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Original article

# Synthesis and biological evaluation of new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives via click chemistry approach

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ABSTRACT

Synthesis of new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives (**4a**–**h**) using 1,3-dipolar cycloaddition (click chemistry) reaction of 3-(azidomethyl)-2-chloro-quinoline derivatives (**3a**–**h**) with phenyl acetylene in the presence of Cu(I) catalyst has been achieved in very high yield. These molecules were evaluated *in vitro* for their antifungal and antibacterial activity. Most of the compounds exhibited significant antifungal and antibacterial activity against all the tested strains.



## 1. Introduction

Quinolines have been the interest of research for many years as a large number of natural products contain these heterocycles and they are found in numerous commercial products including pharmaceuticals, fragrances, and dyes [1]. Quinoline alkaloids such as quinine, chloroquine, mefloquine and amodiaquine are used as efficient drugs for the treatment of malaria [2]. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmaceutical properties. Quinolines possess interesting physiological properties and as phthalideisoquinoline alkaloids play interesting roles such as noscapine, a non-narcotic cough cure and (+)-biculine, an effective antagonist of an inhibitory neurotransmitter γ-aminobutyric acid (GABA) [3]. Quinoline derivatives, protoberbines and 8-oxoberbines are known to possess biological properties such as antileukemic, antitumor and anticancer activities [4]. The potent antitumor agents Dynamicin A and Virantmycin are important natural products containing the quinoline core [5].

Triazoles have been shown to possess a number of desirable features in the context of medicinal chemistry. Triazoles are stable to acidic/basic hydrolysis and also reductive/oxidative conditions, indicative of a high aromatic stabilization. This moiety is relatively resistant to metabolic degradation. Tazobactam, a β-lactamase inhibitor is the best known examples of triazole containing structures with the broad spectrum antibiotic piperacillin [6–8]. Also several members of the 1,2,3-triazole family have indeed shown interesting biological properties, such as antiallergic [9–11], antibacterial [12] and antiHIV activity [13]. Additionally, 1,2,3-triazoles are found in herbicides, fungicides, and dyes [14].

Click chemistry is a newer approach for the synthesis of drug-like molecules that can accelerate the drug discovery process by utilizing a few practical and reliable reactions. Of the reactions comprising the click universe, the perfect example is the Huisgen 1,3-dipolar cycloaddition [15–17] of alkynes to azides to form 1,4-disubstituted-1,2,3-triazoles. The copper (I) catalyzed reaction is a mild and very efficient, requiring no protecting groups and no purification in many cases [18,19]. Copper (I) catalysis of this transformation, which accelerates the rate of reaction up to $10^7$ times, has placed it in a class of its own and has enabled many novel applications [20–25].

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Herein, we wish to report for the first time the synthesis of title compounds in regards to develop our on going research work [26–30] by click approach.

## 2. Results and discussion

### 2.1. Chemistry

In our approach to synthesize title compounds, we have performed click reaction to connect 2-chloro quinolyl part containing terminal azide i.e. compounds (**3a**–**h**) and phenyl acetylene in the presence of Cu(I) catalyst to form new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives (**4a**–**h**) (Scheme 1). Accordingly, we have firstly synthesized (2-chloro quinolin-3-yl) methanol derivatives (**1a**–**h**) by reported method, [26] then by reacting these (**1a**–**h**) compounds with methane sulphonyl chloride in the presence of triethyl amine (TEA) in acetone at 0 °C to form the corresponding (2-chloro quinolin-3-yl)methyl methanesulfonate derivatives (**2a**–**h**). Further compounds (**2a**–**h**) reacted with sodium azide in dimethylformide (DMF) at room temperature to form 3-(azidomethyl)-2-chloro-quinoline derivatives (**3a**–**h**) in good yields.

### 2.2. Spectroscopic analysis

IR spectrum of compounds (**2a**–**h**) showed absorption due to asymmetric (S=O) stretching in the range of 1333–1347 $cm^{-1}$, also symmetric (S=O) stretching in the range of 1133–1152 $cm^{-1}$ (Table 1). In proton NMR spectrum, resonance corresponding to (Ar–$CH_2$) group was observed at $\delta$ 4.83 ppm, also in $^{13}C$ NMR spectrum, at $\delta$ 43.1 ppm and $\delta$ 51.5 ppm are corresponds to (O–$SO_2$–C) and (Ar–C–$OSO_2$) carbons for compound (**2a**) respectively. The presence of azido group in the compounds (**3a**–**h**) was confirmed by IR spectrum in the range of 2101–2121 $cm^{-1}$ (Table 2). In proton NMR spectrum, at $\delta$ 4.59 ppm value indicates the presence of (Ar–$CH_2$) group, also at $\delta$ 51.6 ppm we have observed (Ar–C–$N_3$) carbon in the $^{13}C$ NMR spectrum for the compound (**3a**).

**Table 1**
Synthesis of compounds (**2a**–**h**).

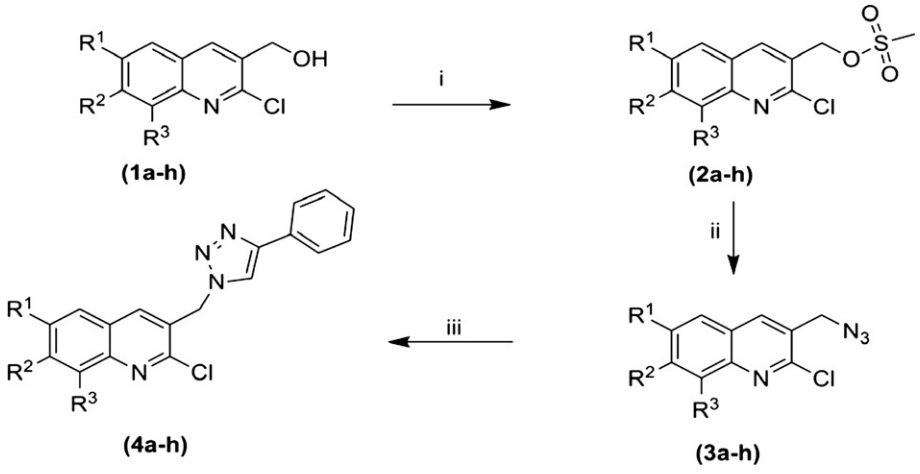
| Compounds | $R^1$ | $R^2$ | $R^3$ | M.P. (°C) | Yield (%)[a] | IR (KBr, $\nu$max/$cm^{-1}$) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Asym. S=O Stret. | Sym. S=O Stret. |
| **2a** | H | H | H | 110–112 | 91 | 1333 | 1135 |
| **2b** | Me | H | H | 124–126 | 90 | 1342 | 1137 |
| **2c** | H | Me | H | 72–74 | 85 | 1342 | 1144 |
| **2d** | H | H | Me | 116–118 | 94 | 1338 | 1152 |
| **2e** | OMe | H | H | 86–88 | 82 | 1347 | 1136 |
| **2f** | H | OMe | H | 92–94 | 87 | 1347 | 1129 |
| **2g** | OEt | H | H | 68–70 | 89 | 1342 | 1133 |
| **2h** | H | H | Et | 88–90 | 78 | 1339 | 1138 |

[a] Isolated Yields.

In IR spectrum of compounds (**4a**–**h**) showed absorption due to (C–N) stretch in the range 1012–1042 $cm^{-1}$ (Table 3). Protons at (Ar–$CH_2$) position for all (**4a**–**h**) compounds have been observed in the region of $\delta$ 5.83–5.90 ppm, also proton in triazole ring significantly observed in the region of $\delta$ 8.63–8.76 ppm. Carbon at (Ar–C–triazole) position was observed in the region of $\delta$ 50.8–51.7 ppm in $^{13}C$ NMR spectrum for all (**4a**–**h**) compounds.

### 2.3. Antimicrobial activity

*In vitro* antibacterial and antifungal activity was screened by considering zone of inhibition of growth. The synthesized compounds (**4a**–**h**) were screened with their different concentrations with standard antibiotics such as streptomycin (5 μg/mL) and griseofluvin (5 μg/mL) (Table 4). The results showed that most of the our designed compounds had moderate antibacterial and antifungal activities in between 10 and 25 μg/mL MIC values against standard antibiotics *in vitro* as shown in Table 4. Compounds **4c** ($R^1 = R^3 = H$; $R^2 = Me$), **4e** ($R^2 = R^3 = H$; $R^1 = OMe$), **4f** ($R^1 = R^3 = H$; $R^2 = OMe$) and **4h** ($R^1 = R^2 = H$; $R^3 = Et$) have the zone of inhibition (16.6, 16.7, 16.0 and 16.1 mm respectively) as that of the standard streptomycin (16.5 mm) against *Bacillus subtilis*. Against *Escherichia coli* the compounds **4f** ($R^1 = R^3 = H$; $R^2 = OMe$) and **4h** ($R^1 = R^2 = H$;




**Scheme 1.** Reagents and conditions: (i) Methanesulfonyl chloride, TEA/acetone, 0 °C, 2 h; (ii) $NaN_3$/DMF, rt, 3h; (iii) Phenyl acetylene, sodium ascorbate (40 mol%), $CuSO_4 \cdot 5H_2O$ (5 mol%), THF/$H_2O$ (9:1), rt, 11–12 h.

**Table 2**
Synthesis of compounds (**3a**–**h**).

| Compounds | $R^1$ | $R^2$ | $R^3$ | M.P. (°C) | Yield (%)[a] | IR (KBr, $\nu$max/cm$^{-1}$) |
|---|---|---|---|---|---|---|
| | | | | | | Azido group |
| **3a** | H | H | H | 42–44 | 94 | 2102 |
| **3b** | Me | H | H | 48–50 | 95 | 2108 |
| **3c** | H | Me | H | 72–74 | 92 | 2121 |
| **3d** | H | H | Me | 62–64 | 91 | 2105 |
| **3e** | OMe | H | H | 68–70 | 89 | 2114 |
| **3f** | H | OMe | H | 70–72 | 90 | 2121 |
| **3g** | OEt | H | H | 66–68 | 83 | 2121 |
| **3h** | H | H | Et | 60–62 | 77 | 2101 |

[a] Isolated Yields.

$R^3$ = Et) showed (16.4 and 15.9 mm) zone of inhibition respectively as that of the standard streptomycin (16.1 mm). The data indicate that a change in the substituent might also affect the antibacterial activity of title compounds (**4a**–**h**). Comparison of biological activities among (**4a**–**h**) shows functional groups as $R^1$ = OMe, $R^2$ = Me/OMe and $R^3$ = Et to be potentially more active against *Bacillus subtilis*. Also antibacterial potency of compounds among (**4a**–**h**) shows functional groups as $R^2$ = OMe and $R^3$ = Et shows more active against *E. coli*.

In antifungal activity, compounds **4a** ($R^1$ = $R^2$ = $R^3$ = H), **4c** ($R^1$ = $R^3$ = H; $R^2$ = Me) and **4g** ($R^2$ = $R^3$ = H; $R^1$ = OEt) have showed (16.0, 16.4, 16.5 mm) zone of inhibition against *Candida albicans* which might be indication that the functional groups ($R^1$ = $R^2$ = $R^3$ = H), $R^2$ = Me and $R^1$ = OEt involve in the antifungal potency of respective compounds as that of standard griseofluvin (16.9 mm). Against *Aspergillus niger* (16.1 and 16.3 mm) zone of inhibition of compounds **4b** ($R^2$ = $R^3$ = H; $R^1$ = Me) and **4e** ($R^2$ = $R^3$ = H; $R^1$ = OMe) respectively indicate that the functional groups at $R^1$ = Me or OMe position interferes in the antifungal potency of title compounds (**4a**–**h**).

## 3. Conclusion

In conclusion, we have synthesized new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives and their antimicrobial activities have been evaluated. All compounds demonstrated potent inhibition against all the strains tested. The importance of such work lies in the possibility that the new compounds might be more efficacious drugs against bacteria and fungi, which could be helpful in designing more potent antibacterial and antifungal agents for therapeutic use.

## 4. Experimental section

All chemicals and solvents were purchased from Merck (Darmstadt, Germany), Spectrochem (Mumbai, India) and S. D. Fine-chem. (Mumbai, India). Melting points were determined in open capillaries on Kumar's melting point apparatus (India) and are uncorrected. IR spectra were recorded on JASCO FT-IR 4100, Japan using KBr discs. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker DRX-300 and NMR Spectrometer AC200. Mass spectra were recorded on Single-Quadrupole Mass Detector 3100, Waters. Elemental analyses were performed on CHNS analyzer Flash 1112, Thermo Finnigan. The progress of the reactions was monitored by TLC on Merck silica plates. Results are presented as, chemical shift $\delta$ in ppm, multiplicity, $J$ values in Hertz (Hz), number of protons, proton's position. Multiplicities are shown as the abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), m (multiplet). Solvents were commercially available materials of reagent grade.

**Table 3**
Synthesis of compounds (**4a**–**h**).

| Compounds | $R^1$ | $R^2$ | $R^3$ | M.P. (°C) | Yield (%)[a] | IR (KBr, $\nu$max/cm$^{-1}$) |
|---|---|---|---|---|---|---|
| | | | | | | (C–N) Stret. |
| **4a** | H | H | H | 146–148 | 91 | 1032 |
| **4b** | Me | H | H | 140–142 | 90 | 1042 |
| **4c** | H | Me | H | 142–144 | 95 | 1042 |
| **4d** | H | H | Me | 146–148 | 94 | 1017 |
| **4e** | OMe | H | H | 104–106 | 92 | 1012 |
| **4f** | H | OMe | H | 124–126 | 89 | 1029 |
| **4g** | OEt | H | H | 188–190 | 87 | 1030 |
| **4h** | H | H | Et | 114–116 | 81 | 1041 |

[a] Isolated yields.

**Table 4**
Antibacterial and antifungal activity of compounds (**4a**–**h**).

| Compounds | *Bacillus subtilis* | *Escherichia coli* | *Candida albicans* | *Aspergillus niger* |
|---|---|---|---|---|
| | ZI[a](MIC)[b] | ZI(MIC) | ZI(MIC) | ZI(MIC) |
| **4a** | 13.5(15) | 12.0(15) | **16.0**(**15**) | 10.0(20) |
| **4b** | 11.4(25) | 14.0(15) | 14.7(15) | **16.1**(**10**) |
| **4c** | **16.6**(**10**) | 14.0(15) | **16.4**(**10**) | – |
| **4d** | 12.0(20) | 12.0(20) | 13.4(25) | 12.7(20) |
| **4e** | **16.7**(**10**) | – | 15.7(15) | **16.3**(**15**) |
| **4f** | **16.0**(**10**) | **16.4**(**10**) | 14.0(15) | – |
| **4g** | – | – | **16.5**(**10**) | 12.8(20) |
| **4h** | **16.1**(**10**) | **15.9**(**15**) | 14.0(15) | – |
| Strept. | 16.5(05) | 16.1(05) | n. t.[c] | n. t. |
| Gris. | n. t. | n. t. | 16.9(05) | 16.6(05) |

Bold values indicates better results.
[a] Zone of inhibition in mm.
[b] Minimum inhibitory concentration in μg/mL.
[c] n. t. not tested.

### 4.1. General procedure for the synthesis of compounds (*2a*–*h*)

To a mixture of (2-chloro quinolin-3-yl)methanol **1** (1 equiv) in acetone, triethyl amine (2 equiv) was added at 0 °C. Methane sulphonyl chloride (1.5 equiv) in acetone was added dropwise in 10 min at 0 °C, and stirred for 5 h. The progress of the reaction was monitored on TLC. After completion of the reaction, reaction mixture was poured on crushed ice. The solid obtained was extracted with chloroform (4 × 50 mL) and washed with brine (2 × 20 mL). Thus organic layer was separated, dried over anhydrous $Na_2SO_4$. The solvent was removed under reduced pressure. The obtained crude product was purified by column chromatography on silica gel by EtOAc:petroleum ether (2:8) as an eluent to obtain pure products **2**.

### 4.2. (2-Chloroquinolin-3-yl)methyl methanesulfonate(*2a*)

$^1$H NMR (300 MHz, $CDCl_3$, $\delta$ ppm): 2.25 (s, 3H, $CH_3$), 4.83 (s, 2H, Ar–$CH_2$), 7.60 (t, 1H, $J$ = 7.5 Hz, Ar–H), 7.75 (t, 1H, $J$ = 7.5 Hz, Ar–H), 7.83 (d, 1H, $J$ = 7.8 Hz, Ar–H), 8.02 (d, 1H, $J$ = 8.4 Hz, Ar–H), 8.27 (s, 1H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$, $\delta$ ppm): 43.1 (O–$SO_2$–C), 51.5 (Ar–C–$OSO_2$), 127.1 127.5 127.6, 128.3 129.0 130.9, 138.6, 147.3 149.6 (Ar–C); Elemental analysis: $C_{11}H_{10}ClNO_3S$ Calcd.: C: 48.62%; H: 3.71%; N: 5.15%; S: 11.80%; Found: C: 48.56%; H: 3.55%; N: 5.23%: S: 11.54%.

### 4.3. General procedure for the synthesis of compounds (*3a*–*h*)

To a solution of (2-chloroquinolin-3-yl)methyl methanesulfonate **2** (1 equiv) in dry DMF, sodium azide (2 equiv) was added and stirred at room temperature for 3 h. The progress of the reaction was monitored on TLC. After completion of reaction, reaction mixture was poured on crushed ice. The solid obtained was extracted with EtOAc (2 × 50 mL). The organic extract was washed

with water and brine. The solvent was removed under reduced pressure to afford crude product **3**, which was purified by column chromatography on silica gel by hexane:EtOAc (8:2) as an eluent.

### 4.4. 3-(Azidomethyl)-2-chloro-6-methylquinoline (**3a**)

$^1$H NMR (300 MHz, $CDCl_3$, $\delta$ ppm): 4.59 (s, 2H, Ar–$CH_2$), 7.53 (t, 1H, $J$ = 7 Hz, Ar–H), 7.68–7.78 (m, 2H, Ar–H), 7.98 (d, 1H, $J$ = 9 Hz, Ar–H), 8.08 (s, 1H, Ar–H); $^{13}$C NMR (75 MHz, $CDCl_3$, $\delta$ ppm): 51.6 (Ar–C–$N_3$), 126.6, 127.1, 127.2, 127.6, 127.8, 130.4, 137.1, 146.7, 149.0 (Ar–C); MS: $m/z$ 219 (m + 1), 221 (m + 3); Elemental analysis: $C_{10}H_7ClN_4$ Calcd.: C: 54.93%; H: 3.23%; N: 25.62%; Found: C: 54.67%; H: 3.40%; N: 25.74%.

### 4.5. General procedure for the synthesis of compounds (**4a**–**h**)

The azide compounds (**3a**–**h**) (1.3 equiv) and phenyl acetylene (1 equiv) were dissolved in THF/$H_2O$ (9:1). To this solution, $CuSO_4 \cdot 5H_2O$ (0.05 equiv) and sodium ascorbate (0.40 equiv) were added. The reaction mixture was stirred for 11–12 h at room temperature. After completion of reaction, reaction mixture was poured on crushed ice. The solid obtained was extracted with EtOAc (2 × 50 mL). The organic extract was washed with water and brine. The solvent was removed under reduced pressure to afford crude product (**4a**–**h**), which was purified by column chromatography on silica gel by MeOH:$CH_2Cl_2$ (2:8) as an eluent to obtain compounds (**4a**–**h**).

### 4.6. 2-Chloro-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)quinoline (**4a**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 5.9 (s, 2H, Ar–$CH_2$), 7.29–7.88 (m, 7H, Ar–H), 7.99 (d, 1H, $J$ = 9 Hz, Ar–H), 8.08 (d, 1H, $J$ = 6 Hz, Ar–H), 8.39 (s, 1H, Ar–H), 8.67 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 50.9 (Ar–C–triazole), 122.0, 125.2, 126.9, 127.3, 127.6, 127.8, 127.9, 128.2, 128.9, 130.6, 131.4, 133.4, 137.5, 139.8, 146.5, 146.7, 149.2 (Ar–C); MS: $m/z$ 321 (m + 1), 323 (m + 3); Elemental analysis: $C_{18}H_{13}ClN_4$ Calcd.: C: 67.40%; H: 4.08%; N: 17.47%; Found: C: 67.65%; H: 4.15%; N: 17.51%.

### 4.7. 2-Chloro-6-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl) quinoline (**4b**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 2.48 (s, 3H, $CH_3$), 5.89 (s, 2H, Ar–$CH_2$), 7.30–7.89 (m, 8H, Ar–H), 8.50 (s, 1H, Ar–H), 8.66 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 21.0 ($CH_3$), 50.8 (Ar–C–triazole), 121.9, 122.8, 125.2, 126.8, 127.2, 127.3, 127.9, 128.9, 129.1, 129.6, 130.6, 133.4, 137.5, 139.1, 145.3, 146.5, 148.2 (Ar–C); MS: $m/z$ 335 (m + 1), 337 (m + 3); Elemental analysis: $C_{19}H_{15}ClN_4$ Calcd.: C: 68.16%; H: 4.52%; N: 16.73%; Found: C: 68.24%; H: 4.41%; N: 16.65%.

### 4.8. 2-Chloro-7-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl) quinoline (**4c**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 2.25 (s, 3H, $CH_3$), 5.84 (s, 2H, Ar–$CH_2$), 7.26–7.83 (m, 8H, Ar–H), 8.57 (s, 1H, Ar–H), 8.71 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 21.5 ($CH_3$), 51.7 (Ar–C–triazole), 120.7, 122.6, 124.2, 126.7, 127.1, 127.3, 127.9, 129.0, 129.1, 129.7, 130.3, 133.4, 137.5, 138.6, 146.0, 146.4, 150.1 (Ar–C); MS: $m/z$ 335 (m + 1), 337 (m + 3); Elemental analysis: $C_{19}H_{15}ClN_4$ Calcd.: C: 68.16%; H: 4.52%; N: 16.73%; Found: C: 68.32%; H: 4.61%; N: 16.61%.

### 4.9. 2-Chloro-8-methyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl) quinoline (**4d**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 2.31 (s, 3H, $CH_3$), 5.87 (s, 2H, Ar–$CH_2$), 7.14–7.64 (m, 8H, Ar–H), 8.34 (s, 1H, Ar–H), 8.51 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 21.3 ($CH_3$), 51.9 (Ar–C–triazole), 1119.7, 122.3, 124.6, 126.5, 127.3, 127.8, 128.2, 129.4, 129.8, 130.1, 130.7, 133.3, 137.6, 138.2, 146.7, 147.1, 152.4 (Ar–C); MS: $m/z$ 335 (m + 1), 337 (m + 3); Elemental analysis: $C_{19}H_{15}ClN_4$ Calcd.: C: 68.16%; H: 4.52%; N: 16.73%; Found: C: 68.27%; H: 4.54%; N: 16.61%.

### 4.10. 2-Chloro-6-methoxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl) methyl)quinoline (**4e**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 3.76 (s, 3H, $OCH_3$), 5.83 (s, 2H, Ar–$CH_2$), 7.27–7.94 (m, 8H, Ar–H), 8.29 (s, 1H, Ar–H), 8.63 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 50.8 (Ar–C–triazole), 55.70 ($OCH_3$), 106.4, 119.7, 120.2, 121.9, 122.0, 124.5, 125.3, 127.9, 128.9, 129.4, 130.6, 135.9, 139.7, 146.6, 148.8, 149.5, 161.7 (Ar–C); MS: $m/z$ 351 (m + 1), 353 (m + 3); Elemental analysis: $C_{19}H_{15}ClN_4O$ Calcd.: C: 65.05%; H: 4.31%; N: 15.97%; Found: C: 65.24%; H: 4.24%; N: 15.75%.

### 4.11. 2-Chloro-7-methoxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl) methyl)quinoline (**4f**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 3.34 (s, 3H, $OCH_3$), 5.84 (s, 2H, Ar–$CH_2$), 7.32–7.83 (m, 8H, Ar–H), 8.09 (s, 1H, Ar–H), 8.76 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 51.1 (Ar–C–triazole), 55.4 ($OCH_3$), 105.7, 120.7, 121.1, 121.4, 122.6, 124.7, 125.9, 127.0, 128.7, 129.3, 130.9, 135.6, 140.7, 145.7, 147.9, 149.6, 159.8 (Ar–C); MS: $m/z$ 351 (m + 1), 353 (m + 3); Elemental analysis: $C_{19}H_{15}ClN_4O$ Calcd.: C: 65.05%; H: 4.31%; N: 15.97%; Found: C: 65.31%; H: 4.44%; N: 15.83%.

### 4.12. 2-Chloro-6-ethoxy-3-((4-phenyl-1H-1,2,3-triazol-1-yl) methyl)quinoline (**4g**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 1.38 (t, 3H, $J$ = 6 Hz, $CH_3$–$OCH_2$), 4.15 (q, 2H, $J$ = 6 Hz, $OCH_2$), 5.89 (s, 2H, Ar–$CH_2$), 7.31–7.89 (m, 8H, Ar–H), 8.11 (s, 1H, Ar–H), 8.69 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 14.5 ($CH_3$–$CH_2$), 50.8 (Ar–C–triazole), 63.8 ($CH_2$–$CH_3$), 105.0, 106.6, 119.6, 120.4, 121.5, 122.1, 123.9, 125.2, 127.6, 127.9, 128.2, 128.9, 130.6, 135.8, 137.9, 142.5, 157.3 (Ar–C); MS: $m/z$ 365 (m + 1), 367 (m + 3); Elemental analysis: $C_{20}H_{17}ClN_4O$ Calcd.: C: 65.84%; H: 4.70%; N: 15.36%; Found: C: 65.58%; H: 4.65%; N: 15.41%.

### 4.13. 2-Chloro-8-ethyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl) quinoline (**4h**)

$^1$H NMR (300 MHz, DMSO-$d_6$, $\delta$ ppm): 1.24 (t, 3H, $J$ = 6 Hz, $CH_3$–$CH_2$), 3.10 (q, 2H, $J$ = 6 Hz, $CH_3$–$CH_2$), 5.88 (s, 2H, Ar–$CH_2$), 7.27–7.86 (m, 8H, Ar–H), 8.33 (s, 1H, Ar–H), 8.65 (s, 1H, triazole–H); $^{13}$C NMR (75 MHz, DMSO-$d_6$, $\delta$ ppm): 15.0 ($CH_3$–$CH_2$), 23.7 ($CH_2$–$CH_3$) 50.9 (Ar–C–triazole), 106.1, 120.4, 121.8, 122.0, 125.3, 126.1, 127.1, 127.7, 127.9, 128.9, 129.8, 130.6, 140.3, 141.2, 145.2, 146.6, 148.3 (Ar–C); MS: $m/z$ 349 (m + 1), 351 (m + 3); Elemental analysis: $C_{20}H_{17}ClN_4$ Calcd.: C: 68.86%; H: 4.91%; N: 16.06%; Found: C: 68.71%; H: 4.84%; N: 16.18%.

## 5. Biological assays

The compounds were diluted in dimethylsulfoxide (DMSO) with required concentrations for bioassay. Antimicrobial activity was evaluated by screening of the compounds by standard method i.e. agar cup plate method against a panel of human pathogenic microorganisms: one Gram positive (*Bacillus subtilis* NCIM 2250), one Gram negative (*E. coli* ATCC 25922) were used for the antibacterial assay, while for the antifungal assay, (*C. albicans* MTCC 277) and (*A. niger* NCIM 545) were used for the studies. Microorganisms were maintained at 37 °C on Mueller Hinton (MH) agar slants. Moreover the MH agar and Czapek Dox broth were used to evaluate antibacterial and antifungal activity respectively. To make a judgment of antibacterial and antifungal potency of the synthesized compounds (**4a**–**i**) commercial antibiotics such as streptomycin (Strept.) and griseofluvin (Gris.) in DMSO served as reference standards to compare inhibition of growth. The plate containing bacterial organism were incubated at 37 ± 0.5 °C and plates containing fungal organism were incubated at 28 ± 0.5 °C for 48 h. The zone of inhibition was calculated by measuring the diameter of zone of inhibition for bacterial and fungal growth around the disc. Averages of three independent determinations were recorded. The minimum inhibitory concentration (MIC) of the samples by cup plate method on MH agar plates containing the following concentrations (μg/mL): 0 (control), 1, 2, 3, 5, 10, 15, 20, 30 and 40. MH agar was molted and poured in Petri dishes according to National Committee for Clinical Laboratory Standards (NCCLS, M7-A5 January 2000). The plates were incubated at 37 °C, examined after 24 h and incubated further for 72 h, where necessary. The MIC was defined as the lowest and their antimicrobial activities have been evaluated. All compounds demonstrated potent inhibition against all the strains tested. The importance of such work lies in the possibility that the new compounds might be more efficacious drugs against bacteria and fungi, which could be helpful in designing more potent antibacterial and antifungal agents for therapeutic use.

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