

Direct and Metal-free Oxidative Amination of sp^3 C-H Bonds for the Construction of 2-Hetarylquinazolin-4(3*H*)-ones

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Table of contents

1. General information.....	S2
2. General experimental procedures for the synthesis of 3.....	S2
3. Spectra data.....	S2
4. References.....	S13
5. ¹ H NMR and ¹³ C NMR spectra.....	S14

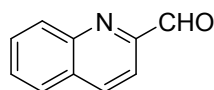
1. General information

2-Aminobenzamides¹ were prepared according to literature procedures. Other reagents were commercially available and were used without further purification. All reactions were monitored by thin-layer chromatography (TLC). Melting points were determined on an XD-4 digital micro melting point apparatus. IR spectra were recorded with an IR spectrophotometer VERTEX 70 FTIR (Bruker Optics). ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 400 (400 MHz) or 300 (300 MHz) spectrometer, using CDCl₃ as solvent and tetramethylsilane (TMS) as internal standard. HRMS spectra were determined on a Q-TOF6510 spectrograph (Agilent).

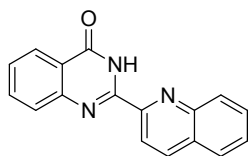
2. General experimental procedures for the synthesis of 3

A 25 mL flask equipped with a magnetic stirring bar was charged with substituted 2-aminobenzamides **1** (0.3 mmol), (2-azaaryl)methanes **2** (0.3 mmol), Ph₂PO₂H (0.3 mmol), TBAI (0.3 mmol) and TBHP (1.2 mmol) in DMSO (5 mL). The mixture was allowed to stir under air at 90 °C, 10 h. After that, the reaction was cooled to room temperature, filtered through a short silica gel column eluting with ethyl acetate. The filtrate was diluted with brine (60 mL) and extracted with ethyl acetate twice (2×30 mL). The combined organic layers were dried with MgSO₄ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to provide the desired product.

3. Spectra data

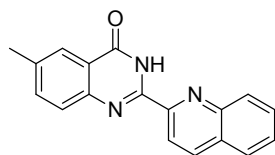


Quinoline-2-carbaldehyde²: white solid. ¹H NMR (CDCl₃, 400 MHz, ppm): δ 10.24 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.84-7.81 (m, 1H), 7.72-7.70 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 193.8, 152.6, 147.9, 137.4, 130.5, 130.4, 130.1, 129.2, 127.9, 117.4; HRMS calcd. for: C₁₀H₈NO [M+H]⁺ 158.0600, found 158.0600.



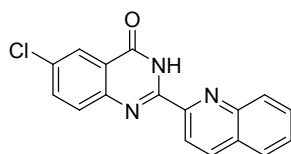
3a

2-(Quinolin-2-yl)quinazolin-4(3H)-one 3a³: white solid (76.2 mg, 93%). ¹H NMR (CDCl₃, 400 MHz, ppm): δ 11.21 (s, 1H), 8.67 (d, *J* = 8.5 Hz, 1H), 8.39 (t, *J* = 9.2 Hz, 2H), 8.18 (d, *J* = 8.3 Hz, 1H), 7.92 (t, *J* = 8.2 Hz, 2H), 7.83 (t, *J* = 7.6 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 161.4, 149.2, 149.0, 148.1, 146.8, 137.6, 134.6, 130.5, 129.7, 129.3, 128.3, 127.8, 127.5, 126.8, 122.7, 118.5; HRMS calcd. for: C₁₇H₁₂N₃O [M+H]⁺ 274.0975, found 274.0946.



3b

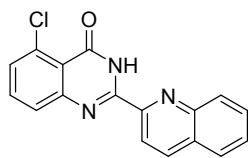
6-Methyl-2-(quinolin-2-yl)quinazolin-4(3H)-one 3b³: white solid (79.2 mg, 92%). ¹H NMR (CDCl₃, 400 MHz, ppm): δ 11.21 (s, 1H), 8.66 (d, *J* = 8.6 Hz, 1H), 8.37 (d, *J* = 8.6 Hz, 1H), 8.18 (t, *J* = 7.2 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 9.2 Hz, 2H), 7.67 (t, *J* = 7.6 Hz, 2H), 2.53 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 161.5, 148.3, 148.2, 147.1, 146.8, 138.0, 137.6, 136.0, 130.5, 129.7, 129.2, 128.2, 128.0, 127.7, 126.3, 122.4, 118.4, 21.4; HRMS calcd. for: C₁₈H₁₄N₃O [M+H]⁺ 288.1131, found 288.1129.



3c

6-Chloro-2-(quinolin-2-yl)quinazolin-4(3H)-one 3c³: yellow solid (71.8 mg, 78%). ¹H NMR (CDCl₃, 300 MHz, ppm): δ 11.26 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.39 (t, *J* = 6.0 Hz, 2H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.85-7.80 (m, 2H), 7.77 (dd, *J*₁ = 8.7 Hz, *J*₂ = 2.4 Hz, 1H), 7.69-7.64 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 160.4, 149.2, 147.8, 147.7, 146.8, 137.8, 135.0, 133.5, 130.6,

129.8, 129.7, 129.4, 128.4, 127.8, 126.3, 123.8, 118.4; HRMS calcd. for: C₁₇H₁₁ClN₃O [M+H]⁺ 308.0585, found 308.0582.



3d

5-Chloro-2-(quinolin-2-yl)quinazolin-4(3H)-one 3d: yellow solid (66.3 mg, 72%). Mp = 269-270 °C;

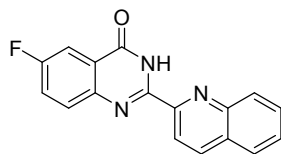
IR (neat, cm⁻¹): 3447, 3321, 1620, 1547, 1293, 1117, 950, 834, 811, 620; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 11.07 (s, 1H), 8.61 (d, *J* = 8.6 Hz, 1H), 8.37 (d, *J* = 8.6 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.92

(d, *J* = 8.2 Hz, 1H), 7.84-7.76 (m, 2H), 7.68-7.62 (m, 2H), 7.51 (dd, *J*₁ = 7.8 Hz, *J*₂ = 1.0 Hz, 1H); ¹³C

NMR (CDCl₃, 100 MHz, ppm): δ 159.5, 151.6, 149.5, 147.5, 146.8, 137.7, 134.5, 133.9, 130.6, 130.2,

129.8, 129.4, 128.4, 127.8, 127.5, 119.9, 118.4; HRMS calcd. for: C₁₇H₁₁ClN₃O [M+H]⁺ 308.0585,

found 308.0585.



3e

6-Fluoro-2-(quinolin-2-yl)quinazolin-4(3H)-one 3e: yellow solid (78.6 mg, 90%). Mp = 254-255 °C;

IR (neat, cm⁻¹): 3445, 3174, 3080, 1690, 1622, 1566, 1485, 1415, 1336, 1191, 1138, 929, 845, 761, 724, 625; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 11.16 (s, 1H), 8.56 (d, *J* = 8.6 Hz, 1H), 8.31 (d, *J* = 8.6 Hz,

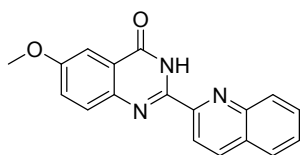
1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.97 (dd, *J*₁ = 8.4 Hz, *J*₂ = 3.0 Hz, 1H), 7.87-7.75 (m, 3H), 7.63-7.59 (m,

1H), 7.50-7.46 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 162.6 (d, *J* = 248.0 Hz, 1C), 160.6 (d, *J*

= 3.0 Hz, 1C), 148.3, 147.8, 146.7, 145.7, 137.6, 130.6 (d, *J* = 9.0 Hz, 1C), 129.6, 129.2, 128.3, 127.7,

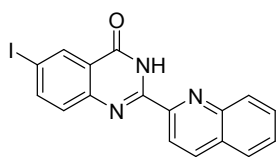
124.1 (d, *J* = 9.0 Hz, 1C), 123.1 (d, *J* = 23.0 Hz, 1C), 118.3, 112.0 (d, *J* = 24.0 Hz, 1C); HRMS calcd.

for: C₁₇H₁₁FN₃O [M+H]⁺ 292.0881, found 292.0881.



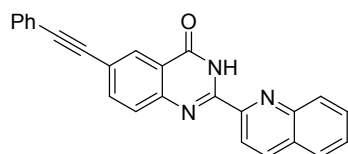
3f

6-Methoxy-2-(quinolin-2-yl)quinazolin-4(3H)-one 3f: white solid (72.7 mg, 80%). Mp = 240-241 °C; IR (neat, cm^{-1}): 3126, 3062, 2950, 2845, 1677, 1618, 1591, 1560, 1489, 1416, 1358, 1291, 1220, 1139, 1020, 868, 833, 758; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 11.21 (s, 1H), 8.60 (d, J = 8.6 Hz, 1H), 8.32 (d, J = 8.6 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.81-7.73 (m, 3H), 7.63 (t, J = 7.4 Hz, 1H), 7.40 (dd, J_1 = 8.9 Hz, J_2 = 2.9 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.3, 159.1, 148.2, 147.0, 146.8, 143.5, 137.5, 130.4, 129.8, 129.6, 129.1, 128.1, 127.7, 124.8, 123.5, 118.3, 106.3, 55.9; HRMS calcd. for: $\text{C}_{18}\text{H}_{14}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 304.1081, found 304.1083.



3g

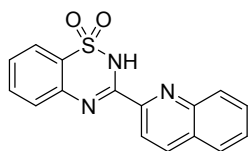
6-Iodo-2-(quinolin-2-yl)quinazolin-4(3H)-one 3g: yellow solid (80.2 mg, 67%). Mp = 299-300 °C; IR (neat, cm^{-1}): 3443, 3115, 1673, 1593, 1558, 1464, 1398, 829, 756; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 11.25 (s, 1H), 8.70 (d, J = 2.0 Hz, 1H), 8.62 (d, J = 8.6 Hz, 1H), 8.36 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.07 (dd, J_1 = 8.6 Hz, J_2 = 2.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.83-7.79 (m, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.59 (d, J = 8.6 Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 159.9, 149.5, 148.5, 147.7, 146.8, 143.4, 137.7, 135.7, 130.6, 129.9, 129.7, 129.4, 128.4, 127.8, 124.2, 118.4, 92.3, 92.2; HRMS calcd. for: $\text{C}_{17}\text{H}_{11}\text{IN}_3\text{O}$ $[\text{M}+\text{H}]^+$ 399.9941, found 399.9940.



3h

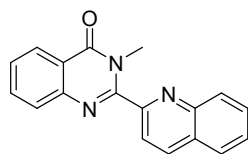
6-(Phenylethynyl)-2-(quinolin-2-yl)quinazolin-4(3H)-one 3h: yellow solid (106.3 mg, 95%). Mp =

264-265 °C; IR (neat, cm⁻¹): 3318, 3289, 3052, 2923, 2202, 1693, 1594, 1497, 1417, 1341, 1295, 1144, 915, 840, 756, 693, 621; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 11.21 (s, 1H), 8.65 (d, *J* = 8.6 Hz, 1H), 8.52 (d, *J* = 1.7 Hz, 1H), 8.35 (d, *J* = 8.6 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.90-7.87 (m, 2H), 7.84-7.78 (m, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.57-7.55 (m, 2H), 7.38-7.36 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 160.6, 149.4, 148.6, 147.9, 146.8, 137.6, 137.1, 131.7, 130.5, 130.1, 129.7, 129.4, 128.6, 128.4, 128.3, 127.7, 122.9, 122.8, 118.5, 91.5, 88.5; HRMS calcd. for: C₂₅H₁₆N₃O [M+H]⁺ 374.1288, found 374.1293.



3i

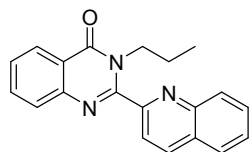
3-(Quinolin-2-yl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide 3i⁴: yellow solid (64.0 mg, 69%). ¹H NMR (CDCl₃, 300 MHz, ppm): δ 10.80 (s, 1H), 8.55 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 8.7 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.06 (dd, *J*₁ = 7.8 Hz, *J*₂ = 0.9 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.88-7.83 (m, 1H), 7.74-7.63 (m, 2H), 7.49-7.44 (m, 1H), 7.40 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 150.4, 146.6, 146.5, 138.4, 134.1, 133.2, 130.9, 129.9, 129.5, 129.0, 128.1, 127.0, 125.0, 122.3, 119.0, 117.4; HRMS calcd. for: C₁₆H₁₂N₃O₂S [M+H]⁺ 310.0645, found 310.0649.



3j

3-Methyl-2-(quinolin-2-yl)quinazolin-4(3H)-one 3j³: white solid (74.9 mg, 87%). ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.39 (d, *J* = 6.9 Hz, 2H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.97 (t, *J* = 10.3 Hz, 2H), 7.83 (t, *J* = 8.3 Hz, 3H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.54 (s, 1H), 3.72 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 162.6, 154.0, 153.1, 147.1, 147.0, 137.7, 134.3, 130.5, 129.8, 128.0, 127.7, 127.6, 127.5, 126.9, 121.3,

121.1, 33.6; HRMS calcd. for: C₁₈H₁₄N₃O [M+H]⁺ 288.1131, found 288.1170.



3k

3-Propyl-2-(quinolin-2-yl)quinazolin-4(3H)-one 3k: white solid (80.3 mg, 85%). Mp = 134-135 °C;

IR (neat, cm⁻¹): 3444, 3060, 2967, 2875, 1685, 1588, 1503, 1465, 1391, 1333, 1298, 1239, 1180, 1115,

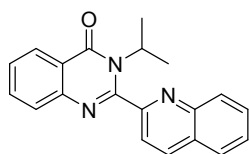
1080, 874, 832, 764, 693, 532; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.39 (d, *J* = 8.2 Hz, 2H), 8.16 (d, *J*

= 8.4 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.83-7.77 (m, 3H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.55 (q, *J* = 4.0 Hz,

1H), 4.28 (t, *J* = 7.7 Hz, 2H), 1.86 (q, *J* = 7.6 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 100

MHz, ppm): δ 162.3, 154.0, 153.4, 147.1, 146.9, 137.5, 134.2, 130.4, 129.8, 127.9, 127.7, 127.6, 127.4,

126.9, 121.6, 121.3, 47.1, 22.4, 11.2; HRMS calcd. for: C₂₀H₁₈N₃O [M+H]⁺ 316.1444, found 316.1452.



3l

3-Isopropyl-2-(quinolin-2-yl)quinazolin-4(3H)-one 3l: yellow solid (77.5 mg, 82%). Mp = 162-163

°C; IR (neat, cm⁻¹): 3443, 2973, 2927, 1669, 1554, 1465, 1353, 1289, 1173, 1075, 838, 770, 696; ¹H

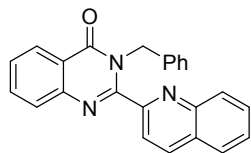
NMR (CDCl₃, 400 MHz, ppm): δ 8.39 (d, *J* = 8.4 Hz, 1H), 8.36-8.33 (m, 1H), 8.18 (d, *J* = 8.4 Hz, 1H),

7.94 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.82-7.79 (m, 1H), 7.76-7.75 (m, 2H), 7.68-7.64 (m,

1H), 7.54-7.50 (m, 1H), 4.46 (t, *J* = 6.8 Hz, 1H), 1.68 (d, *J* = 6.8 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz,

ppm): δ 162.6, 154.9, 153.9, 147.2, 146.6, 137.6, 134.1, 130.5, 129.9, 127.9, 127.8, 127.7, 127.3, 126.5,

122.5, 120.8, 54.4, 19.9; HRMS calcd. for: C₂₀H₁₈N₃O [M+H]⁺ 316.1444, found 316.1441.



3m

3-Benzyl-2-(quinolin-2-yl)quinazolin-4(3H)-one 3m: white solid (89.3 mg, 82%). Mp = 128-129 °C;

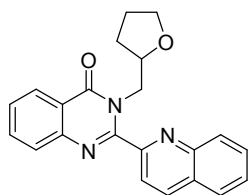
IR (neat, cm^{-1}): 3444, 3059, 1680, 1583, 1498, 1465, 1383, 1238, 1146, 1023, 970, 840, 774, 691; ^1H

NMR (CDCl_3 , 400 MHz, ppm): δ 8.44 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.83-7.79 (m, 3H), 7.67-7.55 (m, 3H), 7.10-7.03 (m, 3H), 6.84 (d, J = 7.1

Hz, 2H), 5.80 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 162.4, 153.7, 153.1, 146.9, 146.6, 137.2,

137.1, 134.5, 130.4, 129.6, 128.3, 128.0, 127.9, 127.7, 127.63, 127.58, 127.4, 127.31, 127.26, 121.6,

121.2, 47.2; HRMS calcd. for: $\text{C}_{24}\text{H}_{18}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 364.1444, found 364.1440.



3n

2-(Quinolin-2-yl)-3-((tetrahydrofuran-2-yl)methyl)quinazolin-4(3H)-one 3n: white solid (82.5 mg,

77%). Mp = 103-104 °C; IR (neat, cm^{-1}): 3427, 3063, 2959, 2853, 1664, 1558, 1467, 1383, 1333, 1236,

1150, 1062, 831, 775, 695; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 8.38 (q, J = 4.1 Hz, 2H), 8.14 (d, J =

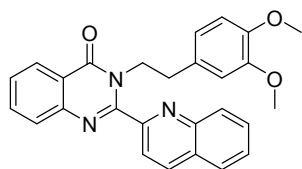
8.4 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.81-7.76 (m, 3H), 7.66-7.62 (m, 1H),

7.54-7.50 (m, 1H), 4.74-4.66 (m, 2H), 4.19-4.14 (m, 1H), 3.42-3.37 (m, 1H), 2.98 (q, J = 7.1 Hz, 1H),

1.92-1.85 (m, 1H), 1.65-1.59 (m, 1H), 1.49-1.46 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 162.5,

154.6, 154.2, 147.2, 146.4, 137.0, 134.3, 130.2, 129.5, 127.7, 127.6, 127.3, 127.0, 122.7, 121.2, 47.4,

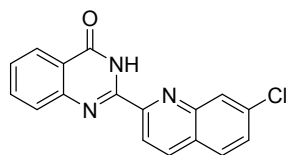
29.0, 25.5; HRMS calcd. for: $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 358.1550, found 358.1550.



3o

3-(3,4-Dimethoxyphenethyl)-2-(quinolin-2-yl)quinazolin-4(3H)-one 3o: white solid (94.4 mg, 72%).

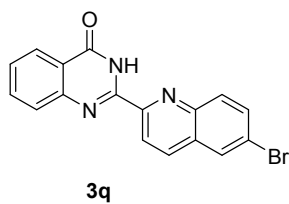
Mp = 184-185 °C; IR (neat, cm^{-1}): 3442, 3056, 2941, 2831, 1682, 1587, 1513, 1466, 1391, 1330, 1262, 1233, 1146, 1026, 831, 769, 697; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 8.43-8.41 (m, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.1 Hz, 1H), 7.83-7.77 (m, 3H), 7.68 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.59-7.55 (m, 1H), 6.62 (d, J = 8.1 Hz, 1H), 6.46 (dd, J_1 = 8.1 Hz, J_2 = 1.9 Hz, 1H), 6.20 (d, J = 1.8 Hz, 1H), 4.61 (t, J = 7.5 Hz, 2H), 3.81 (s, 3H), 3.34 (s, 3H), 3.12 (t, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 162.3, 153.9, 153.4, 148.9, 147.7, 147.1, 146.5, 137.3, 134.4, 130.8, 130.4, 129.6, 127.9, 127.8, 127.6, 127.5, 126.9, 121.7, 121.3, 120.8, 111.5, 111.2, 55.9, 55.2, 47.1, 34.6; HRMS calcd. for: $\text{C}_{27}\text{H}_{24}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 438.1812, found 438.1815.



3p

2-(7-Chloroquinolin-2-yl)quinazolin-4(3H)-one 3p: white solid (79.2 mg, 86%). Mp = 301-302 °C;

IR (neat, cm^{-1}): 3146, 1683, 1603, 1475, 1414, 1333, 1235, 1133, 941, 909, 846, 766, 683, 620; ^1H NMR (CDCl_3 , 300 MHz, ppm): δ 11.11 (s, 1H), 8.72 (d, J = 8.7 Hz, 1H), 8.41-8.34 (m, 2H), 8.18 (d, J = 2.1 Hz, 1H), 7.93-7.80 (m, 3H), 7.63-7.54 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz, ppm): δ 161.3, 149.1, 148.8, 147.2, 137.6, 136.6, 134.7, 129.4, 129.0, 128.6, 128.2, 127.8, 127.7, 126.9, 122.7, 118.9; HRMS calcd. for: $\text{C}_{17}\text{H}_{11}\text{ClN}_3\text{O}$ $[\text{M}+\text{H}]^+$ 308.0585, found 308.0589.



2-(6-Bromoquinolin-2-yl)quinazolin-4(3H)-one 3q: yellow solid (67.4 mg, 64%). Mp = 275-276 °C;

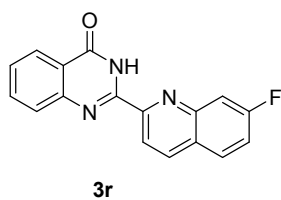
IR (neat, cm^{-1}): 3444, 3146, 2923, 2853, 1686, 1596, 1473, 1438, 1382, 1134, 888, 834, 765; ^1H NMR

(CDCl_3 , 400 MHz, ppm): δ 11.10 (s, 1H), 8.69 (d, J = 8.6 Hz, 1H), 8.39 (d, J = 7.8 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 2.0 Hz, 1H), 8.03 (d, J = 8.9 Hz, 1H), 7.89-7.80 (m, 3H), 7.57 (t, J = 7.2 Hz,

1H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.4, 149.0, 148.61, 148.56, 145.4, 136.6, 134.6, 134.1,

131.2, 130.3, 129.9, 128.3, 127.7, 126.8, 122.7, 122.5, 119.4; HRMS calcd. for: $\text{C}_{17}\text{H}_{11}\text{BrN}_3\text{O}$ $[\text{M}+\text{H}]^+$

352.0080, found 352.0079.



2-(7-Fluoroquinolin-2-yl)quinazolin-4(3H)-one 3r: white solid (69.0 mg, 79%). Mp = 247-248 °C;

IR (neat, cm^{-1}): 3444, 3146, 3090, 1683, 1598, 1511, 1476, 1425, 1336, 1236, 1205, 1134, 982, 919,

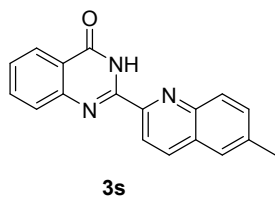
848, 765; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 11.11 (s, 1H), 8.69 (d, J = 8.6 Hz, 1H), 8.37-8.34 (m,

2H), 7.93-7.87 (m, 2H), 7.83-7.73 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44-7.42 (m, 1H); ^{13}C NMR

(CDCl_3 , 100 MHz, ppm): δ 164.8 (d, J = 251.0 Hz, 1C), 161.1, 148.7, 148.5, 147.8, 147.7, 137.7, 134.7,

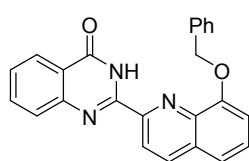
129.9 (d, J = 10.0 Hz, 1C), 128.0 (d, J = 21.0 Hz, 1C), 126.8, 126.4, 122.6, 119.1, 118.8, 118.1, 113.3

(d, J = 21.0 Hz, 1C); HRMS calcd. for: $\text{C}_{17}\text{H}_{11}\text{FN}_3\text{O}$ $[\text{M}+\text{H}]^+$ 292.0881, found 292.0876.



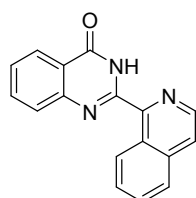
2-(6-Methylquinolin-2-yl)quinazolin-4(3H)-one 3s: white solid (77.5 mg, 90%). Mp = 251-252 °C;

IR (neat, cm^{-1}): 3440, 3321, 1681, 1603, 1434, 1379, 1330, 1111, 880, 832, 749; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 11.26 (s, 1H), 8.73 (d, $J = 8.6$ Hz, 1H), 8.39 (dd, $J_1 = 7.9$ Hz, $J_2 = 1.4$ Hz, 1H), 8.29 (d, $J = 8.6$ Hz, 1H), 8.07 (d, $J = 8.6$ Hz, 1H), 7.99 (d, $J = 8.1$ Hz, 1H), 7.85-7.83 (m, 1H), 7.67-7.62 (m, 2H), 7.57-7.55 (m, 1H), 2.58 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.1, 149.3, 148.4, 146.5, 145.4, 138.9, 137.1, 134.8, 133.0, 129.5, 129.3, 127.8, 127.7, 126.9, 126.6, 122.5, 118.8, 21.8; HRMS calcd. for: $\text{C}_{18}\text{H}_{14}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 288.1131, found 288.1128.



3t

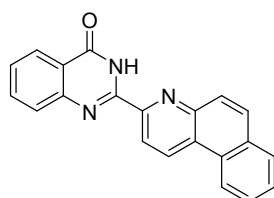
2-(8-(Benzyloxy)quinolin-2-yl)quinazolin-4(3H)-one 3t: yellow solid (85.3 mg, 75%). Mp = 168-169 $^{\circ}\text{C}$; IR (neat, cm^{-1}): 3521, 3439, 3029, 2913, 1680, 1592, 1557, 1458, 1379, 1330, 1242, 1143, 1099, 989, 959, 889, 844, 766, 734, 692, 620; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 11.25 (s, 1H), 8.66 (d, $J = 8.6$ Hz, 1H), 8.38 (d, $J = 7.8$ Hz, 1H), 8.29 (d, $J = 8.6$ Hz, 1H), 7.87-7.78 (m, 2H), 7.58 (q, $J = 7.3$ Hz, 3H), 7.48-7.41 (m, 4H), 7.36 (t, $J = 7.3$ Hz, 1H), 7.11 (d, $J = 7.2$ Hz, 1H), 5.44 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.4, 154.6, 149.3, 149.1, 146.9, 139.1, 137.5, 136.7, 134.5, 130.6, 128.8, 128.6, 128.2, 128.1, 127.4, 127.0, 126.8, 122.7, 119.7, 119.0, 111.1, 70.8; HRMS calcd. for: $\text{C}_{24}\text{H}_{18}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 380.1394, found 380.1388.



3u

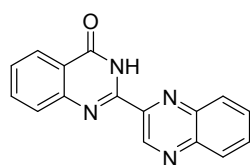
2-(Isoquinolin-1-yl)quinazolin-4(3H)-one 3u⁵: white solid (72.1 mg, 88%). ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 10.15 (s, 1H), 10.16 (t, $J = 5.0$ Hz, 1H), 8.57 (d, $J = 5.5$ Hz, 1H), 8.39 (dd, $J_1 = 7.9$ Hz,

$J_2 = 1.3$ Hz, 1H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.90-7.87 (m, 1H), 7.84-7.75 (m, 4H), 7.57-7.53 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.4, 150.2, 148.9, 145.7, 140.5, 137.7, 134.4, 130.6, 129.1, 128.5, 128.2, 127.7, 127.3, 127.2, 126.6, 124.7, 122.4; HRMS calcd. for: $\text{C}_{17}\text{H}_{12}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 274.0975, found 274.0982.



3v

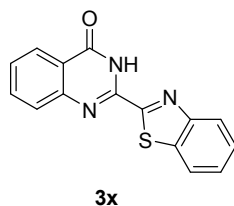
2-(Benzo[f]quinolin-3-yl)quinazolin-4(3H)-one 3v: white solid (79.5 mg, 82%). Mp = 278-279 °C; IR (neat, cm^{-1}): 3443, 3329, 2922, 1684, 1605, 1468, 1434, 1338, 1134, 873, 832, 743; ^1H NMR (CDCl_3 , 300 MHz, ppm): δ 11.23 (s, 1H), 9.15 (d, $J = 8.7$ Hz, 1H), 8.81 (d, $J = 8.7$ Hz, 1H), 8.70-8.67 (m, 1H), 8.40 (dd, $J_1 = 8.1$ Hz, $J_2 = 1.2$ Hz, 1H), 8.09-7.96 (m, 3H), 7.91 (dd, $J_1 = 8.1$ Hz, $J_2 = 0.6$ Hz, 1H), 7.85 (dd, $J_1 = 7.2$ Hz, $J_2 = 1.5$ Hz, 1H), 7.79-7.68 (m, 2H), 7.57 (td, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz, ppm): δ 161.4, 149.3, 149.0, 147.4, 147.0, 134.6, 132.3, 132.2, 132.1, 129.2, 128.9, 128.23, 128.18, 127.7, 127.6, 127.4, 127.1, 126.8, 123.2, 122.6, 119.0; HRMS calcd. for: $\text{C}_{21}\text{H}_{14}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 324.1131, found 324.1135.



3w

2-(Quinoxalin-2-yl)quinazolin-4(3H)-one 3w: yellow solid (67.4 mg, 82%). ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 10.85 (s, 1H), 10.04 (s, 1H), 8.40 (d, $J = 7.6$ Hz, 1H), 8.24-8.16 (m, 2H), 7.95-7.83 (m, 4H), 7.60 (t, $J = 7.4$ Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 161.1, 148.7, 147.6, 143.7, 143.6, 142.5, 140.5, 134.8, 131.7, 131.2, 129.6, 128.5, 128.2, 126.9, 122.8; HRMS calcd. for: $\text{C}_{16}\text{H}_{11}\text{N}_4\text{O}$

[M+H]⁺ 275.0927, found 275.0928.



2-(Benzo[d]thiazol-2-yl)quinazolin-4(3H)-one 3x³: white solid (71.1 mg, 85%). ¹H NMR (CDCl₃, 400 MHz, ppm): δ 10.35 (s, 1H), 8.37 (d, *J* = 7.5 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.87-7.82 (m, 2H), 7.60-7.50 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 161.2, 160.6, 153.0, 148.5, 145.5, 136.8, 134.9, 128.2, 128.1, 127.2, 127.1, 127.0, 124.4, 122.9, 122.2; HRMS calcd. for: C₁₅H₁₀N₃OS [M+H]⁺ 280.0539, found 280.0548.

4. References

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- (5) Wu, X.-F.; He, L.; Neumann, H.; Beller, M. *Chem. - Eur. J.* **2013**, 19, 12635.

5. ^1H NMR and ^{13}C NMR spectra

