Supplementary Information

Design, synthesis and antibacterial evaluation of some novel 3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline] -2,4'(3'*H*)-dione derivatives

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EXERIMENTAL

General

Melting points were obtained in open capillary tubes and were measured on an electro-thermal 9200 apparatus. Mass spectra were recorded on a Shimadzu QP 1100 BX mass spectrometer. The IR spectra were recorded on KBr pellets on a Shimadzu IR-470 spectrophotometer. ^1H and ^{13}C NMR spectra were determined on a Bruker 300 DRX Avance instrument at 300 and 75 MHz. Elemental analysis for C, H and N were performed using a Heraus CHN rapid analyzer.

General procedure for preparation of 3'-(phenylamino)-1'*H*- spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (3a-m)

A mixture of isatoic anhydride **1** (1 mmol), isatin **2** (1 mmol), phenyl hydrazine **3** (1 mmol), 0.3 g (0.6 mmol) alum, and 10 ml EtOH in a 50 ml flask was stirred at reflux for time period as indicated in Table 1. After completion of the reaction (monitored by TLC, ethylacetate/n-hexane, 1:1), 25 ml EtOH was added to the reaction mixture, and recrystallized from ethanol to afford pure product.

Spectral data for Products:

3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (4a):

yellow powder (92%); mp: 174-176 °C. IR (KBr): ν_{max} = 3296, 3067, 1736, 1656, 1613 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.67-7.92 (15H, m, H-Ar, 2NH), 10.45 (1H, s, NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.7, 110.5, 110.8, 113.5, 113.9, 114.4, 117.9, 119.7, 122.2, 125.6, 127.7, 127.9, 128.7, 131.1, 134.4, 143.3, 146.7, 148.9, 165.6, 175.8 ppm; MS: m/z (%)= 356(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{N}_4\text{O}_2$: C, 70.77; H, 4.53; N, 15.72%. Found: C, 70.71; H, 4.48; N, 15.64%.

5-bromo-3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (4b):

yellow powder (97%); mp: **172-174** °C. IR (KBr): $\nu_{\max}$ = 3295, 1736, 1657, 1610 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.69-8.02 (14H, m, H-Ar, 2NH), 10.59 (1H, s, NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.7, 112.4, 113.5, 113.8, 114.4, 118.1, 119.9, 127.7, 128.7, 130.1, 133.8, 134.5, 142.6, 146.5, 148.7, 175.4 ppm; MS: m/z (%)= 434(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{15}\text{BrN}_4\text{O}_2$: C, 57.95; H, 3.47; N, 12.87%. Found: C, 57.89; H, 3.41; N, 12.82%.

1-methyl-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4c):

yellow powder (97%); mp: **259-261** °C. IR (KBr): $\nu_{\max}$ = 3453, 3232, 3257, 1721, 1658, 1605 cm^{-1} ; ^1H NMR (CDCl_3) δ = 3.10 (3H, s, CH_3), 6.66-7.87(15H, m, H-Ar, 2NH) ppm; ^{13}C NMR (CDCl_3) δ = 56.5, 78.5, 109.3, 113.5, 114.0, 114.5, 118.1, 119.7, 122.9, 125.2, 127.3, 127.7, 128.7, 131.2, 134.4, 144.6, 146.6, 148.8, 165.5, 174.1 ppm; MS: m/z (%)= 370(M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_4\text{O}_2$: C, 71.34; H, 4.90; N, 15.13%. Found: C, 71.29; H, 4.82; N, 15.07%.

1-benzyl-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4d):

yellow powder (97%); mp: **138-140** °C. IR (KBr): $\nu_{\max}$ = 3299, 2923, 1728, 1662, 1613 cm^{-1} ; ^1H NMR (CDCl_3) δ = 4.77(1H, d, $^3J_{\text{HH}}$ =15.0, CH), 5.00(1H, d, $^3J_{\text{HH}}$ =15.0, CH), 6.72-8.12(20H, m, H-Ar, 2NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.7, 110.0, 113.7, 114.5, 118.1, 119.9, 125.6, 127.8, 128.7, 129.0, 131.1, 134.5, 135.9, 143.6, 146.7, 174.4 ppm; MS: m/z (%)= 446(M^+). Anal. Calcd for $\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_2$: C, 75.32; H, 4.97; N, 12.55%. Found: C, 75.25; H, 4.91; N, 12.46%.

5-nitro-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4e):

yellow powder (97%); mp: **188-190** °C. IR (KBr): $\nu_{\max}$ = 3297, 2924, 2854, 1744, 1658, 1615 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.69-8.42(14H, m, H-Ar, 2NH), 10.45 (1H, s, NH) ppm; MS: m/z (%)= 401(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{15}\text{N}_5\text{O}_4$: C, 62.84; H, 3.77; N, 17.45%. Found: C, 62.79; H, 3.71; N, 17.40%. (Due to very low solubility of the product 4e, we cannot report the ^{13}C NMR data for this product).

5-bromo-1-methyl-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4f):

yellow powder (85%); mp: **178-180** °C. IR (KBr): $\nu_{\max}$ = 3295, 3019, 1729, 1655, 1608 cm^{-1} ; ^1H NMR (CDCl_3) δ = 3.10(3H, s, CH_3), 6.67-8.00(14H, m, H-Ar, 2NH) ppm; MS: m/z (%)= 448(M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{17}\text{BrN}_4\text{O}_2$: C, 58.81; H, 3.81; N, 12.47%. Found: C, 58.75; H, 3.83; N, 12.41%. (Due to very low solubility of the product 4f, we cannot report the ^{13}C NMR data for this product).

5-bromo-1-ethyl-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4g):

yellow powder (93%); mp: 244-246 °C. IR (KBr): $\nu_{\max}$ = 3319, 3253, 1716, 1654, 1605 cm^{-1} ; ^1H NMR (CDCl_3) δ = 0.96-1.23(3H, m, CH_3), 3.45-3.66(2H, m, CH_2), 6.66-8.03(14H, m, H-Ar, 2NH) ppm; MS: m/z (%)= 462(M^+). Anal. Calcd for $\text{C}_{23}\text{H}_{19}\text{BrN}_4\text{O}_2$: C, 59.62; H, 4.13; N, 12.09%. Found: C, 59.54; H, 4.05; N, 12.01%. (Due to very low solubility of the product 4g, we cannot report the ^{13}C NMR data for this product).

1-methyl-5-nitro-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4h):

yellow powder (90%); mp: **257-259** °C. IR (KBr): $\nu_{\max}$ = 3297, 2944, 1741, 1661, 1610 cm^{-1} ; ^1H NMR (CDCl_3) δ = 3.20(3H, s, CH_3), 6.70-8.46 (14H, m, H-Ar, 2NH) ppm; ^{13}C NMR (CDCl_3) δ = 27.0, 78.0, 109.9, 113.3, 113.9, 114.7, 118.7, 120.0, 120.5, 127.9, 128.3, 128.8, 134.7, 142.8, 146.1, 148.3 ppm; MS: m/z (%)= 415(M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{17}\text{N}_5\text{O}_4$: C, 63.61; H, 4.12; N, 16.86%. Found: C, 63.54; H, 4.05; N, 16.77%.

1-ethyl-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4i):

yellow powder (60%); mp: **283-285** °C. IR (KBr): $\nu_{\max}$ = 3314, 3250, 1708, 1654, 1605 cm^{-1} ; ^1H NMR (CDCl_3) δ = 1.03-1.23(3H, m, CH_3), 3.65-3.67(2H, m, CH_2), 6.46-7.92 (15H, m, H-Ar, 2NH) ppm; MS: m/z (%)= 384(M^+). Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2$: C, 71.86; H, 5.24; N, 14.57%. Found: C, 71.79; H, 5.18; N, 14.52%. (Due to very low solubility of the product 4i, we cannot report the ^{13}C NMR data for this product).

5-bromo-5'-chloro-3'-(phenylamino)-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione (4j):

yellow powder (87%); mp: **188-190** °C. IR (KBr): $\nu_{\max}$ = 3292, 1737, 1663, 1609 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.70-8.13(13H, m, H-Ar, 2NH), 10.67(1H, s, NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.5, 112.5, 113.5, 113.9, 115.2, 116.5, 120.0, 121.9, 126.7, 128.8, 129.6, 134.0, 134.2, 142.6, 145.3, 148.4, 164.2, 175.2 ppm; MS: m/z (%)= 468(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{14}\text{BrClN}_4\text{O}_2$: C, 53.70; H, 3.00; N, 11.93%. Found: C, 53.63; H, 3.04; N, 11.86%.

5'-chloro-3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (4k):

yellow powder (90%); mp: 268-270 °C. IR (KBr): $\nu_{\max}$ = 3294, 1733, 1666, 1610 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.68-8.04(14H, m, H-Ar, 2NH), 10.51(1H, s, NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.5, 110.6, 113.5, 116.5, 119.8, 125.7, 126.6, 128.7, 131.3, 134.1, 145.6, 148.7, 163.2, 174.5 ppm; MS: m/z (%)= 390(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{15}\text{ClN}_4\text{O}_2$: C, 64.54; H, 3.87; N, 14.34 %. Found: C, 64.48; H, 3.77; N, 14.27%.

5'-chloro-5-nitro-3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (4l):

yellow powder (94%); mp: **198-200** °C. IR (KBr): $\nu_{\max}$ = 3302, 174.7, 1668, 1613 cm^{-1} ; ^1H NMR (CDCl_3) δ = 6.68-8.44(13H, m, H-Ar, 2NH), 11.28(1H, s, NH) ppm; ^{13}C NMR (CDCl_3) δ = 78.2, 110.9, 113.3, 120.2, 126.8, 128.5, 128.8, 145.1 ppm; MS: m/z (%)= 435(M^+). Anal. Calcd for $\text{C}_{21}\text{H}_{14}\text{ClN}_5\text{O}_4$: C, 57.87; H, 3.24; N, 16.07%. Found: C, 57.79; H, 3.15; N, 16.02%.

5'-chloro-1-methyl-3'-(phenylamino)-1'*H*-spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (4m):

yellow powder (88%); mp: **171-173** °C. IR (KBr): $\nu_{\max}$ = 3302, 1727, 1657, 1608 cm^{-1} ; ^1H NMR (CDCl_3) δ = 3.11(3H, s, CH_3), 6.68-7.99(14H, m, H-Ar, 2NH) ppm; ^{13}C NMR (CDCl_3) δ = 26.6, 78.3, 109.5, 113.4, 115.4, 116.6, 119.8, 121.8, 123.0, 126.7, 128.7, 131.4, 134.1, 138.6, 145.5, 148.5 ppm; MS: m/z (%)= 404(M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{17}\text{ClN}_4\text{O}_2$: C, 65.27; H, 4.23; N, 13.84%. Found: C, 65.17; H, 4.14; N, 13.75%.

13C (175) NMR