SUPPORTING INFORMATION

A Convenient and Scalable Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-one Derivatives and their Anticancer Activity

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1.1 General Experimental Details:

All solvents and reagents were used, as received from the suppliers. TLC was performed on Merck Kiesel gel 60, F254 plates with the layer thickness of 0.25 mm. Melting points were determined on a Fisher John's melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer RX-1 FT-IR system. ^1H NMR spectral data were collected at 300, 400 & 500 MHz, while ^{13}C NMR were recorded at 75, 100 and 125 MHz. ^1H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s- singlet; d- doublet; dd- doublet of doublet; t- triplet; q- quartet; m- multiplet), number of protons and coupling constants. ^{13}C NMR chemical shifts are expressed in ppm. HRMS (ESI) spectral data were collected using ORBITRAP High Resolution Mass Spectrometer.

1.2 General Procedure for Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-ones (3a-3aa)

Indiumtribromide (0.5 mol %) was added to a solution of 2-amino benzanilide or 2-amino-5-chloro benzamide (1 mmol) and desired aldehydes (1 mmol) in acetonitrile (3mL). The mixture was stirred at room temperature for the specified period of time. The progress of the reaction was monitored by TLC. After completion of reaction, solvent was evaporated at reduced pressure, and solid was partitioned between ethyl acetate (15.0 mL) and water (15.0 mL), and transferred to a separatory funnel. The organic layer was washed with water, and brine, dried over anhydrous Na_2SO_4 (s) and concentrated *in vacuo*. The residue was purified by recrystallization from CH_2Cl_2 /Hexane to afford the corresponding pure 2,3-dihydroquinazolin-4(1*H*)-ones (**3a-3aa**) as solids with excellent yields.

1.3 Analytical data for all the products (3a-3aa)

2,3-Diphenyl-2,3-dihydroquinazolin-4(1H)-one (3a).¹

Yield: 94 %; White solid; m.p. 204-206 °C; IR (neat): $\nu_{\max}$, 3287, 2884, 1387, 772 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 8.01 (d, J = 7.8 Hz, 1H), 7.38 – 7.26 (m, 8H), 7.18 (d, J = 7.6 Hz, 3H), 6.87 (t, J = 7.5 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.08 ppm (s, 1H); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6+\text{CDCl}_3$): δ 161.5, 145.2, 139.6, 139.3, 132.4, 127.3, 127.1, 127.0, 126.9, 125.4, 125.1, 124.9, 116.5, 114.4, 113.6, 72.3 ppm; MS (ESI): m/z : 301 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{20}\text{H}_{17}\text{ON}_2$: 301.13354 $[\text{M}+\text{H}]^+$; found: 301.13271.

3-Phenyl-2-(*p*-tolyl)-2,3-dihydroquinazolin-4(1H)-one (3b).¹

Yield: 96 %; White solid; m.p. 214-216 °C; IR (neat): $\nu_{\max}$, 3289, 2885, 1380, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 7.88 (d, J = 7.7 Hz, 1H), 7.38 – 7.15 (m, 7H), 7.05 (d, J = 7.8 Hz, 2H), 6.74 (dd, J = 16.7, 7.6 Hz, 3H), 6.08 (s, 1H), 2.27 ppm (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6+\text{CDCl}_3$): δ 162.3, 145.5, 140.2, 137.3, 136.8, 132.9, 128.2, 127.9, 127.6, 125.8, 125.7, 125.5, 117.3, 115.2, 114.1, 73.0, 20.2 ppm; MS (ESI): m/z : 315 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{21}\text{H}_{19}\text{ON}_2$: 315.14919 $[\text{M}+\text{H}]^+$; found: 315.14846.

2-(4-Isopropylphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3c).²

Yield: 97 %; White solid; m.p. 200-202 °C; IR (neat): $\nu_{\max}$, 3285, 2882, 1373, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 7.96 (d, J = 7.5 Hz, 1H), 7.31 – 7.16 (m, 8H), 7.10 (d, J = 8.0 Hz, 2H), 6.82 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.07 (s, 1H), 2.83 (m, 1H), 1.18 ppm (d, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6+\text{CDCl}_3$): δ 161.6, 147.6, 145.2, 139.8, 136.8, 132.3, 127.3, 127.0, 125.5, 125.3, 125.1, 124.9, 116.5, 114.4,

113.6, 72.2, 32.2, 22.5 ppm; MS (ESI): m/z : 343 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{23}H_{23}ON_2$: 343.18049 $[M+H]^+$; found: 343.17959.

2-(4-Methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3d).³

Yield: 98 %; White solid; m.p. 204-205 °C; IR (neat): $\nu_{\max}$, 3288, 2851, 1382, 772 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 8.01 (dd, J = 7.8, 1.1 Hz, 1H), 7.72 (dd, J = 5.8, 3.3 Hz, 1H), 7.53 (dd, J = 5.6, 3.3 Hz, 1H), 7.27 (dd, J = 9.9, 4.6 Hz, 4H), 7.18 (t, J = 3.2 Hz, 2H), 6.87 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 8.7 Hz, 2H), 6.62 (d, J = 8.0 Hz, 1H), 6.05 (s, 1H), 3.74 ppm (s, 3H); ^{13}C NMR (125 MHz, $DMSO-d_6+CDCl_3$): δ 160.8, 157.5, 144.9, 139.2, 131.8, 130.9, 126.8, 126.3, 126.2, 124.6, 124.3, 115.8, 113.8, 113.1, 111.8, 71.2, 53.3 ppm; MS (ESI): m/z : 331 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{21}H_{19}O_2N_2$: 331.14410 $[M+H]^+$; found: 331.14335.

2-(3,4-Dimethoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3e).⁴

Yield: 95 %; Pale yellow solid; m.p. 243-245 °C; IR (neat): $\nu_{\max}$, 3290, 2852, 1385, 771 cm^{-1} ; 1H NMR (300 MHz, $DMSO-d_6$): δ 7.82 (d, J = 7.0 Hz, 1H), 7.25 (m, , 6H), 7.10 (s, 1H), 6.98 (s, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.76 (d, J = 6.9 Hz, 2H), 6.09 (s, 1H), 3.75 ppm (d, J = 14.3 Hz, 6H); ^{13}C NMR (75 MHz, $DMSO-d_6+CDCl_3$): δ 161.4, 147.3, 147.1, 145.1, 139.5, 137.7, 132.1, 127.1, 126.6, 124.9, 124.6, 119.2, 117.7, 116.2, 113.4, 109.2, 108.7, 71.7, 54.1 ppm; MS (ESI): m/z : 361 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{22}H_{21}O_3N_2$: 361.15467 $[M+H]^+$; found: 361.15278.

3-Phenyl-2-(3,4,5-trimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3f).⁴

Yield: 96 %; White solid; m.p. 193-195 °C; IR (neat): $\nu_{\max}$, 3289, 2881, 1389, 772 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J

= 7.8 Hz, 1H), 7.32 (dd, J = 15.6, 7.9 Hz, 3H), 7.20 (dd, J = 7.2, 5.2 Hz, 3H), 6.91 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.55 (s, 2H), 6.04 (s, 1H), 4.76 (s, 1H), 3.75 ppm (d, J = 22.5 Hz, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ 163.1, 153.1, 145.5, 140.4, 135.2, 133.8, 130.9, 128.8, 127.0, 126.8, 120.5, 119.5, 116.6, 114.7, 103.9, 74.6, 60.7, 55.9 ppm; MS (ESI): m/z : 391 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{23}\text{H}_{23}\text{O}_4\text{N}_2$: 391.16523 $[\text{M}+\text{H}]^+$; found: 391.16481.

2-(4-Fluorophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3g).¹

Yield: 96 %; White solid; m.p. 236-238 °C; IR (neat): ν_{max} , 3290, 2882, 1388, 772 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 8.02 (d, J = 7.9 Hz, 1H), 7.36 – 7.29 (m, 5H), 7.18 (dd, J = 13.3, 7.3 Hz, 3H), 6.94 (t, J = 9.0 Hz, 3H), 6.65 (d, J = 8.1 Hz, 1H), 6.12 (s, 1H), 4.76 ppm (s, 1H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6+\text{CDCl}_3$): δ 162.3, 161.1, 144.9, 139.2, 135.1, 132.2, 127.7, 127.1, 126.6, 124.9, 124.7, 116.3, 113.7, 113.4, 113.3, 71.2 ppm; MS (ESI): m/z : 319 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{20}\text{H}_{16}\text{ON}_2\text{F}$: 319.12412 $[\text{M}+\text{H}]^+$; found: 319.12329.

2-(2,4-Dichlorophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3h).⁵

Yield: 94 %; White solid; m.p. 190-192 °C; IR (neat): ν_{max} , 3288, 2879, 1386, 772 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 8.02 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.35 (dd, J = 20.1, 4.8 Hz, 5H), 7.23 – 7.16 (m, 3H), 6.88 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 6.39 (s, 1H), 5.23 ppm (s, 1H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6+\text{CDCl}_3$): δ 161.9, 144.6, 139.3, 135.0, 133.8, 132.9, 131.6, 128.6, 128.1, 127.9, 127.3, 126.4, 125.8, 125.4, 117.5, 114.4, 114.1, 69.2 ppm; MS (ESI): m/z 369 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{ON}_2\text{Cl}_2$: 369.05560 $[\text{M}+\text{H}]^+$; found, 369.05501.

2-(4-Bromophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3i).¹

Yield: 97 %; White solid; m.p. 222-224 °C; IR (neat): $\nu_{\max}$, 3288, 2883, 1384, 772 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.88 (d, J = 7.7 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.1 Hz, 1H), 7.25 – 7.15 (m, 6H), 6.78 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.58 (d, J = 2.1 Hz, 1H), 6.05 ppm (s, 1H); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6 + \text{CDCl}_3$): δ 162.4, 145.3, 140.1, 139.1, 133.3, 130.9, 128.3, 128.0, 125.9, 125.8, 121.8, 120.3, 118.0, 115.5, 114.4, 72.8 ppm; MS (ESI): m/z : 381 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{20}\text{H}_{16}\text{ON}_2\text{Br}$: 379.04405 $[\text{M}+\text{H}]^+$; found: 379.04354.

2-([1,1'-Biphenyl]-4-yl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3j).⁶

Yield: 96 %; White solid; m.p. 202-204 °C; IR (neat): $\nu_{\max}$, 3291, 2885, 1385, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 7.84 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 2.8 Hz, 2H), 7.40 (d, J = 2.4 Hz, 2H), 7.31 (d, J = 7.6 Hz, 3H), 7.20 (dd, J = 11.5, 7.0 Hz, 6H), 6.85 – 6.52 (m, 3H), 6.08 ppm (s, 1H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6 + \text{CDCl}_3$): δ 162.5, 145.5, 140.4, 140.2, 139.3, 138.9, 133.1, 128.3, 128.1, 128.0, 127.9, 126.8, 126.5, 126.3, 126.2, 125.8, 120.2, 117.7, 114.3, 73.0 ppm; MS (ESI): m/z : 377 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{26}\text{H}_{21}\text{ON}_2$: 377.16484 $[\text{M}+\text{H}]^+$; found, 377.16450.

4-(4-Oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)benzonitrile (3k).⁴

Yield: 93 %; White solid; m.p. 204-206 °C; IR (neat): $\nu_{\max}$, 3287, 2882, 2227, 1393, 771 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 7.83 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 0.8 Hz, 1H), 7.57 (d, J = 4.3 Hz, 3H), 7.27 (dd, J = 23.9, 6.9 Hz, 5H), 6.79 – 6.71 (m, 2H), 6.19 ppm (d, J = 2.9 Hz, 1H); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6 + \text{CDCl}_3$): δ 162.0, 145.2, 145.0, 140.0, 133.3, 131.5, 128.3, 127.9, 126.8, 125.9, 125.4, 118.0, 117.6, 115.4, 114.4,

111.4, 72.4 ppm; MS (ESI): m/z : 326 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{21}H_{16}ON_3$: 326.12879 $[M+H]^+$; found: 326.12824.

2-(Naphthalen-1-yl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3l).

Yield: 94 %; White solid; m.p. 242-244 °C; IR (neat): $\nu_{\max}$, 3291, 2883, 1379, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 8.53 (d, J = 8.2 Hz, 1H), 7.96 – 7.72 (m, 4H), 7.66 – 7.45 (m, 3H), 7.35 (t, J = 7.6 Hz, 1H), 7.26 – 7.10 (m, 4H), 7.07 (d, J = 6.7 Hz, 1H), 6.96 (s, 1H), 6.74 ppm (dd, J = 17.9, 7.8 Hz, 2H); ^{13}C NMR (125 MHz, $\text{DMSO-}d_6+\text{CDCl}_3$): δ 162.6, 145.2, 139.3, 134.0, 133.0, 132.8, 132.5, 129.0, 128.2, 127.5, 127.3, 127.2, 125.5, 125.1, 124.6, 123.7, 122.8, 119.6, 116.8, 114.4, 113.9, 71.0 ppm; MS (ESI): m/z : 351 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{24}H_{19}ON_2$: 351.14919 $[M+H]^+$; found: 351.14716.

6-Chloro-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (3m).⁷

Yield: 97 %; White solid; m.p. 248-250 °C; IR (neat): $\nu_{\max}$, 3300, 2876, 1648, 1362, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 8.18 (s, 1H), 7.73 (d, J = 2.4 Hz, 1H), 7.67 (s, 1H), 7.57 (d, J = 6.3 Hz, 2H), 7.40 (d, J = 2.9 Hz, 2H), 7.18 (dd, J = 8.6, 2.2 Hz, 1H), 6.72 (dd, J = 23.1, 8.5 Hz, 1H), 5.83 ppm (s, 1H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6+\text{CDCl}_3$): δ 162.1, 145.4, 139.3, 131.8, 128.2, 127.7, 127.2, 125.9, 125.7, 120.7, 115.0, 66.4 ppm; MS (ESI): m/z : 259 $[M+H]^+$; HRMS (ESI): m/z : calcd for $C_{14}H_{12}ON_2\text{Cl}$: 259.06327 $[M+H]^+$; found: 259.06265.

6-Chloro-2-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (3n).⁷

Yield: 95 %; White solid; m.p. 250-252 °C; IR (neat): $\nu_{\max}$, 3313, 2853, 1659, 1363, 772 cm^{-1} ; ^1H NMR (500 MHz, $\text{DMSO-}d_6$): δ 8.16 (s, 1H), 7.71 (d, J = 5.4 Hz, 1H), 7.59 (s, 1H), 7.43 (d, J = 6.5 Hz, 2H), 7.20 (d, J = 6.4 Hz, 2H), 6.75 (d, J = 8.4

Hz, 1H), 5.78 (s, 1H), 2.36 ppm (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 161.5, 145.1, 136.3, 131.3, 129.5, 127.4, 125.4, 125.2, 120.0, 114.7, 114.5, 65.6, 27.7 ppm; MS (ESI): m/z : 273 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{15}\text{H}_{14}\text{ON}_2\text{Cl}$: 273.07892 $[\text{M}+\text{H}]^+$; found: 273.07687.

6-Chloro-2-(4-isopropylphenyl)-2,3-dihydroquinazolin-4(1H)-one (3o).

Yield: 96 %; Pale yellow solid; m.p. 225-227 °C; IR (neat): ν_{max} , 3293, 2881, 1651, 1361, 772 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 8.25 (s, 1H), 7.91 (s, 1H), 7.49 (d, $J = 8.0$ Hz, 1H), 7.34 – 7.24 (m, 4H), 6.61 (d, $J = 8.6$ Hz, 1H), 5.86 (s, 1H), 5.30 (s, 1H), 3.01 – 2.89 (m, 1H), 1.27 ppm (d, $J = 7.0$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 162.4, 148.8, 145.7, 136.6, 132.0, 126.2, 126.0, 125.4, 121.0, 115.2, 115.0, 66.7, 32.6, 22.9 ppm; MS (ESI): m/z : 301 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{17}\text{H}_{18}\text{ON}_2\text{Cl}$: 301.11022 $[\text{M}+\text{H}]^+$; found: 301.10953.

6-Chloro-2-(4-methoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3p).⁷

Yield: 98 %; White solid; m.p. 220-222 °C; IR (neat): ν_{max} , 3308, 2884, 1662, 1358, 772 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 8.24 (s, 1H), 7.92 (s, 1H), 7.72 (d, $J = 3.2$ Hz, 1H), 7.51 (d, $J = 8.7$ Hz, 2H), 6.96 (d, $J = 8.7$ Hz, 2H), 6.62 (d, $J = 8.5$ Hz, 1H), 5.84 (s, 1H), 3.85 ppm (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 161.7, 158.4, 145.3, 131.4, 131.1, 126.9, 125.3, 120.2, 114.8, 114.6, 112.2, 65.6, 53.7 ppm; MS (ESI): m/z : 289 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{15}\text{H}_{14}\text{O}_2\text{N}_2\text{Cl}$: 289.07383 $[\text{M}+\text{H}]^+$; found: 289.07325.

6-Chloro-2-(3,4-dimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3q).

Yield: 96 %; White solid; m.p. 232-234 °C; IR (neat): ν_{max} , 3349, 2876, 1676, 1351, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ

8.06 (s, 1H), 7.96 (s, 1H), 7.64 (d, $J = 2.3$ Hz, 1H), 7.19 (d, $J = 2.5$ Hz, 1H), 7.16 (s, 1H), 6.92 (d, $J = 6.7$ Hz, 1H), 6.77 (d, $J = 8.6$ Hz, 1H), 5.74 (s, 1H), 3.85 ppm (d, $J = 4.7$ Hz, 6H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 161.6, 147.8, 147.3, 145.2, 131.4, 129.5, 127.1, 125.2, 120.1, 117.9, 114.8, 109.4, 109.0, 65.7, 54.2 ppm; MS (ESI): m/z : 319 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{16}\text{H}_{16}\text{O}_3\text{N}_2\text{Cl}$: 319.08440 $[\text{M}+\text{H}]^+$; found: 319.08377.

6-Chloro-2-(3,4,5-trimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3r).⁹

Yield: 95 %; White solid; m.p. 240-242 °C; IR (neat): ν_{max} , 3315, 2878, 1640, 1347, 772 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 8.18 (s, 1H), 7.63 (s, 1H), 7.21 (dd, $J = 8.6, 2.1$ Hz, 1H), 6.84 (s, 2H), 6.79 (d, $J = 8.6$ Hz, 1H), 5.78 (s, 1H), 3.86 (s, 6H), 3.81 ppm (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 162.7, 152.3, 145.7, 137.4, 134.5, 132.4, 126.3, 121.8, 115.5, 115.3, 103.4, 67.3, 59.7, 55.2 ppm; MS (ESI): m/z : 349 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{17}\text{H}_{18}\text{O}_4\text{N}_2\text{Cl}$: 349.09496 $[\text{M}+\text{H}]^+$; found: 349.09428.

6-Chloro-2-(4-fluorophenyl)-2,3-dihydroquinazolin-4(1H)-one (3s).⁷

Yield: 94 %; White solid; m.p. 249-251 °C; IR (neat): ν_{max} , 3318, 2882, 1646, 1336, 772 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ 8.13 (s, 1H), 7.89 (s, 1H), 7.53 (dd, $J = 8.6, 5.4$ Hz, 1H), 7.19 – 7.04 (m, 4H), 6.75 (d, $J = 8.6$ Hz, 1H), 5.79 ppm (s, 1H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6 + \text{CDCl}_3$): δ 162.5, 161.4, 144.9, 135.3, 131.4, 127.4, 125.1, 120.0, 114.7, 113.7, 113.4, 64.8 ppm; MS (ESI): m/z : 277 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{14}\text{H}_{11}\text{ON}_2\text{ClF}$: 277.05385 $[\text{M}+\text{H}]^+$; found, 277.05335.

6-Chloro-2-(2,4-dichlorophenyl)-2,3-dihydroquinazolin-4(1H)-one (3t).

Yield: 93 %; White solid; m.p. 218-220 °C; IR (neat): ν_{max} , 3316, 2881, 1662, 1357, 772 cm^{-1} ; ^1H NMR (300 MHz,

DMSO-*d*₆): δ 7.78 (s, 1H), 7.59(s,1H), 7.55 (s, 1H), 7.43 (d, *J* = 1.9 Hz, 1H), 7.31 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.21 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.23 ppm (s, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆+CDCl₃): δ 162.8, 145.5, 135.9, 134.4, 132.9, 132.6, 129.2, 128.7, 127.0, 126.6, 122.0, 116.0, 115.3, 63.1 ppm; MS (ESI): *m/z*: 329 [M+H]⁺; HRMS (ESI): *m/z*: calcd for C₁₄H₁₀ON₂Cl₃: 326.98532 [M+H]⁺; found: 326.98487.

2-(4-Bromophenyl)-6-chloro-2,3-dihydroquinazolin-4(1*H*)-one (3u).⁸

Yield: 96 %; White solid; m.p. 205-207 °C; IR (neat): $\nu_{\max}$, 3315, 2883, 1653, 1356, 772 cm⁻¹; ¹H NMR (300 MHz, DMSO-*d*₆): δ 8.28 (s, 1H), 7.63 (s, 1H), 7.49 (dd, *J* = 22.1, 8.4 Hz, 4H), 7.18 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 5.79 ppm (s, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆+CDCl₃): δ 162.8, 145.5, 138.7, 132.7, 130.9, 128.3, 126.6, 122.2, 122.1, 115.6, 115.5, 66.6 ppm; MS(ESI): *m/z* 339 [M+H]⁺; HRMS (ESI): *m/z*: calcd for C₁₄H₁₁ON₂BrCl: 336.97378 [M+H]⁺; found, 336.97340.

2-([1,1'-Biphenyl]-4-yl)-6-chloro-2,3-dihydroquinazolin-4(1*H*)-one (3v).⁶

Yield: 95 %; White solid; m.p. 250-252 °C; IR (neat): $\nu_{\max}$, 3310, 2882, 1646, 1358, 773 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.31 (d, *J* = 8.2 Hz, 1H), 7.77 (s, 1H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.66 – 7.56 (m, 5H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.19 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 1H), 5.87 ppm (s, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆+CDCl₃): δ 162.6, 145.7, 140.9, 139.2, 138.4, 133.7, 132.3, 127.9, 126.8, 126.2, 125.9, 124.5, 121.5, 115.4, 115.3, 66.7 ppm; MS (ESI): *m/z*: 335 [M+H]⁺; HRMS (ESI): *m/z*: calcd for C₂₀H₁₆ON₂Cl: 335.09457 [M+H]⁺; found: 335.09401.

4-(6-Chloro-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)benzonitrile (3w).

Yield: 93 %; Pale yellow solid; m.p. 234-236 °C; IR (neat): $\nu_{\max}$, 3377, 2915, 2225, 1678, 1368, 772 cm⁻¹; ¹H NMR (300

MHz, DMSO- d_6): δ 8.21 (s, 1H), 8.06 (s, 1H), 7.75 – 7.67 (m, 4H), 7.20 (d, J = 8.6 Hz, 1H), 6.75 (d, J = 10.3 Hz, 1H), 5.87 ppm (s, 1H); ^{13}C NMR (75 MHz, DMSO- d_6 + CDCl_3): δ 162.4, 145.9, 145.3, 132.7, 131.6, 127.2, 126.4, 121.7, 117.7, 115.8, 115.5, 111.5, 65.7 ppm; MS (ESI): m/z : 284 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{15}\text{H}_{11}\text{ON}_3\text{Cl}$: 284.05852 $[\text{M}+\text{H}]^+$; found: 284.05658.

6-Chloro-2-(naphthalen-1-yl)-2,3-dihydroquinazolin-4(1H)-one (3x).

Yield: 95 %; White solid; m.p. 183-185 °C; IR (neat): ν_{max} , 3326, 2882, 1645, 1334, 772 cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6): δ 8.55 (d, J = 8.9 Hz, 1H), 8.23 (s, 1H), 7.99 – 7.88 (m, 2H), 7.80 – 7.73 (m, 2H), 7.59 – 7.49 (m, 3H), 7.19 (dd, J = 8.6, 2.4 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 6.50 ppm (s, 1H); ^{13}C NMR (125 MHz, DMSO- d_6 + CDCl_3): δ 161.6, 145.4, 132.9, 132.1, 131.2, 128.9, 127.8, 126.9, 125.1, 124.4, 124.4, 124.1, 123.4, 122.7, 119.8, 114.7, 114.4, 64.5 ppm; MS (ESI): m/z : 309 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{18}\text{H}_{14}\text{ON}_2\text{Cl}$: 309.07892 $[\text{M}+\text{H}]^+$; found, 309.07645.

6-Chloro-2-(4-nitrophenyl)-2,3-dihydroquinazolin-4(1H)-one (3y).⁷

Yield: 94 %; Yellow solid; m.p. 218-220 °C; IR (neat): ν_{max} , 3270, 2923, 1660, 1347, 772 cm^{-1} ; ^1H NMR (300 MHz, DMSO- d_6): δ 8.38 (s, 1H), 8.21 (d, J = 7.9 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.68 (s, 1H), 7.19 (d, J = 8.5 Hz, 1H), 6.76 (d, 1H), 5.92 ppm (s, 1H); ^{13}C NMR (75 MHz, DMSO- d_6 + CDCl_3): δ 162.7, 147.4, 147.4, 145.1, 132.9, 127.4, 126.7, 123.0, 122.4, 115.8, 115.6, 65.8 ppm; MS (ESI): m/z : 304 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{14}\text{H}_{11}\text{O}_3\text{N}_3\text{Cl}$: 304.04835 $[\text{M}+\text{H}]^+$; found: 304.04685.

2-Butyl-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3z).

Yield: 75%; White solid; m.p. 121-123 °C; IR (neat): $\nu_{\max}$, 3298, 2955, 2929, 2859, 1640, 1585, 1520, 1438, 749, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ 7.80 (s, 1H), 7.56 (d, J = 7.8 Hz, 2H), 7.46 (d, J = 7.4 Hz, 1H), 7.35 (t, J = 7.9 Hz, 3H), 7.26 – 7.23 (m, 2H), 7.14 (t, J = 7.4 Hz, 1H), 6.70 (t, J = 7.7 Hz, 1H), 1.32 – 1.20 (m, 2H), 0.94 – 0.86 (m, 4H), 0.81 ppm (t, J = 5.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 167.5, 148.8, 137.7, 132.7, 129.0, 127.1, 124.4, 120.5, 117.4, 116.7, 116.1, 77.4, 33.1, 31.1, 22.4, 13.8 ppm; MS (ESI): m/z : 281 $[\text{M}+\text{H}]^+$.

2-Pentyl-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (3aa).

Yield: 79%; Pale yellow solid; m.p. 110-112 °C; IR (neat): $\nu_{\max}$, 3295, 2955, 2929, 2859, 1642, 1586, 1521, 1438, 749, 692 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ 7.82 (s, 1H), 7.55 (dd, J = 8.5, 1.0 Hz, 2H), 7.46 (d, J = 7.1 Hz, 1H), 7.37 – 7.33 (m, 3H), 7.26 – 7.22 (m, 2H), 7.15 – 7.12 (m, 1H), 6.69 (t, J = 7.4 Hz, 1H), 2.32 (t, J = 7.5 Hz, 2H), 1.65 – 1.59 (m, 2H), 1.33 – 1.30 (m, 4H), 0.89 ppm (t, J = 5.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 167.5, 148.8, 137.7, 132.6, 128.9, 127.1, 124.4, 120.5, 117.4, 116.8, 116.2, 77.2, 33.8, 31.1, 24.3, 22.2, 13.8 ppm; MS (ESI): m/z 295 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z : calcd for $\text{C}_{19}\text{H}_{23}\text{ON}_2$: 295.18049 $[\text{M}+\text{H}]^+$; found: 295.18022.

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1.5 ^1H and ^{13}C NMR Spectra of Compounds 3a-3y:

¹H and ¹³C NMR spectra of Imine intermediate (II)

1.6 Cytotoxicity evaluation

Cytotoxicity evaluation of the compounds was done *in vitro* by measurement of growth inhibition of tumor cell lines in 96 well plates using the MTT assay which is based on the cell-mediated reduction of tetrazolium salt to water insoluble formazan crystals using doxorubicin as standard. The cytotoxicity was assessed against a panel of four different human tumor cell lines: A549 derived from human alveolaradenocarcinoma epithelial cells (ATCC No. CCL-185), HeLa derived from human cervical cancer cells (ATCC No. CCL-2), MCF-7 derived from human breast adenocarcinoma cells (ATCC No. HTB-22) and DU-145 derived from human prostate cancer cells (ATCC No. HTB-81) were obtained from American Type Culture Collection, Manassas, VA, USA. The IC₅₀ values (50% inhibitory concentration) were calculated from the plotted absorbance data for the dose–response curves. The IC₅₀ values (in μM) were expressed as the means ± SD of three independent experiments.

Table 3. *In vitro* cytotoxicity evaluation of compounds **3a** – **3y**

Compounds ($\mu\text{g mL}^{-1}$)	IC ₅₀ values (in μM) ^a			
	A549 (Lung cancer)	MCF7 (Breast cancer)	HeLa (Cervical cancer)	DU145 (Prostate cancer)
3a	21.5 $\pm$ 0.22	– ^b	22.4 $\pm$ 0.32	– ^b
3b	25.2 $\pm$ 0.32	– ^b	22.4 $\pm$ 0.26	– ^b
3c	– ^b	– ^b	– ^b	– ^b
3d	– ^b	82.4 $\pm$ 0.52	– ^b	80.4 $\pm$ 0.48
3e	– ^b	– ^b	– ^b	– ^b
3f	19.7 $\pm$ 0.18	– ^b	18.7 $\pm$ 0.19	– ^b
3g	– ^b	– ^b	– ^b	– ^b
3h	20.6 $\pm$ 0.21	50.1 $\pm$ 0.48	18.3 $\pm$ 0.32	60.2 $\pm$ 0.12
3i	– ^b	– ^b	– ^b	– ^b
3j	38.6 $\pm$ 0.42	– ^b	34.8 $\pm$ 0.43	– ^b
3k	28.9 $\pm$ 0.32	15.0 $\pm$ 0.24	25.8 $\pm$ 0.25	12.1 $\pm$ 0.21
3l	38.5 $\pm$ 0.24	24.3 $\pm$ 0.18	34.8 $\pm$ 0.34	21.3 $\pm$ 0.13
3m	12.5 $\pm$ 0.18	44.2 $\pm$ 0.42	10.7 $\pm$ 0.26	61.8 $\pm$ 0.52
3n	13.9 $\pm$ 0.12	12.7 $\pm$ 0.26	11.2 $\pm$ 0.18	11.4 $\pm$ 0.24
3o	10.5 $\pm$ 0.08	6.0 $\pm$ 0.16	8.8 $\pm$ 0.15	4.1 $\pm$ 0.11
3p	– ^b	12.0 $\pm$ 0.14	– ^b	9.6 $\pm$ 0.22
3q	22.5 $\pm$ 0.22	9.9 $\pm$ 0.26	20.1 $\pm$ 0.17	7.2 $\pm$ 0.08
3r	32.9 $\pm$ 0.18	14.5 $\pm$ 0.32	31.2 $\pm$ 0.27	11.7 $\pm$ 0.16
3s	46.9 $\pm$ 0.26	17.4 $\pm$ 0.33	44.6 $\pm$ 0.21	14.3 $\pm$ 0.40
3t	20.9 $\pm$ 0.24	12.9 $\pm$ 0.15	19.1 $\pm$ 0.25	10.4 $\pm$ 0.21
3u	8.9 $\pm$ 0.18	11.9 $\pm$ 0.21	7.8 $\pm$ 0.14	9.8 $\pm$ 0.16
3v	– ^b	9.6 $\pm$ 0.09	– ^b	8.1 $\pm$ 0.27
3w	41.3 $\pm$ 0.32	8.8 $\pm$ 0.12	39.2 $\pm$ 0.29	7.9 $\pm$ 0.20
3x	7.9 $\pm$ 0.15	8.2 $\pm$ 0.22	6.3 $\pm$ 0.09	5.1 $\pm$ 0.19
3y	14.1 $\pm$ 0.21	10.4 $\pm$ 0.36	14.05 $\pm$ 0.42	9.1 $\pm$ 0.13
Doxorubicin (Standard)	0.1 $\pm$ 0.04	0.1 $\pm$ 0.08	0.09 $\pm$ 0.02	0.06 $\pm$ 0.04

^a Results are expressed as the means $\pm$ SD of three independent experiments.^b No activity.