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Full Paper

Design and Synthesis of Some New Quinoline Based 1,2,3-Triazoles as Antimicrobial and Antimalarial Agents

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Abstract: A series of novel 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j)** were synthesized in good yields from the intermediates (6-bromo-2-chloro-quinolin-3-yl)-methanol **(2)**, methanesulfonic acid (6-bromo-2-chloroquinolin-3-yl)methyl methanesulfonate **(3)** and 3-azidomethyl-6-bromo-2-chloro-quinoline **(4)**. The synthetic route leading to the title compounds is commenced from commercially available 6-bromo-2-chloro-quinolin-3-carbaldehyde **(1)**. The chemical structures of the newly synthesized compounds were elucidated by their IR, ^{1}H and ^{13}C NMR, mass spectral data and elemental analysis. Further, all the target compounds were screened for their antimicrobial activity against various microorganisms and antimalarial activity towards *P. falciparum*.

Keywords: quinolone; triazoles; antimicrobial activity; antimalarial

1. INTRODUCTION

1,2,3-Triazoles have been the subject of considerable research, mainly due to their usefulness in synthetic organic chemistry and also due to their variety of interesting biological activities such as antibacterial and antituberculosis [1], neuraminidase inhibitors [2], anticancer [3], antiviral [4], analgesic [5], fungicidal [6], protein tyrosine phosphatase inhibitors [7], assorted biomolecules (nucleosides and nucleotides) [8], herbicidal, cytostatic, virostatic, anti-inflammatory [9], anti-HIV [10] and β-adrenergic receptor agonists [11]. The importance of the quinoline nucleus has been well demonstrated as illustrated by the large number of patents employing such species as chemotherapeutic agents. A number of biological activities have been associated with quinoline-containing compounds such as anti-inflammatory, antiallergic [12], antimalarial [13], antibacterial [14], antiproliferative [15], anticancer [16] and antiparasitic [17] activities.

2. MATERIAL AND METHODS

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60–120 mesh. IR spectra were obtained on a Perkin-Elmer BX serried FTIR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a Varian 300 MHz spectrometer for ^{1}H NMR and 100 MHz spectrometer ^{13}C NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

Synthesis of (6-bromo-2-chloro-quinolin-3-yl)-methanol (2)

A mixture of 6-bromo-2-chloro-quinolin-3-carbaldehyde **(1)** (0.01 mol) and sodium borohydrate (0.01 mol) in methanol (20 ml) was constantly stirred at room temperature for 4 h. After completion of the reaction (monitored by TLC), the resultant solution was poured in ice-cold water and the separated solid was filtered, dried and recrystallised from pet-ether to get pure (6-bromo-2-chloro-quinolin-3-yl)-methanol **(2)**.

Synthesis of (6-bromo-2-chloroquinolin-3-yl)methyl methanesulfonate (3)

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A mixture of (6-bromo-2-chloro-quinolin-3-yl)-methanol **(2)** (0.01 mol) and mesyl chloride (0.01 mol) was stirred uniformly at 0 ^{0}C for 5 h. After completion of the reaction (monitored by TLC), the mixture is poured in ice-cold water to get the crude product which is purified by recrystallization from methanol to give pure methanesulfonic acid (6-bromo-2-chloroquinolin-3-yl)methylmethanesulfonate **(3)**

Synthesis of 3-azidomethyl-6-bromo-2-chloro-quinoline (4)

An equimolar mixture of (6-bromo-2-chloroquinolin-3-yl)methyl methanesulfonate **(3)** (0.01 mol) and sodium azide (0.01 mol) was refluxed in DMF for 4 h. After completion of the reaction (monitored by TLC), solvent was removed under reduced pressure and the residue was poured over crushed ice to get crude solid which is recrystallized from methanol to yield the pure 3-azidomethyl-6-bromo-2-chloro-quinoline **(4)**.

Synthesis of 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives (5a-j)

A mixture of 3-azidomethyl-6-bromo-2-chloro-quinoline **(4)** (0.01 mol), aromatic alkyne (0.01 mol), CuI (0.01 mol), N,N-diisopropylethylamine (0.01 mol) and NBS (0.01 mol) in THF (10 ml) was stirred constantly at room temperature for 12-15 hours. After completion of the reaction (monitored by TLC), solvent was removed under reduced pressure and the crude product was purified by silica gel (60-120 mesh) column chromatography using ethyl acetate/hexane as eluent to get the corresponding 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j)** in pure form.

Physical and Spectral Data

(6-Bromo-2-chloro-quinolin-3-yl)-methanol (2): Pale yellow solid, Yield: 77%, mp 140–142^{0}C, IR (KBr): ν/cm^{-1} 3215 (O-H), 3012 (C-H, Ar), 2945 (C-H, CH_2), 1576 (C=C, Ar), 1442 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.84 (d, 1H, J = 7.2 Hz, Ar-H), 7.74 (d, 1H, J = 7.2 Hz, Ar-H), 7.61 (s, 1H, Ar-H), 7.57, (s, 1H, Ar-H), 5.25 (s, 1H, OH), 4.20 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.0, 148.6, 136.7, 133.7, 131.0, 128.4, 126.4, 123.2, 121.5, 57.6. MS: *m/z* 270 (M^+). Anal. Calcd. for $C_{10}H_7BrClNO$: C-44.07, H-2.59, Br-29.32, Cl-13.01, N-5.14, O-5.87. Found: C-43.26, H-2.36, Br-28.54, Cl-12.69, N-4.98, O-5.21.

(6-Bromo-2-chloroquinolin-3-yl)methyl methanesulfonate (3): Yellow solid, Yield: 71%, mp 129–131^{0}C; IR (KBr): ν/cm^{-1} 3026 (C-H, Ar), 2968 (C-H, CH_2), 1580 (C=C, Ar), 1436 (C=N), 1240 (C-S), 1045 (S=O). ^{1}H NMR (300 MHz, DMSO-d_6): δ δ 7.79 (d, 1H, J = 7.0 Hz, Ar-H), 7.71 (d, 1H, J = 7.0 Hz, Ar-H), 7.54 (s, 1H, Ar-H), 7.52, (s, 1H, Ar-H), 4.24 (s, 2H, CH_2), 3.70 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.6, 146.3, 136.1, 134.8, 133.4, 125.7, 124.3 121.5, 120.3, 59.2, 36.3. MS: *m/z* 350 (M^+); Anal. Calcd. for $C_{11}H_9BrClNO_3S$: C-37.68, H-2.59, Br-22.79, Cl-10.11, N-3.99, O-13.69, S-9.15. Found: C-36.57, H-2.36, Br-21.95, Cl-9.84, N-3.62, O-12.97, S-8.93.

3-Azidomethyl-6-bromo-2-chloro-quinoline (4): White solid, Yield: 72%, mp 155-157^{0}C, IR (KBr): ν/cm^{-1} 3022 (C-H, Ar), 2975 (C-H, CH_2), 2150 (N=N), 1588 (C=C, Ar), 1446 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.82 (d, 1H, J = 7.3 Hz, Ar-H), 7.78 (d, 1H, J = 7.3 Hz, Ar-H), 7.63 (s, 1H, Ar-H), 7.59, (s, 1H, Ar-H), 4.27 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.6, 148.3, 133.7, 132.5, 131.0, 126.7, 124.7, 122.8, 120.7, 48.3. MS: *m/z* 297 (M^+); Anal. Calcd. for $C_{10}H_6BrClN_4$: C-40.37, H-2.03, Br-26.86, Cl-11.92, N-18.83. Found: C-39.84, H-1.98, Br-25.98, Cl-10.92, N-17.85.

6-Bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline (5a): Yellow solid, Yield: 70%, mp 130-132^{0}C, IR (KBr): ν/cm^{-1} 3026 (C-H, Ar), 2954 (C-H, CH_2), 2163 (N=N), 1598 (C=C, Ar), 1448 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.05 (s, 1H, CH), 7.82 (d, 1H, J = 6.8 Hz, Ar-H), 7.74 (d, 1H, J = 6.8 Hz, Ar-H), 7.70-7.64 (m, 5H, Ar-H), 7.62 (s, 1H, Ar-H), 7.55, (s, 1H, Ar-H), 4.31 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.7, 148.6, 137.6, 135.6, 134.5, 133.7, 132.7, 131.2, 128.3 (2), 127.2 (2), 126.5, 125.8, 125.6, 123.5, 120.5, 52.3. MS: *m/z* 399 (M^+); Anal. Calcd. for $C_{18}H_{12}BrClN_4$: C-54.09, H-3.03, Br-19.99, Cl-8.87, N-14.02. Found: C-53.02, H-2.99, Br-18.89, Cl-7.98, N-13.56.

6-Bromo-2-chloro-3-(4-m-tolyl-[1,2,3]triazol-1-ylmethyl)-quinoline (5b): Brown solid, Yield: 76%, mp 147-149^{0}C, IR (KBr): ν/cm^{-1} 3032 (C-H, Ar), 2960 (C-H, CH_2), 2154 (N=N), 1586 (C=C, Ar), 1448 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.12 (s, 1H, CH), 7.70 (d, 1H, J = 7.4 Hz, Ar-H), 7.68 (d, 1H,

J = 7.4 Hz, Ar-H), 7.67-7.60 (m, 3H, Ar-H), 7.58 (s, 1H, Ar-H), 7.56, (s, 1H, Ar-H), 7.49 (s, 1H, Ar-H), 4.49 (s, 1H, CH), 4.36 (s, 2H, CH_2), 3.21 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.2, 145.2, 138.6, 136.2, 135.7, 134.7, 132.8, 131.0, 130.2, 128.6, 127.4, 126.3, 125.7, 123.4, 122.4, 121.2, 120.8, 52.3, 23.6. MS: *m/z* 413 (M^+); Anal. Calcd. for $C_{19}H_{14}BrClN_4$: C-55.16, H-3.41, Br-19.31, Cl-8.57, N-13.54. Found: C-54.36, H-3.24, Br-18.95, Cl-8.12, N-12.95.

6-Bromo-2-chloro-3-[4-(3-methoxy-phenyl)-[1,2,3]triazol-1-ylmethyl]-quinoline (5c)*:* Pale yellow solid, Yield: 70%, mp 122-124^{0}C, IR (KBr): *ν*/cm^{-1} 3021 (C-H, Ar), 2968 (C-H, CH_2), 2161 (N=N), 1568 (C=C, Ar), 1434 (C=N), 1142 (C-O). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.16 (s, 1H, CH), 7.81 (d, 1H, J = 7.2 Hz, Ar-H), 7.74 (d, 1H, J = 7.2 Hz, Ar-H), 7.70-7.63 (m, 3H, Ar-H), 7.60 (s, 1H, Ar-H), 7.59 (s, 1H, Ar-H), 7.55, (s, 1H, Ar-H), 4.60 (s, 1H, CH), 4.36 (s, 2H, CH_2), 3.02 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 160.3, 145.3, 138.6, 137.5, 135.8, 134.9, 133.7, 132.5, 130.2, 129.6, 128.6, 123.3, 122.5, 118.6, 115.3, 124.7, 57.8, 52.3. MS: *m/z* 430 (M^+); Anal. Calcd. for $C_{19}H_{14}BrClN_4O$: C-53.11, H-3.28, Br-18.60, Cl-8.25, N-13.04, O-3.72. Found: C-52.36, H-3.14, Br-17.46, Cl-8.01, N-12.65, O-3.20.

6-Bromo-2-chloro-3-[4-(3-fluoro-phenyl)-[1,2,3]triazol-1-ylmethyl]-quinoline (5d)*:* White solid, Yield: 73%, mp 150-152^{0}C, IR (KBr): *ν*/cm^{-1} 3018 (C-H, Ar), 2958 (C-H, CH_2), 2149 (N=N), 1584 (C=C, Ar), 1438 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.98 (s, 1H, CH), 7.85 (d, 1H, J = 7.6 Hz, Ar-H), 7.76 (d, 1H, J = 7.6 Hz, Ar-H), 7.69-7.61 (m, 3H, Ar-H), 7.65 (s, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.49, (s, 1H, Ar-H), 4.63 (s, 1H, CH), 4.32 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.3, 157.6, 146.4, 138.6, 137.5, 136.2, 135.2, 133.1, 132.8, 130.1, 128.6, 126.7, 125.2, 124.7, 121.4, 116.3, 113.6, 56.3. MS: *m/z* 417 (M^+); Anal. Calcd. for $C_{18}H_{11}BrClFN_4$: C-51.76, H-2.69, Br-19.13, Cl-8.49, F-4.55, N-13.41. Found: C-50.36, H-2.41, Br-18.54, Cl-7.98, F-4.21, N-12.95.

6-Bromo-2-chloro-3-[4-(3-chloro-phenyl)-[1,2,3]triazol-1-ylmethyl]-quinoline (5e)*:* Brown solid, Yield: 70%, mp 160-162^{0}C, IR (KBr): *ν*/cm^{-1} 3032 (C-H, Ar), 2952 (C-H, CH_2), 2148 (N=N), 1583 (C=C, Ar), 1448 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.08 (s, 1H, CH), 7.78 (d, 1H, J = 7.4 Hz, Ar-H), 7.74 (d, 1H, J = 7.4 Hz, Ar-H), 7.70-7.63 (m, 3H, Ar-H), 7.60 (s, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.55, (s, 1H, Ar-H), 4.59 (s, 1H, CH), 4.36 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 147.1, 139.3, 138.5, 137.4, 136.5, 135.0, 134.8, 131.2, 130.2, 129.8, 128.6, 126.3, 124.8, 125.4, 123.5, 121.0, 56.3. MS: *m/z* 434 (M^+); Anal. Calcd. for $C_{18}H_{11}BrCl_2N_4$: C-49.80, H-2.55, Br-18.41, Cl-16.33, N-12.91. Found: C-48.36, H-2.25, Br-17.48, Cl-15.68, N-12.02.

6-Bromo-2-chloro-3-[4-(2,4-difluoro-phenyl)-[1,2,3]triazol-1-ylmethyl]-quinoline (5f)*:* Yellow solid, Yield: 71%, mp 136-138^{0}C, IR (KBr): *ν*/cm^{-1} 3020 (C-H, Ar), 2959 (C-H, CH_2), 2162 (N=N), 1584 (C=C, Ar), 1436 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.23 (s, 1H, CH), 7.74 (d, 1H, J = 7.5 Hz, Ar-H), 7.70 (d, 1H, J = 7.5 Hz, Ar-H), 7.68 (s, 1H, Ar-H), 7.66 (s, 1H, Ar-H), 7.64 (d, 1H, J = 6.8 Hz, Ar-H), 7.60 (d, 1H, J = 6.8 Hz, Ar-H), 7.58, (s, 1H, Ar-H), 4.58 (s, 1H, CH), 4.29 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.2, 143.6, 138.5, 136.7, 135.0, 134.6, 133.2, 132.4, 130.2, 129.7, 127.8, 126.5, 125.4, 124.7, 123.0, 122.3, 120.3, 49.6. MS: *m/z* 388 (M^+); Anal. Calcd. for $C_{18}H_{10}BrClF_2N_4$: C-49.62, H-2.31, Br-18.34, Cl-8.14, F-8.72, N-12.86. Found: C-48.36, H-2.12, Br-17.65, Cl-7.98, F-8.25, N-12.02.

6-Bromo-3-[4-(3-bromo-phenyl)-[1,2,3]triazol-1-ylmethyl]-2-chloro-quinoline (5g): Pale yellow solid, Yield: 72%, mp 152-154 ^{0}C, IR (KBr): *ν*/cm^{-1} 3036 (C-H, Ar), 2948 (C-H, CH_2), 2151 (N=N), 1552 (C=C, Ar), 1442 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.11 (s, 1H, CH), 7.68 (d, 1H, J = 7.2 Hz, Ar-H), 7.62 (d, 1H, J = 7.2 Hz, Ar-H), 7.58 (s, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.48-7.36 (m, 3H, Ar-H), 4.63 (s, 1H, CH), 4.33 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.4, 148.6, 139.5, 136.5, 135.6, 133.5, 132.0, 131.9, 131.2, 130.5, 129.5, 128.6, 126.8, 125.4, 124.5, 123.0, 122.3, 52.3; MS: *m/z* 478 (M^+); Anal. Calcd. for $C_{18}H_{11}Br_2ClN_4$: C-45.17, H-2.32, Br-33.39, Cl-7.41, N-11.71. Found: C-44.67, H-2.23, Br-32.95, Cl-7.02, N-10.98.

6-Bromo-3-[4-(4-bromo-phenyl)-[1,2,3]triazol-1-ylmethyl]-2-chloro-quinoline (5h)*:* Brown solid, Yield: 77%, mp 120-122 ^{0}C, IR (KBr): *ν*/cm^{-1} 3040 (C-H, Ar), 2942 (C-H, CH_2), 2157 (N=N), 1564 (C=C, Ar), 1450 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.99 (s, 1H, CH), 7.66 (d, 1H, J = 7.6 Hz, Ar-H), 7.65 (d, 1H, J = 7.6 Hz, Ar-H), 7.62 (s, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.45 (d, 2H, J = 7.4 Hz, Ar-H), 7.36 (d, 2H, J = 7.4 Hz, Ar-H), 4.59 (s, 1H, CH), 4.39 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.2, 149.6, 137.8, 135.2, 134.1, 132.6, 131.7 (2), 130.2, 129.8, 128.7 (2), 125.8, 126.7, 125.8, 124.8, 123.2, 55.7; MS: *m/z* 478 (M^+); Anal. Calcd. for $C_{18}H_{11}Br_2ClN_4$: C-45.17, H-2.32, Br-33.39, Cl-7.41,

N-11.71. Found: C-44.67, H-2.23, Br-32.95, Cl-7.02, N-10.98.

6-Bromo-3-[4-(4-chloro-phenyl)-[1,2,3]triazol-1-ylmethyl]-2-chloro-quinoline (5i): White solid, Yield: 74%, mp 144-146 ^{0}C, IR (KBr): *ν*/cm^{-1} 3036 (C-H, Ar), 2938 (C-H, CH_2), 2150 (N=N), 1558 (C=C, Ar), 1446 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.19 (s, 1H, CH), 7.70 (d, 1H, J = 7.5 Hz, Ar-H), 7.63 (d, 1H, J = 7.5 Hz, Ar-H), 7.58 (s, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.50 (d, 2H, J = 7.3 Hz, Ar-H), 7.47 (d, 2H, J = 7.3 Hz, Ar-H), 4.68 (s, 1H, CH), 4.47 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.1, 148.2, 136.4, 134.2, 133.5, 132.3, 131.9 (2), 130.8, 130.2, 129.3, 128.5 (2), 125.8, 124.6, 123.8, 122.7, 53.6; MS: *m/z* 434 (M^+); Anal. Calcd. for $C_{18}H_{11}BrCl_2N_4$: C-49.80, H-2.55, Br-18.41, Cl-16.33, N-12.91. Found: C-48.36, H-2.25, Br-17.48, Cl-15.68, N-12.02.

***6-Bromo-3-[4-(4-methoxy-phenyl)-[1,2,3]triazol-1-ylmethyl]-2-chloro-quinoline (5j)*:** Yellow solid, Yield: 70%, mp 132-134 ^{0}C, IR (KBr): *ν*/cm^{-1} 3044 (C-H, Ar), 2942 (C-H, CH_2), 2147 (N=N), 1565 (C=C, Ar), 1452 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.20 (s, 1H, CH), 7.72 (d, H, J = 7.5 Hz, Ar-H), 7.61 (d, 1H, J = 7.5 Hz, Ar-H), 7.55 (s, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.48 (d, 2H, J = 7.3 Hz, Ar-H), 7.42 (d, 2H, J = 7.3 Hz, Ar-H), 4.74 (s, 1H, CH), 4.36 (s, 2H, CH_2), 3.12 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.4, 149.6, 138.4, 136.4, 134.7, 133.2, 132.4 (2), 131.0, 130.8. 129.2, 127.4 (2), 126.3, 125.2, 124.1, 123.6, 56.3, 53.6; MS: *m/z* 430 (M^+); Anal. Calcd. for $C_{19}H_{14}BrClN_4O$: C-53.11, H-3.28, Br-18.60, Cl-8.25, N-13.04, O-3.72. Found: C-52.36, H-3.14, Br-17.46, Cl-8.01, N-12.65, O-3.20.)

3. RESULTS AND DISCUSSION

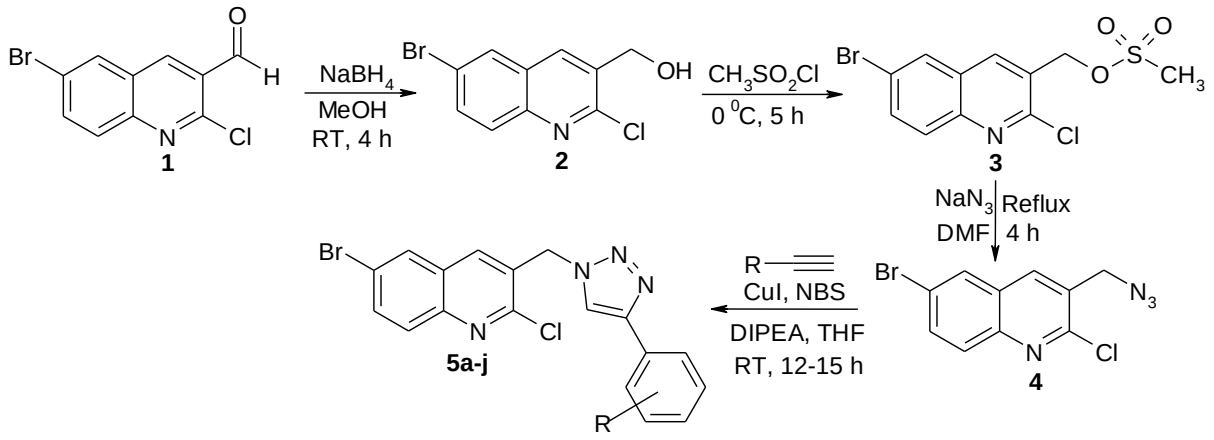
Inspired by the biological profile of 1,2,3-triazole derivatives and quinoline nucleus, and their increasing importance in pharmaceutical and biological fields, and also in continuation of our work on the synthesis of biologically active heterocycles, it was thought worthwhile to undertake the synthesis of 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j),** with the view to obtain certain new chemical entities with two active pharmacophores in a single molecular framework for the intensified biological activities. Scanning of the existing literature reveals that there is no report on the synthesis of 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j)** from any compound including 6-bromo-2-chloro-quinolin-3-carbaldehyde **(1)**. The synthetic route leading to the title compounds is summarized in Scheme 1.

Accordingly, in this manuscript, we describe the synthesis of target compounds 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j)**. The synthesis of the compounds **5a-j** commenced from commercially available 6-bromo-2-chloro-quinolin-3-carbaldehyde **(1)**. The initial intermediate (6-bromo-2-chloro-quinolin-3-yl)-methanol **(2)** has been prepared from the reduction of the starting material 6-bromo-2-chloro-quinolin-3-carbaldehyde **(1)** with sodium borohydride in methanol on constant stirring at ambient temperature for 4 hours. The subsequent reaction of compound **2** with methanesulfonyl chloride (mesyl chloride) at 0 ^{0}C temperature on constant stirring for 5 hours afforded the key intermediate (6-bromo-2-chloroquinolin-3-yl)methyl methanesulfonate **(3)** in good yield. Compound 3-azidomethyl-6-bromo-2-chloro-quinoline **(4)** which is used to synthesis of the title compounds were prepared in good yield from the reaction of compound **3** with sodium azide in DMF at reflux temperature for 4 hours. To achieve the title compounds, 6-bromo-2-chloro-3-(4-phenyl-[1,2,3]triazol-1-ylmethyl)-quinoline and its derivatives **(5a-j)** through cyclization reaction in good to excellent yields, we treated the intermediate **4** with different aromatic alkynes in presence of *N*,*N*-Diisopropylethylamine, CuI, N-bromosuccinamide in THF on uniform stirring at room temperature 12-15 h. The chemical structures of the newly synthesized compounds were elucidated by their IR, ^{1}H and ^{13}C NMR, mass spectral data and elemental analysis. Finally, all the target compounds were used to screen for their antimicrobial activity against various microorganisms and antimalarial activity towards *P. falciparum*.

Antimicrobial Activity

The *in vitro* antimicrobial activity was carried out by cup-plate method [18]. All the synthesized compounds were screened for antibacterial activity against *Escherichia coli*, *Micrococus luteus* and *Staphylococcus aureus* using Chloramphenicol (0.001 mole/ml) as standard. The antifungal activity was investigated against *Aspergellius flavus*, *Aspergillus niger* and *Curvuliaria lunata* using Flucanazole (0.001 mole/ml) as reference. Inhibition was recorded by measuring the diameter of the inhibition zone at

the end of 24 hr for bacteria and 48 hr for fungi. Each experiment was repeated thrice and the average of the three independent determinations was recorded. The results are summarized in Table 1. Amongst the compounds tested for antibacterial activity, the compound **5e** was found to display considerable activity against all the bacteria, whereas compound **5f** was found to exhibit promising activity against *E. coli* and *M. luteus*. The compound **5g** showed good antifungal activity against *A. flavus* compare compared to standard and the compound **5h** also exhibited good antifungal activity against *A. flaves* and *A. niger* and was found to be near active compare with standard against *C. lunata*. The remaining compounds showed lower to moderate activity against two organisms employed. It is interesting to note that, none of the compound is inactive against all the tested microorganisms and this remarkable property may achieve to the compounds due to the two active pharmacophores (quinoline and 1,2,3-triazole) in a single molecular skeleton.



Scheme 1. **5 a)** R = H, **b)** = 3-CH_3, **c)** = 3-OCH_3, **d)** = 3-F, **e)** = 3-Cl, **f)** = 2,4-F, **g)** = 3-Br, **h)** = 4-Br, **i)** = 4-Cl, **j)** = 4-OCH_3

Table 1. Antimicrobial activity of compounds **5a-j.**

Compound	Antibacterial activity (Zone of inhibition in mm)			Antifungal activity (Zone of inhibition in mm)		
	E. coli	*M. luteus*	*S. aureus*	*A. flavus*	*A. niger*	*C. lunata*
5a	15	20	22	08	12	10
5b	18	18	24	10	09	08
5c	12	16	28	09	11	09
5d	14	15	19	12	08	12
5e	30	31	33	13	11	14
5f	31	30	25	13	14	13
5g	28	26	17	16	15	13
5h	21	34	20	15	17	16
5i	12	16	18	11	10	11
5j	14	16	17	10	12	12
Chloramphenicol	37	36	42	-	-	-
Flucanazole	-	-	-	17	20	17

Antiplasmodial Activity

The newly synthesized compounds **5a-j** were also tested for their anti plasmodial activity against the W2 strain of *P. falciparum*, which is resistant to chloroquine and other antimalarial drugs. The target compounds were diluted and incubated with cultured W2-strain of *P. falciparum* for 48 h. Parasites were fixed and stained, and parasitemias of treated and control cultures were determined. Results are means, compared to untreated controls, from three experiments. Error bars represent standard deviations of results. The test compounds showed toxicity to erythrocytes at concentrations above 20 mM, about three orders of magnitude above concentrations with antimalarial activity. All the ten compounds were

found to be active against strain W2 of *P. falciparum* in culture. The most active compounds were 5c, 5d and 5g with respective IC50 values of 5.09 μM, 3.25 μM and 2.13 μM respectively. From the study of the structure-activity relationships, it appears that the presence of a methoxy group on meta position of phenyl ring decreases the anti plasmodial activity of compound **5c** compared to compound **5d** that bears a fluoro group on the same carbon of phenyl ring. Furthermore, compound with bromo group at meat position confers significant activity to compound **5g** (Table 2). The rest of all target compounds performed lower to moderate anti-plasmodial activity**.**

Table 2. The IC50 values of compounds **5a-j** against strain W2 of *P. falciparum* in culture.

Compound	***5a***	***5b***	***5c***	***5d***	***5e***	***5f***	***5g***	***5h***	***5i***	***5j***
IC 50[a]	8.18	9.12	5.09	3.25	9.00	9.52	2.13	8.62	9.26	7.85
± SD (μM)	±0.07	±0.06	±0.04	±0.07	±0.002	±0.04	±0.02	±0.08	±0.06	±0.03

[a]Concentration that killed 50 % parasites relative to negative control; SD = standard deviation; the compounds were tested in triplicate

4. REFERENCES AND NOTES

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