

Supporting Information

Metal-free C5-selective halogenation of quinolines under aqueous condition

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Materials and methods

1. General

All reactions were carried out in oven-dried glassware. Melting points (m.p.) were taken on an XT-4 micro melting point apparatus and uncorrected. IR spectra were recorded in KBr on a Nicolet Impact 410 grating infrared spectrophotometer (ν_{max} in cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on Bruker-300 spectrometers, and were referenced to the residual peaks of CDCl_3 at 7.26 ppm or $\text{DMSO}-d_6$ at 2.50 ppm (^1H NMR) and CDCl_3 at 77.0 ppm or $\text{DMSO}-d_6$ at 39.5 ppm (^{13}C NMR). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (Hz), and integration. High Resolution Mass measurement was performed on Agilent QTOF 6520 mass spectrometer with electron spray ionization (ESI) as the ion source. Flash column chromatography was carried out using commercially available 200-300 mesh under pressure.

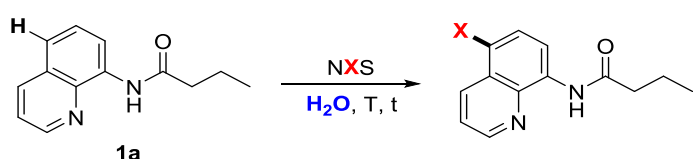
2. Materials

Unless otherwise indicated, all reagents were obtained from commercial suppliers used without further purification. PE refers to petroleum ether (b.p. 60-90 °C) and EA refers to ethyl acetate, and all reaction solvents were freshly distilled prior to use.

Preparation of substrates

All substrates were synthesized according to the literature procedures and the ^1H NMR spectrum data for them showed good agreement with the literature data.¹

Table S1 Optimization of reaction conditions of chlorination and iodination^a



1a

Entry	NXS (equiv.)	T (°C)	t (min)	Yield ^b (%)
1	NCS (1.5)	25	15	trace
2	NCS (1.5)	50	15	23
3	NCS (1.5)	80	15	37
4	NCS (1.5)	100	15	41
5	NCS (1.5)	100	30	52
6	NCS (2.0)	100	30	65
7 ^c	NCS (2.0)	100	30	76
8	NCS (3.0)	100	30	81

9 ^c	NCS (3.0)	100	30	88
10	NIS (1.5)	25	15	0
11	NIS (1.5)	50	15	trace
12	NIS (1.5)	80	15	24
13	NIS (1.5)	100	15	39
14	NIS (1.5)	100	30	46
15	NIS (2.0)	100	30	62
16 ^c	NIS (2.0)	100	30	75
17	NIS (3.0)	100	30	80
18 ^c	NIS (3.0)	100	30	93

^a Reaction conditions: **1a** (0.2 mmol), NXS, H₂O (1.5 mL), under air. ^b Isolated yields. ^c NXS in two portions, each NXS of 1.5 equiv. for 15 min.

General procedure for bromination of quinolines

To a 15 mL round-bottom flask with a magnetic stirring bar were added aminoquinoline derivatives (**1**, 0.2 mmol), NBS (0.3 mmol) and H₂O (1.5 mL). The reaction mixture was carried out at room temperature or 50 °C, and vigorously stirred for 15 min, followed to be extracted with EtOAc (5 mL × 3). The combined solvents were washed brine, dried with anhydrous Na₂SO₄, removed under reduced pressure. Finally, the crude reaction mixture was purified by flash chromatography using *PE/EA* = 30:1 as an eluent to give the desired products **2a-2o** and **3a-3o**.

General procedure for chlorination and iodination of quinolines

To a 1.5 mL H₂O solution of aminoquinoline derivatives (**1**, 0.2 mmol) in 15 mL round-bottom flask with a magnetic stirring bar were added NCS or NIS (0.6 mmol) in two portions (each 0.3 mol NCS or NIS for 15 min). The reaction mixture was vigorously stirred at 100 °C. Upon completion, it was cooled to ambient temperature and extracted with EtOAc (5 mL × 3). The combined solvents were washed brine, dried with anhydrous Na₂SO₄ and removed under reduced pressure. Finally, the crude reaction mixture was purified by flash chromatography using *PE/EA* = 30:1 as an eluent to afford the chlorinated and iodinated products **4a-4j** and **4a'-4j'**, respectively.

General procedure for hydrolysis of halogenated products

To a solution of **2a** (0.2 mmol) in EtOH (2.0 mL), 0.5 mL of concentrated hydrochloric acid (10 M) was added. The mixture was refluxed for 1 h and then concentrated under reduced pressure. The residue was dissolved in CH₂Cl₂ (10.0 mL), washed by saturated NaHCO₃ aqueous solution (5 mL × 2), brine (5 mL × 2), and dried over anhydrous Na₂SO₄. The organic solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel using *PE/EA* = 10 : 1 as an eluent to give the brominated 8-aminoquinoline **5a**.

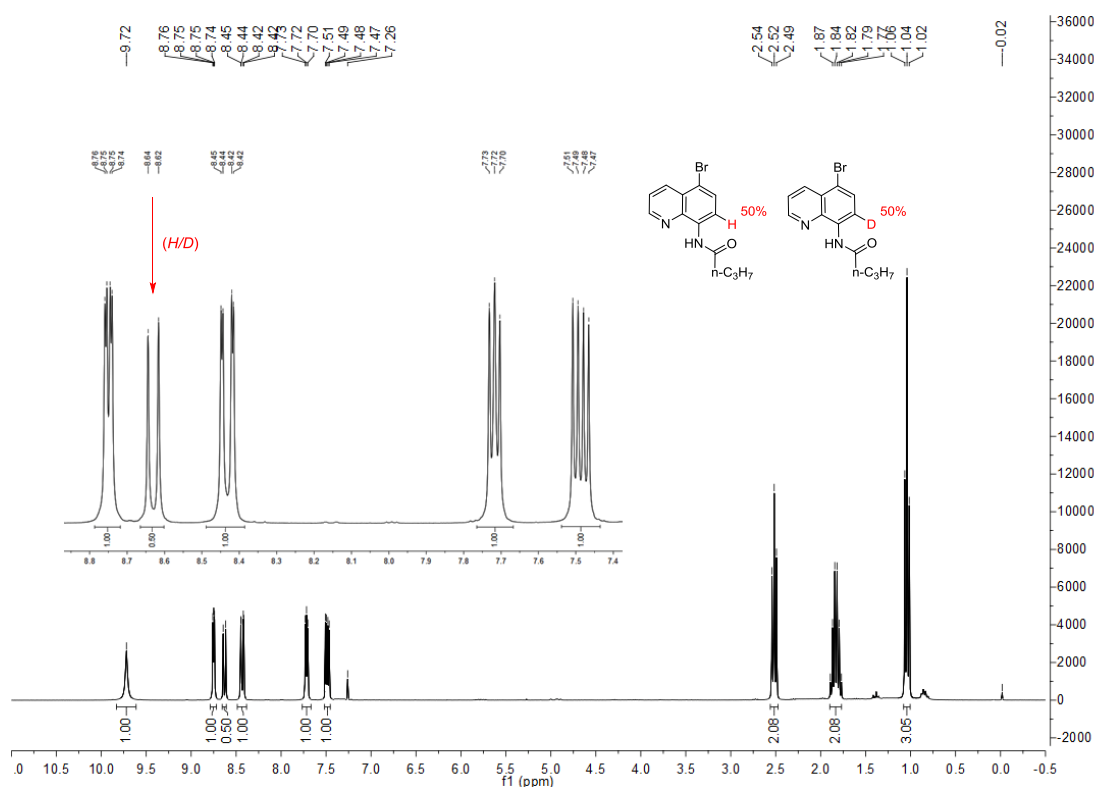
Radical inhibition experiment

The reaction was carried out according to the general bromination procedure, and another 3 equiv of TEMPO or BHT was added prior to NBS. At the end of the reaction, the yield of the target product **2a** decreased dramatically to trace.

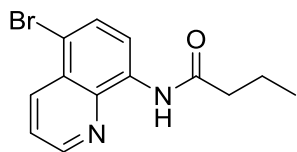
Kinetic isotope experiment

To demonstrate the intermolecular kinetic isotope effect (KIE), a 1:1 mixture of **1a** and the dideuterated substrate d_2 -**1a** was subjected to the standard reaction condition for 15 min and the products were isolated by flash column chromatography. Yield: 91%. From the ^1H -NMR analysis of the H/D ratio at the 7-position of the quinoline ring reveals a nearly equal mixture of isotopes, corresponding to an intermolecular KIE of $k_{\text{H}}/k_{\text{D}} = 1.0$. This result indicates that the breakage of the C-H bond is not a rate-determining step.

^1H -NMR spectrum of the product in the intermolecular KIE experiment:

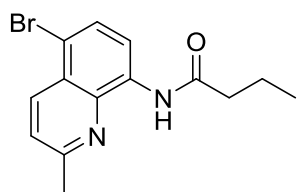


Analytical data for the products



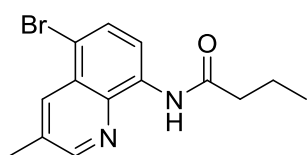
***N*-(5-bromoquinolin-8-yl)butanamide (2a)**

Obtained as a white solid (56.3 mg, 96%); m.p. 88 – 90 °C; IR (KBr), cm^{-1} : 3347, 2965, 2936, 2875, 1688, 1519, 1475, 1383, 1359, 1318, 1182, 1149, 958, 903, 854, 780; ^1H NMR (300 MHz, CDCl_3) δ 9.79 (s, 1H), 8.82 (dd, $J = 4.2, 1.5$ Hz, 1H), 8.69 (d, $J = 8.4$ Hz, 1H), 8.53 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.79 (d, $J = 8.4$ Hz, 1H), 7.57 (dd, $J = 8.5, 4.2$ Hz, 1H), 2.54 (t, $J = 7.5$ Hz, 2H), 1.89 – 1.79 (m, 2H), 1.06 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.64, 148.43, 138.81, 135.75, 134.30, 130.75, 126.95, 122.47, 116.71, 113.84, 40.01, 18.95, 13.73; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{14}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 293.0284, found 293.0289.



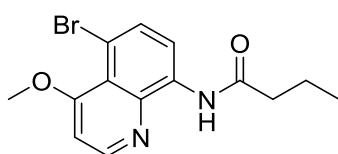
***N*-(5-bromo-2-methylquinolin-8-yl)butanamide (2b)**

Obtained as a white solid (52.8 mg, 86%); m.p. 91 – 93 °C; IR (KBr), cm^{-1} : 3340, 2959, 1686, 1601, 1563, 1522, 1485, 1396, 1369, 1327, 1158, 956, 903, 836, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.81 (s, 1H), 8.64 (d, $J = 8.4$ Hz, 1H), 8.37 (d, $J = 8.6$ Hz, 1H), 7.69 (d, $J = 8.4$ Hz, 1H), 7.40 (d, $J = 8.6$ Hz, 1H), 2.77 (s, 3H), 2.54 (t, $J = 7.5$ Hz, 2H), 1.90 – 1.80 (m, 2H), 1.07 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.57, 157.75, 138.23, 135.77, 133.67, 129.68, 125.19, 123.33, 116.70, 113.86, 40.01, 24.96, 18.91, 13.76; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 307.0441, found 307.0443.



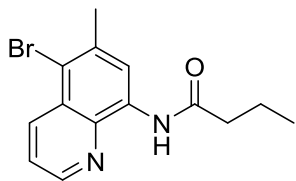
***N*-(5-bromo-3-methylquinolin-8-yl)butanamide (2c)**

Obtained as a white solid (51.0 mg, 83%); m.p. 122 – 124 °C; IR (KBr), cm^{-1} : 3336, 2963, 2926, 1686, 1518, 1466, 1364, 1320, 1189, 981, 881, 851; ^1H NMR (300 MHz, CDCl_3) δ 9.72 (s, 1H), 8.62 (d, $J = 1.8$ Hz, 1H), 8.58 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 0.9$ Hz, 1H), 7.72 (d, $J = 8.4$ Hz, 1H), 2.56 (s, 3H), 2.53 (t, $J = 7.7$ Hz, 2H), 1.88 – 1.78 (m, 2H), 1.05 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.65, 150.32, 137.23, 134.49, 134.29, 132.36, 130.81, 126.81, 115.87, 113.34, 40.06, 18.99, 18.76, 13.75; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 307.0441, found 307.0446.



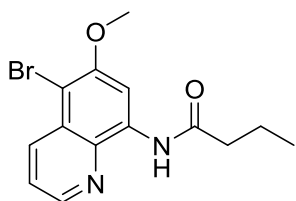
***N*-(5-bromo-4-methoxyquinolin-8-yl)butanamide (2d)**

Obtained as a white solid (50.4 mg, 78%); m.p. 145 – 147 °C; IR (KBr), cm^{-1} : 3327, 2963, 2938, 2844, 1678, 1540, 1485, 1453, 1316, 1038, 969, 820, 696; ^1H NMR (300 MHz, CDCl_3) δ 9.89 (s, 1H), 8.63 – 8.58 (m, 2H), 7.74 (d, $J = 8.5$ Hz, 1H), 6.84 (d, $J = 5.3$ Hz, 1H), 4.03 (s, 3H), 2.56 – 2.47 (m, 2H), 1.87 – 1.77 (m, 2H), 1.04 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.60, 162.88, 148.96, 140.53, 134.04, 132.94, 119.37, 116.91, 107.84, 101.93, 55.35, 40.11, 18.97, 13.73; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{ClN}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 323.0390, found 323.0395.



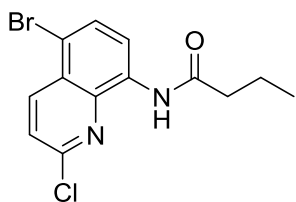
***N*-(5-bromo-6-methylquinolin-8-yl)butanamide (2e)**

Obtained as a white solid (52.2 mg, 85%); m.p. 88 – 90 °C; IR (KBr), cm^{-1} : 3347, 2961, 2922, 2851, 1687, 1530, 1468, 1402, 1380, 1364, 1190, 898, 877, 780; ^1H NMR (300 MHz, CDCl_3) δ 9.72 (s, 1H), 8.76 – 8.70 (m, 2H), 8.55 (dd, J = 8.6, 1.5 Hz, 1H), 7.50 (dd, J = 8.6, 4.2 Hz, 1H), 2.61 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 1.92 – 1.82 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.72, 147.45, 137.69, 137.64, 135.56, 133.48, 127.32, 122.49, 119.03, 115.21, 40.04, 24.25, 18.99, 13.75; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 307.0441, found 307.0440.



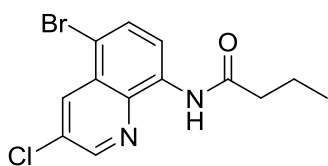
***N*-(5-bromo-6-methoxyquinolin-8-yl)butanamide (2f)**

Obtained as a white solid (58.8 mg, 91%); m.p. 130 – 132 °C; IR (KBr), cm^{-1} : 3332, 2966, 2944, 2868, 1678, 1620, 1531, 1459, 1397, 1343, 1246, 1191, 1085, 902, 854, 780; ^1H NMR (300 MHz, CDCl_3) δ 9.85 (s, 1H), 8.84 (s, 1H), 8.68 – 8.61 (m, 1H), 8.49 (dd, J = 8.6, 1.0 Hz, 1H), 7.50 (dd, J = 8.6, 4.2 Hz, 1H), 4.07 (s, 3H), 2.56 (t, J = 7.4 Hz, 2H), 1.88 – 1.78 (m, 2H), 1.07 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.99, 154.41, 145.98, 135.25, 134.59, 134.41, 127.88, 122.94, 104.21, 99.14, 56.87, 40.01, 18.83, 13.74; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 323.0390, found 323.0395.



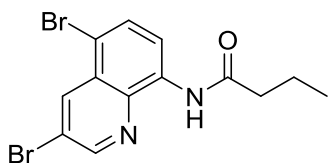
***N*-(5-bromo-2-chloroquinolin-8-yl)butanamide (2g)**

Obtained as a white solid (63.5 mg, 97%); m.p. 101 – 102 °C; IR (KBr), cm^{-1} : 3361, 2963, 2935, 2872, 1695, 1580, 1519, 1389, 1324, 1276, 1261, 1181, 1142, 1093, 956, 906, 838, 749; ^1H NMR (300 MHz, CDCl_3) δ 9.36 (s, 1H), 8.73 (d, J = 8.5 Hz, 1H), 8.47 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 8.5 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 2.55 (t, J = 7.5 Hz, 2H), 1.90 – 1.80 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.70, 149.83, 138.76, 138.16, 133.52, 131.17, 125.68, 123.65, 118.10, 113.62, 39.91, 18.82, 13.72; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{BrClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 326.9894, found 326.9900.



***N*-(5-bromo-3-chloroquinolin-8-yl)butanamide (2h)**

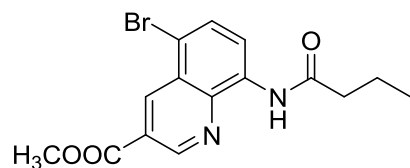
Obtained as a white solid (64.2 mg, 98%); m.p. 112 – 114 °C; IR (KBr), cm^{-1} : 3358, 2960, 2929, 1673, 1527, 1464, 1416, 1359, 1276, 1261, 1104, 966, 896, 847, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.59 (s, 1H), 8.69 (dd, J = 7.2, 5.4 Hz, 2H), 8.50 (d, J = 2.2 Hz, 1H), 7.81 (d, J = 8.5 Hz, 1H), 2.53 (t, J = 7.5 Hz, 2H), 1.88 – 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.59, 147.62, 136.54, 134.36, 133.88, 132.05, 130.46, 127.22, 116.88, 112.47, 77.42, 77.00, 76.58, 39.96, 18.87, 13.72; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{BrClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 326.9894, found 326.9898.



***N*-(3,5-dibromoquinolin-8-yl)butanamide (2i)**

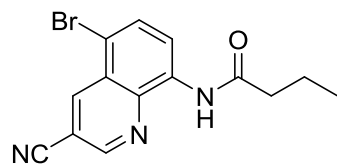
Obtained as a white solid (67.7 mg, 91%); m.p. 142 – 144 °C; IR (KBr), cm^{-1} : 3367, 2957, 2921, 1677, 1525, 1462, 1388, 1315, 1122, 963, 932, 894, 848; ^1H NMR (300 MHz, CDCl_3) δ 9.59 (s, 1H), 8.80 (d, J = 2.1 Hz, 1H), 8.69 (t, J = 5.3 Hz, 2H), 7.81 (d, J = 8.5 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.88 – 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz,

CDCl₃) δ 171.68, 149.56, 137.21, 136.84, 134.51, 132.08, 127.89, 119.24, 117.11, 112.48, 40.01, 18.92, 13.74; HRMS (ESI) calculated for C₁₃H₁₃BrN₂O [M + H]⁺ 372.9375, found 372.9374;



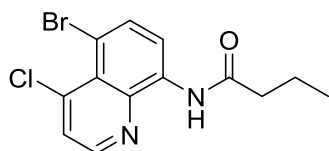
***N*-(5-bromo-3-methoxycarbonylquinolin-8-yl)butanamide (2j)**

Obtained as a white solid (65.3 mg, 93%); m.p. 139 – 141 °C; IR (KBr), cm⁻¹: 2956, 2920, 2850, 1727, 1687, 1521, 1468, 1432, 1365, 1274, 1178, 1112, 998, 764; ¹H NMR (300 MHz, CDCl₃) δ 9.67 (s, 1H), 9.28 (d, *J* = 1.8 Hz, 1H), 9.09 (d, *J* = 1.8 Hz, 1H), 8.76 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 4.04 (s, 3H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.91–1.81 (m, 2H), 1.06 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.69, 165.07, 148.21, 140.15, 138.17, 134.46, 131.75, 125.82, 124.40, 118.85, 114.82, 52.63, 39.98, 18.89, 13.71; HRMS (ESI) calculated for C₁₅H₁₆BrN₂O₃ [M+H]⁺ 351.0339, found 351.0342.



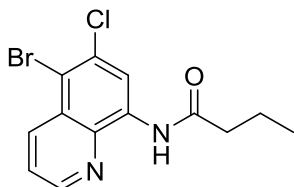
***N*-(5-bromo-3-cyanoquinolin-8-yl)butanamide (2k)**

Obtained as a white solid (52.2 mg, 82%); m.p. 147 – 149 °C; IR (KBr), cm⁻¹: 3357, 2956, 2921, 2874, 2850, 1673, 1566, 1529, 1465, 1411, 1361, 1321, 987, 914, 851; ¹H NMR (300 MHz, CDCl₃) δ 9.54 (s, 1H), 8.92 (d, *J* = 1.9 Hz, 1H), 8.87 (d, *J* = 1.9 Hz, 1H), 8.84 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.88 – 1.78 (m, 2H), 1.06 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.81, 148.17, 141.42, 134.76, 133.00, 125.60, 119.95, 116.39, 113.89, 108.34, 77.42, 77.00, 76.58, 40.03, 18.90, 13.70; HRMS (ESI) calculated for C₁₄H₁₃BrN₃O [M + H]⁺ 318.0237, found 318.0239.



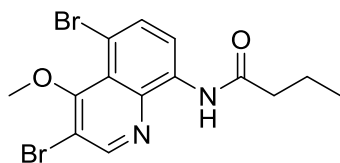
***N*-(5-bromo-4-chloroquinolin-8-yl)butanamide (2l)**

Obtained as a white solid (53.1 mg, 81%); m.p. 153 – 155 °C; IR (KBr), cm⁻¹: 3337, 2962, 2921, 1687, 1528, 1468, 1354, 1309, 1131, 1122, 829, 690; ¹H NMR (300 MHz, CDCl₃) δ 9.83 (s, 1H), 8.65 (d, *J* = 8.5 Hz, 1H), 8.58 (d, *J* = 4.6 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 4.6 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 1.87 – 1.77 (m, 2H), 1.05 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.73, 146.92, 142.98, 140.56, 135.81, 135.03, 125.27, 124.03, 117.34, 109.22, 40.15, 18.95, 13.75; HRMS (ESI) calculated for C₁₃H₁₃BrClN₂O [M + H]⁺ 326.9894, found 326.9897.



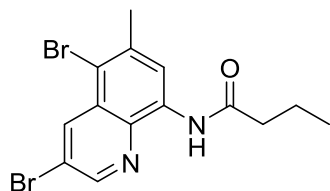
***N*-(5-bromo-6-chloroquinolin-8-yl)butanamide (2m)**

Obtained as a white solid (55.0 mg, 84%); m.p. 150 – 152 °C; IR (KBr), cm⁻¹: 3339, 2963, 2925, 1697, 1566, 1513, 1463, 1364, 1319, 1183, 1154, 960, 949, 865, 780; ¹H NMR (300 MHz, CDCl₃) δ 9.74 (s, 1H), 8.93 (s, 1H), 8.82 – 8.74 (m, 1H), 8.54 (d, *J* = 8.6 Hz, 1H), 7.57 (dd, *J* = 8.6, 4.2 Hz, 1H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.90 – 1.80 (m, 2H), 1.05 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.67, 148.21, 137.18, 136.04, 134.43, 134.29, 127.82, 123.29, 117.50, 113.30, 39.91, 18.84, 13.71; HRMS (ESI) calculated for C₁₃H₁₃BrClN₂O [M + H]⁺ 326.9894, found 326.9900.



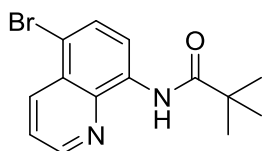
***N*-(3,5-dibromo-4-methoxyquinolin-8-yl)butanamide (2n)**

Obtained as a white solid (57.9 mg, 72%); m.p. 149 – 151 °C; IR (KBr), cm^{-1} : 2922, 2850, 1691, 1561, 1510, 1345, 1276, 1261, 1012, 969, 764, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.67 (s, 1H), 8.79 (s, 1H), 8.63 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.5 Hz, 1H), 4.02 (s, 3H), 2.51 (t, J = 7.5 Hz, 2H), 1.86–1.76 (m, 2H), 1.04 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.71, 160.77, 151.15, 139.93, 134.91, 123.56, 119.05, 117.33, 113.09, 106.68, 62.31, 40.12, 18.96, 13.73; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 402.9480, found 402.9477.



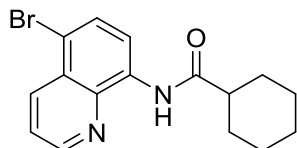
***N*-(3,5-dibromo-4-methylquinolin-8-yl)butanamide (2o)**

Obtained as a white solid (73.3 mg, 95%); m.p. 128 – 130 °C; IR (KBr), cm^{-1} : 3350, 2962, 2929, 2872, 1689, 1558, 1519, 1456, 1396, 1368, 1308, 1185, 956, 929, 890; ^1H NMR (300 MHz, CDCl_3) δ 9.49 (s, 1H), 8.73 (s, 1H), 8.67 (d, J = 1.0 Hz, 2H), 2.60 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 1.87–1.77 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.77, 148.54, 139.34, 137.08, 135.83, 133.72, 128.35, 119.42, 119.27, 113.87, 40.05, 24.40, 18.97, 13.75; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{15}\text{Br}_2\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 384.9546, found 384.9543.



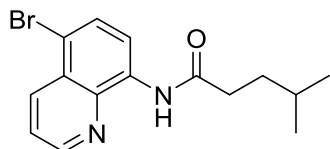
***N*-(5-bromoquinolin-8-yl)pivalamide (3a)**

Obtained as a white solid (58.4 mg, 95%); m.p. 91 – 93 °C; IR (KBr), cm^{-1} : 3371, 2966, 2921, 2871, 1678, 1552, 1481, 1383, 1363, 1318, 1178, 1144, 932, 835, 782, 679; ^1H NMR (300 MHz, CDCl_3) δ 10.21 (s, 1H), 8.79 (dd, J = 4.2, 1.5 Hz, 1H), 8.66 (d, J = 8.4 Hz, 1H), 8.45 (dd, J = 8.5, 1.6 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 8.5, 4.2 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.15, 148.57, 139.32, 135.75, 134.51, 130.80, 127.00, 122.46, 116.60, 113.79, 40.30, 27.61; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 307.0441, found 307.0438.



***N*-(5-bromoquinolin-8-yl)cyclohexanecarboxamide (3b)**

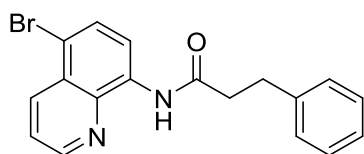
Obtained as a white solid (54.6 mg, 82%); m.p. 99 – 101 °C; IR (KBr), cm^{-1} : 3357, 2927, 2852, 1686, 1519, 1476, 1384, 1363, 948, 836, 786; ^1H NMR (300 MHz, CDCl_3) δ 9.86 (s, 1H), 8.82 (dd, J = 4.2, 1.5 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 8.51 (dd, J = 8.5, 1.5 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.55 (dd, J = 8.5, 4.2 Hz, 1H), 2.50–2.42 (m, 1H), 2.09–2.05 (m, 2H), 1.90–1.85 (m, 2H), 1.75–1.56 (m, 2H), 1.45–1.25 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.78, 148.51, 139.15, 135.87, 134.55, 130.89, 127.10, 122.51, 116.87, 113.82, 46.82, 29.67, 25.72, 25.69; HRMS (ESI) calculated for $\text{C}_{16}\text{H}_{18}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 333.0597, found 333.0598.



4-methyl-*N*-(5-bromoquinolin-8-yl)pentanamide (3c)

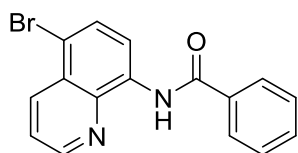
Obtained as a white solid (62.3 mg, 97%); m.p. 108– 110 °C; IR (KBr), cm^{-1} : 3344, 2952, 2924, 2867, 1667, 1522, 1484, 1421, 1362, 1275, 1261, 914, 842, 789, 765, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.78 (s, 1H), 8.82 (dd, J = 4.2, 1.5 Hz, 1H), 8.67 (d, J = 8.4 Hz, 1H), 8.51 (dd, J = 8.5, 1.6 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.55 (dd, J = 8.5, 4.2 Hz, 1H), 2.56 (t, J = 7.4 Hz, 2H), 1.75–1.68 (m, 3H), 0.97 (d, J = 6.4 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.04,

148.52, 138.95, 135.89, 134.43, 130.88, 127.08, 122.56, 116.82, 113.91, 36.20, 34.29, 27.77, 22.33; HRMS (ESI) calculated for $C_{15}H_{18}BrN_2O$ $[M + H]^+$ 321.0597, found 321.0600.



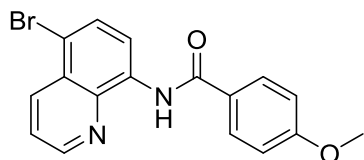
***N*-(5-bromoquinolin-8-yl)phenylpropanamide (3d)**

Obtained as a white solid (66.8 mg, 94%); m.p. 118–120 °C; IR (KBr), cm^{-1} : 3347, 2961, 2921, 2852, 1687, 1522, 1477, 1386, 1363, 1316, 1144, 1080, 923, 785, 747; 1H NMR (300 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.78 (dd, $J = 4.2, 1.6$ Hz, 1H), 8.68 (d, $J = 8.4$ Hz, 1H), 8.51 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.79 (d, $J = 8.4$ Hz, 1H), 7.55 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.32–7.25 (m, 4H), 7.24–7.18 (m, 1H), 3.14 (t, $J = 7.7$ Hz, 2H), 2.88 (t, $J = 7.7$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.64, 148.42, 140.54, 138.78, 135.76, 134.20, 130.76, 128.49, 128.31, 126.96, 126.21, 122.50, 116.81, 114.01, 39.59, 31.28; HRMS (ESI) calculated for $C_{18}H_{16}BrN_2O$ $[M + H]^+$ 355.0441, found 355.0443.



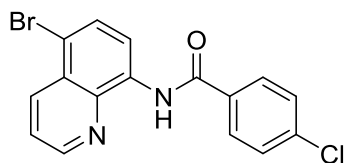
***N*-(5-bromoquinolin-8-yl)benzamide (3e)**

Obtained as a white solid (56.3 mg, 86%); m.p. 130–132 °C; IR (KBr), cm^{-1} : 3362, 3352, 2920, 2850, 1671, 1530, 1495, 1477, 1384, 1364, 1322, 1262, 918, 843, 786; 1H NMR (300 MHz, $CDCl_3$) δ 10.72 (s, 1H), 8.87 (dd, $J = 4.2, 1.5$ Hz, 1H), 8.84 (d, $J = 8.4$ Hz, 1H), 8.56 (dd, $J = 8.5, 1.5$ Hz, 1H), 8.07 (dd, $J = 7.9, 1.6$ Hz, 2H), 7.86 (d, $J = 8.4$ Hz, 1H), 7.63–7.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.27, 148.68, 139.29, 135.89, 134.73, 134.38, 131.95, 130.86, 128.78, 127.20, 127.13, 122.65, 116.91, 114.35; HRMS (ESI) calculated for $C_{16}H_{12}BrN_2O$ $[M + H]^+$ 327.0128, found 327.0133.



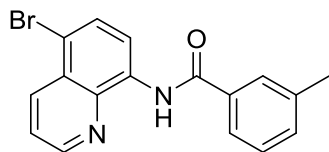
4-methoxy-*N*-(5-bromoquinolin-8-yl)benzamide (3f)

Obtained as a white solid (59.3 mg, 83%); m.p. 166–168 °C; IR (KBr), cm^{-1} : 3357, 2957, 2936, 2854, 1687, 1616, 1526, 1461, 1396, 1369, 1203, 1083, 897, 852, 772; 1H NMR (300 MHz, $CDCl_3$) δ 10.63 (s, 1H), 8.86 (d, $J = 2.8$ Hz, 1H), 8.82 (d, $J = 8.4$ Hz, 1H), 8.59–8.50 (m, 1H), 8.04 (d, $J = 8.8$ Hz, 2H), 7.84 (d, $J = 8.4$ Hz, 1H), 7.58 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.04 (d, $J = 8.8$ Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.91, 162.66, 148.65, 139.44, 136.34, 135.97, 134.70, 130.99, 129.16, 127.24, 127.14, 122.64, 116.84, 114.03, 55.45; HRMS (ESI) calculated for $C_{17}H_{14}BrN_2O_2$ $[M + H]^+$ 357.0233, found 357.0234.



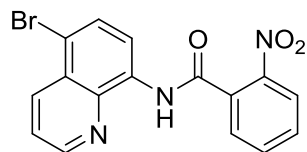
4-chloro-*N*-(5-bromoquinolin-8-yl)benzamide (3g)

Obtained as a white solid (58.6 mg, 81%); m.p. 154–156 °C; IR (KBr), cm^{-1} : 3369, 2932, 2850, 1685, 1534, 1475, 1386, 1364, 1323, 1260, 1091, 919, 843, 784, 744; 1H NMR (300 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.86 (d, $J = 4.1$ Hz, 1H), 8.79 (d, $J = 8.4$ Hz, 1H), 8.55 (d, $J = 8.5$ Hz, 1H), 8.00 (d, $J = 8.4$ Hz, 2H), 7.84 (d, $J = 8.3$ Hz, 1H), 7.59 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.52 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.96, 148.67, 139.11, 138.22, 135.87, 134.04, 132.97, 130.76, 128.97, 128.56, 127.04, 122.66, 116.88, 114.55; HRMS (ESI) calculated for $C_{16}H_{11}BrClN_2O$ $[M + H]^+$ 360.9738, found 360.9740.



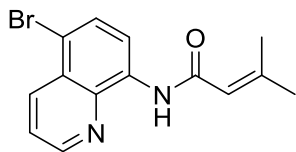
4-methyl-N-(5-bromoquinolin-8-yl)benzamide(3h)

Obtained as a white solid (59.4 mg, 87%); m.p. 121 – 123 °C; IR (KBr), cm^{-1} : 3363, 2920, 2851, 1673, 1587, 1522, 1474, 1383, 1363, 1319, 1270, 932, 835, 784; ^1H NMR (300 MHz, CDCl_3) δ 10.68 (s, 1H), 8.89 (dd, J = 4.2, 1.5 Hz, 1H), 8.85 (d, J = 8.4 Hz, 1H), 8.57 (dd, J = 8.5, 1.6 Hz, 1H), 7.86 (d, J = 8.5 Hz, 3H), 7.60 (dd, J = 8.5, 4.2 Hz, 1H), 7.42 (dd, J = 9.2, 7.8 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.50, 148.67, 139.36, 138.66, 135.88, 134.80, 134.52, 132.70, 130.90, 128.62, 127.99, 127.16, 124.14, 122.61, 116.95, 114.26, 21.42; HRMS (ESI) calculated for $\text{C}_{17}\text{H}_{14}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 341.0284, found 341.0286.



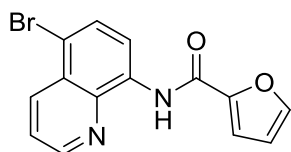
2-nitro-N-(5-bromoquinolin-8-yl)benzamide(3i)

Obtained as a white solid (61.0 mg, 82%); m.p. 165 – 167 °C; IR (KBr), cm^{-1} : 2956, 2924, 2853, 1701, 1676, 1655, 1535, 1484, 1319, 1345, 1319, 918, 833, 815, 786; ^1H NMR (300 MHz, CDCl_3) δ 10.13 (s, 1H), 8.79 (d, J = 8.3 Hz, 2H), 8.57 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.77 (s, 2H), 7.73 – 7.64 (m, 1H), 7.58 (dd, J = 8.5, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.02, 164.22, 148.85, 139.06, 136.10, 134.05, 133.83, 132.80, 130.93, 130.91, 128.58, 127.27, 124.79, 122.83, 117.56, 115.28; HRMS (ESI) calculated for $\text{C}_{16}\text{H}_{11}\text{BrN}_3\text{O}_3$ $[\text{M} + \text{H}]^+$ 371.9978, found 371.9985.



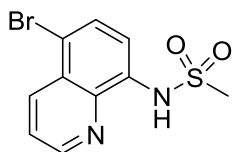
3-methyl-N-(5-bromoquinolin-8-yl)but-2-enamide (3j)

Obtained as a white solid (47.6 mg, 78%); m.p. 147 – 149 °C; IR (KBr), cm^{-1} : 3342, 2920, 2849, 1680, 1642, 1515, 1476, 1363, 1315, 1244, 1158, 1140, 916, 830, 780; ^1H NMR (300 MHz, CDCl_3) δ 9.70 (s, 1H), 8.80 (dd, J = 4.2, 1.5 Hz, 1H), 8.73 (d, J = 8.4 Hz, 1H), 8.51 (dd, J = 8.5, 1.6 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.55 (dd, J = 8.5, 4.2 Hz, 1H), 6.01 – 5.93 (m, 1H), 2.29 (d, J = 1.0 Hz, 3H), 1.96 (d, J = 1.0 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.23, 153.93, 148.44, 139.12, 135.92, 134.90, 130.96, 127.17, 122.55, 119.11, 116.63, 113.71, 27.50, 20.02; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{14}\text{BrN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 305.0284, found 305.0283.



N-(5-bromoquinolin-8-yl)furan-2-carboxamide(3k)

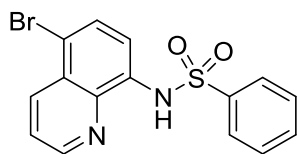
Obtained as a white solid (59.6 mg, 94%); m.p. 194 – 196 °C; IR (KBr), cm^{-1} : 3355, 3334, 2920, 2850, 1683, 1588, 1532, 1472, 1388, 1323, 1269, 1006, 909, 830; ^1H NMR (300 MHz, CDCl_3) δ 10.75 (s, 1H), 8.91 (dd, J = 4.2, 1.5 Hz, 1H), 8.77 (d, J = 8.4 Hz, 1H), 8.56 (dd, J = 8.5, 1.6 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 0.9 Hz, 1H), 7.60 (dd, J = 8.5, 4.3 Hz, 1H), 7.31 (d, J = 2.8 Hz, 1H), 6.60 (dd, J = 3.5, 1.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.30, 148.87, 148.20, 144.62, 139.34, 135.94, 134.17, 130.92, 127.29, 122.73, 117.12, 115.36, 114.56, 112.50; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{10}\text{BrN}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 316.9920, found 316.9922.



N-(5-bromoquinolin-8-yl)methanesulfonamide (3l)

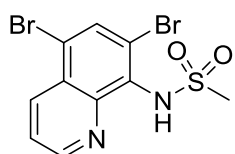
Obtained as a white solid (30.7 mg, 51%); m.p. 151 – 153 °C; IR (KBr), cm^{-1} : 3202, 2922, 2850, 1606, 1488, 1325, 1301, 1156, 972, 836, 796; ^1H NMR (300 MHz, CDCl_3) δ 8.93 (d, J = 4.0 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.68 (s, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.50 (dd, J = 7.3, 4.2 Hz, 1H), 3.48 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 150.48, 143.75, 136.39, 133.77, 131.37,

127.85, 126.60, 122.09, 121.01, 43.17; HRMS (ESI) calculated for $C_{10}H_{10}BrN_2O_2S$ $[M + H]^+$ 300.9641, found 300.9645.



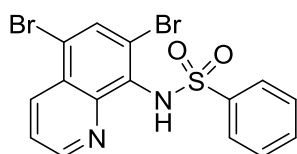
***N*-(5-bromoquinolin-8-yl)benzenesulfonamide (3m)**

Obtained as a white solid (32.0 mg, 44%); m.p. 170 – 172 °C; IR (KBr), cm^{-1} : 3230, 2920, 2850, 1605, 1585, 1489, 1450, 1334, 1169, 1122, 1093, 834, 794, 752, 726, 689, 645; 1H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, $J = 4.1$ Hz, 1H), 8.07 (d, $J = 8.2$ Hz, 2H), 7.78 – 7.73 (m, 3H), 7.55 (d, $J = 8.8$ Hz, 1H), 7.44 (t, $J = 7.0$ Hz, 1H), 7.31 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.92, 143.53, 140.08, 135.96, 133.46, 132.59, 131.78, 128.28, 127.66, 127.32, 126.51, 121.71, 121.27; HRMS (ESI) calculated for $C_{15}H_{12}BrN_2O_2S$ $[M + H]^+$ 362.9797, found 362.9803.



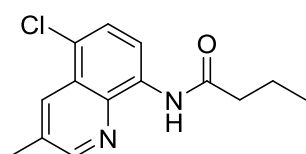
***N*-(3,5-bromoquinolin-8-yl)methanesulfonamide (3n)**

Obtained as a white solid (70.7 mg, 93%); m.p. 227 – 229 °C; IR (KBr), cm^{-1} : 3298, 3238, 3083, 2957, 2924, 2853, 1569, 1479, 1453, 1386, 1369, 1323, 1311, 1154, 1085, 1043, 980, 868, 818, 800; 1H NMR (300 MHz, DMSO) δ 9.70 (s, 1H), 9.06 (d, $J = 4.0$ Hz, 1H), 8.50 (d, $J = 8.5$ Hz, 1H), 8.29 (s, 1H), 7.77 (dd, $J = 8.1, 3.8$ Hz, 1H), 3.29 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 152.00, 145.39, 135.58, 133.97, 133.51, 126.76, 124.88, 123.61, 120.13, 43.21; HRMS (ESI) calculated for $C_{10}H_9Br_2N_2O_2S$ $[M + H]^+$ 380.8731, found 380.8733.



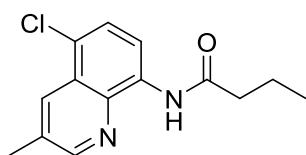
***N*-(3,5-bromoquinolin-8-yl)benzenesulfonamide (3o)**

Obtained as a white solid (76.0 mg, 86%); m.p. 233 – 235 °C; IR (KBr), cm^{-1} : 3238, 3103, 3031, 1577, 1481, 1452, 1421, 1357, 1335, 1170, 1137, 1095, 930, 871, 794, 755; 1H NMR (300 MHz, DMSO) δ 10.20 (s, 1H), 8.46 (d, $J = 4.1$ Hz, 1H), 8.40 (d, $J = 8.5$ Hz, 1H), 8.28 (s, 1H), 7.65 (d, $J = 7.9$ Hz, 2H), 7.62 – 7.53 (m, 2H), 7.43 (t, $J = 7.2$ Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 151.06, 145.12, 141.46, 135.18, 133.65, 133.52, 132.21, 128.42, 126.93, 126.57, 124.84, 123.27, 120.35; HRMS (ESI) calculated for $C_{15}H_{11}Br_2N_2O_2S$ $[M + H]^+$ 442.8896, found 442.8888.



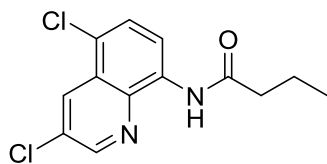
***N*-(5-chloro-3-methylquinolin-8-yl)butanamide (4a)**

Obtained as a white solid (42.5 mg, 81%); m.p. 98 – 100 °C; IR (KBr), cm^{-1} : 3335, 2970, 2929, 2872, 1679, 1528, 1472, 1393, 1376, 1325, 1196, 988, 883, 851, 710; 1H NMR (300 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.62 (d, $J = 8.4$ Hz, 2H), 8.26 (dd, $J = 1.9, 0.9$ Hz, 1H), 7.52 (d, $J = 8.4$ Hz, 1H), 2.56 – 2.50 (m, 5H), 1.88 – 1.78 (m, 2H), 1.05 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.55, 150.24, 137.05, 133.60, 131.96, 131.80, 127.05, 125.48, 123.34, 115.20, 39.99, 18.96, 18.72, 13.71; HRMS (ESI) calculated for $C_{14}H_{16}ClN_2O$ $[M + H]^+$ 263.0946, found 263.0950.



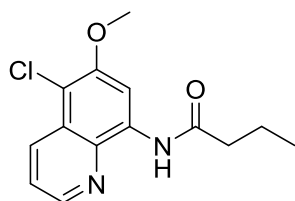
***N*-(5-chloro-3-methylquinolin-8-yl)butanamide (4a)**

Obtained as a white solid (42.6 mg, 81%); m.p. 98 – 100 °C; IR (KBr), cm^{-1} : 3335, 2970, 2929, 2872, 1679, 1528, 1472, 1393, 1376, 1325, 1196, 988, 883, 851, 710; 1H NMR (300 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.62 (d, $J = 8.4$ Hz, 2H), 8.26 (dd, $J = 1.9, 0.9$ Hz, 1H), 7.52 (d, $J = 8.4$ Hz, 1H), 2.56 – 2.50 (m, 5H), 1.88 – 1.78 (m, 2H), 1.05 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.55, 150.24, 137.05, 133.60, 131.96, 131.80, 127.05, 125.48, 123.34, 115.20, 39.99, 18.96, 18.72, 13.71; HRMS (ESI) calculated for $C_{14}H_{16}ClN_2O$ $[M + H]^+$ 263.0946, found 263.0950.



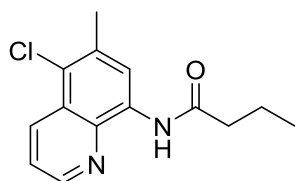
***N*-(3,5-dichloroquinolin-8-yl)butanamide (4b)**

Obtained as a white solid (41.9 mg, 74%); m.p. 101 – 103 °C; IR (KBr), cm^{-1} : 3361, 2958, 2921, 1676, 1569, 1531, 1465, 1417, 1363, 1319, 1183, 1106, 975, 896, 849; ^1H NMR (300 MHz, CDCl_3) δ 9.55 (s, 1H), 8.72 (dd, J = 5.4, 3.1 Hz, 2H), 8.51 (d, J = 2.3 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.91 – 1.79 (dd, J = 14.9, 7.4 Hz, 2H), 1.07 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.69, 147.86, 133.98, 131.65, 130.37, 128.61, 127.57, 126.28, 123.01, 116.57, 40.07, 18.98, 13.75; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 283.0399, found 283.0402.



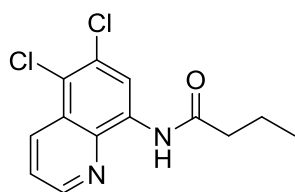
***N*-(5-chloro-6-methoxyquinolin-8-yl)butanamide (4c)**

Obtained as a white solid (47.9 mg, 86%); m.p. 123 – 125 °C; IR (KBr), cm^{-1} : 3342, 2967, 2944, 1680, 1623, 1535, 1462, 1400, 1348, 1191, 1089, 908, 855, 802, 781; ^1H NMR (300 MHz, CDCl_3) δ 9.80 (s, 1H), 8.83 (s, 1H), 8.66 (dd, J = 4.2, 1.5 Hz, 1H), 8.48 (dd, J = 8.6, 1.5 Hz, 1H), 7.49 (dd, J = 8.6, 4.2 Hz, 1H), 4.07 (s, 3H), 2.55 (t, J = 7.5 Hz, 2H), 1.88 – 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.86, 153.20, 145.92, 134.55, 134.03, 131.98, 126.59, 122.56, 108.31, 104.28, 56.74, 39.97, 18.82, 13.71; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{ClN}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$ 279.0895, found 279.0899.



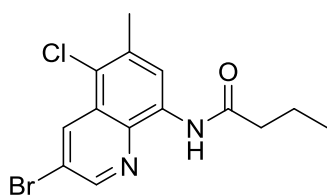
***N*-(5-chloro-6-methylquinolin-8-yl)butanamide (4d)**

Obtained as a white solid (44.7 mg, 85%); m.p. 95 – 97 °C; IR (KBr), cm^{-1} : 3364, 2962, 2920, 2850, 1681, 1523, 1468, 1406, 1116, 904, 781, 764; ^1H NMR (300 MHz, CDCl_3) δ 9.69 (s, 1H), 8.74 (dd, J = 4.2, 1.4 Hz, 1H), 8.71 (s, 1H), 8.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.50 (dd, J = 8.5, 4.2 Hz, 1H), 2.56 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 1.88 – 1.80 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.53, 147.28, 137.54, 134.99, 132.81, 132.72, 125.80, 122.67, 122.02, 118.86, 39.94, 20.89, 18.93, 13.69; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{ClN}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 263.0946, found 263.0951.



***N*-(3,5-dichloroquinolin-8-yl)butanamide (4e)**

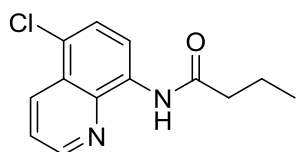
Obtained as a white solid (46.4 mg, 82%); m.p. 130 – 132 °C; IR (KBr), cm^{-1} : 3340, 2962, 2922, 1698, 1516, 1466, 1368, 1323, 1178, 971, 865, 781; ^1H NMR (300 MHz, CDCl_3) δ 9.70 (s, 1H), 8.90 (s, 1H), 8.80 (dd, J = 4.2, 1.5 Hz, 1H), 8.53 (dd, J = 8.6, 1.5 Hz, 1H), 7.57 (dd, J = 8.6, 4.2 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.90 – 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.76, 148.33, 137.47, 135.43, 134.03, 133.46, 132.01, 126.58, 123.05, 117.67, 39.99, 18.94, 13.74; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 283.0399, found 283.0400.



***N*-(5-chloro-3-bromo-6-methylquinolin-8-yl)butanamide (4f)**

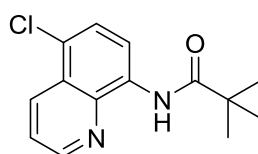
Obtained as a white solid (51.9 mg, 76%); m.p. 111 – 113 °C; IR (KBr), cm^{-1} : 3367, 2962, 2927, 2873, 1693, 1562, 1521, 1459, 1399, 1370, 1313, 1181, 957, 891, 764, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.51 (s, 1H), 8.74 (s, 2H), 8.71 (d, J = 2.1 Hz, 1H), 2.58 (s, 3H), 2.52 (d, J = 7.6 Hz, 2H), 1.89 – 1.81 (m, 2H), 1.06 (t, J = 7.4 Hz,

3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.67, 148.47, 136.79, 135.73, 134.40, 133.11, 126.86, 121.68, 119.36, 118.89, 40.01, 21.10, 18.96, 13.74; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{15}\text{BrClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 341.0051, found 341.0053.



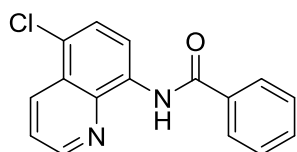
***N*-(5-chloroquinolin-8-yl)butanamide (4g)**

Obtained as a white solid (43.8 mg, 88%); m.p. 60 – 62 °C; IR (KBr), cm^{-1} : 3358, 2963, 2927, 1689, 1522, 1480, 1387, 1319, 1184, 958, 837, 787; ^1H NMR (300 MHz, CDCl_3) δ 9.73 (s, 1H), 8.82 (dd, J = 4.2, 1.5 Hz, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.53 (dd, J = 8.5, 1.5 Hz, 1H), 7.59 – 7.50 (m, 2H), 2.53 (t, J = 7.5 Hz, 2H), 1.91– 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.67, 148.51, 138.86, 133.81, 133.32, 127.21, 125.86, 124.01, 122.21, 116.28, 40.09, 19.02, 13.75; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{14}\text{ClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 249.0789, found 249.0791.



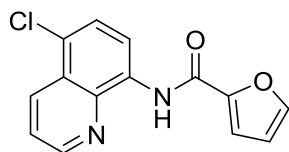
***N*-(5-chloroquinolin-8-yl)pivalamide (4h)**

Obtained as a white solid (43.6 mg, 83%); m.p. 85 – 87 °C; IR (KBr), cm^{-1} : 3371, 2963, 2922, 2867, 2832, 1677, 1525, 1483, 1386, 1366, 1320, 1178, 1143, 947, 835, 783, 749; ^1H NMR (300 MHz, CDCl_3) δ 10.20 (s, 1H), 8.83 (dd, J = 4.0, 1.3 Hz, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.51 (dd, J = 8.5, 1.5 Hz, 1H), 7.61 – 7.50 (m, 2H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.20, 148.61, 139.23, 133.90, 133.24, 127.17, 125.80, 123.91, 122.18, 116.06, 40.30, 27.63; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{ClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 263.0916, found 263.0952.



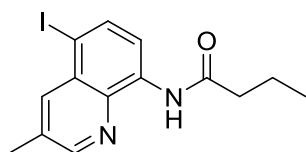
***N*-(5-chloroquinolin-8-yl)benzamide (4i)**

Obtained as a white solid (46.4 mg, 82%); m.p. 137 – 139 °C; IR (KBr), cm^{-1} : 3336, 2920, 1676, 1525, 1478, 1386, 1323, 1262, 939, 835, 786, 692; ^1H NMR (300 MHz, CDCl_3) δ 10.69 (s, 1H), 8.89 (dd, J = 4.9, 3.4 Hz, 2H), 8.59 (dd, J = 8.5, 1.5 Hz, 1H), 8.07 (dd, J = 7.8, 1.6 Hz, 2H), 7.67 – 7.53 (m, 5H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.17, 148.61, 139.11, 134.73, 133.71, 133.24, 131.88, 128.73, 127.16, 127.13, 125.81, 124.34, 122.26, 116.30; HRMS (ESI) calculated for $\text{C}_{16}\text{H}_{12}\text{ClN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 283.0633, found 283.0635.



***N*-(5-chloroquinolin-8-yl)furan-2-carboxamide (4j)**

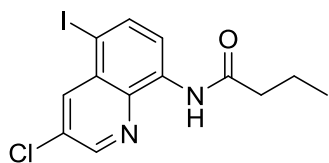
Obtained as a white solid (47.4 mg, 87%); m.p. 167 – 169 °C; IR (KBr), cm^{-1} : 3336, 2926, 1682, 1590, 1533, 1475, 1390, 1325, 1271, 1008, 948, 923, 873, 831, 787, 772, 759; ^1H NMR (300 MHz, CDCl_3) δ 10.70 (s, 1H), 8.91 (dd, J = 4.2, 1.5 Hz, 1H), 8.80 (d, J = 8.4 Hz, 1H), 8.56 (dd, J = 8.5, 1.5 Hz, 1H), 7.65 – 7.55 (m, 3H), 7.30 (dd, J = 3.5, 0.7 Hz, 1H), 6.59 (dd, J = 3.5, 1.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.28, 148.84, 148.12, 144.61, 139.13, 133.43, 133.33, 127.19, 125.97, 124.60, 122.39, 116.50, 115.33, 112.49; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{10}\text{ClN}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 273.0425, found 273.0430.



***N*-(5-iodoquinolin-8-yl)butanamide (4a')**

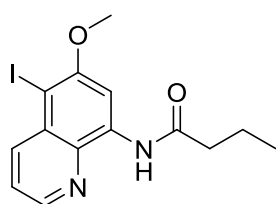
Obtained as a white solid (59.5 mg, 84%); m.p. 138 – 140 °C; IR (KBr), cm^{-1} : 3338, 2967, 2923, 2869, 1686, 1514, 1466, 1357, 1318, 1195, 1081, 981, 881, 852, 678; ^1H NMR (300 MHz, CDCl_3) δ 9.76 (s, 1H), 8.59 (d, J = 1.8 Hz, 1H), 8.48 (d, J = 8.3 Hz, 1H), 8.10 (s, 1H), 8.02 (d, J = 8.3 Hz, 1H), 2.59 (s, 3H), 2.53 (t, J = 7.3 Hz, 2H), 1.90 – 1.78 (m, 2H), 1.05 (t, J = 7.4

Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.64, 150.33, 139.20, 138.08, 137.00, 135.20, 132.80, 129.10, 116.74, 88.43, 40.05, 18.96, 18.66, 13.74; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{IN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 355.0302, found 355.0308.



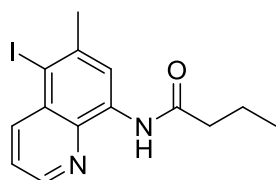
***N*-(5-iodo-3-chloroquinolin-8-yl)butanamide (4b')**

Obtained as a white solid (65.9 mg, 88%); m.p. 147 – 149 °C; IR (KBr), cm^{-1} : 3348, 2960, 2927, 2867, 1671, 1561, 1528, 1464, 1350, 1316, 1180, 1103, 964, 885, 844; ^1H NMR (300 MHz, CDCl_3) δ 9.57 (s, 1H), 8.61 (d, J = 2.0 Hz, 1H), 8.53 (d, J = 8.3 Hz, 1H), 8.32 (d, J = 2.0 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 2.53 (t, J = 7.5 Hz, 2H), 1.90 – 1.77 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.75, 147.84, 139.53, 138.83, 136.69, 135.47, 131.05, 129.97, 117.91, 87.25, 40.08, 18.94, 13.75; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{ClIN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 374.9756, found 374.9765.



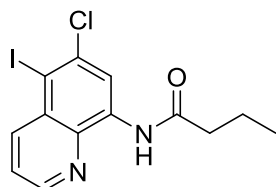
***N*-(5-iodo-4-methoxyquinolin-8-yl)butanamide (4c')**

Obtained as a white solid (70.3 mg, 95%); m.p. 136 – 138 °C; IR (KBr), cm^{-1} : 3357, 2957, 2936, 2854, 1687, 1616, 1526, 1461, 1396, 1369, 1203, 1083, 897, 852, 772; ^1H NMR (300 MHz, CDCl_3) δ 9.88 (s, 1H), 8.80 (s, 1H), 8.60 (dd, J = 4.1, 1.3 Hz, 1H), 8.41 (dd, J = 8.6, 1.3 Hz, 1H), 7.46 (dd, J = 8.6, 4.2 Hz, 1H), 4.06 (s, 3H), 2.56 (t, J = 7.5 Hz, 2H), 1.92 – 1.79 (m, 2H), 1.07 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.77, 157.06, 145.89, 139.11, 136.07, 134.58, 130.10, 123.20, 103.41, 76.40, 56.91, 39.92, 18.69, 13.67; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{IN}_2\text{O}_2$ $[\text{M} + \text{H}]^+$ 371.0251, found 371.0257.



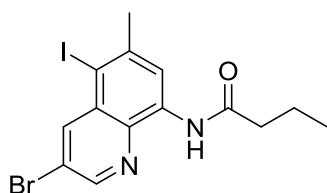
***N*-(5-iodo-6-methylquinolin-8-yl)butanamide (4d')**

Obtained as a white solid (65.9 mg, 93%); m.p. 108 – 110 °C; IR (KBr), cm^{-1} : 3352, 2961, 2924, 1686, 1523, 1466, 1395, 1363, 1186, 895, 781; ^1H NMR (300 MHz, CDCl_3) δ 9.77 (s, 1H), 8.80 (s, 1H), 8.69 (d, J = 4.1 Hz, 1H), 8.50 (dd, J = 8.6, 1.3 Hz, 1H), 7.49 (dd, J = 8.6, 4.2 Hz, 1H), 2.70 (s, 3H), 2.54 (t, J = 7.5 Hz, 2H), 1.91 – 1.79 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.68, 147.58, 142.32, 140.54, 137.43, 134.34, 129.87, 122.97, 118.45, 95.14, 40.08, 30.21, 18.98, 13.75; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{IN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 355.0302, found 355.0309.



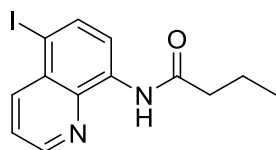
***N*-(5-iodo-6-chloroquinolin-8-yl)butanamide (4e')**

Obtained as a white solid (67.4 mg, 90%); m.p. 169 – 171 °C; IR (KBr), cm^{-1} : 3338, 2961, 2920, 1695, 1560, 1511, 1460, 1358, 1341, 1315, 1121, 869, 805, 779, 685; ^1H NMR (300 MHz, CDCl_3) δ 9.75 (s, 1H), 8.93 (s, 1H), 8.70 (dd, J = 4.2, 1.5 Hz, 1H), 8.43 (dd, J = 8.6, 1.5 Hz, 1H), 7.51 (dd, J = 8.6, 4.2 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.90 – 1.78 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.80, 148.38, 141.61, 139.63, 137.18, 135.60, 131.02, 123.93, 117.34, 92.84, 40.06, 18.93, 13.74; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{13}\text{ClIN}_2\text{O}$ $[\text{M} + \text{H}]^+$ 374.9756, found 374.9759.



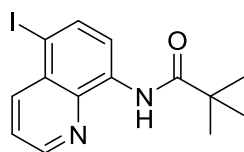
***N*-(5-iodo-3-bromo-6-methylquinolin-8-yl)butanamide (4f')**

Obtained as a white solid (78.8 mg, 91%); m.p. 132 – 134 °C; IR (KBr), cm^{-1} : 3362, 2960, 2920, 2851, 1686, 1552, 1515, 1457, 1390, 1365, 1305, 1185, 947, 925, 888, 750; ^1H NMR (300 MHz, CDCl_3) δ 9.54 (s, 1H), 8.79 (s, 1H), 8.65 (s, 2H), 2.69 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 1.90 – 1.78 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.70, 148.62, 143.96, 141.97, 135.48, 134.51, 130.93, 119.74, 118.77, 93.34, 40.07, 30.35, 18.93, 13.74; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{15}\text{BrIN}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 432.9407, found 432.9411.



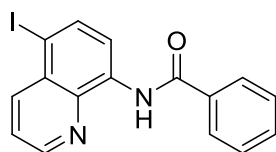
***N*-(5-iodoquinolin-8-yl)butanamide (4g')**

Obtained as a white solid (63.3 mg, 93%); m.p. 128 – 130 °C; IR (KBr), cm^{-1} : 3353, 2963, 2920, 1691, 1521, 1477, 1382, 1353, 951, 895, 853, 749; ^1H NMR (300 MHz, CDCl_3) δ 9.81 (s, 1H), 8.77 (d, J = 4.1 Hz, 1H), 8.57 (d, J = 8.5 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.53 (dd, J = 8.5, 4.2 Hz, 1H), 2.54 (t, J = 7.4 Hz, 2H), 1.93 – 1.77 (m, 2H), 1.06 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.67, 148.55, 140.56, 138.80, 138.17, 135.35, 129.42, 122.99, 117.67, 88.95, 40.08, 18.97, 13.75; HRMS (ESI) calculated for $\text{C}_{13}\text{H}_{14}\text{IN}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 341.0145, found 341.0151.



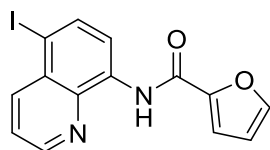
***N*-(5-iodoquinolin-8-yl)pivalamide (4h')**

Obtained as a white solid (66.6 mg, 94%); m.p. 88 – 90 °C; IR (KBr), cm^{-1} : 3363, 2960, 1684, 1518, 1478, 1357, 1315, 1275, 1261, 1143, 926, 837, 764, 750; ^1H NMR (300 MHz, CDCl_3) δ 10.26 (s, 1H), 8.78 (dd, J = 4.2, 1.5 Hz, 1H), 8.57 (d, J = 8.3 Hz, 1H), 8.35 (dd, J = 8.5, 1.5 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.52 (dd, J = 8.5, 4.2 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.18, 148.66, 140.50, 139.22, 138.13, 135.46, 129.38, 122.96, 117.49, 88.89, 40.32, 27.61; HRMS (ESI) calculated for $\text{C}_{14}\text{H}_{16}\text{IN}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 355.0302, found 355.0307.



***N*-(5-iodoquinolin-8-yl)benzamide (4i')**

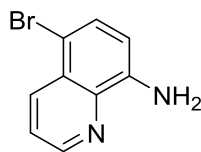
Obtained as a white solid (68.1 mg, 91%); m.p. 157 – 159 °C; IR (KBr), cm^{-1} : 3351, 2921, 2850, 1674, 1522, 1473, 1381, 1358, 1319, 1262, 906, 836, 785, 692; ^1H NMR (300 MHz, CDCl_3) δ 10.71 (s, 1H), 8.79 (dd, J = 4.2, 1.3 Hz, 1H), 8.69 (d, J = 8.3 Hz, 1H), 8.36 (dd, J = 8.5, 1.3 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.06 (dd, J = 7.7, 1.5 Hz, 2H), 7.61 – 7.49 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.33, 148.79, 140.70, 139.28, 138.27, 135.45, 134.82, 131.98, 129.60, 128.80, 127.25, 123.16, 117.84, 89.47; HRMS (ESI) calculated for $\text{C}_{16}\text{H}_{12}\text{IN}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 374.9989, found 374.9995.



***N*-(5-iodoquinolin-8-yl)furan-2-carboxamide (4j')**

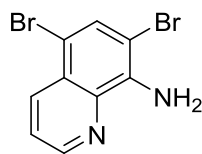
Obtained as a white solid (62.6 mg, 86%); m.p. 183 – 185 °C; IR (KBr), cm^{-1} : 3332, 2978, 2923, 1671, 1583, 1565, 1526, 1473, 1385, 1356, 1320, 1006, 902, 872, 832, 788, 765; ^1H NMR (300 MHz, CDCl_3) δ 10.74 (s, 1H), 8.83 (d, J = 3.4 Hz, 1H), 8.62 (d, J = 8.3 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 7.62 (s, 1H), 7.53 (dd, J = 8.5, 4.2 Hz, 1H), 7.30 (d, J = 3.4 Hz, 1H), 6.59 (d, J = 1.6 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.28, 148.93, 148.16, 144.63, 140.65,

139.16, 138.21, 135.09, 129.64, 123.20, 117.93, 115.38, 112.50, 89.67; HRMS (ESI) calculated for $C_{14}H_{10}IN_2O_2$ $[M + H]^+$ 364.9781, found 364.9787.



5-bromoquinolin-8-amine (5a)

Obtained as a slightly yellow solid (42.4 mg, 95%); m.p. 99 – 101 °C; R (KBr), cm^{-1} : 3421, 3324, 2920, 2850, 1611, 1501, 1464, 1356, 1262, 1122, 1031, 922, 819, 783; 1H NMR (300 MHz, $CDCl_3$) δ 8.77 (dd, J = 4.1, 1.5 Hz, 1H), 8.43 (dd, J = 8.6, 1.5 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.48 (dd, J = 8.5, 4.2 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 5.06 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.69, 143.94, 138.90, 135.35, 130.75, 127.69, 122.35, 110.09, 107.29; HRMS (ESI) calculated for $C_9H_8BrN_2$ $[M + H]^+$ 222.9865, found 222.9867.



3,5-dibromoquinolin-8-amine (5b)

Obtained as a yellow solid (37.4 mg, 62%); m.p. 119 – 120 °C; R (KBr), cm^{-1} : 3421, 2967, 2922, 1607, 1364, 1122, 867, 806, 785, 653; 1H NMR (300 MHz, $CDCl_3$) δ 8.74 (dd, J = 4.2, 1.5 Hz, 1H), 8.37 (dd, J = 8.5, 1.6 Hz, 1H), 7.78 (s, 1H), 7.48 (dd, J = 8.5, 4.2 Hz, 1H), 5.45 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.41, 142.13, 138.46, 135.56, 133.13, 126.72, 122.45, 106.82, 103.10; HRMS (ESI) calculated for $C_9H_7Br_2N_2$ $[M + H]^+$ 302.8956, found 302.8954.

Copies of ^1H and ^{13}C NMR spectra for the title compounds

