Supporting Information
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SUPPLEMENTARY MATERIAL

Regioselective Palladium Catalyzed Cross-Coupling Reactions of 2,4,7-Trichloroquinazoline

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Experimental procedures and spectral data for all new compounds.
**General.** All glassware was dried in an oven at 140 °C for 2 h prior to use. All air and moisture-sensitive reactions were performed under a dry N₂ atmosphere. Reactions carried out at 0 °C employed an ice bath or a cryocool and an isopropanol/ethanol bath. THF and DME were distilled from sodium/benzophenone ketyl and degassed prior to use. 2,4,7-dichloroquinazoline was prepared according to a literature procedure.¹ All other materials were obtained from commercial sources and used as received.

Melting points were determined using a Laboratory Devices Mel-Temp II in open capillary tubes and are uncorrected. Infrared spectra were determined as neat solids on a Smiths Detection IdentifyIR FT-IR spectrometer. Mass spectra were obtained on a Micromass Autospec double focusing instrument. ¹H and ¹³C NMR spectra were obtained on a Bruker Avance 300 MHz or 600 MHz in DMSO-d₆ unless otherwise noted. Chemical shifts (δ) were reported in parts per million with the residual solvent peak used as an internal standard δ¹H / ¹³C (Solvent); 2.50 / 39.52 (DMSO); and are tabulated as follows: chemical shift, multiplicity (s = singlet, d= doublet, t = triplet, app t = apparent triplet, q = quartet, sept = septet, m = multiplet), number of protons, and coupling constant(s). ¹³C NMR spectra were obtained at 75 MHz or 150 MHz using a proton-decoupled pulse sequence and are tabulated by observed peak. Reactions were monitored by thin-layer chromatography analysis using pre-coated silica gel 60 F₂₅₄ plates (EMD, 250 µm thickness) and visualization was accomplished with a 254 nm UV light. Flash chromatography was performed using SiO₂ (Silicycle, Silia-P Flash Silica Gel, 40-63 µm). Concentrating under reduced pressure refers to the use of a rotary evaporator connected to a membrane vacuum pump to remove solvent.

2,7-Dichloro-4-(isopropylthio)quinazoline (1). To a solution of 2,4,7-trichloroquinazoline (0.300 g, 1.28 mmol) in freshly distilled and degassed THF (13.0 mL) cooled to 0 °C was added a premixed solution of i-PrSH (0.12 mL, 1.28 mmol) and NaH (0.032 g, 1.35 mmol) in THF (2.0 mL) dropwise. The mixture was stirred for 16 h, warmed to room temperature, poured into ice cold H₂O, extracted with EtOAc (5 x 25 mL), and washed with H₂O. The combined organic extracts were dried (MgSO₄) and concentrated to give a light yellow residue. The residue was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to provide 1 (0.291 g, 83%) as a light yellow crystalline solid: Mp 89.1-90.1 °C (EtOAc); IR (ATR) 3075, 2965, 2881, 1551, 1459, 1321, 1224, 1133, 852 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.07 (d, 1 H, J = 9.0 Hz), 7.98 (d, 1 H, J = 2.1 Hz), 7.72 (dd, 1 H, J = 9.0, 2.1 Hz), 4.18 (sept, 1 H, J = 6.9 Hz), 1.46 (d, 6 H, J = 6.9 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 174.8, 156.0, 149.7, 140.1, 128.9, 126.6, 125.9, 120.2, 36.0, 22.3 (2 C); MS (EI) m/z 272 ([M]+, 33), 230 (100), 195 (48), 161 (37); HRMS (EI) m/z calcd for C₁₁H₁₀Cl₂N₂S 271.9942, found 271.9946.

7-Chloro-4-(isopropylthio)-2-(thiophen-2-yl)quinazoline (2). General Protocol A. To a reaction vial was added 1 (0.025 g, 0.092 mmol), Pd(OAc)₂ (0.0010 g, 0.0046 mmol), PPh₃
(0.0036 g, 0.014 mmol), Na₂CO₃ (0.030 g, 0.28 mmol), and thiophene-2-boronic acid (0.023 g, 0.18 mmol). The reaction mixture was flushed with N₂. Freshly distilled and degassed DME and H₂O (DME/H₂O, 10:1) were added via syringe to generate a 0.1 M solution of 1, and the reaction mixture was stirred at 75 °C under a N₂ atmosphere for 24 h. H₂O (1 mL) was added and the mixture was extracted with CH₂Cl₂ (4 x 5 mL). The combined organic layers were washed with brine (5 mL), dried (MgSO₄), and concentrated under reduced pressure. The crude residue was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to give 2 (0.029 g, 99%) as a light yellow solid: Mp 122.7-124.7 °C (DMSO); IR (ATR) 2973, 2917, 2855, 1524, 1437, 1327, 1236, 988, 837, 773, 714 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.06 (dd, 1 H, J = 3.6, 1.2 Hz), 8.00 (d, 1 H, J = 8.7 Hz), 7.95 (d, 1 H, J = 2.1 Hz), 7.84 (dd, 1 H, J = 5.1, 1.5 Hz), 7.61 (dd, 1 H, J = 9.0, 2.1 Hz), 7.29 (dd, 1 H, J = 4.8, 3.6 Hz), 4.30 (sept, 1 H, J = 6.9 Hz), 1.53 (d, 6 H, J = 6.9 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 171.2, 156.0, 149.0, 142.8, 139.2, 131.7, 129.8, 128.8, 127.6, 127.0, 125.8, 120.0, 35.7, 22.4 (2 C); MS (ESI) m/z 321 ([M+1]⁺, 100), 277 (65); HRMS (ESI) m/z calcd for C₁₃H₁₄ClN₂S₂ (M+1) 321.0287, found 321.0271.

![Image](image_url)

**7-Chloro-4-(isopropylthio)-2-phenylquinazoline (3).** According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)₂ (0.0016 g, 0.0073 mmol), PPh₃ (0.0058 g, 0.022 mmol), Na₂CO₃ (0.048 g, 0.45 mmol), and phenylboronic acid (0.027 g, 0.22 mmol) were heated at 75 °C for 33 h and provided a crude residue that was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to afford 3 (0.042 g, 92%) as a pale green fluffy solid: Mp 130.3-131.1 °C
(DMSO); IR (ATR) 2956, 2924, 2863, 1552, 1530, 1329, 1301, 844, 773 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.57-8.52 (m, 2 H), 8.08 (d, 1 H, J = 9.0 Hz), 8.06 (d, 1 H, J = 1.5 Hz), 7.68 (dd, 1 H, J = 8.7, 2.1 Hz), 7.62-7.57 (m, 3 H), 4.42 (sept, 1 H, J = 6.9 Hz), 1.55 (d, 6 H, J = 6.9 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 171.2, 158.9, 149.2, 139.1, 137.0, 131.3, 128.8 (2 C), 128.2 (2 C), 128.1, 127.5, 125.7, 120.4, 35.4, 22.4 (2 C); HRMS (ESI) m/z calcd for C₁₇H₁₆ClN₂S (M+H) 315.0723, found 315.0726.

![Chemical Structure](attachment:image.png)

**7-Chloro-4-(isopropylthio)-2-m-tolylquinazoline (4).** According to General Protocol A, 1 (0.030 g, 0.11 mmol), Pd(OAc)₂ (0.0012 g, 0.0055 mmol), PPh₃ (0.0044 g, 0.016 mmol), Na₂CO₃ (0.036 g, 0.34 mmol), and 3-methylphenylboronic acid (0.018 g, 0.13 mmol) were heated at 75 °C for 36 h and provided a crude residue that was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to afford 4 (0.032 g, 90%) as a white crystalline solid: Mp 114.4-115.1 °C (DMSO); IR (ATR) 2969, 2920, 2859, 1530, 1329, 768, 719 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.37-8.30 (m, 2H), 8.07 (d, 1 H, J = 6.5 Hz), 8.06 (s, 1 H), 7.67 (dd, 1 H, J = 8.9, 2.0 Hz), 7.47 (app t, 1 H, J = 7.6 Hz), 7.40 (d, 1 H, J = 7.6 Hz), 4.40 (sept, 1 H, J = 6.8 Hz), 2.44 (s, 3 H), 1.55 (d, 6 H, J = 6.8 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 171.2, 159.0, 149.2, 139.0, 138.0, 137.0, 131.9, 128.8, 128.7, 128.0, 127.5, 125.7, 125.5, 120.3, 35.4, 22.4 (2 C), 21.2; MS (El) m/z 328 ([M⁺], 47), 286 (100), 253 (87), 91 (75); HRMS (El) m/z calcd for C₁₈H₁₇ClN₂S 328.0801, found 328.0804.
7-Chloro-2-(4-ethylphenyl)-4-(isopropylthio)quinazoline (5). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022 mmol), Na$_2$CO$_3$ (0.048 g, 0.45 mmol), and 4-ethylphenylboronic acid (0.033 g, 0.22 mmol) were heated at 75 °C for 33 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:50, EtOAc:hexanes) to afford 5 (0.048 g, 95%) as a pale green solid: Mp 124.1-125.9 °C (DMSO); IR (ATR) 3064, 2920, 1552, 1532, 1329, 1301, 990, 762, 699 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) $\delta$ 8.46 (d, 2 H, $J = 8.4$ Hz), 8.07 (d, 1 H, $J = 9.0$ Hz), 8.04 (d, 1 H, $J = 2.1$ Hz), 7.66 (dd, 1 H, $J = 8.7$, 2.1 Hz), 7.42 (d, 2 H, $J = 8.1$ Hz), 4.41 (sept, 1 H, $J = 6.9$ Hz), 2.71 (q, 2 H, $J = 7.5$ Hz), 1.55 (d, 6 H, $J = 6.9$ Hz), 1.24 (t, 3 H, $J = 7.5$ Hz); $^{13}$C NMR (DMSO-d$_6$, 150 MHz) $\delta$ 171.1, 159.0, 149.2, 147.4, 139.0, 134.6, 128.31 (2 C), 128.27 (2 C), 127.9, 127.4, 125.7, 120.3, 35.4, 28.2, 22.4 (2 C), 15.4; HRMS (ESI) $m/z$ calcd for C$_{19}$H$_{20}$ClN$_2$S (M+H) 343.1036, found 343.1015.

2-(4-tert-Butylphenyl)-7-chloro-4-(isopropylthio)quinazoline (6). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022...
mmol), Na$_2$CO$_3$ (0.048 g, 0.45 mmol), and 4-tert-butylbenzeneboronic acid (0.039 g, 0.22 mmol) were heated at 75 °C for 25 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:50, EtOAc:hexanes) to afford 6 (0.051 g, 93%) as a tan colored sticky solid: IR (ATR) 2959, 2864, 1551, 1528, 1465, 1327, 991, 848, 779 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) δ 8.46 (d, 2 H, $J = 8.5$ Hz), 8.06 (d, 1 H, $J = 8.7$ Hz), 8.04 (d, 1 H, $J = 1.3$ Hz), 7.66 (dd, 1 H, $J = 8.7, 2.1$ Hz), 7.60 (d, 2 H, $J = 8.5$ Hz), 4.40 (sept, 1 H, $J = 6.8$ Hz), 1.55 (d, 6 H, $J = 6.8$ Hz), 1.34 (s, 9 H); $^{13}$C NMR (DMSO-d$_6$, 150 MHz) δ 171.5, 159.4, 154.6, 149.7, 139.44, 134.76, 128.5 (2 C), 128.3, 127.9, 126.2, 126.1 (2 C), 120.7, 35.9, 35.2, 31.4 (3 C), 22.9 (2 C); MS (EI) m/z 370 ([M]$^+$, 50), 328 (95), 313 (100), 240 (48); HRMS (EI) m/z calcd for C$_{21}$H$_{23}$ClN$_2$S 370.1270, found 370.1259.

7-Chloro-4-(isopropylthio)-2-(4-(trifluoromethyl)phenyl)quinazoline (7). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022 mmol), Na$_2$CO$_3$ (0.048 g, 0.45 mmol), and 4-trifluoromethylphenylboronic acid (0.042 g, 0.22 mmol) were heated at 75 °C for 13 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:50, EtOAc:hexanes) to afford 7 (0.049 g, 88%) as an off-white solid: Mp 142.1-144.0 °C (DMSO); IR (ATR) 2963, 2928, 2866, 1536, 1551, 1319, 1303, 1105, 1064, 852, 779 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 323 K, 300 MHz) δ 8.69 (d, 2 H, $J = 8.0$ Hz), 8.09 (d, 1 H, $J = 8.9$ Hz), 8.05 (d, 1 H, $J = 2.0$ Hz), 7.92 (d, 2 H, $J = 8.3$ Hz), 7.69 (dd, 1 H, $J = 8.8, 2.1$ Hz), 4.43 (sept, 1 H, $J = 6.8$ Hz), 1.57 (d, 6 H, $J = 6.8$ Hz); $^{13}$C NMR (DMSO-d$_6$, 323 K, 75 MHz) δ
171.1, 157.4, 148.7, 140.6, 139.0, 130.7 (d, 1 C, $J^2 = 32.3$ Hz), 128.5 (2 C), 127.3, 125.4, 125.3 (q, 2 C, $J^3 = 3.8$ Hz), 123.9 (d, 1 C, $J^1 = 270.8$ Hz), 120.3, 35.3, 22.2 (2 C); MS (ESI) $m/z$ 383 ([M+1]$^+$, 100), 313 (10); HRMS (ESI) $m/z$ calcd for C$_{18}$H$_{15}$ClF$_3$N$_2$S (M+H) 383.0597, found 383.0563.

![Chemical Structure](image)

7-Chloro-4-(isopropylthio)-2-(3-methoxyphenyl)quinazoline (8). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022 mmol), Na$_2$CO$_3$ (0.048 g, 0.45 mmol), and 3-methoxyphenylboronic acid (0.034 g, 0.22 mmol) were heated at 75 °C for 17 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:50, EtOAc:hexanes) to afford 8 (0.045 g, 89%) as an off-white solid: Mp 109.7-111.3 °C (EtOAc/hexanes); IR (ATR) 3068, 2920, 2859, 1599, 1552, 1452, 1329, 1047, 772 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) $\delta$ 8.10 (d, 1 H, $J = 7.8$ Hz), 8.07-7.99 (m, 3 H), 7.64 (dd, 1 H, $J = 8.9$, 2.0 Hz), 7.48 (app t, 1 H, $J = 8.0$ Hz), 7.14 (dd, 1 H, $J = 8.2$, 2.5 Hz), 4.35 (sept, 1 H, $J = 6.8$ Hz), 3.86 (s, 3 H), 1.54 (d, 6 H, $J = 6.8$ Hz); $^{13}$C NMR (DMSO-d$_6$, 75 MHz) $\delta$ 171.1, 159.6, 158.6, 149.0, 139.0, 138.4, 129.9, 128.1, 127.5, 125.7, 120.6, 120.3, 116.9, 113.2, 55.2, 35.5, 22.4 (2 C); MS (ESI) $m/z$ 345 ([M+1]$^+$, 100), 227 (27), 229 (21); HRMS (ESI) $m/z$ calcd for C$_{18}$H$_{18}$ClN$_2$OS (M+H) 345.0801, found 345.0828.
2-(Benzofuran-2-yl)-7-chloro-4-(isopropylthio)quinazoline (9). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022 mmol), Na$_2$CO$_3$ (0.048 g, 0.45 mmol), and benzo[b]furan-boronic acid (0.036 g, 0.22 mmol) were heated at 75 °C for 33 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:100, EtOAc:hexanes) to afford 9 (0.041 g, 79%) as a pale green solid: Mp 168.7-169.9 °C (EtOAc/hexanes); IR (ATR) 3056, 2961, 2920, 2864, 1579, 1547, 1528, 1470, 1336, 954, 848, 754 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) $\delta$ 8.11 (d, 1 H, $J = 2.0$ Hz), 8.08 (d, 1 H, $J = 8.8$ Hz), 7.93 (s, 1 H), 7.84 (d, 1 H, $J = 7.7$ Hz), 7.78 (d, 1 H, $J = 8.1$ Hz), 7.70 (dd, 1 H, $J = 8.8$, 1.9 Hz), 7.48 (app t, 1 H, $J = 7.6$ Hz), 7.36 (app t, 1 H, $J = 7.7$ Hz), 4.41 (sept, 1 H, $J = 6.8$ Hz), 1.55 (d, 6 H, $J = 6.8$ Hz); $^{13}$C NMR (DMSO-d$_6$, 308 K, 75 MHz) $\delta$ 171.3, 155.4, 153.1, 152.5, 148.7, 139.2, 128.2, 127.7, 127.3, 126.5, 125.6, 123.5, 122.4, 120.4, 111.7, 110.8, 35.5, 22.3 (2 C); MS (EI) m/z 354 ([M]+, 43), 312 (100), 279 (50); HRMS (EI) m/z calcd for C$_{19}$H$_{15}$ClN$_2$OS 354.0594, found 354.0590.

7-Chloro-4-(isopropylthio)-2-(pyridin-4-yl)quinazoline (10). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)$_2$ (0.0016 g, 0.0073 mmol), PPh$_3$ (0.0058 g, 0.022 mmol),
Na₂CO₃ (0.048 g, 0.45 mmol), and pyridine-4-boronic acid (0.027 g, 0.22 mmol) were heated at 75 °C for 48 h and provided a crude residue that was purified by chromatography on SiO₂ (1:100 to 1:5, EtOAc:hexanes) to afford 10 (0.025 g, 53%) as a tan-colored solid: Mp 154.3-155.8 °C (DMSO); IR (ATR) 3023, 2969, 2920, 2864, 1599, 1547, 1526, 1464, 1331, 1310, 1239, 993, 824, 775 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.85-8.81 (m, 2 H), 8.41-8.36 (m, 2 H), 8.15 (s, 1 H), 8.13 (d, 1 H, J = 5.8 Hz), 7.77 (dd, 1 H, J = 8.9, 2.1 Hz), 4.45 (sept, 1 H, J = 6.8 Hz), 1.56 (d, 6 H, J = 6.8 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 171.8, 157.0, 150.3, 148.6, 144.0, 139.1, 128.7, 127.5, 125.5, 121.6, 120.7, 35.4, 22.2 (2 C); MS (EI) m/z 317 ([M+2]⁺, 22), 315 ([M]⁺, 38), 272 (18), 240 (40), 78 (61); HRMS (EI) m/z calcd for C₁₆H₁₄ClN₃S 315.0597, found 315.0602.

7-Chloro-2-(1H-indol-5-yl)-4-(isopropylthio)quinazoline (11). According to General Protocol A, 1 (0.040 g, 0.15 mmol), Pd(OAc)₂ (0.0047 g, 0.0029 mmol), PPh₃ (0.0058 g, 0.022 mmol), Na₂CO₃ (0.048 g, 0.45 mmol), and indole-5-boronic acid (0.027 g, 0.22 mmol) were heated at 75 °C for 48 h and provided a crude residue that was purified by chromatography on SiO₂ (1:100 to 1:10, EtOAc:hexanes) to afford 11 (0.031 g, 60%) as a tan colored solid: Mp 191.7-193.2 °C (DMSO); IR (ATR) 3176, 2958, 2920, 2863, 1470, 1526, 1333, 1318, 1232, 850, 764, 731 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 11.38 (s, 1 H), 8.82 (s, 1 H), 8.35 (dd, 1 H, J = 8.6, 1.6 Hz), 7.98 (d, 1 H, J = 8.9 Hz), 7.97 (d, 1 H, J = 2.0 Hz), 7.56 (dd, 1 H, J = 8.6, 2.2 Hz), 7.54 (d, 1 H, J = 8.6 Hz), 7.44 (app t, 1 H, J = 2.7 Hz), 6.62 (app t, 1 H, J = 2.0 Hz), 4.42 (sept, 1 H, J = 6.8 Hz), 1.55 (d, 6 H, J = 6.8 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 171.8, 157.0, 150.3, 148.6, 144.0, 139.1, 128.7, 127.5, 125.5, 121.6, 120.7, 35.4, 22.2 (2 C); MS (EI) m/z 317 ([M+2]⁺, 22), 315 ([M]⁺, 38), 272 (18), 240 (40), 78 (61); HRMS (EI) m/z calcd for C₁₆H₁₄ClN₃S 315.0597, found 315.0602.
Hz), 1.55 (d, 6 H, $J = 6.8$ Hz); $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 170.4, 160.4, 149.5, 138.7, 137.9, 128.0, 127.9, 127.1, 127.0, 126.7, 125.6, 121.6, 121.4, 121.3, 120.0, 111.6, 102.5, 35.2, 22.5 (2 C); MS (EI) $m/z$ 353 ([M]$^+$, 10), 311 (12), 278 (18); HRMS (EI) $m/z$ calcd for C$_{19}$H$_{16}$ClN$_3$S 353.0753, found 353.0756.

7-Chloro-4-phenyl-2-(thiophen-2-yl)quinazoline (12). General Protocol B. To a reaction vial was added 2 (0.025 g, 0.078 mmol), CuTC (0.033 g, 0.17 mmol), Pd(PPh$_3$)$_4$ (0.0041 g, 0.0039 mmol), and phenylboronic acid (0.021 g, 0.17 mmol). The reaction mixture was flushed with N$_2$ and freshly distilled and degassed THF was added via syringe to generate a 0.06 M solution of 2. The reaction mixture was stirred vigorously at 50 °C under a N$_2$ atmosphere for 13 h. A saturated solution of NaHCO$_3$ (1 mL) was added and the solution was extracted with CH$_2$Cl$_2$ (4 x 5 mL), dried (MgSO$_4$), and concentrated under reduced pressure. The crude residue was purified by chromatography on SiO$_2$ (1:50, EtOAc:hexanes) to afford 12 (0.024 g, 97%) as an off-white flaky solid: Mp 172.9-174.0 °C (DMSO); IR (ATR) 3066, 2917, 1526, 1426, 770, 701 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 8.16-8.10 (m, 2 H), 8.05 (d, 1 H, $J = 9.0$ Hz), 7.88-7.81 (m, 3 H), 7.72-7.63 (m, 4 H), 7.27 (dd, 1 H, $J = 5.1, 3.6$ Hz); $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 168.4, 157.2, 151.8, 142.9, 139.4, 136.2, 131.7, 130.5, 130.0, 129.3, 128.8, 128.1, 126.8, 119.6; MS (EI) $m/z$ 322 ([M]$^+$, 100), 321 ([M-1]$^+$, 74), 287 (75), 245 (30); HRMS (EI) $m/z$ calcd for C$_{18}$H$_{11}$ClN$_2$S$_2$ 322.0331, found 322.0327.
7-Chloro-2-(4-ethylphenyl)-4-m-tolylquinazoline (13). According to General Protocol B, 5 (0.028 g, 0.083 mmol), CuTC (0.035 g, 0.18 mmol), Pd(PPh₃)₄ (0.0053 g, 0.0041 mmol), and 3-methylphenylboronic acid (0.025 g, 0.18 mmol) were heated at 50 °C for 19 h and provided a crude residue that was purified by chromatography on SiO₂ (1:100, EtOAc:hexanes) to afford 13 (0.027 g, 89%) as a pale yellow sticky solid: IR (ATR) 2963, 2935, 2883, 1599, 1552, 1528, 1336, 846, 786, 701 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.49 (d, 2 H, J = 8.3 Hz), 8.17 (d, 1 H, J = 2.0 Hz), 8.07 (d, 1 H, J = 8.9 Hz), 7.69 (dd, 1 H, J = 9.0, 2.1 Hz), 7.68 (s, 1 H), 7.64 (d, 1 H, J = 7.5 Hz), 7.54 (t, 1 H, J = 7.5 Hz), 7.48 (d, 1 H, J = 7.6 Hz), 7.41 (d, 2 H, J = 8.4 Hz), 2.71 (q, 2 H, J = 7.6 Hz), 2.47 (s, 3 H), 1.24 (t, 3 H, J = 7.6 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 168.3, 160.1, 151.9, 147.3, 139.0, 138.2, 136.6, 134.7, 131.0, 130.4, 129.2, 128.6, 128.4, 128.2, 127.23, 127.20, 119.7, 28.2, 21.1, 15.4; MS (EI) m/z 358 ([M]+, 32), 357 ([M-1]+, 81), 91 (100); HRMS (EI) m/z calcd for C₂₃H₁₉ClN₂ 358.1237, found 358.1230.

7-Chloro-2-phenyl-4-m-tolylquinazoline (14). According to General Protocol B, 3 (0.028 g, 0.090 mmol), CuTC (0.038 g, 0.20 mmol), Pd(PPh₃)₄ (0.0057 g, 0.0045 mmol), and 3-
methylphenylboronic acid (0.027 g, 0.20 mmol) were heated at 50 °C for 26 h and provided a crude residue that was purified by chromatography on SiO₂ (1:100, EtOAc:hexanes) to afford 14 (0.028 g, 89%) as a pale yellow sticky solid: IR (ATR) 3058, 3030, 2914, 2851, 1556, 1532, 1336, 913, 766, 695, 682 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.63-8.56 (m, 2 H), 8.22 (d, 1 H, J = 2.1 Hz), 7.73 (dd, 1 H, 9.0, 2.1 Hz), 7.70 (s, 1 H), 7.67 (d, 1 H, J = 7.6 Hz), 7.62-7.57 (m, 3 H), 7.54 (d, 1 H, J = 7.5 Hz), 7.49 (d, 1 H, J = 7.4 Hz), 2.47 (s, 3 H); ¹³C NMR (DMSO-d₆, 75 MHz) δ 168.3, 160.0, 151.9, 139.1, 138.1, 137.1, 136.6, 131.2, 131.0, 130.4, 129.1, 128.8 (2 C), 128.6, 128.4, 128.3 (2 C), 127.3, 127.2, 119.8, 21.1; MS (EI) m/z 330 ([M⁺], 17), 329 ([M-1⁺], 43), 238 (43), 91 (100); HRMS (EI) m/z calcd for C₂₁H₁₅ClN₂ 330.0924, found 330.0930.

2-(4-tert-Butylphenyl)-7-chloro-4-(4-ethylphenyl)quinazoline (15). According to General Protocol B, 6 (0.047 g, 0.13 mmol), CuTC (0.053 g, 0.28 mmol), Pd(PPh₃)₄ (0.0080 g, 0.0063 mmol), and 4-ethylphenylboronic acid (0.042 g, 0.28 mmol) were heated at 50 °C for 19 h and provided a crude residue that was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to afford 15 (0.043 g, 86%) as a white crystalline solid: IR (ATR) 2959, 2866, 1599, 1552, 1528, 1472, 1388, 1336, 850, 786, 703 cm⁻¹; ¹H NMR (DMSO-d₆, 600 MHz) δ 8.46 (d, 2 H, J = 8.5 Hz), 8.12 (d, 1 H, J = 2.1 Hz), 8.06 (d, 1 H, J = 8.9 Hz), 7.77 (d, 2 H, J = 8.0 Hz), 7.64 (dd, 1 H, J = 8.9, 2.1 Hz), 7.56 (d, 2 H, J = 8.6 Hz), 7.46 (d, 2 H, J = 8.1 Hz), 2.74 (q, 2 H, J = 7.6 Hz),
1.32 (s, 9 H), 1.26 (t, 3 H, J = 7.6 Hz); $^{13}$C NMR (DMSO-d$_6$, 150 MHz) δ 167.9, 160.1, 153.9, 152.0, 146.4, 138.9, 134.5, 134.1, 130.1 (2 C), 129.1, 128.2 (2 C), 128.12 (2 C), 128.09, 127.2, 125.5 (2 C), 119.6, 34.6, 31.0 (3 C), 28.1, 15.5; HRMS (ESI) m/z calcd for C$_{26}$H$_{26}$ClN$_2$ (M+H) 401.1785, found 401.1775.

![Chemical Structure](image)

7-Chloro-2-(4-ethylphenyl)-4-(3-methoxyphenyl)quinazoline (16). According to General Protocol B, 5 (0.046 g, 0.13 mmol), CuTC (0.057 g, 0.30 mmol), Pd(PPh$_3$)$_4$ (0.0086 g, 0.0067 mmol), and 3-methoxyphenylboronic acid (0.045 g, 0.30 mmol) were heated at 50 °C for 22 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:200 to 1:20, EtOAc:hexanes) to afford 16 (0.042 g, 83%) as a yellow solid: Mp 88.3-89.7 °C (EtOAc/hexanes); IR (ATR) 3064, 3002, 2959, 2930, 2827, 1597, 1554, 1528, 1334, 1247, 1236, 1042, 909, 783 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) δ 8.51 (d, 2 H, J = 8.3 Hz), 8.19 (d, 1 H, J = 2.1 Hz), 8.11 (d, 1 H, J = 9.0 Hz), 7.71 (dd, 1 H, J = 8.9, 2.2 Hz), 7.58 (t, 1 H, J = 8.3 Hz), 7.45-7.38 (m, 4 H), 7.27-7.22 (m, 1 H), 3.87 (s, 3 H), 2.71 (q, 2 H, J = 7.6 Hz), 1.24 (t, 3 H, J = 7.6 Hz); $^{13}$C NMR (DMSO-d$_6$, 75 MHz) δ 168.0, 160.1, 159.3, 151.9, 147.3, 139.1, 138.0, 134.7, 129.92, 129.88, 129.2, 128.5 (2 C), 128.3 (2 C), 127.2, 122.2, 119.8, 115.9, 115.3, 55.4, 28.2, 15.4; MS (ESI) m/z 375 ([M+1]$^+$, 100), 227 (30); HRMS (ESI) m/z calcd for C$_{23}$H$_{26}$ClN$_2$O (M+H) 375.1264, found 375.1259.
7-Chloro-2-(4-methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)quinazoline (17). According to General Protocol B, 8 (0.031 g, 0.091 mmol), CuTC (0.038 g, 0.20 mmol), Pd(PPh₃)₄ (0.0058 g, 0.0045 mmol), and 4-trifluoromethylphenylboronic acid (0.038 g, 0.20 mmol) were heated at 50 °C for 19 h and provided a crude residue that was purified by chromatography on SiO₂ (1:50, EtOAc:hexanes) to afford 17 (0.033 g, 87%) as a white solid: Mp 159.0-159.9 °C (DMSO); IR (ATR) 2950, 2918, 2844, 1538, 1321, 1278, 1167, 1122, 1053, 1043, 777 cm⁻¹; ¹H NMR (DMSO-d₆, 600 MHz) δ 8.22 (d, 1 H, J = 2.0 Hz), 8.15 (d, 1 H, J = 7.7 Hz), 8.09 (d, 2 H, J = 8.1), 8.08 (s, 1 H), 8.05 (d, 1 H, J = 8.9 Hz), 8.02 (d, 2 H, J = 8.2 Hz), 7.71 (dd, 1 H, J = 8.9, 2.0 Hz), 7.48 (t, 1 H, J = 8.0 Hz), 7.15 (dd, 1 H, J = 8.0, 2.3 Hz), 3.86 (s, 3 H); ¹³C NMR (DMSO-d₆, 150 MHz) δ 166.9, 159.8, 159.7, 151.8, 140.5, 139.4, 138.3, 130.9 (2 C), 130.4 (q, 1 C, J² = 31.5 Hz), 128.82, 128.79, 127.4, 125.7 (q, 2 C, J³ = 4.5 Hz), 124.1 (d, 1 C, J⁴ = 270.0 Hz), 120.8, 119.8, 119.1, 117.0, 113.4, 55.3; HRMS (ESI) m/z calcd for C₂₂H₁₅ClF₃N₂O (M+H) 415.0825, found 415.0806.
2-(Benzofuran-2-yl)-4-(4-tert-butylphenyl)-7-chloroquinoxaline (18). According to General Protocol B, 9 (0.036 g, 0.10 mmol), CuTC (0.043 g, 0.22 mmol), Pd(PPh₃)₄ (0.0064 g, 0.0051 mmol), and 4-tert-butylphenylboronic acid (0.040 g, 0.22 mmol) were heated at 50 °C for 27 h and provided a crude residue that was purified by chromatography on SiO₂ (1:100, EtOAc:hexanes) to afford 18 (0.039 g, 91%) as a yellow crystalline solid: Mp 193.7-195.4 °C (DMSO); IR (ATR) 2961, 2920, 2864, 1552, 1523, 1474, 1334, 846, 783, 759 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 8.26 (d, 1H, J = 1.8 Hz), 8.14 (d, 1 H, J = 8.9 Hz), 7.96 (s, 1 H), 7.84 (d, 2 H, J = 8.2 Hz), 7.83-7.72 (m, 3 H), 7.70 (d, 2 H, J = 8.2 Hz), 7.48 (t, 1 H, J = 7.6 Hz), 7.36 (t, 1 H, J = 7.5 Hz), 1.40 (s, 9 H); ¹³C NMR (DMSO-d₆, 323 K, 75 MHz) δ 168.1, 155.2, 153.6, 153.3, 153.1, 151.4, 139.1, 133.2, 129.5 (2 C), 129.0, 128.4, 127.7, 126.9, 126.3, 125.2 (2 C), 123.3, 122.1, 119.7, 111.5, 110.3, 34.4, 30.7 (3 C); MS (EI) m/z 414 ([M+2]+, 35), 412 ([M]+, 100), 397 (59), 355 (33), 251 (74); HRMS (EI) m/z calcd for C₂₆H₂₁ClN₂O 412.1342, found 412.1338.
7-Chloro-2-(4-ethylphenyl)-4-(1H-indol-5-yl)quinazoline (19). According to General Protocol B, 5 (0.015 g, 0.044 mmol), CuTC (0.018 g, 0.096 mmol), Pd(PPh₃)₄ (0.0028 g, 0.0022 mmol), and indole-5-boronic acid (0.016 g, 0.096 mmol) were heated at 50 °C for 48 h and provided a crude residue that was purified by chromatography on SiO₂ (1:20, THF:toluene) to afford 19 (0.012 g, 66%) as a yellow solid: Mp 172.8-174.2 °C (THF/Toluene); IR (ATR) 3213, 3205, 2956, 2915, 2848, 1599, 1551, 1530, 1461, 1336, 852, 772, 729 cm⁻¹; ¹H NMR (DMSO-d₆, 300 MHz) δ 11.48 (s, 1 H), 8.53 (d, 2 H, J = 8.3 Hz), 8.23 (d, 1 H, J = 9.0 Hz), 8.15 (d, 1 H, J = 2.1 Hz), 8.13 (s, 1 H), 7.70 (dd, 1 H, J = 8.9, 2.2 Hz), 7.66 (s, 2 H), 7.53 (t, 1 H, J = 2.8 Hz), 7.42 (d, 2 H, J = 8.4 Hz), 6.65 (dd, 1 H, J = 2.8, 2.0 Hz), 2.71 (q, 2 H, J = 7.6 Hz), 1.24 (t, 3 H, J = 7.6 Hz); ¹³C NMR (DMSO-d₆, 75 MHz) δ 169.3, 160.0, 152.2, 147.1, 138.6, 137.1, 135.0, 129.8, 128.4 (2 C), 128.2 (2 C), 127.9, 127.6, 127.5, 127.1, 127.0, 123.3, 122.9, 119.9, 111.7, 102.3, 28.2, 15.4; MS (ESI) m/z 384 ([M+1]+, 100), 343 (80); HRMS (ESI) m/z calcd for C₂₄H₁₉ClN₃ (M+H) 384.1268, found 384.1273.
2-(4-tert-Butylphenyl)-4-(4-ethylphenyl)-7-(3-methoxyphenyl)quinazoline (20). According to General Protocol A, 15 (0.038 g, 0.094 mmol), Pd(OAc)$_2$ (0.0021 g, 0.0094 mmol), PPh$_3$ (0.0075 g, 0.028 mmol), Na$_2$CO$_3$ (0.062 g, 0.58 mmol), and 3-methoxyphenylboronic acid (0.057 g, 0.38 mmol) were heated at reflux for 22 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:200 to 1:50, EtOAc:hexanes) to afford 20 (0.038 g, 86%) as a pale green solid: Mp 89.2-91.0 °C (EtOAc); IR (ATR) 3063, 2959, 2866, 1552, 1528, 1338, 852, 773 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) $\delta$ 8.55 (d, 2 H, $J = 8.6$ Hz), 8.37 (d, 1 H, $J = 1.7$ Hz), 8.18 (d, 1 H, $J = 8.7$ Hz), 8.03 (dd, 1 H, $J = 8.8$, 1.8 Hz), 7.86 (d, 2 H, $J = 8.1$ Hz), 7.61 (d, 2 H, $J = 8.6$ Hz), 7.52 (d, 2 H, $J = 8.2$ Hz), 7.51-7.49 (m, 1 H), 7.47 (dd, 2 H, $J = 7.1$, 1.7 Hz), 7.11-7.03 (m, 1 H), 3.89 (s, 3 H), 2.78 (q, 2 H, $J = 7.5$ Hz), 1.35 (s, 9 H), 1.30 (t, 3 H, $J = 7.6$ Hz); $^{13}$C NMR (DMSO-d$_6$, 75 MHz) $\delta$ 167.6, 159.9, 159.6, 153.6, 151.8, 146.3, 145.4, 140.0, 134.9, 134.5, 130.4, 130.1 (2 C), 128.2 (2 C), 128.1 (2 C), 127.6, 126.9, 125.6, 125.5 (2 C), 120.2, 119.7, 114.7, 112.7, 55.3, 34.7, 31.1 (3 C), 28.1, 15.5; MS (EI) $m/z$ 472 ([M]$^+$, 100), 457 (79); HRMS (EI) $m/z$ calcd for C$_{33}$H$_{32}$N$_2$O 472.2515, found 472.2510.
According to General Protocol A, 17 (0.028 g, 0.067 mmol), Pd(OAc)$_2$ (0.0015 g, 0.0067 mmol), PPh$_3$ (0.0053 g, 0.020 mmol), Na$_2$CO$_3$ (0.044 g, 0.42 mmol), and 4-ethylphenylboronic acid (0.040 g, 0.27 mmol) were heated at reflux for 34 h and provided a crude residue that was purified by chromatography on SiO$_2$ (1:100, EtOAc:hexanes) to afford 21 (0.026 g, 81%) as an off-white solid: Mp 173.0-174.1 °C (EtOAc/hexanes); IR (ATR) 2963, 2922, 2850, 1618, 1538, 1333, 1105, 1068, 788 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 600 MHz) $\delta$ 8.40 (d, 1 H, $J$ = 1.7 Hz), 8.22 (d, 1 H, $J$ = 7.8 Hz), 8.16 (d, 1 H, $J$ = 2.5 Hz), 8.15 (d, 2 H, $J$ = 8.2 Hz), 8.12 (d, 1 H, $J$ = 8.7 Hz), 8.07 (dd, 1 H, $J$ = 8.1, 1.7 Hz), 8.05 (d, 2 H, $J$ = 8.0 Hz), 7.88 (d, 2 H, $J$ = 8.2 Hz), 7.51 (t, 1 H, $J$ = 7.9 Hz), 7.42 (d, 2 H, $J$ = 8.2 Hz), 7.16 (dd, 1 H, $J$ = 8.0, 2.5 Hz), 3.88 (s, 3 H), 2.7 (q, 2 H, $J$ = 7.6 Hz), 1.25 (t, 3 H, $J$ = 7.6 Hz); $^{13}$C NMR (DMSO-d$_6$, 150 MHz) $\delta$ 166.4, 159.7, 159.2, 151.8, 145.9, 144.9, 140.9, 138.8, 135.6, 130.9 (2 C), 130.3 (d, 1 C, $J^c$ = 31.5 Hz), 129.9, 128.8 (2 C), 127.4 (2 C), 127.28, 127.25, 125.7, 125.63, 125.08, 125.1, 124.2 (d, 1 C, $J^d$ = 270.0 Hz), 120.7, 120.0, 116.7, 113.2, 55.3, 27.9, 15.5; HRMS (ESI) $m/z$ calcd for C$_{30}$H$_{24}$F$_3$N$_2$O (M+H) 485.1841, found 485.1835.
2-(4-ethylphenyl)-7-(1H-indol-5-yl)-4-(3-methoxyphenyl)quinazoline (22). According to General Protocol A, 16 (0.025 g, 0.067 mmol), Pd(OAc)$_2$ (0.0015 g, 0.0067 mmol), PPh$_3$ (0.0053 g, 0.020 mmol), Na$_2$CO$_3$ (0.044 g, 0.41 mmol), and indole-5-boronic acid (0.043 g, 0.27 mmol) were heated at reflux for 48 h and provided a crude residue that was purified by chromatography on SiO$_2$ (toluene to 1:20, THF/toluene) to afford 22 (0.020 g, 66%) as a yellow solid: Mp 81.7-82.2 °C (EtOAc); IR (ATR) 3418, 2958, 2926, 2851, 1716, 1606, 1532, 1340, 1236, 1044, 794 cm$^{-1}$; $^1$H NMR (DMSO-d$_6$, 300 MHz) δ 11.31 (s, 1H), 8.55 (d, 2 H, $J$ = 8.3 Hz), 8.34 (d, 1 H, $J$ = 1.3 Hz), 8.16-8.12 (m, 2 H), 8.09 (dd, 1 H, $J$ = 8.8, 1.6 Hz), 7.69 (dd, 1 H, $J$ = 8.6, 1.7 Hz), 7.63-7.55 (m, 2 H), 7.48-7.40 (m, 5 H), 7.25 (ddd, 1 H, $J$ = 8.3, 2.5, 0.9 Hz), 6.59-6.55 (m, 1 H), 3.89 (s, 3 H), 2.72 (q, 2 H, $J$ = 7.6 Hz), 1.26 (t, 3 H, $J$ = 7.6 Hz); $^{13}$C NMR (DMSO-d$_6$, 75 MHz) δ 167.4, 159.5, 159.4, 151.9, 147.4, 146.8, 138.5, 136.3, 135.3, 129.8, 129.3, 128.4, 128.3, 128.2, 127.3, 127.2, 126.6, 124.5, 122.2, 120.7, 119.5, 119.4, 115.6, 115.3, 112.3, 102.0, 55.4, 28.2, 15.4. HRMS (ESI) $m/z$ calcd for C$_{31}$H$_{26}$N$_3$O (M+H) 456.2076, found 456.2091.
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