinyl-H, *J*=8.0 Hz); MS (m/z): 507 (M+1). Anal. Calcd. (%) for $C_{24}H_{16}F_6N_4O_2$: C, 56.92; H, 3.18; N, 11.06. Found C, 56.93; H, 3.19; N, 11.07.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(4-methylthio phenyl)prop-2-en-1-one (4d) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3072 (Ar-H), 1659 (C=O), 1588 (C=C), 1095 (C-F); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.53 (s, 3H, CH_3), 2.59 (s, 3H, *S*-CH_3), 7.65 (d, 2H, 4-methylthiophenyl-H, *J*=8.4 Hz), 7.70 (d, 2H, 4-methylthiophenyl-H, *J*=8.4 Hz), 7.82-7.86 (m, 2H, quinolinyl-H), 7.90 (s, 1H, quinolinyl-H), 7.94 (d, 1H, CH=CH, *J*=15.7 Hz), 8.05 (d, 1H, CH=CH, *J*=15.8 Hz), 8.32 (d, 1H, quinolinyl-H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 10.04, 15.05, 115.93, 119.123, 121.363, 121.68, 121.86, 124.40, 125.06, 125.88, 126.83, 129.26, 129.63, 129.85, 130.65, 130.71, 131.10, 140.30, 141.54, 143.02, 144.12, 144.23, 145.12, 148.72, 149.08, 183.80; DEPT (100 MHz, $CDCl_3$, δ ppm): 10.04, 15.05, 115.92, 121.36, 125.88, 126.83, 129.26, 129.63, 130.71, 144.23; Anal. Calcd. (%) for $C_{24}H_{16}F_6N_4OS$: C, 55.17; H, 3.09; N, 10.72; Found C, 55.15; H, 3.08; N, 10.71.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(3,4-dimethoxy phenyl)prop-2-en-1-one (4f) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3072 (Ar-H), 1690 (C=O), 1578 (C=C), 1180 (C-F); ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 2.29 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 7.02-7.08 (m, 3H, 3,4-dimethoxyphenyl-H), 7.43 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.57 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 7.75 (s, 1H, quinolinyl-H), 7.90 (d, 1H, CH=CH, *J*=16 Hz), 8.05 (d, 1H, CH=CH, *J*=16 Hz), 8.37 (d, 1H, quinolinyl-H, *J*=8.0 Hz); MS (m/z): 537 (M^+); Anal. Calcd. (%) for $C_{25}H_{18}F_6N_4O_3$: C, 55.98; H, 3.38; N, 10.44; Found C, 55.97; H, 3.37; N, 10.45.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]trazol-4-yl}-3-(3,4 dimethoxy-2-nitro phenyl)prop-2-en-1-one (4g) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3070 (Ar-H), 1700 (C=O), 1581 (C=C), 1535, 1380 (NO_2), 1105 (C-F); ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.52 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 7.47 (d, 1H, nitrodimethoxyphenyl-H, *J*=8.0 Hz), 7.70 (d, 1H, nitrodimethoxyphenyl-H, *J*=8.0 Hz), 7.88 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.94 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 8.01 (s, 1H, quinolinyl-H), 8.03 (d, 1H, CH=CH, *J*=15.8 Hz), 8.22 (d, 1H, CH=CH, *J*=15.8 Hz), 8.63 (d, 1H, quinolinyl-H, *J*=8.0 Hz); MS (m/z): 582 (M^+); Anal. Calcd. (%) for $C_{25}H_{17}F_6N_5O_5$: C, 51.64, H, 2.95, N, 12.05; Found C, 51.63, H, 2.96, N, 12.06.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(4-chlorophenyl)prop-2-en-1-one (4j) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 2980 (Ar-H), 1664 (C=O), 1600 (C=C), 1164 (C-F), 772 (C-Cl); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 2.60 (s, 3H, CH_3), 7.43 (d, 2H, 4-chlorophenyl, *J*=8.2 Hz), 7.68 (d, 2H, 4-chlorophenyl, *J*=8.2 Hz), 7.83-7.87 (m, 2H, quinolinyl-H), 7.90 (s, 1H, quinolinyl-H), 7.93 (d, 1H, CH=CH, *J*=15.6 Hz), 8.08 (d, 1H, CH=CH, *J*=15.6 Hz), 8.33 (d, 1H, quinolinyl-H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 10.04, 115.92, 119.11, 121.85, 121.91, 124.39, 124.40, 125.03, 126.76, 129.32, 129.66, 130.02, 130.68, 130.73, 133.17, 136.86, 140.48, 141.48, 143.22, 143.98, 145.13, 148.74, 149.11, 183.67; DEPT (100 MHz, $CDCl_3$, δ ppm): 10.05, 115.91, 122.90, 126.77, 29.32, 129.67, 130.03, 130.73, 143.21; MS (m/z): 510 (M^+); Anal. Calcd. (%) for $C_{23}H_{13}ClF_6N_4O$: C, 54.08; H, 2.57; N, 10.97. Found C, 54.09; H, 2.57; N, 10.96.

1-{1-[2,8-Bis(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-[1,2,3]triazol-4-yl}-3-(pyridin-3-yl)prop-2-en-1-one (4n) : IR (KBr, $\gamma_{max,}$ cm^{-1}): 3020 (Ar-H), 1698 (C=O), 1590 (C=N), 1579 (C=C), 1199 (C-F); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 2.61 (s, 3H, CH_3), 7.43 (t, 1H, pyridyl-H, *J*=5.0 Hz), 7.68 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 7.85 (t, 1H, quinolinyl-H, *J*=8.0 Hz), 7.89 (s, 1H, quinolinyl-H), 7.96 (d, 1H, CH=CH, *J*=15 Hz), 7.99 (d, 1H, pyridyl-H, *J*=7.8 Hz), 8.15 (d, 1H, CH=CH, *J*=15 Hz), 8.33 (d, 1H, quinolinyl-H, *J*=8.0 Hz), 8.41-8.48 (m, 1H, pyridyl-H), 8.71(s, 1H, pyridyl-H); Anal. Calcd. (%) for $C_{22}H_{13}F_6N_5O$: C, 55.35; H, 2.74; N, 14.67; Found C, 55.33; H, 2.73; N, 14.65.

APPLICATIONS

The synthesized 1,2,3-triazole derivatives were evaluated for qualitative (zone of inhibition) and quantitative antimicrobial activity (MIC). Preliminary pharmacological observations revealed that some of the derivatives shown promising in vitro antibacterial and antifungal activity.

CONCLUSIONS

The study reports the synthesis of title compounds by 1,3-dipolar addition in normal to good yield and anti microbial activity of these derivatives containing quinoline derivative against wide range of bacterial and fungal strains. The investigation of SAR of the above new 1,2,3-triazoles containing different substituents on position 4 of the triazole ring revealed that electron releasing substituents in the phenyl ring show relatively significant antimicrobial activity. On the other hand, above derivatives with electron withdrawing substituents in the phenyl ring shows marginal activity. Naphtyl ring cause dramatic reduction in the activity, while pyridyl and biphenyl rings enhance the activity. These results suggest that the effect of 4-substitution on the triazole moiety on antimicrobial activity is mostly due to the electronic and steric factors of the groups.

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