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Design And Two-Step Synthesis, Characterization Of 1,2,3-Triazol-Benzo- Oxazolo And Benzo-Imidazo [1,8] Naphthyridines

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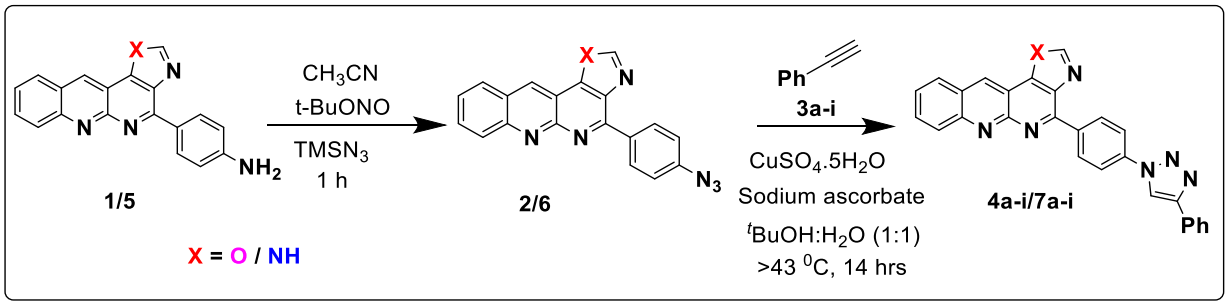
ABSTRACT

Herein, we have depicted the two step series of phenyl-1H-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridines 4a-4i & phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridines 7a-7i through azide formation followed [3+2] click protocol cyclo addition with various terminal alkynes 3a-3i by means of $CuSO_4.5H_2O$ and sodium ascorbate namely Sharpless catalyst to give promising yields, shown in Scheme I & II and further confirmed by spectral and elemental analysis.

Keywords: *1,2,3-triazole,1,8-naphthyridine, imidazole, oxazole, cyclo-addition, $CuSO_4.5H_2O$ and sodium ascorbate, $TMSN_3$*



Graphical Abstract

INTRODUCTION

N-heterocycles are employed in adhesives, elastic chemicals, colorants, and medicines.[1]

For a medicinal chemist, designing a new agent is one of the most challenging undertakings. Over the past few decades, there has been a growing interest in the synthesis of high Nitrogen-Containing heterocyclic compounds due to their potential applications in pyrotechnics, propellants, explosives, and specifically in chemotherapy. For twenty years, medicinal chemists have been very interested in1,2,3 triazole because of its excellent pharmacokinetic and pharmacodynamic profiles, minimal toxicity, and wide range of impacts,[2] low toxicity, strong pharmacokinetic and pharmacodynamic profiles, 1,2,3 & 1,2,4-triazole has drawn considerable interest from the 1,2,3-triazole to medicinal chemists of two decades. The triazoles manufactured from aminoguanidine set-up on large scale, useful as herbicides.[3] *N*-substituted triazole and 1,8-naphthyridine with another substituent and it exhibited biological activity

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such as anti-inflammatory, [4] anti-convulsant [5], anti-cancer [6], anti-mycobacterial [7], anti-oxidant [8], and anti-malarial abilities.[9] Herein, we design, synthesis and characterization of targets phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine 4a-4i and phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine 7a-7i are shown in Fig.1.

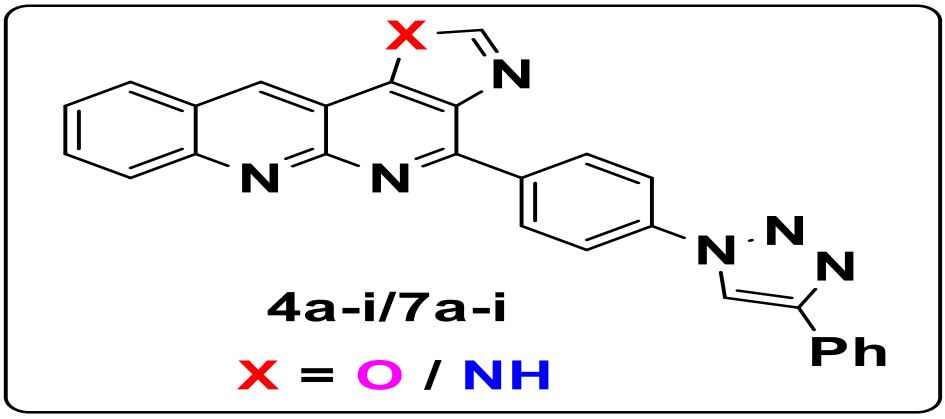

Fig.1. Designed Targets

MATERIAL AND METHOD

All reagents were procured from Sigma-Aldrich, and are of laboratory grade. The melting points reported here-in are uncorrected and were determined in open capillaries using Thiele's melting point apparatus. Reactions were monitored by thin layer chromatography (TLC), which were performed on coated Silica gel G plates activated for 30 min.(120°C) and spots were visualized by exposure to iodine vapours. ^{1}H NMR spectra were determined on Mercury Plus 400MHz NMR Spectrometer in DMSO-d6 with TMS, δ 0 ppm as an internal standard. ^{13}C NMR spectra were recorded with DMSO-d6 at100MHz on a Mercury Plus NMR Spectrometer. Mass spectra were collected using a Jeol JMC-300 spectrometer (ESI, 70 eV). The Carlo Erba 106 and PerkinElmer model 240 analysers were used to analyse the elements.

RESULTS AND DISCUSSIONS

General procedure for the synthesis of 4-(4-azidophenyl) benzo[b] oxazolo [5,4-f] [1,8] naphthyridine (2) Step I: 4-(benzo[b]oxazolo[5,4-f] [1,8] naphthyridin-4-yl) aniline (1) (200 mg, 2.14 mmol) was dissolved in CH_3CN (4 mL) in a 25 mL round-bottomed flask and cooled to 0°C in an ice bath. To this stirred mixture was added t-BuONO (331 mg, 380 µL, 3.21 mmol) followed by $TMSN_3$ (300 mg, 340 µL, 2.56 mmol) drop-wise. The resulting solution was stirred at room temperature for 1 h. [10-11] The reaction mixture was concentrated under vacuum and the crude product was purified by silica gel chromatography (hexane) to give 4-(4-azidophenyl) benzo[b] oxazolo [5,4-f] [1,8] naphthyridine (2) from step one. General procedure for the synthesis of series of phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridines 4a-4i, 4-(4-(4-phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine 4a: Step II: In a 100 ml RB flask, the phenylacetylene(3a) 0.102 gm (1 mmol), 4-(4-azidophenyl) benzo[b] oxazolo [5,4-f] [1,8] naphthyridine (2) 0.48 gm (1.2 mmol), $CuSO_4.5H_2O$ 0.025 gm (10 mol%) and sodium ascorbate 0.0396 gm (0.2 mmol) Sharpless catalyst, [3+2] click protocol cyclo addition in 5 mL of $tBuOH/H_2O$ (1:1) solution, were added. The resulting reaction mixture was heated at 43°C for 14 hours. The progress of the reaction as analyzed by TLC, then the reaction mixture was extracted twice with 10 ml of water-ethyl acetate and the organic layer was dried using Na_2SO_4, filtered and the excess of organic layer was concentrated under rotary evaporator. Finally, the crude product was purified by column chromatography using (1:1) ethyl acetate/hexane as eluent to afford the pure product 4-(4-(4-phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine 4a in 80% yield. Similar procedure was applied to synthesize the rest of the compounds by taking various substituted phenyl acetylenes. [12-15]. By following the same protocols, we have synthesized 4b-4i.

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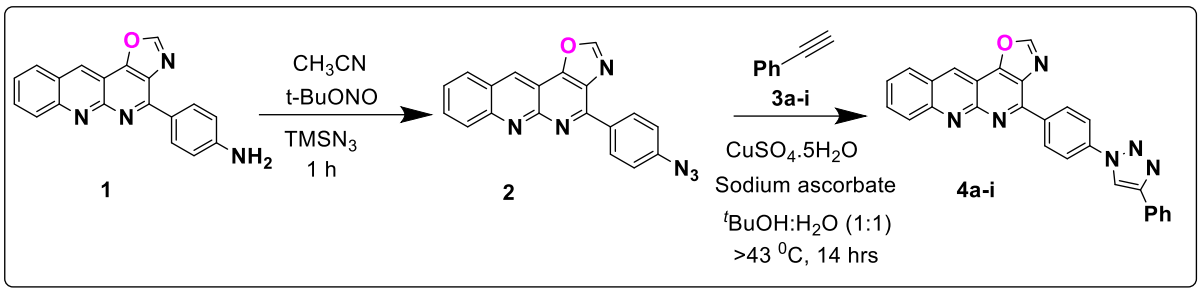

Scheme -I Synthesis of series of phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridines 4a-4i, 4-(4-(4-phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine 4a: Yellow - orange, m.p.243–245 °C, Yield 80 %.^{1}H NMR (DMSO-d_6): δ 8.81 (s, 1H), 8.42 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.95 (s, 1H), 7.81 (s, 3H), 7.60 (d, *J* = 16.4 Hz, 3H), 7.41 (d, *J* = 15.9 Hz, 3H), 7.28 (s, 1H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 133.00, 132.62, 131.94, 130.44, 128.86, 127.61, 127.37, 126.28, 125.77, 125.27, 124.33, 122.86, 121.60, 117.88, 110.74; ESI-MS: 441 [M+H]+, Found: C, 74.63; H, 3.67; N, 19.05 ; calcd for $C_{27}H_{16}N_6O$: C, 73.63; H, 3.66; N, 19.08. 4-(4-(4-(p-tolyl)-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo [5,4-f] [1,8] naphthyridine 4b: Yellowish - brown, m.p.250–252 °C, Yield 78 %.^{1}H NMR (DMSO-d6): δ 8.81 (s, 1H), 8.48 – 8.34 (m, 2H), 8.10 (d, *J* = 18.0 Hz, 2H), 7.95 (s, 1H), 7.87 – 7.74 (m, 3H), 7.60 (s, 1H), 7.57 – 7.46 (m, 2H), 7.43 (s, 1H), 7.34 – 7.19 (m, 2H), 2.35 – 2.31 (m, 3H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 136.14, 133.00, 132.62, 131.94, 130.39, 128.90, 127.61, 127.37, 126.37, 125.27, 124.33, 122.86, 121.60, 117.88, 110.74, 21.12; ESI-MS: 455 [M+H]+, Found: C, 73.42; H, 3.97; N, 18.45; calcd for $C_{28}H_{18}N_6O$: C, 74.00; H, 3.99; N, 18.49. 4-(4-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4-f][1,8]naphthyridine 4c: Brighter - yellow, m.p.280–282 °C, Yield 74 %.^{1}H NMR (DMSO-d6): δ 8.81 (s, 1H), 8.49 – 8.34 (m, 2H), 8.10 (d, *J* = 17.8 Hz, 2H), 7.95 (s, 1H), 7.84 – 7.78 (m, 3H), 7.62 – 7.49 (m, 3H), 7.43 (s, 1H), 7.08 – 6.94 (m, 2H), 3.83 – 3.79 (m, 3H);^{13}C NMR (DMSO-d_6): δ 159.63, 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 133.00, 132.62, 131.94, 130.46, 127.61, 127.37, 125.92, 125.27, 124.61, 124.33, 122.86, 121.60, 117.88, 114.40, 110.74, 56.03; ESI-MS: 471 [M+H]+, Found: C, 72.02; H, 3.84; N, 17.83; calcd for $C_{28}H_{18}N_6O_2$:C, 71.48; H, 3.86; N, 17.86. 4-(4-(4-(4-nitrophenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4f][1,8]naphthyridine 4d: Maroon, m.p.350–352 °C, Yield 76 %.^{1}H NMR (DMSO-d6):δ 9.43 (s, 1H), 8.81 (s, 1H), 8.50 – 8.36 (m, 2H), 8.36 – 8.22 (m, 2H), 8.12 (s, 1H), 7.95 (s, 1H), 7.93 – 7.71 (m, 5H), 7.60 (s, 1H), 7.43 (s, 1H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 146.40, 139.85, 137.43, 134.60, 133.00, 132.62, 131.94, 130.46, 127.61, 127.37, 125.27, 124.81, 124.39, 122.86, 121.60, 117.88, 110.74; ESI-MS: 486 [M+H]+, Found: C, 66.92; H, 3.13; N, 20.17;calcd for $C_{27}H_{15}N_7O_3$: C, 66.80; H, 3.11; N, 20.20. 4-(4-(4-(4-chlorophenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4 f][1,8]naphthyridine 4e: Pale-yellow, m.p.290–292 °C, Yield 80 %.^{1}H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.44 – 8.30 (m, 2H), 8.07 (d, *J* = 13.7 Hz, 2H), 7.95 (s, 1H), 7.81 – 7.72 (m, 3H), 7.58 (s, 1H), 7.56 – 7.44 (m, 2H), 7.44 – 7.35 (m, 3H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 134.14, 133.00, 132.62, 131.94, 130.46, 129.56, 129.20, 128.28, 127.61, 127.37, 125.27, 124.33, 122.86, 121.60, 117.88, 110.74; ESI-MS: 474[M]$^+$, 475[M+1],476 [M+2], Found: C, 68.39; H, 3.20; N, 17.66;calcd for $C_{27}H_{15}ClN_6O$: C, 68.29; H, 3.18; Cl, 7.46; N, 17.70. 4-(4-(4-(4-bromophenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4-f][1,8]naphthyridine 4f: Yellow, m.p.258–260 °C, Yield 82 %.^{1}H NMR (DMSO-d6):δ 8.78 (s, 1H), 8.44 – 8.30 (m, 2H), 8.07 (d, *J* = 13.9 Hz, 2H), 7.95 (s, 1H), 7.88 – 7.72 (m, 3H), 7.60 – 7.50 (m, 3H), 7.50 – 7.44 (m, 2H), 7.42 (s, 1H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 133.00, 132.62, 132.37, 131.94, 130.46, 128.37, 127.72, 125.27, 124.33, 123.35, 122.86, 121.60, 117.88, 110.74; ESI-MS: 518[M]$^+$, 520 [M+2], Found: C, 63.02; H, 2.93; N, 16.13; calcd for $C_{27}H_{15}BrN_6O$: C, 62.44; H, 2.91; N, 16.18. 4-(1-(4-(benzo[b]oxazolo[5,4-f][1,8]naphthyridin-4-yl)phenyl)-

1*H*-1,2,3-triazol-4-yl)benzonitrile 4g:Bright-yellow, m.p.310–312 °C, Yield 80 %.^{1}H NMR (DMSO-d6):δ 9.36 (s, 1H), 8.81 (s, 1H), 8.50 – 8.36 (m, 2H), 8.12 (s, 1H), 7.95 (s, 1H), 7.89 – 7.68 (m, 7H), 7.60 (s, 1H), 7.43 (s, 1H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 133.00, 132.55, 131.94, 130.46, 130.14, 127.61, 127.37, 125.27, 124.33, 122.86, 121.60, 119.12, 117.88, 113.07, 110.74; ESI-MS: 466 [M+H]+, Found: C, 72.35; H, 3.27; N, 21.02; calcd for $C_{28}H_{15}N_7O$: C, 72.25; H, 3.25; N, 21.06. 4-(4-(4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4-f][1,8]naphthyridine 4h: Bright-yellow, m.p.320–322 °C, Yield 84 %.^{1}H NMR (DMSO-d6):δ 9.34 (s, 1H), 8.81 (s, 1H), 8.49 – 8.35 (m, 2H), 8.12 (s, 1H), 7.95 (s, 1H), 7.88 – 7.73 (m, 3H), 7.72 – 7.54 (m, 5H), 7.43 (s, 1H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 139.85, 137.43, 134.71, 133.00, 132.62, 131.94, 130.46, 128.16, 127.98, 127.73, 127.58, 127.37, 127.05, 125.46, 125.27, 124.63, 123.41, 122.86, 121.60, 121.32, 117.88, 110.74; ESI-MS: 508 $[M]^+$, Found: C, 66.14; H, 2.97; N, 16.53;calcd for $C_{28}H_{15}F_3N_6O$: C, 66.14; H, 2.97; N, 16.53. 4-(4-(4-(4-ethylphenyl)-1*H*-1,2,3-triazol-1-yl)phenyl)benzo[b]oxazolo[5,4-f][1,8]naphthyridine 4i: Yellow, m.p.270–272 °C, Yield 82 %.^{1}H NMR (DMSO-d6):δ 8.81 (s, 1H), 8.48 – 8.34 (m, 2H), 8.10 (d, *J* = 18.0 Hz, 2H), 7.95 (s, 1H), 7.87 – 7.74 (m, 3H), 7.63 – 7.50 (m, 3H), 7.43 (s, 1H), 7.37 – 7.23 (m, 2H), 2.67 – 2.54 (m, 2H), 1.33 – 1.29 (m, 3H);^{13}C NMR (DMSO-d_6): δ 157.94, 155.66, 155.41, 150.51, 146.98, 143.15, 139.85, 137.43, 133.00, 132.62, 131.94, 130.54, 129.43, 127.61, 127.37, 125.27, 124.62, 124.33, 122.86, 121.60, 117.88, 110.74, 28.23, 13.21; ESI-MS: 469 $[M+H]^+$, Found: C, 74.64; H, 4.33; N, 17.84; calcd for $C_{29}H_{20}N_6O$: C, 74.34; H, 4.30; N, 17.94.

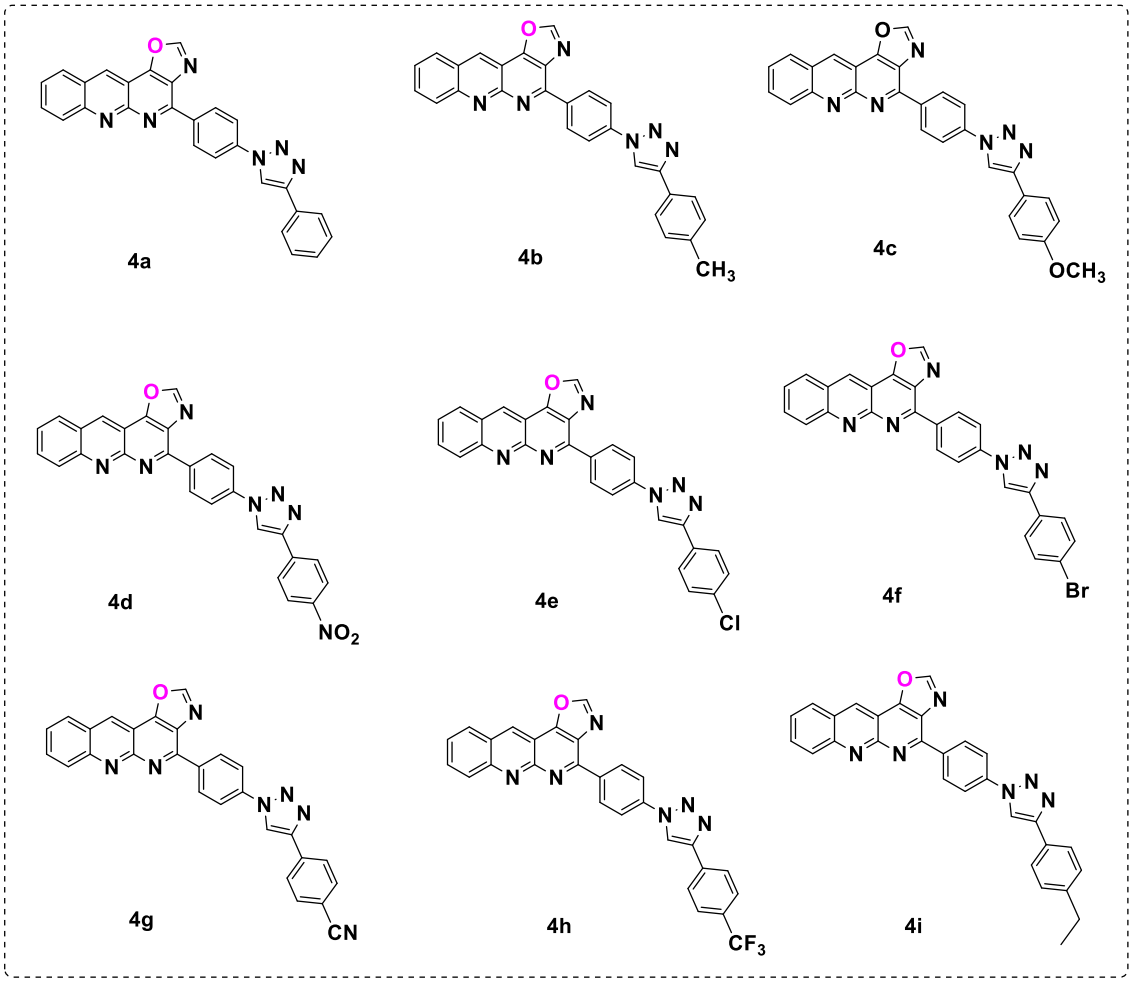

Fig. 2. Structures of designed target phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridines 4a-4i

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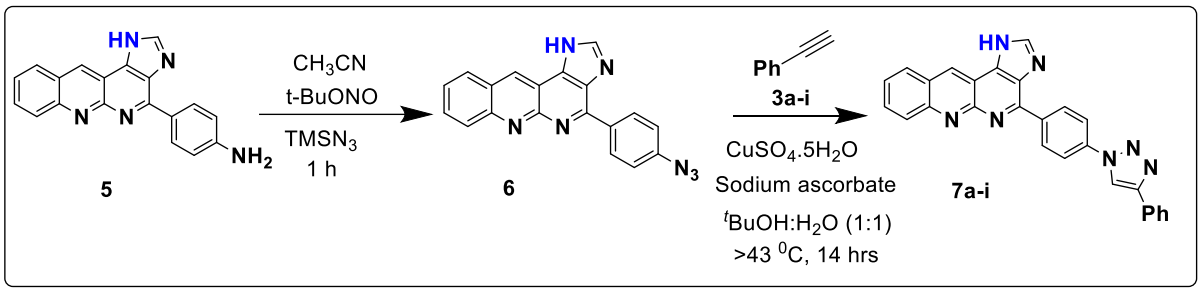
General procedure for the synthesis of 4-(4-azidophenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8] naphthyridine (6) Step I: 4-(1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridin-4-yl) aniline (5) (200 mg, 2.14 mmol) was dissolved in CH_3CN (4 mL) in a 25 mL round-bottomed flask and cooled to 0°C in an ice bath. To this stirred mixture was added t-BuONO (331 mg, 380 µL, 3.21 mmol) followed by $TMSN_3$ (300 mg, 340 µL, 2.56 mmol) drop-wise. The resulting solution was stirred at room temperature for 1 h. [10-11] The reaction mixture was concentrated under vacuum and the crude product was purified by silica gel chromatography (hexane) to give 4-(4-azidophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (6) from step one. General procedure for the synthesis of series of phenyl-1*H*-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridines 7a-7i, 4-(4-(4-phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1*H*-benzo[b]imidazo[4,5-f] [1,8] naphthyridine 7a: Step II: In a 100 ml RB flask, the phenylacetylene(3a) 0.102 gm (1 mmol), 4-(4-azidophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (6) 0.48 gm (1.2 mmol), $CuSO_4.5H_2O$ 0.025 gm (10 mol%) and sodium ascorbate 0.0396 gm (0.2 mmol) Sharpless catalyst, [3+2] click protocol cyclo addition in 5 mL of tBuOH/H_2O (1:1) solution, were added. The resulting reaction mixture was heated at 43°C for 14 hours. The progress of the reaction as analyzed by TLC, then the reaction mixture was extracted twice with 10 ml of water-ethyl acetate and the organic layer was dried using Na_2SO_4, filtered and the excess of organic layer was concentrated under rotary evaporator. Finally, the crude product was purified by column chromatography using (1:1) ethyl acetate/hexane as eluent to afford the pure product 4-(4-(4-phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine 7a in 82% yield. Similar procedure was applied to synthesize the rest of the compounds by taking various substituted phenyl acetylenes. By following the same protocols, we have synthesized 7b-7i.



Scheme -II Synthesis of series of phenyl-1*H*-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b] imidazo [4,5-f] [1,8] naphthyridines 7a-7i 4-(4-(4-phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1*H*-benzo[b]imidazo[4,5-f] [1,8] naphthyridine 7a: Yellow, m.p.306–308 °C, Yield 82 %.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.80 (t, *J* = 7.8 Hz, 3H), 7.71 (s, 1H), 7.60 (d, *J* = 10.2 Hz, 3H), 7.40 (t, *J* = 12.3 Hz, 3H), 7.30 (s, 1H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 133.31, 132.62, 130.44, 128.86, 127.61, 127.37, 126.28, 125.77, 125.27, 124.33, 122.86, 121.60, 119.16, 112.90; ESI-MS: 440 $[M+H]^+$, Found: C, 73.61; H, 3.92; N, 22.26; calcd for $C_{27}H_{17}N_7$: C, 73.79; H, 3.90; N, 22.31. 4-(4-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7b: Pale-yellow, m.p.285–287 °C, Yield 78 %.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (s, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.80 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.61 (s, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.43 (s, 1H), 7.26 (d, *J* = 7.5 Hz, 2H), 2.33 (s, 3H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.42, 147.95, 145.55, 139.54, 137.43, 136.20, 133.31, 132.62, 130.39, 129.01, 127.61, 127.38, 126.57, 125.37, 124.33, 122.87, 121.80, 119.16 , 112.90 , 21.13; ESI-MS: 454 $[M+H]^+$, Found: C, 75.06; H, 4.25; N, 21.51; calcd for $C_{28}H_{19}N_7$: C, 74.16; H, 4.22; N, 21.62. 4-(4-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7c: Canary -yellow, m.p.276–278 °C, Yield 74%.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (s, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.56 (d, *J* = 7.5 Hz, 3H),

7.42 (td, *J* = 7.5, 1.4 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 2H), 3.81 (s, 3H);^{13}C NMR (DMSO-d_6): δ 159.63, 156.84, 155.42, 147.95, 145.55, 139.54, 137.43, 136.26, 133.31, 132.62, 130.47, 127.61, 127.38, 126.12 , 125.37, 124.62, 124.33, 122.87, 121.80, 119.16, 114.59, 112.90, 56.04; ESI-MS: 470 [M+H]+, Found: C, 72.02; H, 4.11; N, 20.68; calcd for $C_{28}H_{19}N_7O$: C, 71.63; H, 4.08; N, 20.88. 4-(4-(4-(4-nitrophenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7d:Orange-brown, m.p.320–322 °C, Yield 79 %.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.59 (s, 1H), 7.52 (d, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 11.1 Hz, 3H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 146.40, 145.55, 139.53, 137.43, 136.26, 134.60, 133.31, 132.62, 130.46, 127.61, 127.37, 125.27, 124.81, 124.39, 122.86, 121.60 ,119.16, 112.90; ESI-MS: 485 [M+H]+, Found: C, 67.02; H, 3.36; N, 23.03; calcd for $C_{27}H_{16}N_8O_2$: C, 66.94; H, 3.33; N, 23.13. 4-(4-(4-(4-chlorophenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7e: Bright-yellow, m.p.305–307 °C, Yield 78%.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.59 (s, 1H), 7.52 (d, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 11.1 Hz, 3H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 134.14, 133.31, 132.62, 130.46, 129.56, 129.20, 128.28, 127.61, 127.37, 125.27, 124.33, 122.86, 121.60, 119.16, 112.90; ESI-MS: 473[M]$^+$, 474[M+1], 475,[M+2], Found: C, 69.03; H, 3.43; N, 20.59;calcd for $C_{27}H_{16}ClN_7$: C, 68.43; H, 3.40; N, 20.69. 4-(4-(4-(4-bromophenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7f: Yellow - orange, m.p.310–312 °C, Yield 76 %.^{1}H NMR (DMSO-d6):δ 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 7.5 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.79 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 3H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.43 (s, 1H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 133.31, 132.62, 132.37, 130.46, 128.37, 127.72, 125.27, 124.33, 123.35, 122.86, 121.60, 119.16, 112.90; ESI-MS: 517[M]$^+$,519[M+2], Found: C, 63.06; H, 3.14; N, 18.84;calcd for $C_{27}H_{16}BrN_7$: C, 62.56; H, 3.11; N, 18.91.4-(1-(4-(1H-benzo[b]imidazo[4,5-f][1,8]naphthyridin-4-yl)phenyl)-1*H*-1,2,3-triazol-4-yl)benzonitrile 7g: Bright-yellow, m.p.330–332 °C, Yield 80 %.^{1}H NMR (DMSO-d6):δ 9.36 (s, 1H), 8.72 (s, 1H), 8.41 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 7.97 (s, 1H), 7.85 – 7.69 (m, 8H), 7.59 (s, 1H), 7.44 (s, 1H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 133.31, 132.55, 130.46, 130.14, 127.61, 127.37, 125.27, 124.33, 122.86, 121.60, 119.14, 113.07, 112.90; ESI-MS: 465[M+H]+, Found: C, 73.04; H, 3.49; N, 24.02; calcd for $C_{28}H_{16}N_8$: C, 72.40; H, 3.47; N, 24.12.4-(4-(4-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7h: Pale-yellow , m.p.340–342 °C, Yield 79 %.^{1}H NMR (DMSO-d6):δ 9.34 (s, 1H), 8.72 (s, 1H), 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 7.5 Hz, 1H), 7.97 (s, 1H), 7.80 (d, *J* = 7.4 Hz, 3H), 7.71 (s, 1H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 10.3 Hz, 3H), 7.42 (s, 1H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 134.71, 133.31, 132.62, 130.46, 128.16, 127.98, 127.72, 127.58, 127.37, 127.05, 125.46, 125.27, 124.63, 123.41, 122.86 , 121.60, 121.32, 119.16, 112.90; ESI-MS: 508 [M+H]+, Found: C, 67.05; H, 3.21; N, 19.22; calcd for $C_{28}H_{16}F_3N_7$: C, 66.27; H, 3.18; N, 19.32.4-(4-(4-(4-ethylphenyl)-1H-1,2,3-triazol-1-yl)phenyl)-1*H*-benzo[b]imidazo[4,5-f][1,8]naphthyridine 7i: Yellow - orange, m.p.260–262 °C, Yield 81 %.^{1}H NMR (DMSO-d6):δ 8.40 (d, *J* = 7.5 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 7.80 (d, *J* = 7.5 Hz, 3H), 7.71 (s, 1H), 7.57 (d, *J* = 7.4 Hz, 3H), 7.42 (s, 1H), 7.30 (d, *J* = 7.5 Hz, 2H);^{13}C NMR (DMSO-d_6): δ 156.84, 155.41, 147.95, 145.55, 139.53, 137.43, 136.26, 134.71, 133.31, 132.62, 130.46, 128.16, 127.98, 127.8, 127.6, 127.4, 127.05, 125.46, 125.27, 124.63, 123.41, 122.86, 121.60, 121.32, 119.16, 112.90; ESI-MS: 468 [M+H]+, Found: C, 75.05; H, 4.56; N, 20.81; calcd for $C_{29}H_{21}N_7$: C, 74.50; H, 4.53; N, 20.97.

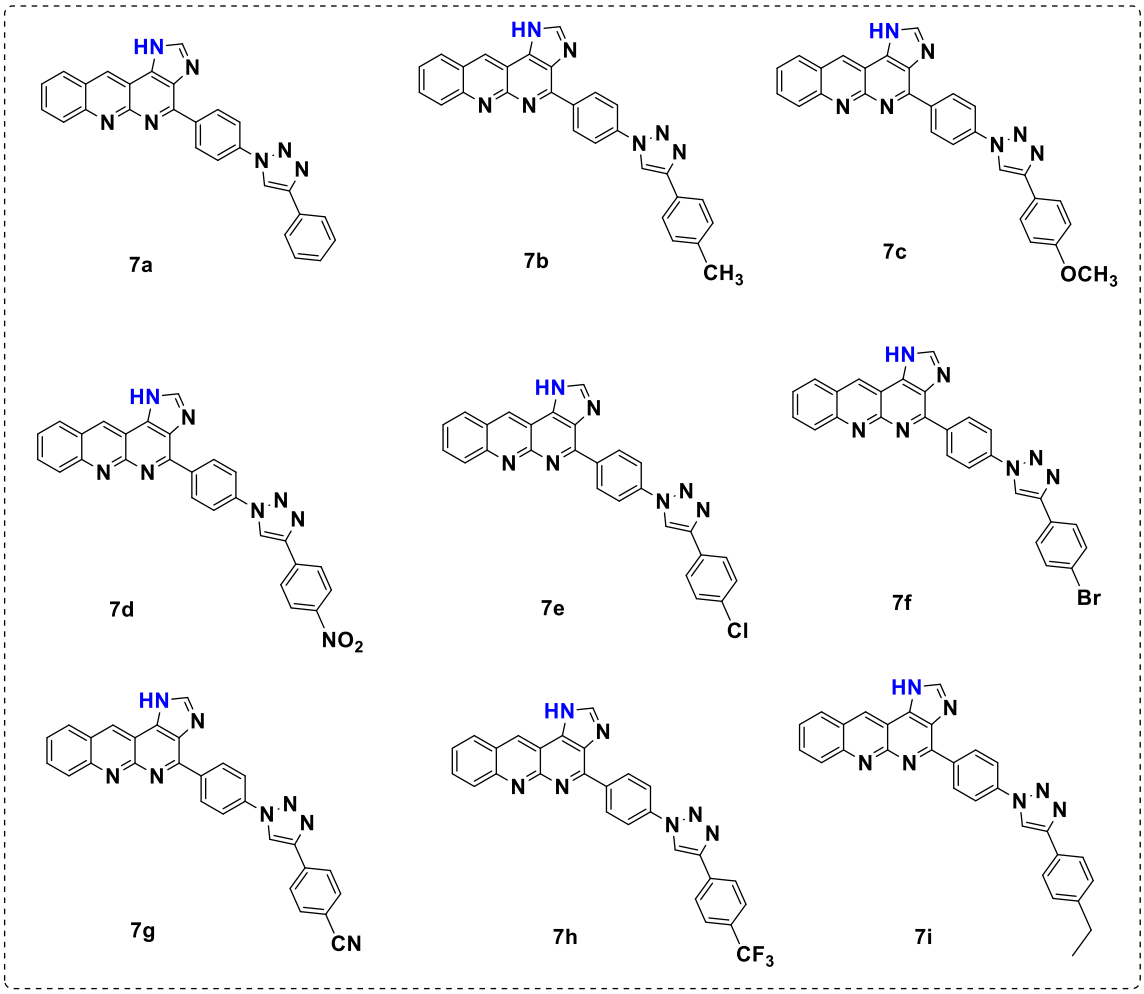


Fig.3. Structures of designed target phenyl-1*H*-1,2,3-triazol-1-yl) phenyl)-1H-benzo[b]imidazo [4,5-f] [1,8] naphthyridines 7a-7i

CONCLUSION

Two-Step Synthesis of series of phenyl-1*H*-1,2,3-triazol-1-yl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridines 4a-4i and phenyl-1H-1,2,3-triazol-1-yl) phenyl)-1*H*-benzo[b]imidazo [4,5-f] [1,8] naphthyridines 7a-7i were developed with promising yields, and further confirmed by spectral and elemental analysis.

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