An Efficient Aldol-Type Direct Reaction of Isatin with TMSCH$_2$CN

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Supporting Information

All the reactions were performed under dry nitrogen. Cesium fluoride was purchased from Sigma Aldrich and used directly. The Bruker AV-300 instrument (300 MHz and 75 MHz, respectively) was used to record $^1$H and $^{13}$C NMR spectra in deuterated solvents with residual protonated solvent signals as internal reference. $^1$H NMR’s data is reported as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), integration, coupling constant (Hz). $^{13}$C NMR’s data is recorded in terms of chemical shift (δ, ppm). Perkin Elmer FT-IR Spectrometer was used to record infrared spectra and are reported in frequency of absorption. MS-TOF mass spectrometer and ESI mass spectrometer were used to record low resolution and high resolution mass spectra. Column chromatographic separations were carried out on silica gel (100–200 mesh).

Materials: 2-trimethylsilylacetonitrile 2 was purchased from Sigma-aldrich and used without further purification. N-protected Isatins 1A-S were prepared according to known literature procedures.$^1$
General procedure for Cyanomethylation of isatin: To a solution of CsF (20 mol%) in dimethyl formamide (1 ml) was added ketone 1 (0.2 mmol) and trimethylsilyl acetonitrile (0.3 mmol) at 0 °C under N₂ atmosphere. The resulting mixture was warmed at room temperature and stirred for next 48 h. The progress of the reaction was monitored by TLC (thin layer chromatography). Once the reaction was completed, it was quenched by addition of methanol and 1M HCl (1.0 mL) solution. The resulting mixture was extracted with ethyl acetate (5 mL × 3). The combined organic layer was dried over Na₂SO₄, filtered, and concentrated under reduced pressure to provide an oily residue that was purified by flash chromatography on silica gel (eluent: EtOAc/Petroleum ether = 1/3, v/v).

2-(3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3a): white solid (8.6 mg, yield = 23%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, DMSO-d₆): δ 2.92 (d, J = 16.51 Hz, 1H), 3.02 (d, J = 16.51 Hz, 1H), 6.58 (s, 1H), 6.85 (d, J = 7.52 Hz, 1H), 7.01 (t, J = 7.52 Hz, 1H), 7.26 (t, J = 7.52 Hz, 1H), 7.44 (d, J = 7.34 Hz, 1H), 10.53 (s, 1H); ¹³C-NMR (75 MHz, DMSO-d₆): δ 26.12, 72.02, 110.07, 117.08, 122.00, 124.15, 129.78, 130.02, 141.59, 176.70; FTIR (KBr) cm⁻¹, 3425, 2361, 1655, 1001, 765. HRMS ESI: [M+Na]⁺, Calcd for C₁₀H₈O₂N₂Na 211.0477; found 211.0496.

2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetonitrile (3b): white solid (13 mg, yield = 32%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, CDCl₃): δ 2.70 (d, J = 16.51 Hz, 1H), 3.05 (d, J = 16.51 Hz, 1H), 3.24 (s, 3H), 6.91 (d, J = 7.34 Hz, 1H), 7.17 (t, J = 7.15 Hz, 1H), 7.41 (t, J = 7.15 Hz, 1H), 7.66 (d, J = 6.79 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): δ 26.57, 27.47, 72.58, 109.13, 115.27, 123.99, 124.28, 127.48, 131.02, 142.86, 175.32; FTIR (KBr) cm⁻¹, 3422, 2316, 1655, 1001, 824, 765. HRMS ESI: [M+Na]⁺, Calcd for C₁₁H₁₀O₂N₂Na 225.0634; found 225.0639.
2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3c): white solid (39 mg, yield = 71%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^1H-NMR (300 MHz, CDCl_3): δ 2.71 (d, J = 16.20 Hz, 1H), 3.03 (d, J = 16.01 Hz, 1H), 4.74 (d, J = 14.13 Hz, 1H), 4.88 (d, J = 14.88, 1H), 6.71 (d, J = 6.03 Hz, 1H), 7.08 (bs, 1H), 7.24 (bs, 6H), 7.58 (d, J = 5.09 Hz, 1H); ^13C-NMR (75 MHz, CDCl_3): δ 27.56, 44.24, 72.66, 110.20, 115.19, 123.98, 124.35, 127.24, 127.46, 128.01, 128.98, 130.96, 134.68, 142.12, 175.43; FTIR (KBr) cm^{-1}, 3419, 2216, 1652, 1011, 826, 769. HRMS ESI: [M+Na]^+, Calcd for C_{17}H_{14}O_{2}N_{2}Na 301.0946; found 301.0947.

2-(3-hydroxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)acetonitrile (3d): white solid (34 mg, yield = 55%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^1H-NMR (300 MHz, CDCl_3): δ 2.67 (d, J = 16.58 Hz, 1H), 3.01 (d, J = 16.58 Hz, 1H), 3.68 (s, 3H), 4.66 (d, J = 15.45 Hz, 1H), 4.79 (d, J = 15.26 Hz, 1H), 6.67-6.78 (m, 3H), 7.03 (t, J = 7.54 Hz, 1H), 7.13-7.25 (m, 3H), 7.55 (d, J = 7.16 Hz, 1H); ^13C-NMR (75 MHz, CDCl_3): δ 27.35, 43.64, 55.20, 72.69, 110.19, 114.29, 115.34, 123.87, 124.27, 126.65, 127.65, 128.62, 130.76, 141.98, 159.21, 175.61; FTIR (KBr) cm^{-1}, 3432, 2910, 2260, 1659, 1508, 1158, 741. HRMS ESI: [M+Na]^+, Calcd for C_{18}H_{16}O_{3}N_{2}Na 331.1053; found 331.1043.

2-(3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3e): white solid (67 mg, yield = 78%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^1H-NMR (300 MHz, CDCl_3): δ 2.76 (d, J = 16.20 Hz, 1H), 2.95 (d, J = 16.2 Hz, 1H), 6.31 (d, J = 7.54 Hz, 1H), 6.91-6.99 (m, 2H), 7.15-7.20 (m, 9H), 7.37-7.44 (m, 7H); ^13C-NMR (75 MHz, CDCl_3): δ 28.14, 72.80, 75.12, 77.20, 115.37, 116.82, 123.45, 127.20, 127.44, 127.86, 129.22, 129.45, 141.26, 142.93, 177.26; FTIR (KBr) cm^{-1}, 3402, 2924, 2362, 1725, 1603, 1455, 1077, 738, 700. HRMS ESI: [M+Na]^+, Calcd for C_{29}H_{22}O_{2}N_{2}Na 453.1573; found 453.1540.
2-(3-hydroxy-5-methyl-2-oxo-1-tritylindolin-3-yl)acetonitrile (3f): white solid (64.8 mg, yield = 73%). R$_f$ = 0.4 (ethyl acetate/petroleum ether = 2/3); $^1$H-NMR (300 MHz, DMSO-d$_6$): $\delta$ 2.21 (s, 3H), 3.15 (s, 2H), 6.10 (d, $J$ = 8.26 Hz, 1H), 6.68 (s, 1H), 6.80 (d, $J$ = 7.93 Hz, 1H), 7.17-7.27 (m, 9H), 7.42-7.45 (m, 6H); $^{13}$C-NMR (75 MHz, DMSO-d$_6$): $\delta$ 20.29, 26.69, 54.87, 71.89, 73.59, 115.30, 117.09, 124.15, 126.70, 127.64, 128.74, 129.66, 131.43, 139.75, 141.84, 176.70; FTIR (KBr) cm$^{-1}$, 3407, 2923, 2360, 1705, 1625, 1488, 1158, 741, 700. HRMS ESI: [M+Na]$^+$, Calcd for C$_{30}$H$_{24}$O$_2$N$_2$Na 467.1730; found 467.1710.

2-(3-hydroxy-5-methoxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3g): white solid (66.4 mg, yield = 72%). R$_f$ = 0.4 (ethyl acetate/petroleum ether = 2/3); $^1$H-NMR (300 MHz, DMSO-d$_6$): $\delta$ 3.19 (s, 2H), 3.67 (s, 3H), 6.13 (d, $J$ = 8.85 Hz, 1H), 6.59 (d, $J_1$ = 2.83 Hz, $J_2$ = 9.04 Hz, 1H), 6.75 (s, 1H), 7.11 (d, $J$ = 2.83 Hz, 1H), 7.18-7.23 (m, 2H), 7.25-7.30 (m, 6H), 7.44-7.47 (m, 6H); $^{13}$C-NMR (75 MHz, DMSO-d$_6$): $\delta$ 26.64, 55.36, 72.04, 73.55, 79.15, 110.34, 113.03, 116.10, 126.69, 127.64, 128.72, 130.92, 135.09, 141.83, 154.96, 176.4; FTIR (KBr) cm$^{-1}$, 3439, 2928, 1722, 1598, 1487, 1194, 748, 704. HRMS ESI: [M+Na]$^+$, Calcd for C$_{30}$H$_{24}$O$_3$N$_2$Na 483.1679; found 483.1683.

2-(5-fluoro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3h): white solid (65.5 mg, yield = 73%). R$_f$ = 0.4 (ethyl acetate/petroleum ether = 2/3); $^1$H-NMR (300 MHz, DMSO-d6): $\delta$ 3.24 (s, 2H), 6.21 (dd, $J_1$ = 4.14, $J_2$ = 8.85 Hz), 6.87-6.94 (m, 2H), 7.18-7.23 (m, 2H), 7.25-7.35 (m, 7H), 7.43-7.45 (m, 6H); $^{13}$C-NMR (75 MHz, DMSO-d$_6$): $\delta$ 26.41, 71.89, 73.77, 111.16 (d, $J$ = 24.15 Hz), 114.79 (d, $J$ = 23.05 Hz), 116.56 (d, $J$ = 7.68 Hz), 116.95, 126.87, 127.78, 128.71, 131.54 (d, $J$ = 8.23 Hz), 138.24 (d, $J$ = 2.20 Hz), 141.58, 156.37 (d, $J$ = 240 Hz), 176; FTIR (KBr) cm$^{-1}$, 3423, 2252, 1658, 1448, 1027, 824, 763. HRMS ESI: [M+Na]$^+$, Calcd for C$_{29}$H$_{21}$O$_2$N$_2$FNa 471.1479; found 471.1476.
2-(5-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3i): white solid (65.9 mg, yield = 71%). R\textsubscript{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \textsuperscript{1}H-NMR (300 MHz, DMSO-d\textsubscript{6}): δ 3.26 (s, 2H), 6.23 (d, J = 8.62 Hz, 1H), 6.91 (s, 1H), 7.10 (dd, J\textsubscript{1} = 2.02 Hz, J\textsubscript{2} = 8.62 Hz, 1H), 7.19-7.31 (m, 8H), 7.42-7.44 (m, 6H), 7.51 (d, J = 1.83 Hz, 1H); \textsuperscript{13}C-NMR (75 MHz, DMSO-d\textsubscript{6}): δ 26.31, 71.74, 73.86, 79.17, 116.94, 123.76, 126.74, 126.90, 127.80, 128.33, 128.68, 131.72, 141.05, 141.46, 176.29; FTIR (KBr) cm\textsuperscript{-1}, 3430, 2252, 1651, 1598, 1025, 824, 764. HRMS ESI: [M+Na]+, Calcd for C\textsubscript{29}H\textsubscript{21}O\textsubscript{2}N\textsubscript{2}ClK 503.0923; found 503.0966.

2-(5-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3j): white solid (71.2 mg, yield = 70%). R\textsubscript{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \textsuperscript{1}H-NMR (300 MHz, DMSO-d\textsubscript{6}): δ 3.27 (s, 2H), 6.19 (d, J = 8.67 Hz, 1H), 6.91 (s, 1H), 7.19-7.23 (m, 2H), 7.26-7.31 (m, 7H), 7.42-7.45 (m, 6H), 7.63 (d, J = 1.88 Hz, 1H); \textsuperscript{13}C-NMR (75 MHz, DMSO-d\textsubscript{6}): δ 26.29, 71.66, 73.82, 79.16, 114.52, 116.93, 117.38, 126.52, 126.87, 127.77, 128.66, 131.15, 132.03, 141.42, 176.16; FTIR (KBr) cm\textsuperscript{-1}, 3423, 2253, 1652, 1000, 824, 764. HRMS ESI: [M+Na]+, Calcd for C\textsubscript{29}H\textsubscript{21}O\textsubscript{2}N\textsubscript{2}BrK 547.0418; found 547.0401.

2-(3-hydroxy-5-iodo-2-oxo-1-tritylindolin-3-yl)acetonitrile (3k): white solid (77 mg, yield = 69%). R\textsubscript{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \textsuperscript{1}H-NMR (300 MHz, DMSO-d\textsubscript{6}) δ 3.25 (s, 2H), 6.06 (d, J = 8.44 Hz, 1H), 6.86 (s, 1H), 7.21-7.28 (m, 9H), 7.37-7.44 (m, 6H), 7.77 (s, 1H); \textsuperscript{13}C-NMR (75 MHz, DMSO-d\textsubscript{6}) δ 26.33, 71.53, 73.77, 86.14, 117.01, 117.80, 126.87, 127.78, 128.66, 132.07, 132.21, 136.93, 141.47, 142.00, 176.05; FTIR (KBr) cm\textsuperscript{-1}, 3426, 2253, 2127, 1653, 1026, 825, 764. HRMS ESI: [M+Na]+, Calcd for C\textsubscript{29}H\textsubscript{21}O\textsubscript{2}N\textsubscript{2}INa 579.0540; found 579.0562.
2-(3-hydroxy-2-oxo-5-(trifluoromethyl)-1-tritylindolin-3-yl)acetonitrile (3l): white solid (58 mg, yield = 58%). R_{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \(^1\)H-NMR (300 MHz, DMSO-d\(_6\)): δ 3.32 (s, 2H), 6.44 (d, J = 8.62 Hz, 1H), 6.97 (s, 1H), 7.22-7.32 (m, 9H), 7.43-7.46 (m, 6H), 7.81 (s, 1H); \(^{13}\)C-NMR (75 MHz, DMSO-d\(_6\)): δ 26.18, 71.44, 74.02, 115.68, 116.88, 120.52, 122.60, 123.03, 126.09, 126.94, 127.82, 128.62, 130.59, 141.28, 145.72, 176.64; FTIR (KBr) cm\(^{-1}\), 3405, 2925, 2361, 1737, 1456, 1124, 703. HRMS ESI: [M+K]+, Calcd for C\(_{30}\)H\(_{21}\)O\(_2\)N\(_2\)F\(_3\)K 537.1187; found 537.1174.

2-(3-hydroxy-2-oxo-5-(trifluoromethoxy)-1-tritylindolin-3-yl)acetonitrile (3m): white solid (64.8 mg, yield = 63%). R_{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \(^1\)H-NMR (300 MHz, DMSO-d\(_6\)): δ 3.29 (s, 2H), 6.32 (d, J = 8.67 Hz, 1H), 6.96 (s, 1H), 7.08 (d, J = 8.85 Hz, 1H), 7.19-7.31 (m, 9H), 7.43-7.49 (m, 6H); \(^{13}\)C-NMR (75 MHz, DMSO-d\(_6\)): δ 26.18, 71.44, 74.02, 115.68, 116.88, 120.52, 122.60, 123.03, 126.09, 126.94, 127.82, 128.62, 130.59, 141.28, 145.72, 176.64; FTIR (KBr) cm\(^{-1}\), 3405, 2925, 2361, 1737, 1456, 1124, 703. HRMS ESI: [M+K]+, Calcd for C\(_{30}\)H\(_{21}\)O\(_3\)N\(_2\)F\(_3\)K 553.1136; found 553.1130.

2-(3-hydroxy-2-oxo-5-phenyl-1-tritylindolin-3-yl)acetonitrile (3n): white solid (66mg, yield = 65%). R_{f} = 0.4 (ethyl acetate/petroleum ether = 2/3); \(^1\)H-NMR (300 MHz, DMSO-d\(_6\)): δ 3.28 (s, 2H), 6.31 (d, J = 8.44 Hz, 1H), 6.83 (s, 1H), 7.22-7.24 (m, 2H), 7.27-7.37 (m, 8H), 7.40-7.49 (m, 8H), 7.56-7.58 (m, 2H), 7.79 (s, 1H); \(^{13}\)C-NMR (75 MHz, DMSO-d\(_6\)): δ 26.55, 71.79, 73.70, 115.72, 117.13, 121.91, 126.08, 126.57, 126.76, 127.19, 127.69, 128.68, 128.93, 130.41, 134.29, 139.19, 141.58, 141.72, 176.70; FTIR (KBr) cm\(^{-1}\), 3394, 2926, 2360, 1715, 1477, 1186, 1136, 741, 702. HRMS ESI: [M+Na]+, Calcd for C\(_{35}\)H\(_{26}\)O\(_2\)N\(_2\)Na 529.1886; found 529.1879.
2-(4-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3o): white solid (58 mg, yield = 62%). R<sub>f</sub> = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, DMSO-d<sub>6</sub>): δ 3.23 (s, 2H), 6.11 (s, 1H), 6.87 (s, 1H), 7.10 (d, J = 8.10 Hz, 1H), 7.21-7.26 (m, 2H), 7.29-7.33 (m, 6H), 7.42-7.51 (m, 7H); ¹³C-NMR (75 MHz, DMSO-d<sub>6</sub>): δ 26.35, 71.34, 73.89, 115.23, 116.91, 122.17, 125.08, 126.99, 127.81, 128.59, 128.66, 132.70, 141.24, 143.56, 176.53; FTIR (KBr) cm⁻¹, 3420, 2359, 2126, 1651, 1001, 824, 765. HRMS ESI: [M+Na]+, Calcd for C<sub>29</sub>H<sub>21</sub>O<sub>2</sub>N<sub>2</sub>ClNa 487.1184; found 487.1205.

2-(4-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3p): white solid (75.3 mg, yield = 74%). R<sub>f</sub> = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, DMSO-d<sub>6</sub>): δ 3.17 (d, J = 16.77 Hz, 1H), 3.51 (d, J = 16.58 Hz, 1H), 6.29 (d, J = 8.10 Hz, 1H), 6.94-7.00 (m, 2H), 7.17-7.21 (m, 2H), 7.24-7.31 (m, 7H), 7.42-7.44 (m, 6H); ¹³C-NMR (75 MHz, DMSO-d<sub>6</sub>): δ 23.82, 73.66, 74.07, 115.03, 116.22, 118.31, 126.53, 126.69, 126.90, 127.75, 128.78, 130.23, 141.37, 144.75, 175.73; FTIR (KBr) cm⁻¹, 3424, 2361, 2126, 1653, 1027, 824, 765. HRMS ESI: [M+Na]+, Calcd for C<sub>29</sub>H<sub>21</sub>O<sub>2</sub>N<sub>2</sub>BrNa 531.0679; found 531.0654.

2-(6-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3q): white solid (53.9 mg, yield = 58%). R<sub>f</sub> = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, CDCl<sub>3</sub>): δ 2.76 (d, J = 16.32 Hz, 1H), 2.94 (d, J = 16.14 Hz, 1H), 6.27 (s, 1H), 6.95 (d, J = 7.15 Hz, 1H), 7.20-7.23 (m, 9H), 7.35 (m, 7H); ¹³C-NMR (75 MHz, CDCl<sub>3</sub>): δ 28.07, 72.41, 75.44, 115.12, 117.20, 123.55, 124.36, 125.86, 127.43, 128.01, 129.12, 135.37, 140.84, 144.12, 177.14; FTIR (KBr) cm⁻¹, 3404, 2926, 2360, 1735, 1610, 1085, 741, 703. HRMS ESI: [M+Na]+, Calcd for C<sub>29</sub>H<sub>21</sub>O<sub>2</sub>N<sub>2</sub>ClNa 487.1184; found 487.1186.
2-(6-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3r): white solid (65.2 mg, yield = 64%). R₆ = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, CDCl₃): δ 2.74 (d, J = 16.36 Hz, 1H), 2.94 (d, J = 16.36 Hz, 1H), 6.40 (s, 1H), 7.11-7.25 (m, 11H), 7.31-7.37 (m, 6H); ¹³C-NMR (75 MHz, CDCl₃): δ 27.90, 53.41, 72.48, 75.41, 115.14, 119.91, 123.28, 124.65, 126.43, 127.42, 127.99, 129.10, 140.80, 144.13, 177.07; FTIR (KBr) cm⁻¹, 3419, 2252, 1652, 1001, 824, 764. HRMS ESI: [M+Na]⁺, Calcd for C₂₉H₂₁O₂N₂BrNa 531.0678; found 531.0670.

2-(7-fluoro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3s): white solid (56.4 mg, yield = 63%). R₆ = 0.4 (ethyl acetate/petroleum ether = 2/3); ¹H-NMR (300 MHz, DMSO-d₆) δ 3.25 (s, 2H), 6.90-6.97 (m, 2H), 7.10-7.21 (m, 3H), 7.23-7.28 (m, 6H), 7.38-7.43 (m, 7H); ¹³C-NMR (75 MHz, DMSO-d₆) δ 26.55, 71.73, 74.10, 116.91, 118.74 (d, J = 23.60 Hz), 120.12 (d, J = 2.74 Hz), 124.73 (d, J = 7.14 Hz), 126.51, 127.49, 128.25 (d, J = 2.19 Hz), 128.94 (d, J = 7.68 Hz), 132.50 (d, J = 2.19 Hz), 143.23 (d, J = 2.20 Hz), 144.20 (d, J = 248 Hz), 176.20; FTIR (KBr) cm⁻¹, 3434, 2251, 2125, 1655, 1004, 824, 764. HRMS ESI: [M+Na]⁺, Calcd for C₂₉H₂₁O₂N₂FNa 471.1479; found 471.1462.

2-(3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3a): To a solution of compound 3d (60 mg, 0.139 mmol) in DCM (2 ml), trifluoroacetic acid (39.17 mmol, 3 ml) was dropwise added at room temperature. The resulting reaction mixture was run at same temperature for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was evaporated off under reduced pressure. The organic residue was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 80/20) to give the white solid as product (26.1 mg, yield = 93%); ¹H-NMR (300 MHz, DMSO-d₆): δ 2.92 (d, J = 16.51 Hz, 1H), 3.02 (d, J = 16.51 Hz, 1H), 6.58 (s, 1H), 6.85 (d, J = 7.52 Hz, 1H), 6.87 (s, 1H), 7.11-7.15 (m, 11H), 7.28-7.32 (m, 6H); ¹³C-NMR (75 MHz, DMSO-d₆): δ 27.90, 53.41, 72.48, 75.41, 115.14, 119.91, 123.28, 124.65, 126.43, 127.42, 127.99, 129.10, 140.80, 144.13, 177.07; FTIR (KBr) cm⁻¹, 3419, 2252, 1652, 1001, 824, 764. HRMS ESI: [M+Na]⁺, Calcd for C₂₉H₂₁O₂N₂BrNa 531.0678; found 531.0670.
7.01 (t, J = 7.52 Hz, 1H), 7.26 (t, J = 7.52 Hz, 1H), 7.44 (d, J = 7.34 Hz, 1H), 10.53 (s, 1H); 13C-NMR (75 MHz, DMSO-d6): δ 26.12, 72.02, 110.07, 117.08, 122.00, 124.15, 129.78, 130.02, 141.59, 176.70; FTIR (KBr) cm⁻¹, 3425, 2361, 1655, 1001, 765. HRMS ESI: [M+Na]+, Calcd for C_{10}H_{8}O_{2}N_{2}Na 211.0477; found 211.0496.

2-(6-bromo-3-hydroxy-2-oxoindolin-3-yl)acetonitrile (4): To a solution of compound 3p (50 mg, 0.098 mmol) in DCM (1 ml), trifluoroacetic acid (27.61 mmol, 2.2 ml) was dropwise added at room temperature. The resulting solution was run at same temperature for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was evaporated off under reduced pressure. The organic mixture was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 70/30) to give the white solid as product (24.1 mg, yield = 92%); 1H-NMR (300 MHz, DMSO-d6): δ 2.95 (d, J = 16.58 Hz, 1H), 3.04 (d, J = 16.58 Hz, 1H), 6.68 (s, 1H), 7.02 (d, J = 1.32 Hz, 1H), 7.23 (dd, J₁ =1.51 Hz, J₂ = 7.91 Hz, 1H), 7.38 (d, J = 7.91 Hz, 1H), 10.68 (s, 1H); 13C-NMR (75 MHz, DMSO-d6): δ 25.74, 71.69, 112.83, 116.80, 122.57, 124.59, 125.93, 129.03, 143.24, 176.39; FTIR (KBr) cm⁻¹, 3409, 2252, 1651, 1002, 764. HRMS ESI: [M+Na]+, Calcd for C_{10}H_{7}O_{2}N_{2}Br_{1}Na 288.9583; found 288.9560.

2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetonitrile (3b): To a suspension of NaH (4.4 mg, 0.11 mmol) in dry DMF (1.0 mL), solution of compound 3a (20 mg, 0.1 mmol) in dry DMF (0.5 mL0 was drop wise added at 0°C. The resulting mixture was stirred for 10 minutes at same temperature, then methyl iodide (0.114 mmol, 7 μL) was added to it. Subsequently, the reaction mixture was warmed to room temperature and stirred for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction completed, it was quenched with water. The
biphasic mixture was transferred to the separating funnel with help of EtOAc (2.0 mL). The organic layer was separated and washed with water (2.0 mL x 3). The combined aqueous layer was extracted with EtOAc (2.0 mL). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The resulting residue was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 60/40) to give the white solid product (13.5 mg, yield = 67%). $^1$H-NMR (300 MHz, CDCl$_3$): δ 2.70 (d, $J = 16.51$ Hz, 1H), 3.05 (d, $J = 16.51$ Hz, 1H), 3.24 (s, 3H), 6.91 (d, $J = 7.34$ Hz, 1H), 7.17 (t, $J = 7.15$ Hz, 1H), 7.41 (t, $J = 7.15$ Hz, 1H), 7.66 (d, $J = 6.79$ Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): δ 26.57, 27.47, 72.58, 109.13, 115.27, 123.99, 124.28, 127.48, 131.02, 142.86, 175.32; FTIR (KBr) cm$^{-1}$, 3422, 2316, 1655, 1001, 824, 765. HRMS ESI: [M+Na]$^+$, Calcd for C$_{11}$H$_{10}$O$_2$N$_2$Na 225.0634; found 225.0639.

3-[(cyanomethyl)-2-oxo-1-tritylindolin-3-yl acetate (5): To a solution of compound 3d (20 mg, 0.046 mmol) in dry DCM (1 ml), acetyl chloride (0.28 mmol, 20 μL) was added drop wise at room temperature. The resulting solution was stirred for 5 minutes at same temperature, then K$_2$CO$_3$ (16 mg, 0.115 mmol) was added to it. The reaction was run at room temperature for 12 h. The progress of the reaction was monitored by TLC. Once the reaction completed, the reaction mixture was evaporated off under reduced pressure. The crude mixture was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 30/20) to give the white solid product (12 mg, yield = 55%); $^1$H-NMR (300 MHz, CDCl$_3$): δ 2.02 (s, 3H), 2.45 (d, $J = 16.51$ Hz, 1H), 2.99 (d, $J = 16.51$ Hz, 1H), 6.29 (d, $J = 7.52$ Hz, 1H), 6.90-6.93 (m, 2H), 7.14-7.19 (m, 9H), 7.38-7.41 (m, 7H); $^{13}$C-NMR (75 MHz, CDCl$_3$): δ 20.47, 26.90, 75.19, 75.41, 114.82, 116.76, 122.42, 122.97, 124.86, 127.11, 127.63, 129.37, 129.57, 141.37, 143.17, 167.99, 172.06; FTIR
(KBr) cm$^{-1}$, 3437, 2926, 2362, 1744, 1103, 749, 704. HRMS ESI: [M+Na]$^+$, Calcd for C$_{31}$H$_{24}$O$_3$N$_2$Na 495.1679; found 495.1678.

References

\(^1\)H and \(^{13}\)C NMR Spectra

![NMR Spectra Image](image-url)
Chemical Shift (ppm)

S25