Supporting Information

Regioselective Copper-Diamine-Catalyzed C-H Arylation of 1,2,4-Triazole Ring with Aryl Bromides

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Table of Contents

General Considerations SI 2

Synthesis of Substrates SI 3

General Procedure for Cu-catalyzed C-H Arylation SI 4

Characterization Data for Arylated Products SI 4

References SI 16

Copies of $^1$H and $^{13}$C NMR Spectra of Arylated Products SI 17
General Considerations

All commercially available chemicals and anhydrous solvents were used directly upon purchase from suppliers. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plates (0.2 mm thickness) and visualized using UV radiation on Spectroline Model ENF-24061/F 254 nm. Flash chromatography was performed using Merck silica gel 60 with AR grade solvents. Columns were packed as a silica gel suspension in hexane prior to elution by the appropriate solvent system (hexane/EtOAc). Melting points were determined using OptiMelt automated melting point system and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance DPX 400 spectrophotometer. Chemical shifts for $^1$H and $^{13}$C NMR are reported as δ in units of parts per million (ppm) downfield from SiMe$_4$ and relative to the residual signal of CDCl$_3$ (δ 7.26, singlet for $^1$H NMR; δ 77.06, triplet for $^{13}$C NMR). Multiplicities are reported based on apparent multiplicities and coupling constants ($J$ values) are reported in unit of Hertz (Hz). Numbers of protons are reported based on the appropriate integration of the signals. IR spectra were recorded using Perkin–Elmer Paragon 100 FT-IR spectrophotometer on KBr plates. Mass spectroscopy was performed using Agilent 1100 series LC/MSD.
Synthesis of Substrates

1a was synthesized according to modified literature procedure: To an oven-dried 50-mL RBF equipped with a magnetic stir bar, benzyl bromide (5.0 mmol) and MeCN (20 mL) were added. K₂CO₃ (3.0 equiv.) was then slowly added followed by 1,2,4-triazole (5.0 equiv.). The reaction mixture was then heated at 85 °C under N₂ for overnight. Upon cooling to room temperature, the reaction mixture was passed through a pad of celite with EtOAc washing and the filtrate was then concentrated under reduced pressure. The residue was next redissolved in EtOAc and subsequently washed with concentrated aqueous NaHCO₃ (3 times), water and brine. The organic layer was then dried Na₂SO₄ and concentrated under reduced pressure to afford the analytically pure 1a as light yellow viscous oil which slowly solidified to off-white solid in 78% yield (621 mg). 1b, 1f and 1g were also prepared according to the same procedure using the appropriate starting materials. All compounds were used without further purification except 1f which was further purified by silica gel column chromatography prior to use. 1a,¹ 1b,² 1f¹ and 1g³ are known compounds whose homogeneity and identity were confirmed by comparing its ¹H NMR spectrum with literature.

1c,⁴ 1d⁵ and 1e⁵ are all known compounds which were synthesized according to literature procedures.
General Procedure for Cu-catalyzed C-H Arylation

To an 8-mL screw-capped reaction vial equipped with a magnetic stir bar, a mixture of CuI (20 mol%), 1,2,4-triazole (0.5 mmol), LiO'Bu (2.0 equiv.), DMEDA (20 mol%) and aryl bromide (3.0 equiv.) was mixed in dioxane (0.5 mL). The reaction mixture was then placed into a pre-heated oil bath at 140 °C with vigorous stirring. After 24 h, the reaction mixture was then allowed to cool to room temperature and passed through a short pad of celite with DCM washing. The crude reaction mixture was then dried over Na2SO4 and concentrated under reduced pressure. Purification by silica gel chromatography (hexane: EtOAc) then gave the desired arylated product.

Characterization Data for Arylated Products

1-benzyl-5-phenyl-1H-1,2,4-triazole (3aa).6 Off-white solid (62%, 72.5 mg); Rf (2:1 hexane:EtOAc) = 0.37; m.p 83 – 86 °C; 1H NMR (400 MHz, CDCl3): δ 5.43 (s, 2H), 7.15 – 7.16 (m, 2H), 7.30 – 7.36 (m, 3H), 7.44 – 7.49 (m, 3H), 7.57 – 7.60 (m, 2H), 8.03 (s, 1H); 13C NMR (100 MHz, CDCl3): δ 52.8, 126.9, 127.9, 128.1, 128.8, 128.9, 129.0, 130.3, 135.9, 151.3; νmax (KBr) 3066, 3029, 2959, 1606, 1483, 1454, 1390, 1289, 1234, 1184, 1132, 1074, 1014, 916, 788, 738 cm⁻¹; HRMS (ESI) calcd for C15H14N3 [M+H]: 236.1187, found: 236.1190.
1-butyl-5-phenyl-1H-1,2,4-triazole (3ba). Light yellow oil (40%, 40.3 mg); $R_f$ (2:1 hexane:EtOAc) = 0.37; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.88 (t, $J$ = 7.5 Hz, 3H), 1.25 – 1.32 (m, 2H), 1.83 – 1.89 (m, 2H), 4.20 (t, $J$ = 7.5 Hz, 2H), 7.49 – 7.52 (m, 3H), 7.60 – 7.62 (m, 2H), 7.95 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 13.5, 19.7, 32.0, 49.0, 128.3, 128.7, 128.8, 130.0, 150.7; $\nu_{\text{max}}$ (KBr) 3068, 2960, 2934, 2874, 1484, 1463, 1442, 1385, 1276, 1161, 1013, 922, 881, 777, 731, 699 cm$^{-1}$; HRMS (ESI) calcd for C$_{12}$H$_{16}$N$_3$ [M+H]: 202.1344, found: 202.1348.

(E)-5-phenyl-1-styryl-1H-1,2,4-triazole (3ca). Yellow solid (50%, 61.7 mg); $R_f$ (2:1 hexane:EtOAc) = 0.50; m.p 123 – 126 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.28 – 7.31 (m, 1H), 7.33 – 7.37 (m, 2H), 7.40 – 7.43 (m, 3H), 7.49 – 7.58 (m, 4H), 7.69 – 7.72 (m, 2H), 8.07 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 121.9, 122.5, 126.7, 127.6, 128.4, 128.9, 129.1, 129.4, 130.6, 134.4, 151.6, 154.4; $\nu_{\text{max}}$ (KBr) 3054, 1766, 1654, 1596, 1529, 1486, 1450, 1329, 1261, 1131, 1074, 1008, 941, 886, 775, 755 cm$^{-1}$; HRMS (ESI) calcd for C$_{16}$H$_{14}$N$_3$ [M+H]: 248.1187, found: 248.1190.
1,5-diphenyl-1H-1,2,4-triazole (3da). Off-white solid (43%, 47.3 mg); R_f (2:1 hexane:EtOAc) = 0.54; m.p 78 – 81 °C; ^1H NMR (400 MHz, CDCl_3): δ 7.32 – 7.44 (m, 8H), 7.48 – 7.50 (m, 2H), 8.10 (s, 1H); ^13C NMR (100 MHz, CDCl_3): δ 125.4, 127.6, 127.8, 128.6, 128.9, 129.0, 129.4, 130.1, 138.2, 151.6; ν_max (KBr) 3085, 1598, 1558, 1501, 1440, 1383, 1290, 1200, 1139, 1069, 984, 915, 779, 721 cm^{-1}; HRMS (ESI) calcd for C_{14}H_{12}N_{3} [M+H]: 222.1031, found: 222.1032.

5-phenyl-1-(p-tolyl)-1H-1,2,4-triazole (3ea). Off-white solid (42%, 49.0 mg); R_f (2:1 hexane:EtOAc) = 0.47; m.p 63 – 65 °C; ^1H NMR (400 MHz, CDCl_3): δ 2.41 (s, 3H), 7.20 – 7.25 (m, 4H), 7.32 – 7.36 (m, 2H), 7.37 – 7.41 (m, 1H), 7.49 – 7.51 (m, 2H), 8.08 (s, 1H); ^13C NMR (100 MHz, CDCl_3): δ 21.2, 125.2, 127.9, 128.6, 128.9, 129.97, 130.01, 135.8, 139.1, 151.5, 153.8; ν_max (KBr) 3037, 2920, 1600, 1560, 1514, 1487, 1455, 1381, 1266, 1203, 1136, 1107, 1065, 985, 923, 781, 721 cm^{-1}; HRMS (ESI) calcd for C_{15}H_{14}N_{3} [M+H]: 236.1187, found: 236.1190.
1-benzyl-5-phenyl-1H-1,2,3-triazole (3fa). Off-white solid (22%, 25.4 mg); R<sub>f</sub> (2:1 hexane:EtOAc) = 0.37; m.p 75 – 78 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.55 (s, 2H), 7.06 – 7.09 (m, 2H), 7.24 – 7.30 (m, 5H), 7.40 – 7.44 (m, 3H), 7.75 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 51.9, 127.0, 127.2, 128.2, 128.9, 128.95, 128.98, 129.5, 133.4, 135.6; ν<sub>max</sub> (KBr) 3060, 3033, 2962, 1603, 1479, 1453, 1434, 1365, 1233, 1208, 1127, 1113, 1076, 827, 769, 740, 719, 701 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>15</sub>H<sub>14</sub>N<sub>3</sub> [M+H]: 236.1187, found: 236.1189.

1-benzyl-2-phenyl-1H-imidazole (3ga). Yellow oil (24%, 28.6 mg); R<sub>f</sub> (2:1 hexane:EtOAc) = 0.20; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.21 (s, 2H), 6.97 (s, 1H), 7.08 (d, J = 7.2 Hz, 2H), 7.19 (s, 1H), 7.28 – 7.40 (m, 6H), 7.54 (s, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 50.4, 121.2, 126.6, 127.9, 128.6, 128.8, 128.9, 129.0, 130.4, 136.9, 148.2; ν<sub>max</sub> (KBr) 3065, 3033, 2933, 1605, 1498, 1473, 1454, 1417, 1359, 1277, 1128, 1075, 1019, 914, 772, 729, 699 cm<sup>-1</sup>; HRMS (ESI) calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub> [M+H]: 235.1235, found: 235.1237.
1-benzyl-5-(naphthalene-1-yl)-1H-1,2,4-triazole (3ab). Light tan solid (65%, 93.4 mg); Rf (2:1 hexane:EtOAc) = 0.46; m.p 60 – 64 °C; ¹H NMR (400 MHz, CDCl₃): δ 5.19 (s, 2H), 6.99 – 7.01 (m, 2H), 7.22 – 7.26 (m, 3H), 7.44 – 7.57 (m, 4H), 7.63 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 8.16 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 52.7, 124.9, 125.0, 125.5, 126.6, 127.4, 127.6, 128.1, 128.46, 128.47, 128.7, 130.8, 131.8, 133.6, 135.5, 151.5, 154.0; ν_max (KBr) 3033, 2939, 1594, 1497, 1469, 1455, 1379, 1275, 1177, 1086, 976, 894, 803, 779, 723 cm⁻¹; HRMS (ESI) calcd for C₁₉H₁₆N₃ [M+H]: 286.1344, found: 286.1346.

1-benzyl-5-(naphthalene-2-yl)-1H-1,2,4-triazole (3ac). Off-white solid (74%, 105.9 mg); Rf (2:1 hexane:EtOAc) = 0.43; m.p 124 – 127 °C; ¹H NMR (400 MHz, CDCl₃): δ 5.51 (s, 2H), 7.21 – 7.23 (m, 2H), 7.33 – 7.39 (m, 3H), 7.54 – 7.59 (m, 2H), 7.71 (dd, J₁ = 8.6 Hz, J₂ = 1.8 Hz, 1H), 7.80 – 7.82 (m, 1H), 7.88 – 7.90 (m, 1H), 7.94 (d, J = 8.8 Hz, 1H), 8.05 (s, 1H), 8.08 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 53.0, 125.2, 125.5, 126.9, 127.0, 127.5, 127.9, 128.2, 128.5, 128.8, 129.0, 132.8, 133.8, 136.0, 151.4, 155.3; ν_max (KBr) 3063, 3028, 2956, 1603, 1498, 1475, 1454, 1430, 1367, 1286, 1183, 1116, 1029, 865, 830, 753, 725 cm⁻¹; HRMS (ESI) calcd for C₁₉H₁₆N₃ [M+H]: 286.1344, found: 286.1347.
1-benzyl-5-(p-tolyl)-1H-1,2,4-triazole (3ad). Off-white solid (60%, 75.2 mg); Rf (2:1 hexane:EtOAc) = 0.43; m.p 59 – 60 °C; ^1^H NMR (400 MHz, CDCl₃): δ 2.40 (s, 3H), 5.42 (s, 2H), 7.15 – 7.16 (m, 2H), 7.25 – 7.27 (m, 2H), 7.30 – 7.34 (m, 3H), 7.47 – 7.49 (m, 2H), 8.01 (s, 1H); ^1^C NMR (100 MHz, CDCl₃): δ 21.4, 52.7, 125.0, 126.9, 128.1, 128.6, 128.9, 129.6, 136.0, 140.5, 151.3, 155.4; νmax (KBr) 3025, 2919, 1615, 1491, 1462, 1387, 1272, 1232, 1179, 1124, 1080, 1033, 1015, 903, 877, 824, 784, 732, 696 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₆N₃ [M+H]: 250.1344, found: 250.1345.

1-benzyl-5-(m-tolyl)-1H-1,2,4-triazole (3ae). Off-white solid (66%, 82.6 mg); Rf (2:1 hexane:EtOAc) = 0.46; m.p 51 – 54 °C; ^1^H NMR (400 MHz, CDCl₃): δ 2.35 (s, 3H), 5.40 (s, 2H), 7.15 – 7.16 (m, 2H), 7.28 – 7.35 (m, 6H), 7.41 (s, 1H), 8.00 (s, 1H); ^1^C NMR (100 MHz, CDCl₃): δ 21.2, 52.7, 125.5, 126.9, 127.7, 128.0, 128.6, 128.8, 129.5, 130.9, 135.9, 138.7, 151.1, 155.3; νmax (KBr) 3108, 3028, 1584, 1524, 1492, 1452, 1372, 1274, 1249, 1184, 1123, 1074, 1035, 919, 896, 806, 741 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₆N₃ [M+H]: 250.1344, found: 250.1347.
1-benzyl-5-(o-tolyl)-1H-1,2,4-triazole (3af). Off-white solid (60%, 74.2 mg); Rf (2:1 hexane:EtOAc) = 0.46; m.p 40 – 44 °C; 1H NMR (400 MHz, CDCl3): δ 2.09 (s, 3H), 5.17 (s, 2H), 7.03 – 7.06 (m, 2H), 7.19 – 7.31 (m, 6H), 7.38 – 7.42 (m, 1H), 8.03 (s, 1H); 13C NMR (100 MHz, CDCl3): δ 19.5, 52.5, 125.9, 127.7, 127.8, 128.2, 128.7, 129.7, 130.3, 130.7, 135.5, 138.2, 151.1, 154.7; νmax (KBr) 3030, 1605, 1530, 1453, 1385, 1364, 1273, 1229, 1184, 1136, 1113, 1075, 1015, 917, 885, 774, 749, 716 cm⁻¹; HRMS (ESI) calcd for C16H16N3 [M+H]: 250.1344, found: 250.1347.

1-benzyl-5-(2-methoxyphenyl)-1H-1,2,4-triazole (3ag). Light yellow oil (60%, 75.4 mg); Rf (2:1 hexane:EtOAc) = 0.40; 1H NMR (400 MHz, CDCl3): δ 5.39 (s, 2H), 7.10 – 7.14 (m, 4H), 7.28 – 7.34 (m, 3H), 7.53 – 7.56 (m, 2H), 7.99 (s, 1H); 13C NMR (100 MHz, CDCl3): δ 52.7, 116.0 (d, J = 21.7 Hz), 123.9 (d, J = 3.3 Hz), 126.7, 128.1, 128.9, 130.8 (d, J = 6.8 Hz), 135.6, 151.1, 154.2, 163.7 (d, J = 249.8 Hz); νmax (KBr) 3066, 3034, 2939, 1609, 1486, 1463, 1381, 1275, 1229, 1160, 1123, 1028, 1013, 844, 729 cm⁻¹; HRMS (ESI) calcd for C15H13FN3 [M+H]: 254.1093, found: 254.1095.
1-benzyl-5-(4-chlorophenyl)-1H-1,2,4-triazole (3ah). Light yellow solid (63%, 84.9 mg); R\textsubscript{f} (2:1 hexane:EtOAc) = 0.41; m.p 75 – 78 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 5.42 (s, 2H), 7.13 – 7.15 (m, 2H), 7.31 – 7.37 (m, 3H), 7.42 – 7.44 (m, 2H), 7.50 – 7.53 (m, 2H), 8.02 (s, 1H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 52.9, 126.3, 126.8, 128.3, 129.1, 129.2, 130.1, 135.6, 136.2, 151.4, 154.2; ν\textsubscript{max} (KBr) 3070, 3011, 2934, 1601, 1488, 1457, 1409, 1375, 1286, 1245, 1186, 1094, 1010, 905, 835, 732, 696 cm\textsuperscript{-1}; HRMS (ESI) calcd for C\textsubscript{13}H\textsubscript{13}ClN\textsubscript{3} [M+H]: 270.0798, found: 270.0797.

1-benzyl-5-(4-(trifluoromethyl)phenyl)-1H-1,2,4-triazole (3ai). Off-white solid (46%, 70.4 mg); R\textsubscript{f} (2:1 hexane:EtOAc) = 0.51; m.p 44 – 46 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 5.45 (s, 2H), 7.14 – 7.16 (m, 2H), 7.32 – 7.38 (m, 3H), 7.72 (s, 4H), 8.07 (s, 1H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): δ 53.0, 122.3, 125.0, 125.9 (q, J = 3.7 Hz), 126.8, 127.8, 128.4, 129.1, 129.2, 131.4, 132.2 (q, J = 32.8 Hz), 135.5, 151.5; ν\textsubscript{max} (KBr) 3069, 3033, 2963, 1622, 1544, 1455, 1440, 1384, 1328, 1241, 1131, 1071, 1030, 900, 846, 754, 720 cm\textsuperscript{-1}; HRMS (ESI) calcd for C\textsubscript{16}H\textsubscript{13}F\textsubscript{3}N\textsubscript{3} [M+H]: 304.1061, found: 304.1063.
1-benzyl-5-(3-(trifluoromethyl)phenyl)-1H-1,2,4-triazole (3aj). Off-white solid (55%, 83.9 mg); R_f (2:1 hexane:EtOAc) = 0.43; m.p 50 – 52 °C; ^1H NMR (400 MHz, CDCl₃): δ 5.43 (s, 2H), 7.17 – 7.19 (m, 2H), 7.32 – 7.38 (m, 3H), 7.59 (t, J = 7.8 Hz, 1H), 7.73 – 7.78 (m, 2H), 7.85 (s, 1H), 8.06 (s, 1H); ^13C NMR (100 MHz, CDCl₃): δ 53.1, 122.3, 124.9, 125.8 (q, J = 3.8 Hz), 126.9, 127.0, 128.4, 128.8, 129.1, 129.5, 131.3, 131.7, 132.0, 135.4, 151.4, 153.8; v_max (KBr) 3073, 2934, 1622, 1498, 1457, 1375, 1323, 1276, 1130, 1034, 916, 889, 815, 771, 743, 724 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₃F₃N₃ [M+H]: 304.1061, found: 304.1063.

1-benzyl-5-(2-(trifluoromethyl)phenyl)-1H-1,2,4-triazole (3ak). Yellow solid (31%, 47.1 mg); R_f (2:1 hexane:EtOAc) = 0.38; m.p 86 – 89 °C; ^1H NMR (400 MHz, CDCl₃): δ 5.13 (s, 2H), 7.04 – 7.06 (m, 2H), 7.25 – 7.29 (m, 4H), 7.59 (t, J = 7.4 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 8.04 (s, 1H); ^13C NMR (100 MHz, CDCl₃): δ 52.8, 121.9, 124.7, 126.9 (q, J = 4.8 Hz), 127.8, 128.3, 128.8, 130.1, 130.4, 130.7, 131.8, 132.0, 135.0, 151.2; v_max (KBr) 3068, 3030, 2988, 1605, 1478, 1464, 1362, 1315, 1274, 1229, 1169, 1131, 1065, 1033, 980, 875, 780, 726 cm⁻¹; HRMS (ESI) calcd for C₁₆H₁₃F₃N₃ [M+H]: 304.1061, found: 304.1062.
1-benzyl-5-(4-methoxyphenyl)-1H-1,2,4-triazole (3a1). Light tan solid (56%, 74.8 mg); R_f (2:1 hexane:EtOAc) = 0.26; m.p 79 – 82 °C; 1H NMR (400 MHz, CDCl_3): δ 3.84 (s, 3H), 5.42 (s, 2H), 6.95 – 6.97 (m, 2H), 7.15 – 7.16 (m, 2H), 7.30 – 7.37 (m, 3H), 7.51 – 7.53 (m, 2H), 8.00 (s, 1H); 13C NMR (100 MHz, CDCl_3): δ 52.7, 55.4, 114.3, 120.2, 126.8, 128.1, 129.0, 130.2, 136.0, 151.2, 155.2, 161.1; ν_max (KBr) 3065, 3034, 3005, 2957, 2833, 1611, 1577, 1540, 1472, 1378, 1254, 1178, 1124, 1022, 899, 834, 751, 713 cm⁻¹; HRMS (ESI) calcd for C_{16}H_{16}N_{3}O [M+H]: 266.1293, found: 266.1292.

1-benzyl-5-(3-methoxyphenyl)-1H-1,2,4-triazole (3a3). Yellow oil (61%, 81.2 mg); R_f (2:1 hexane:EtOAc) = 0.37; 1H NMR (400 MHz, CDCl_3): δ 3.73 (s, 3H), 5.43 (s, 2H), 7.00 – 7.02 (m, 1H), 7.11 – 7.16 (m, 4H), 7.29 – 7.36 (m, 4H), 8.02 (s, 1H); 13C NMR (100 MHz, CDCl_3): δ 52.7, 55.3, 113.7, 116.6, 120.8, 126.8, 128.0, 128.9, 129.0, 129.9, 135.9, 151.2, 155.1, 159.8; ν_max (KBr) 3065, 3032, 2939, 2836, 1607, 1584, 1496, 1377, 1288, 1262, 1221, 1181, 1123, 1049, 1028, 864, 792, 739, 728 cm⁻¹; HRMS (ESI) calcd for C_{16}H_{16}N_{3}O [M+H]: 266.1293, found: 266.1294.
1-benzyl-5-(2-methoxyphenyl)-1H-1,2,4-triazole (3an). Off-white solid (43%, 56.7 mg); Rf
(2:1 hexane:EtOAc) = 0.28; m.p 68 – 71 °C; 1H NMR (400 MHz, CDCl3): δ 3.69 (s, 3H),
5.21 (s, 2H), 6.98 (d, J = 8.4 Hz, 1H), 7.02 – 7.08 (m, 3H), 7.24 – 7.29 (m, 3H), 7.37 (dd, J1
= 7.6 Hz, J2 = 1.6 Hz, 1H), 7.45 – 7.49 (m, 1H), 8.02 (s, 1H); 13C NMR (100 MHz, CDCl3): δ
42.8, 55.4, 111.2, 117.4, 121.0, 127.6, 127.8, 128.6, 131.8, 132.0, 135.9, 151.5, 152.9, 157.1;
νmax (KBr) 3014, 2968, 2936, 1781, 1583, 1449, 1381, 1251, 1182, 1104, 1010, 893, 804,
766, 730 cm⁻¹; HRMS (ESI) calcd for C16H16N3O [M+H]: 266.1293, found: 266.1294.

3-(1-benzyl-1H-1,2,4-triazol-5-yl)pyridine (3ao). Yellow solid (34%, 40.7 mg); Rf (1:1
hexane:EtOAc) = 0.18; m.p 54 – 57 °C; 1H NMR (400 MHz, CDCl3): δ 5.45 (s, 2H), 7.13 –
7.15 (m, 2H), 7.31 – 7.36 (m, 3H), 7.38 – 7.42 (m, 1H), 7.90 (dt, J1 = 8.0 Hz, J2 = 2.0 Hz,
1H), 8.07 (s, 1H), 8.72 (d, J = 3.6 Hz, 1H), 8.84 (s, 1H); 13C NMR (100 MHz, CDCl3): δ
53.1, 123.6, 124.4, 126.8, 128.4, 129.1, 135.4, 136.2, 149.2, 151.2, 151.6, 152.5; νmax (KBr)
3065, 3027, 2976, 2935, 1598, 1570, 1489, 1456, 1420, 1379, 1307, 1281, 1196, 1127, 1015,
897, 813, 732, 704 cm⁻¹; HRMS (ESI) calcd for C14H13N4 [M+H]: 237.1140, found: 237.1143.
2-(1-benzyl-1H-1,2,4-triazol-5-yl)pyridine (3ap). Off-white solid (71%, 83.4 mg); Rf (2:1 hexane:EtOAc) = 0.39; m.p 65 – 67 °C; ¹H NMR (400 MHz, CDCl₃): δ 6.13 (s, 2H), 7.22 – 7.36 (m, 6H), 7.82 (td, J₁ = 7.8 Hz, J₂ = 1.6 Hz, 1H), 7.98 (s, 1H), 8.23 (d, J = 8.0 Hz, 1H), 8.69 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 54.1, 123.9, 124.3, 127.8, 128.0, 128.6, 136.7, 137.1, 147.9, 148.8, 150.8, 151.5; v max (KBr) 3098, 2961, 1604, 1585, 1453, 1418, 1320, 1278, 1191, 1139, 1090, 1030, 996, 920, 796, 703 cm⁻¹; HRMS (ESI) calcd for C₁₄H₁₃N₄[M+H]: 237.1140, found: 237.1142.

1-benzyl-5-(thiophen-3-yl)-1H-1,2,4-triazole (3aq). Light tan oil (45%, 53.8 mg); Rf (2:1 hexane:EtOAc) = 0.43; ¹H NMR (400 MHz, CDCl₃): δ 5.50 (s, 2H), 7.11 – 7.15 (m, 2H), 7.30 – 7.37 (m, 3H), 7.39 – 7.41 (m, 2H), 7.56 – 7.57 (m, 1H), 7.99 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 52.8, 126.48, 126.52, 126.9, 127.5, 128.1, 128.3, 129.1, 135.7, 150.9, 151.1; v max (KBr) 3104, 3032, 2953, 1571, 1496, 1454, 1409, 1341, 1307, 1272, 1183, 1121, 1076, 1030, 975, 893, 861, 793, 727 cm⁻¹; HRMS (ESI) calcd for C₁₃H₁₂N₃S [M+H]: 242.0752, found: 242.0754.
1-benzyl-5-(thiophen-2-yl)-1H-1,2,4-triazole (3ar). Light yellow oil (56%, 67.3 mg); Rf (2:1 hexane:EtOAc) = 0.47; 1H NMR (400 MHz, CDCl₃): δ 5.57 (s, 2H), 7.06 – 7.08 (m, 1H), 7.15 – 7.17 (m, 2H), 7.29 – 7.37 (m, 4H), 7.46 – 7.48 (m, 1H), 7.98 (s, 1H); 13C NMR (100 MHz, CDCl₃): δ 53.0, 126.6, 127.9, 128.1, 128.3, 128.9, 129.0, 135.4, 149.5, 151.2; ν max (KBr) 3107, 3033, 2937, 1605, 1568, 1455, 1474, 1386, 1330, 1279, 1231, 1180, 1114, 982, 853, 729 cm⁻¹; HRMS (ESI) calcd for C₁₃H₁₂N₃S [M+H]: 242.0752, found: 242.0754.

References

Introduction

Triazole, also known as pyrrodiazole is one of the simplest forms of the triazole family. It follows from the literature that the triazole nucleus is present as a core structural component in an array of drug categories such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, antihypertensive, antimalarial, local anaesthetic, antianxiety, antidepressant, antihistaminic, and potent activity of triazole and their derivatives has established them as pharmacologically significant scaffolds. Triazole derivatives have been synthesised with molecular formula $\text{C}_n\text{H}_m\text{N}_o\text{X}_p$, where $n$, $m$, $o$, and $p$ are integers, and a molecular weight of 69.06. Triazole is a white to pale yellow crystal line solid with a weak, characteristic odour, it is soluble in water and alcohol, melts at 120°C and boils at 260°C.

The triazole nucleus is one of the most important and well-known heterocycles which is a common and integral feature of a variety of natural products and medicinal agents. Triazole nucleus is present as a core structural feature of a variety of natural products and medicinal agents. Triazole derivatives have been synthesised with molecular formula $\text{C}_n\text{H}_m\text{N}_o\text{X}_p$, where $n$, $m$, $o$, and $p$ are integers, and a molecular weight of 69.06.

The importance of this heterocyclic nucleus is evident from the volume of research that has been carried out on triazole and their derivatives, which has proved the pharmacological significance of this heterocyclic nucleus. The present paper is an attempt to review the pharmacological activities such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, antihypertensive, antimalarial, local anaesthetic, antianxiety, antidepressant, antihistaminic, and anticancer activities that the triazole derivatives possess a wide range of therapeutical values. For example, a series of 1-(substituted biaryloxy)-2,4-disubstituted triazoles such as 3ac, reported for triazole derivatives in the current literature with an update of recent research findings on this nuclei.

Keywords: Triazole, 1,2,3-triazole, 1,2,4-triazole, pharmacological activities such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, antihypertensive, antimalarial, local anaesthetic, antianxiety, antidepressant, antihistaminic, and anticancer activities.

In the past three decades the structure–activity relationship (SAR) of triazole derivatives has been extensively studied. It is evident from these studies that substitutents on the triazole side chain at the N-1 of the triazole nucleus which showed better antifungal activity than standard drug voriconazole. For example, a series of 1-(substituted biaryloxy)-2,4-disubstituted triazoles such as 3ac, compared to the reference in structure and properties is exerted. 25

\[ \text{C}_n\text{H}_m\text{N}_o\text{X}_p \]