Supporting Information

“On water” one-pot synthesis of quaternary centered 3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-ones

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EXPERIMENTAL SECTION

General Information: The starting materials and reagents were purchased from various commercial sources and used without further purification. Several N-Substituted isatins 1h, 1i, 1j, 1l, 1n, 1o, 1p, 1q and 1r were synthesized by following the previously reported procedure. The reactions were performed in reaction vessels at room temperature. ACME silica gel (60-120 mesh) was used for column chromatography. Analytical thin-layer chromatography (TLC) was performed on pre-coated TLC plates with silica gel 60-F254 plates and visualized by UV-light. $^1$H NMR and $^{13}$C NMR spectra were recorded, using tetramethylsilane (TMS) in the solvent of CDCl$_3$+DMSO as the internal standard on a 300, 400, 500 MHz spectrometer ($^1$H NMR: TMS at 0.00 ppm, CDCl$_3$ at 7.26 ppm; $^{13}$C NMR: CDCl$_3$ at 77.0 ppm, DMSO at 39.43). Chemical shifts (δ) were recorded in ppm with respect to TMS as an internal standard and coupling constants are quoted in Hertz (Hz). Mass spectra were recorded on a mass spectrometer by the electrospray ionization (ESI) and the data acquired in positive ionization mode. HRMS spectra were determined on TOF type mass analyzer.

Typical Procedure: An oven-dried flask was charged with stir bar, isatin (73 mg, 0.5 mmol), TMSCN (0.5 mmol) and were stirred vigorously in water (2.0 mL) for 10 min. Then NaN$_3$ (0.6 mmol), Py.HCl (0.01 mmol) were added and the mixture was stirred at room temperature until complete conversion takes place as indicated by the colour change. The resulting reaction mixture was extracted with 2 N HCl (2 x 200 mL) and the combined water phase was then extracted with ethyl acetate (2 x 100 mL). The combined organics were anhydridified with Na$_2$SO$_4$ and dried under vacuum to afford crude light yellow solid product, which was analytically pure by simple workup procedure. To remove color, the product is treated with a mixture of ethyl
acetate (30%) and hexane (70%), and run down a short plug of silica gel to yield a white solid 4 (Table 2).

3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4a, Table 2; entry 1)

Isolated yield: 106 mg, 98%; white solid, mp 216-218 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.4 (s, 1H, NH), 7.27 (d, 2H $J = 7.5$ Hz), 7.22 (bs, 1H), 6.99-6.89 (m, 2H), 2.54 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 71.7, 109.5, 121.3, 124.0, 128.5, 129.2, 141, 173.9. MS (ESI): (m/z) = 240 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_7$N$_5$O$_2$Na = 240.0497, found = 240.0502.

5-chloro-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4b, Table 2; entry 2)

Isolated yield: 118 mg, 94%; white solid, mp 175-178 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.65 (s, 1H, NH), 7.45 (bs, 1H), 7.24 (d, 2H $J = 6.9$ Hz), 6.9 (d, 1H $J = 8.9$ Hz), 2.51 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 95.4, 111.5, 125, 126.2, 129.7, 131.3, 140.6, 155.9, 173.9. MS (ESI): (m/z) = 274 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_6$N$_5$O$_2$ClNa = 274.0107, found = 274.0117.

5-bromo-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4c, Table 2; entry 3)

Isolated yield: 140 mg, 95%; white solid, mp 186-190 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.68 (s, 1H, NH), 7.58-7.54 (m, 1H), 7.45 (bs, 1H), 7.4-7.37 (m, 1H), 6.8-6.75 (dd, 1H), 2.54 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 72.9, 112.5, 113.9, 128.0, 133.0, 138.7, 141.3, 157.5, 175. MS (ESI): (m/z) = 317 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_6$N$_5$O$_2$BrNa = 317.9602, found = 317.9602

3-hydroxy-5-iodo-3-(1H-tetrazol-5-yl)indolin-2-one (4d, Table 2; entry 4)
**Isolated yield**: 157 mg, 92%; white solid, mp 216-218 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.6 (s, 1H, NH), 7.58 (d, 2H, $J$ = 10 Hz), 7.42 (bs, 1H), 6.77 (d, 1H, $J$ = 7.9 Hz), 2.54 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 71.2, 83.2, 111.6, 130.8, 132.4, 137.5, 140.7, 155, 173. MS (ESI): (m/z) = 365 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_6$N$_5$O$_2$INa = 365.9463, found = 365.9475.

**5-fluoro-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4e, Table 2; entry 5)**

**Isolated yield**: 107 mg, 91%; white solid, mp 218-220 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.5 (s, 1H, NH), 7.43 (bs, 1H), 7.0 - 6.95 (m, 2H), 6.90 - 6.86 (m, 1H), 2.54 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 72.3, 110.9, 112.2, 116.2, 130.1, 137.2, 155.7, 159.6, 174.4. MS (ESI): (m/z) = 258 (M+Na)$^+$. HRMS (ESI) (M + H)$^+$ m/z calcd for C$_9$H$_7$N$_5$O$_2$F = 236.0583, found = 236.0594.

**3-hydroxy-5-methyl-3-(1H-tetrazol-5-yl)indolin-2-one (4f, Table 2; entry 6)**

**Isolated yield**: 106 mg, 92%; white solid, mp 158-160 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.3 (s, 1H, NH), 7.2 (bs, 1H), 7.06 (d, 2H, $J$ = 9.2 Hz), 6.82 (d, 1H, $J$ = 7.74 Hz), 2.5 (s, 1H), 2.28 (s, 3H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 20.5, 72.6, 110.1, 125.4, 129.8, 130.6, 131.4, 139.4, 156.7, 174.6. MS (ESI): (m/z) = 254 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_{10}$H$_9$N$_5$O$_2$Na = 254.0653, found = 254.0660.

**7-chloro-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4g, Table 2; entry 7)**

**Isolated yield**: 123 mg, 98%; white solid, mp 176-178 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 10.64 (s, 1H, NH), 7.23 (d, 2H, $J$ = 6.9 Hz), 6.90 (d, 1H, $J$
= 8.9 Hz), 2.51 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 72.3, 111.4, 125.1, 126.9, 129.7, 130.7, 140.3, 155.9, 174.3. MS (ESI): (m/z) = 274 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_6$N$_5$O$_2$NaCl = 274.0107, found = 274.0111.

1-benzyl-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4h, Table 2; entry 8)

**Isolated yield:** 146 mg, 95%; white solid, mp 140-142 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.37-7.31 (m, 5H), 7.28 (s, 1H), 7.26-7.20 (m, 2H), 7.02 (t, 1H, $J = 7.3$ Hz), 6.76-6.74 (m, 1H), 4.92 (s, 1H), 2.54 (s, 1H).

$^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 59.9, 72.6, 110.1, 123.4, 124.8, 127.2, 127.6, 128.7, 129.3, 130.6, 135.7, 142.4, 143.2, 156.9, 173.5. MS (ESI): (m/z) = 330 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_{16}$H$_{13}$N$_5$O$_2$Na = 330.0966, found = 330.0963.

3-hydroxy-1-methyl-3-(1H-tetrazol-5-yl)indolin-2-one (4i, Table 2; entry 9)

**Isolated yield:** 103 mg, 89%; white solid, mp 196-198 °C. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.38 (s, 1H), 7.36 (d, 2H, $J = 7.5$ Hz), 7.06 (t, 1H, $J = 7.5$ Hz), 6.95 (d, 1H, $J = 7.7$ Hz), 3.24 (s, 3H), 2.54 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): 26.0, 71.9, 95.4, 108.6, 122.6, 124.5, 128.8, 130.0, 143.1, 172.7. MS (ESI): (m/z) = 254 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_{10}$H$_9$N$_5$O$_2$Na = 254.0653, found = 254.0659.

1-allyl-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4j, Table 2; entry 10)

**Isolated yield:** 107 mg, 83%; semisolid. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.4 (s, 1H), 7.27 (t, 1H, $J = 7.9$ Hz), 7.03 (t, 1H, $J = 7.9$ Hz), 6.86 (d, 1H, $J = 7.9$ Hz), 5.89-5.82 (m, 1H), 5.32 (d, 1H, $J = 16.8$ Hz), 5.21
(d, 1H, J = 10.8 Hz), 4.32 (m, 2H), 2.5 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta$ 41.7, 72.3, 95.6, 109.1, 117.0, 122.6, 124.8, 129.6, 130.5, 142.2, 157.2, 173.4. MS (ESI): (m/z) = 280 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_{12}$H$_{11}$N$_5$O$_2$Na = 280.0810, found = 280.0811.

3-hydroxy-5-nitro-3-(1H-tetrazol-5-yl)indolin-2-one (4k, Table 2; entry 11)

**Isolated yield:** 126 mg, 96%; pale yellow solid, mp 235-238 °C. IR cm$^{-1}$: 3444, 3115, 1727, 1623, 1342, 1054, 853, 748. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): $\delta$ 11.2 (s, 1H, NH), 8.2 (d, 2H, J = 8.3 Hz), 7.6 (s, 1H), 7.09 (d, 1H, J = 8.3 Hz), 2.54 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta$ 72.0, 110.8, 120.8, 127.6, 130.4, 142.6, 148.2, 155.7, 174.8. MS (ESI): (m/z) = 285 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_9$H$_6$N$_6$O$_4$Na = 285.0348, found = 285.0362.

1-benzyl-5-chloro-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4l, Table 2; entry 12)

**Isolated yield:** 157 mg, 92%; white solid, mp 110-115 °C. IR cm$^{-1}$: 3082, 3027, 1727, 1615, 1478, 1069, 804, 692. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): $\delta$ 7.66-7.62 (m, 1H), 7.39 (s, 1H), 7.35-7.31 (m, 4H), 7.28-7.26 (m, 1H), 7.23 (d, 1H, J = 8.2 Hz), 6.72 (d, 1H, J = 8.2 Hz), 4.96-4.89 (m, 2H), 2.58 (s, 1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta$ 43.4, 72.0, 110.4, 125.1, 126.6, 127.6, 127.2, 127.9, 128.3, 129.7, 130.1, 134.0, 140.6, 151.5, 172.8. MS (ESI): (m/z) = 364 (M+Na)$^+$. HRMS (ESI) (M+Na)$^+$ m/z calcd for C$_{16}$H$_{13}$N$_5$O$_2$Cl = 342.07523, found = 342.07521.

3-hydroxy-3-(1H-tetrazol-5-yl)-5-(trifluoromethoxy)indolin-2-one (4m, Table 2; entry 13)

**Isolated yield:** 148 mg, 98%; white solid, mp 200-202 °C. IR cm$^{-1}$: 3123, 2866, 1735, 1478, 1278, 1166, 828, 628. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-
DMSO): δ 10.4 (s, 1H, NH), 7.49 (s, 1H), 7.26 (s, 1H), 7.15 (d, 1H J = 8.9 Hz), 6.96 (d, 1H J = 8.9 Hz), 2.58 (s, 1H). 13C NMR (100 MHz, d6-DMSO): δ 72.4, 111.0, 118.7, 120.9, 123.0, 130.3, 140.4, 143.9, 155.9, 174.6. MS (ESI): (m/z) = 302 (M+1)⁺. HRMS (ESI) (M+1)⁺ m/z calcd for C10H7F3N5O3=302.04955, found=302.05019.

1-(4-bromobenzyl)-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4n, Table 2; entry 14) Isolated yield: 165 mg, 85%; white solid, mp 160-164 °C. IR cm⁻¹: 3103, 2929, 1719, 1623, 1495, 1374, 1021, 748. 1H NMR (400 MHz, CDCl3+d6-DMSO): δ 7.51 (s, 1H), 7.47-7.41 (m, 4H), 7.27 (d, 2H, J = 8.3 Hz), 7.21 (s, 1H), 6.68 (d, 1H, J = 8.3 Hz), 4.95-4.83 (m, 2H), 2.58 (s,1H). 13C NMR (100 MHz, d6-DMSO): δ 42.5, 72.1, 109.1, 120.7, 122.8, 124.5, 128.2, 128.6, 129.9, 131.1, 133.8, 141.6, 156.2, 173.2. MS (ESI): (m/z) = 386 (M+1)⁺. HRMS (ESI) (M+1)⁺ m/z calcd for C16H13N5O2Br = 386.02471, found= 386.02539.

5-bromo-1-(2-chlorobenzyl)-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4o, Table 2; entry 15) Isolated yield: 179 mg, 85%; pale white solid, mp 138-140 °C. IR cm⁻¹: 3347, 2926, 1719, 1607, 1478, 1166, 1022, 789. 1H NMR (400 MHz, CDCl3+d6-DMSO): δ 7.45-7.32 (m, 3H), 7.26-7.05 (m, 4H), 6.59 (d, 1H J = 8.3 Hz), 4.74-4.62 (m, 2H), 2.04 (s,1H). 13C NMR (100 MHz, d6-DMSO): δ 42.6, 72.0, 110.5, 120.9, 125.0, 127.9, 128.6, 129.7, 130.3, 130.5, 130.9, 131.2, 133.5, 140.3, 140.9, 172.8. MS (ESI): (m/z) = 422 (M+1)⁺. HRMS (ESI) (M+1)⁺ m/z calcd for C16H12N5O2BrCl = 421.98592, found = 421.98419.

1-(2-bromobenzyl)-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4p, Table 2; entry 16) Isolated yield: 169 mg, 88%; white solid, mp 182-184 °C. IR cm⁻¹: 3275,
2931, 1711, 1607, 1470, 1037, 917, 772. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.62 (d, 1H, $J = 7.7$ Hz), 7.5 (s, 1H), 7.45 (d, 1H, $J = 7.1$ Hz), 7.29-7.25 (m, 3H), 7.19-7.09 (m, 2H), 6.7 (d, 1H, $J = 7.7$ Hz), 5.11-4.92 (q, 2H), 2.58 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 43.3, 72.3, 109.6, 121.9, 123.3, 124.8, 127.1, 127.9, 128.8, 129.0, 129.4, 130.5, 132.7, 133.8, 141.9, 173.3. MS (ESI): (m/z) = 386 (M+1)$^+$. HRMS (ESI) (M+1)$^+$ m/z calcd for C$_{16}$H$_{13}$N$_5$O$_2$Br = 386.02616, found = 386.02471.

1-(2-chlorobenzyl)-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4q, Table 2; entry 17)

Isolated yield: 155 mg, 91%; white solid, mp 178-180 °C. IR cm$^{-1}$: 3284, 3002, 2858, 1711, 1607, 1478, 1366, 1045, 757. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.57 (s, 1H), 7.44 (d, 1H, $J = 7.7$ Hz), 7.32-7.21 (m, 4H), 7.09 (t, 1H, $J = 7.5$ Hz), 6.73 (d, 1H, $J = 7.7$ Hz), 5.13-4.95 (q, 2H), 2.59 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 40.7, 72.2, 109.1, 123.1, 124.6, 126.8, 127.2, 128.4, 128.6, 128.7, 129.0, 130.1, 131.6, 132.0, 141.7, 173.5. MS (ESI): (m/z) = 342 (M+1)$^+$. HRMS (ESI) (M+1)$^+$ m/z calcd for C$_{16}$H$_{13}$N$_5$O$_2$Cl = 342.07523, found = 342.07638.

5-chloro-1-(2-chlorobenzyl)-3-hydroxy-3-(1H-tetrazol-5-yl)indolin-2-one (4r, Table 2; entry 18) Isolated yield: 178 mg, 95%; white solid, mp 180-182 °C. IR cm$^{-1}$: 3331, 3106, 2867, 1719, 1615, 1487, 1366, 1054, 821. $^1$H NMR (400 MHz, CDCl$_3$+d$_6$-DMSO): δ 7.64 (s, 1H), 7.51 (d, 1H, $J = 7.3$ Hz), 7.44-7.41 (m, 1H), 7.2-7.19 (m, 4H), 6.66 (d, 1H, $J = 8.2$ Hz), 5.1-4.95 (q, 2H), 2.58 (s,1H). $^{13}$C NMR (100 MHz, d$_6$-DMSO): δ 40.8, 72.0, 110.3, 125.0, 126.8, 127.1, 127.9, 128.5, 129.0, 129.8, 130.3, 131.2, 132.0, 140.3, 155.9, 172.9. MS (ESI): (m/z) = 376 (M+1)$^+$. HRMS (ESI) (M+1)$^+$ m/z calcd for C$_{16}$H$_{12}$N$_5$O$_2$Cl$_2$ = 376.03626, found = 376.03758.
Typical Procedure for the One-pot Synthesis of Compound 5: A slightly modified procedure, isatin (73 mg, 0.5 mmol), aniline (0.5 m mol), AcOH 2-3 drops were added and stirred vigorously in (H2O:EtOH) 1:1 (2.0 mL) for 1 h. Then TMSCN (0.5 mmol), NaN3 (0.6 mmol), Py.HCl (0.01 mmol) were added and the mixture was stirred at room temperature until complete conversion takes place as indicated by the colour change. The resulting reaction mixture was extracted with 2 N HCl (2 x 200 mL) and the combined water phase was then extracted with ethyl acetate (2 x 100 mL). The combined organics were anhydridified with Na2SO4 and concentrated. Then aqueous solution of NaOH (0.25 N) was added, then washed with ethyl acetate and 1 N HCl. Then the aqueous layer was extracted with ethylacetate, washed with 1 N HCl. The organic layer was dried under vacuum to afford crude solid product. To remove color, the product is treated with a mixture of ethyl acetate (30%) and hexane (70%), and run down a short plug of silica gel to yield a white solid 5 (Table 3).

3-(phenylamino)-3-(1H-tetrazol-5-yl)indolin-2-one (5a, Scheme 5; entry 1) Isolated yield:

137 mg, 94%; white solid, mp 170-175 °C. IR cm⁻¹: 3347, 3191, 2959, 2838, 1700, 1620, 1470, 1243, 1054, 888. ¹H NMR (400 MHz, CDCl₃+d₆-DMSO): δ 10.6 (s, 1H), 7.3 (d, 1H, J = 8.0 Hz), 7.24 (t, 1H, J = 8.0 Hz), 6.98-6.94 (m, 5H), 6.64 (t, 1H, J = 8.0 Hz), 6.46 (d, 1H, J = 8.0 Hz), 2.54 (s,1H). ¹³C NMR (100 MHz, d₆-DMSO): δ 72.7, 110.4, 113.9, 117.5, 122.4, 124.2, 125.0, 128.8, 130.1, 130.4, 141.6, 142.0, 145.6, 157.1, 174.9. MS (ESI): (m/z) = 293 (M+1)⁺. HRMS (ESI) (M+Na)⁺ m/z calcd for C₁₅H₁₂N₆ONa = 315.09573, found = 315.09648.

3-(1H-tetrazol-5-yl)-3-(p-tolylamino)indolin-2-one (5b, Scheme 5; entry 2) Isolated yield:

141 mg, 92%; white solid, mp 175-178 °C. IR cm⁻¹: 2923, 1708, 1620, 1492,
1317, 1053, 753. \(^1\)H NMR (400 MHz, CDCl\(_3+d_6\)-DMSO): \(\delta\) 10.7 (s, 1H), 7.33 (d, 1H, \(J = 7.0\) Hz), 7.25 (t, 1H, \(J = 8.0\) Hz), 6.96 (t, 2H, \(J = 7.0\) Hz), 6.79 (d, 2H, \(J = 8.0\) Hz), 6.4 (d, 2H, \(J = 8.0\) Hz), 3.27 (s, 1H), 2.54 (s, 1H), 2.15 (s, 3H). \(^{13}\)C NMR (100 MHz, d\(_6\)-DMSO): \(\delta\) 20.6, 72.3, 110.1, 115.3, 117.8, 120.8, 121.9, 124.5, 126.8, 128.9, 129.3, 138.6, 145.0, 147.6, 156.5, 175.9. 

MS (ESI): (m/z) = 307 (M+1)+. HRMS (ESI) (M+Na)+ m/z calcd for C\(_{16}H_{14}N_6O\) = 329.11184, found = 329.11213.

3-(4-methoxyphenylamino)-3-(1H-tetrazol-5-yl)indolin-2-one (5c, Scheme 5; entry 3) \(\text{Isolated yield: 145 mg, 90%; white solid, mp 179-181^\circ\text{C}. IR cm}^{-1}: 2999, 1711, 1619, 1501, 808, 753. \(^1\)H NMR (400 MHz, CDCl\(_3+d_6\)-DMSO): \(\delta\) 10.4 (s, 1H), 7.33 (d, 1H, \(J = 8.0\) Hz), 7.22 (t, 1H, \(J = 7.0\) Hz), 6.97 (t, 1H, \(J = 8.0\) Hz), 6.55 (d, 2H, \(J = 9.0\) Hz), 6.50 (d, 2H, \(J = 9.0\) Hz), 3.63 (s, 3H), 2.56 (s, 1H). \(^{13}\)C NMR (100 MHz, d\(_6\)-DMSO): \(\delta\) 54.9, 73.7, 110.8, 112.6, 113.7, 116.9, 117.8, 120.8, 125.7, 127.8, 128.9, 134.3, 141.1, 147.5, 155.0, 175.8. MS (ESI): (m/z) = 345 (M+Na)+. HRMS (ESI) (M+Na)+ m/z calcd for C\(_{16}H_{14}N_6O_2\) = 345.10660, found = 345.10704.

3-(phenylamino)-3-(1H-tetrazol-5-yl)-5-(trifluoromethoxy)indolin-2-one (5d, Scheme 5; entry 4) \(\text{Isolated yield: 179 mg, 95%; white solid, mp 178-180^\circ\text{C}. IR cm}^{-1}: 3381, 1723, 1603, 1471, 1433, 1254, 1190, 818. \(^1\)H NMR (400 MHz, CDCl\(_3+d_6\)-DMSO): \(\delta\) 10.8 (s, 1H), 7.5 (s, 1H), 7.1 (d, 1H, \(J = 9.0\) Hz), 7.08-7.0 (m, 3H), 6.72 (t, 1H, \(J = 7.3\) Hz), 6.51 (d, 2H, \(J = 8.4\) Hz), 2.59 (s, 1H). \(^{13}\)C NMR (100 MHz, d\(_6\)-DMSO): \(\delta\) 62.5, 111.1, 114.9, 118.1, 118.8, 121.4, 122.4, 123.3, 128.2, 128.4, 129.5, 140.1, 143.7, 144.1, 156.4, 174.4. MS (ESI): (m/z) = 399 (M+Na)+. HRMS (ESI) (M+Na)+ m/z calcd for C\(_{16}H_{11}O_2N_6F_3Na\) = 399.07864, found = 399.07879.
5-fluoro-3-(phenylamino)-3-(1H-tetrazol-5-yl)indolin-2-one (5e, Scheme 5; entry 5)

**Isolated yield:** 143 mg, 92%; white solid, mp 170-172 °C. **IR cm⁻¹:** 3435, 3002, 106, 1706, 1574, 1415, 1018, 807, 645. **¹H NMR** (400 MHz, CDCl₃+d₆-DMSO): δ 10.7 (s, 1H), 7.1-6.96 (m, 5H), 6.72 (t, 1H, J = 7.3 Hz), 6.51 (d, 2H, J = 7.9 Hz), 2.59 (s,1H). **¹³C NMR** (100 MHz, d₆-DMSO): δ 72.5, 111.1, 111.3, 112.1, 112.3, 114.7, 115.9, 116.1, 118.5, 128.5, 129.5, 137.4, 144.6, 157.2, 174.0. **MS** (ESI): (m/z) = 311 (M+1)⁺. **HRMS** (ESI) (M+1)⁺ m/z calcd for C₁₅H₁₂ON₆F = 311.10481, found = 311.10511.

5-nitro-3-(phenylamino)-3-(1H-tetrazol-5-yl)indolin-2-one (5f, Scheme 5; entry 6)

**Isolated yield:** 158 mg, 94%; pale white solid, mp 120-122 °C. **IR cm⁻¹:** 3106, 1740, 1603, 1340, 1253, 1187, 1052, 837, 749. **¹H NMR** (400 MHz, CDCl₃+d₆-DMSO): δ 11.4 (s, 1H), 8.24 (m, 2H), 7.14 (d, 1H, J = 9.2 Hz), 7.05 (t, 2H, J = 7.74 Hz), 6.73 (t, 1H, J = 7.3 Hz), 6.5 (d, 2H, J = 8.1 Hz), 2.59 (s,1H). **¹³C NMR** (100 MHz, d₆-DMSO): δ 62.0, 110.5, 114.3, 114.6, 118.8, 120.3, 126.3, 128.1, 128.6, 129.0, 142.7, 144.0, 147.4, 156.7, 174.7. **MS** (ESI): (m/z) = 338 (M+1)⁺. **HRMS** (ESI) (M+1)⁺ m/z calcd for C₁₅H₁₂O₃N₇ = 338.09931, found = 338.09961.
X-ray Crystallography

Crystal data (4a): C₉H₇N₅O₂, M = 217.20, monoclinic, space group P2₁/n, a = 9.8335(7) Å, b = 8.2851(6) Å, c = 12.1849(8) Å, β = 102.006(1)°, V = 971.01(12) Å³, Z = 4, D_{calcd} = 1.486 mg m⁻³, T = 294(2)K, μ = 0.112 mm⁻¹, F(000) = 448, λ = 0.71073Å. Data collection yielded 8941 reflections resulting in 1715 unique, averaged reflections, 1647 with I>2σ(I). Full-matrix least-squares refinement led to a final R = 0.0337, wR = 0.0887 and GOF = 1.028. CCDC 857953 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

Crystal data (5a): C₁₅H₁₂N₆O, M = 292.31, monoclinic, space group P2₁/n, a = 12.6583(8) Å, b = 7.1048(4) Å, c = 15.7542(10) Å, β = 104.404(1)°, V = 1372.31(15) Å³, Z = 4, D_{calcd} = 1.415 mg m⁻³, T = 294(2)K, μ = 0.096 mm⁻¹, F(000) = 608, λ = 0.71073Å. Data collection yielded 12706 reflections resulting in 2426 unique, averaged reflections, 2261 with I>2σ(I). Full-matrix least-squares refinement led to a final R = 0.0365, wR = 0.0952 and GOF = 1.092. CCDC 857954 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].
The intensity data were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) by the ω-scan method [1]. Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 7652 reflections in the range of 2.43 < θ < 27.99° for 4a and 9213 reflections in the range of 2.38 < θ < 28.97° for 5a.

Integration and scaling of intensity data were accomplished using the program SAINT [1]. The structures were solved by direct methods using SHELXS97 [2] and refinement was carried out by full-matrix least-squares technique using SHELXL97 [2]. Anisotropic displacement parameters were calculated for all non-hydrogen atoms. The O-bound and N-bound H atoms were located in a difference Fourier density map and refined isotropically. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H = 0.93-0.96 Å, and with U_{iso}(H) = 1.5U_{eq}(C) for methyl H and 1.2U_{eq}(c) for other H atoms.


Figure caption: The molecular structure of 4a, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

Figure caption: The molecular structure of 5a, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.