Direct Sulfanylation of 4-Quinazolinone via C-OH Bond Activation: An Route for 2-Aryl-4-sulfanylquinazolines

\[ \text{Yiyuanpeng@yahoo.com} \]

Supporting Information

List of Contents

1. General experimental method (S2)
2. Experimental procedure for synthesis of compound 7(S2)
3. Characterization data of compound 7 (S2-S11)
4. $^1\text{H}$, $^{13}\text{C}$ NMR and IR spectra of compound 7 (S12-S71)
**General experimental method:**

All reactions were performed in test tubes under nitrogen atmosphere at room temperature. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 μm, standard grade). Analytical thin−layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Solvents were re-distilled prior to use in the reactions. Other commercial reagents were used as received. NMR samples were run in CDCl$_3$ and $^1$H NMR were referenced to TMS, $^{13}$C NMR were referenced to CDCl$_3$. All chemical shift values are quoted in ppm and coupling constants quoted in Hz.

**Experimental procedure for synthesis of product 7**

\[ \text{Quinazolinone (0.1mmol), Et$_3$N (0.3mmol), DMP (5mol%) in CH$_2$Cl$_2$ were added into a round-bottom flask, after 2 mins stirring, TsCl (0.15mmol) was added to the flask, 30 min later, RSH (0.17mmol) was added. The mixture was allowed to stir at room temperature for 5h. After completion of the reaction, the mixture was removed under reduced pressure. The residue was purified by passing through a column of silica gel using petroleum ether/ethyl acetate (100:1) as eluent to give desired compounds 7.} \]
2-Phenyl-4-p-tolylsulfanyl-quinazoline (7a): White solid; yield: 26.6 mg (81%); mp 116-117°C. IR (KBr): 1951.7, 1899, 1822, 1639, 1558, 1539, 1482, 1454, 1442, 1375, 1336, 984, 762, 701, 687 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.49 (s, 3H), 7.34-7.40 (m, 5H), 7.55-7.60 (m, 3H), 7.83-7.87 (m, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.18-8.20 (m, 1H), 8.20-8.26 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.4, 121.9, 123.7, 124.0, 126.8, 128.3, 128.4, 129.0, 129.9, 130.4, 133.7, 136.0, 137.8, 139.7, 149.3, 158.9, 171.3; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₁H₁₇N₂S: 329.1112; Found, 329.1115.

2-Phenyl-4-phenylsulfanyl-quinazoline (7b): White solid; yield: 26.1 mg (83%); mp 120-121°C. IR (KBr): 1639, 1616, 1558, 1375, 1336, 1309, 1080, 986, 699, 686 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.33-7.39 (m, 3H), 7.53-7.56 (m, 3H), 7.60 (s, 1H), 7.70-7.72 (m, 2H), 7.83-7.87 (m, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.18-8.23 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 121.9, 123.7, 126.8, 127.6, 128.3, 128.4, 129.1, 129.2, 129.5, 130.4, 133.7, 136.2, 137.7, 149.4, 158.9, 171.0; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₀H₁₅N₂S: 315.0956; Found, 315.0952.

4-(4-Fluoro-phenylsulfanyl)-2-phenyl-quinazoline (7c): White solid; yield: 28.9 mg (87%); mp148-149°C; IR (KBr): 3056, 1886, 1812, 1614, 1590, 1577, 1538, 1493, 1484, 1340, 1309, 1160, 823, 697, 686 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.24-7.26 (m, 2H), 7.38-7.40 (m, 3H), 7.6 (d, J = 8.4 Hz, 1H), 7.66-7.69 (m, 2H), 7.85-7.87 (m, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.21-8.23 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 116.3 (d, J = 22 Hz), 121.8, 122.8, 123.6, 126.9, 128.3, 129.1, 130.5,
133.8, 137.6, 138.3, 149.4, 158.9, 162.5 (d, J = 249 Hz), 170.7; HRMS (ESI): m/z [M + H]^+ Calcd for C_{20}H_{14}N_{2}SF: 333.0862; Found, 333.0855.

4-(4-Chloro-phenylsulfanyl)-2-phenyl-quinazoline (7d): white solid; yield: 29.7 mg (85%); mp 161-162 °C; IR (KBr): 3090, 1891, 1815, 1640, 1613, 1556, 1540, 1482, 1445, 1338, 1310, 1141, 1088, 987, 756, 705, 658 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.38-7.42 \text{ (m, 3H)}, 7.50-7.52 \text{ (m, 2H)}, 7.55 \text{ (m, 3H)}, 7.84-7.88 \text{ (m, 1H)}, 8.01 \text{ (d, J = 8.4 Hz, 1H)}, 8.14 \text{ (d, J = 8.4 Hz, 1H)}, 8.22-8.24 \text{ (m, 2H)}; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 121.8, 123.6, 126.2, 128.4, 129.1, 129.3, 133.9, 135.9, 137.4, 137.5, 149.4, 158.9, 170.3\); HRMS (ESI): m/z [M + H]^+ Calcd for C_{20}H_{14}ClN_{2}S: 349.0566; Found, 349.0574.

4-(2-Chloro-phenylsulfanyl)-2-phenyl-quinazoline (7e): White solid; yield: 28.3 mg (81%); mp 124-125 °C; IR (KBr): 3057, 1641, 1559, 1538, 1484, 1339, 1309, 1143, 755, 700, 659 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.34-7.41 \text{ (m, 4H)}, 7.51 \text{ (d, J = 1.6 Hz, 1H)}, 7.59 \text{ (s, 1H)}, 7.65 \text{ (dd, J = 0.8, 8.0 Hz, 1H)}, 7.77 \text{ (dd, J = 1.6, 7.6 Hz, 1H)}, 7.86 \text{ (s, 1H)}, 8.02 \text{ (d, J = 8.4 Hz, 1H)}, 8.16-8.21 \text{ (m, 3H)}; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 121.9, 123.7, 127.4, 128.3, 128.4, 129.1, 129.6, 130.2, 131.2, 133.8, 137.6, 138.4, 140.3, 149.5, 158.9, 169.3\); HRMS (ESI): m/z [M + H]^+ Calcd for C_{20}H_{14}ClN_{2}S: 349.0566; Found, 349.0574.
4-Benzylsulfanyl-2-phenyl-quinazoline (7f): Light yellow solid, yield: 26.3 mg (80%), mp 148-149°C; IR (film): 3054, 2987, 2305, 1537, 1483, 1421, 1265, 1028, 738, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 4.78 (s, 2H), 7.26-7.33 (m, 3H), 7.46-7.52 (m, 6H), 7.77-7.82 (m, 1H), 7.99-8.62 (m, 2H), 8.62-8.64 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 33.8, 122.3, 123.8, 126.7, 127.5, 128.5, 128.5, 128.7, 129.0, 130.6, 133.7, 137.2, 138.0, 149.0, 158.8, 170.5; HRMS (ESI): m/z [M + H]^+ Calcd for C₂₁H₁₇N₂S: 329.112; Found, 329.1111.

4-Butylsulfanyl-2-phenyl-quinazoline (7g): Light yellow liquid, yield: 19.9 mg (71%); IR(film): 3054, 2987, 2305, 1614, 1560,1536, 1484, 1265, 740, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 1.13 (t, J = 7.6 Hz, 3H), 1.85-1.90 (m, 2H), 3.42 (t, J = 7.2 Hz, 2H), 7.40-7.51 (m, 4H), 7.71-7.75 (m, 1H), 7.94 (d, J = 8.4Hz, 1H), 7.99 (d, J = 8.0Hz, 1H), 8.60 (dd, J = 1.6, 8.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 13.7, 22.6, 31.6, 122.7, 123.8, 126.5, 129.0, 130.5, 133.5, 138.2, 148.9, 158.8, 171.2; HRMS (ESI): m/z [M + H]^+ Calcd for C₁₇H₁₇N₂S: 281.1112; Found, 281.1115.

2-p-Tolyl-4-p-tolylsulfanyl-quinazoline (7h): White solid, yield: 27.1 mg (79%); mp 173-174°C; IR(film): 3057, 2921, 1906, 1642, 1608, 1559, 1537, 1484, 1450, 1376, 1334, 1308, 988, 759, 733 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.36 (s, 3H), 2.48 (s, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.51-7.55 (m, 1H), 7.56 (d, J =
8.4 Hz, 2H) 7.80-7.84 (m, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.4 Hz, 1H); 13C NMR (100 MHz, CDCl3): δ = 21.4, 121.9, 123.7, 124.2, 126.5, 128.4, 128.9, 129.1, 129.9, 133.6, 135.1, 136.0, 139.6, 140.6, 149.4, 159.0, 171.1; HRMS (ESI): m/z [M + H]+ Calcd for C22H19N2S: 343.1269; Found, 343.1271.

4-Phenylsulfanyl-2-p-tolyl-quinazoline (7i): White solid, yield: 26.6 mg (81%); mp 147-148 °C; IR (KBr): 3060, 2918, 1609, 1559, 1539, 1485, 1450, 1337, 1308, 1177, 756, 687 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ = 2.36 (s, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.51-7.57 (m, 4H), 7.69-7.71 (m, 2H), 7.81-7.85 (m, 1H), 7.98 (d, J = 8.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 2H), 8.16-8.18 (m, 1H); ¹³C NMR (100 MHz, CDCl3): δ = 21.4, 121.8, 123.7, 126.5, 127.7, 128.4, 129.0, 129.1, 129.4, 133.7, 135.0, 136.2, 140.6, 149.5, 159.0, 170.8; HRMS (ESI): m/z [M + H]+ Calcd for C21H17N2S: 329.1112; Found, 329.1115.

4-(4-Fluoro-phenylsulfanyl)-2-p-tolyl-quinazoline (7j): White solid, yield: 29.5 mg (85%); mp 196-197 °C; IR (KBr): 3053, 2917, 2855, 1887, 1818, 1631, 1591, 1451, 1380, 732, 691 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ = 2.37 (s, 3H), 7.17-7.24 (m, 4H), 7.54 (d, J = 7.2 Hz, 1H), 7.65 (dd, J = 6.4, 7.2 Hz, 2H), 7.82 (d, J = 7.2 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.09-8.13 (m, 3H); ¹³C NMR (100 MHz, CDCl3): δ = 21.4, 116.2 (d, J = 22 Hz), 121.7, 122.9, 123.6, 126.7, 128.4, 129.0, 129.1, 133.8, 134.4, 138.3, 140.8, 149.4, 159.0, 162.5 (d, J = 248 Hz), 170.5; HRMS (ESI): m/z [M + H]+ Calcd for C21H16FN2S: 347.1018; Found, 347.1012.
**4-(4-Chloro-phenylsulfanyl)-2-p-tolyl-quinazoline (7k):** White solid, yield: 29.0 mg (80%); mp 206-208; IR (KBr)/cm\(^{-1}\): 3050, 2917, 1898, 1818, 1607, 1576, 1557, 1542, 1478, 1451, 1377, 1324, 1094, 818, 732 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 2.37\) (s, 3H), 7.18 (d, \(J = 8.0\) Hz, 2H), 7.48-7.56 (m, 3H), 7.61 (d, \(J = 8.4\) Hz, 2H), 7.83 (s, 1H), 7.98 (d, \(J = 8.4\) Hz, 1H), 8.10-8.12 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 21.4, 121.7, 123.5, 126.3, 126.9, 128.4, 129.0, 129.2, 129.9, 133.8, 134.8, 135.9, 137.4, 140.8, 149.5, 159.0, 170.1\); HRMS (ESI): \(m/z [\text{M} + \text{H}]^+\) Calcd for C\(_{21}\)H\(_{16}\)ClN\(_2\)S: 363.0723; Found, 363.0732.

**4-(2-Chloro-phenylsulfanyl)-2-p-tolyl-quinazoline (7l):** White solid, yield: 27.9 mg (77%); mp 159-161°C; IR (KBr): 3057, 2917, 1925, 1810, 1608, 1558, 1541, 1482, 1456, 1379, 1335, 987, 753 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 2.36\) (s, 3H), 7.14 (d, \(J = 8.0\) Hz, 2H), 7.39-7.41 (m, 1H), 7.50 (d, \(J = 1.6\) Hz, 1H), 7.56-7.58 (m, 1H), 7.65 (dd, \(J = 1.2, 8.4\) Hz 1H), 7.77 (dd, \(J = 1.6, 7.6\) Hz, 1H), 7.84 (d, \(J = 1.2\) Hz 1H), 7.99 (d, \(J = 8.4\) Hz, 1H), 8.04 (d, \(J = 8.4\) Hz, 2H), 8.16 (d, \(J = 8.4\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 21.4, 121.9, 123.7, 126.5, 127.5, 128.4, 129.0, 129.9, 130.9, 133.7, 134.9, 138.5, 140.3, 140.7, 149.6, 159.0, 169.2\); HRMS (ESI): \(m/z [\text{M} + \text{H}]^+\) Calcd for C\(_{21}\)H\(_{16}\)ClN\(_2\)S: 363.0723; Found, 363.0724.
4-Benzylsulfanyl-2-p-tolyl-quinazoline (7m): White solid, yield: 26.4 mg (77%); mp 136-137°C; IR (KBr): 1815, 1608, 1539, 1450, 1376, 1316, 1249, 1000, 868, 760, 700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3H), 4.78 (s, 2H), 7.26-7.34 (m, 5H), 7.47-7.51 (m, 3H), 7.79 (s 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.51 (d, J = 8.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.5, 33.8, 122.2, 123.7, 126.4, 127.4, 128.5, 128.7, 128.9, 129.2, 129.3, 133.6, 135.7, 137.3, 140.8, 149.1, 158.9, 170.3; HRMS (ESI): m/z [M + H]+ Calcd for C₂₂H₁₉N₂S: 343.1269; Found, 343.1274.

2-(4-Chloro-phenyl)-4-p-tolylsulfanyl-quinazoline (7n): White solid, yield: 28.7 mg (79%); mp 136-137°C; IR (KBr): 3032, 2921, 1957, 1919, 1893, 1816, 1784, 1614, 1593, 1577, 1493, 1451, 1376, 1335, 1252, 1088, 998, 756, 692 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.49 (s, 3H), 7.31-7.35 (m, 4H), 7.54-7.58 (m, 3H), 7.85 (t, J = 8.4 Hz 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.15-8.19 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.5, 121.9, 123.7, 123.9, 127.2, 128.5, 128.6, 129.0, 129.7, 129.9, 133.8, 136.1, 136.3, 136.6, 139.8, 149.2, 158.0, 171.5; HRMS (ESI): m/z [M + H]+ Calcd for C₂₁H₁₆ClN₂S: 363.0723; Found, 363.0725.

2-(4-Chloro-phenyl)-4-phenylsulfanyl-quinazoline (7o): White solid, yield: 25.1 mg (72%); mp 214-215°C; IR (KBr): 3048, 2921, 1816, 1614, 1592, 1560, 1482, 1450, 1382, 1335, 1089, 843, 756, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.31 (d, J = 8.8Hz, 2H), 7.53-7.59 (m, 4H), 7.68-7.70 (m, 2H), 7.86 (d, J = 1.2 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 8.15-8.19 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 121.9, 123.7, 127.0, 127.5, 128.5, 129.0, 129.2, 129.6, 129.7, 133.9, 136.2, 136.3, 136.6, 140.3, 157.9, 171.3; HRMS (ESI):
(7p): White solid, yield: 31.2 mg (85%); mp 247-248°C; IR (KBr): 3056, 2924, 1960, 1922, 1885, 1615, 1592, 1558, 1489, 1451, 1334, 1232, 1089, 1012, 842, 756, 692 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.22-7.26 (m, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.60-7.68 (m, 3H), 7.87 (t, J = 8.4 Hz 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.14-8.18 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 116.5 (d, J = 24 Hz), 121.8, 123.6, 127.1, 128.5, 128.7, 129.0, 129.7, 134.1, 136.0, 136.8, 138.3, 138.4, 149.2, 157.9, 162.9 (d, J = 248 Hz), 171.5; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₀H₁₄ClN₂S: 367.0472; Found, 367.0474.

(7q): White solid, yield: 33.8 mg (88%); m.p.230-231°C; IR (film): 3053, 2924, 2854, 1921, 1854, 1614, 1576, 1451, 1378, 756, 690 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.35 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.60-7.63 (m, 3H), 7.87 (t, J = 8.4 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 121.8, 123.6, 126.0, 128.5, 128.7, 129.1, 129.7, 134.1, 136.1, 136.8, 137.3, 137.4, 149.3, 158.0, 170.6; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₀H₁₃ClF₂N₂S: 383.0177; Found, 383.0182.
5-Fluoro-2-phenyl-4-p-tolylsulfanyl-quinazoline (7r), Light yellow solid, yield: 27.9 mg (78%); mp 161-162°C; IR (KBr): 3067, 2921, 1899.1, 1768, 1625, 1557, 1475, 1450, 1363, 1350, 702 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.50 (s, 3H), 7.22-7.25 (m, 1H), 7.31-7.39 (m, 5H), 7.54(d, J = 8.0 Hz, 2H), 7.73 (d, J = 5.6 Hz,1H), 7.79 (d, J = 8.4 Hz, 1H), 8.10-8.13 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.4, 111.8, 112.6 (d, J = 15 Hz), 124.7 (d, J = 10Hz), 125.0, 128.2 (d, J = 21 Hz), 128.6, 129.3 (d, J = 14 Hz), 130.6, 133.1, 136.1 (d, J = 13 Hz), 137.2, 139.8, 151.6, 157.3 (d, J = 257 Hz), 159.0, 170.0; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₁H₁₆FN₂S: 347.1018; Found, 347.1024.

2-(4-Methoxy-phenyl)-4-phenylsulfanyl-quinazoline (7s): White solid, yield: 27.6 mg (71%); mp 122-123°C; IR (KBr): 2960, 2035, 1903,1607, 1556, 1452, 1376, 1251, 1176, 746, 696 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.49 (s, 3H), 3.84 (s, 3H), 6.86 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.50-7.59 (m, 3H), 7.78-7.82 (m, 1H), 7.95 (d, J = 8.4 Hz, 2H), 8.14-8.19 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.5, 55.3, 113.6, 121.6, 123.7, 124.1, 126.3, 128.7, 129.9, 130.1, 130.4, 133.6, 136.0, 139.6, 149.4, 158.9, 161.6, 171.0; HRMS (ESI): m/z [M + H]⁺ Calcd for C₂₂H₁₉N₂OS: 359.1218; Found, 359.1224.

2-(3,4-Dimethoxy-phenyl)-4-p-tolylsulfanyl-quinazoline (7t): White solid, yield: 28.4 mg (82%); mp 142-143°C; IR (film): 2998, 2837, 2031, 1899, 1600, 1519, 1378, 1234, 1175, 763 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3H), 3.77 (s, 3H), 3.92 (s, 3H), 6.87 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 7.6 Hz, 2H), 7.53-7.60 (m, 3H), 7.69 (s, 1H), 7.80-7.89 (m, 1H), 7.97-8.00 (m, 2H), 8.15 (d, J = 8.4 Hz, 1H); ¹³C NMR (100 MHz,
CDCl₃): δ = 21.3, 55.5, 55.9, 110.6, 110.9, 121.5, 121.6, 123.7, 124.2, 126.4, 128.7, 129.9, 130.5, 133.7, 136.4, 148.4, 139.5, 149.3, 158.5, 161.6, 171.3; HRMS (ESI): m/z [M + H]+ Calcd for C₂₃H₂₁N₂O₂S: 389.1324; Found, 389.1326.