Domino Grignard Addition and Oxidation for the One-Pot Synthesis of C2-Quaternary 2-Hydroxyindoxyls

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1.0 General Information

All experiments were carried out under an inert atmosphere of argon in flame-dried flasks. Solvents were dried using standard procedures. All starting materials were obtained from commercial suppliers and used as received. All the reactions were monitored by thin layer chromatography (TLC) analysis on silica gel 60 F254. Products were purified by flash chromatography on silica gel (100-200 mesh, Merck). Unless otherwise stated, yields refer to analytical pure samples. NMR spectra were recorded in CDCl₃ unless otherwise stated. ¹H NMR spectra were recorded at 500 MHz using Brüker AVANCE 500 MHz and JEOL 400 MHz instruments at 298K. Signals are quoted as δ values in ppm using residual protonated solvent signals as internal standard (CDCl₃: δ 7.26 ppm). Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). ¹³C NMR spectra were recorded on either a JEOL-400 (100 MHz), or a Brüker AVANCE 500 MHz (125 MHz) with complete proton decoupling. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane with the solvent as the internal reference (CDCl₃: δ 77.16 ppm). HRMS analyses were performed with Q-TOF YA263 high resolution (Water Corporation) instruments by +ve mode electrospray ionization.
2.0 Synthesis of *N*-Substituted 3-hydroxy-2-oxindoles 1:

*N*-Substituted 3-hydroxy-2-oxindoles 1 were prepared from *N*-substituted isatins 6 using reported procedure\(^1\) by chemoselective \(\text{NaBH}_4\) reduction at 0 °C-rt for 20 min (Scheme S1). Products obtained after the workup were sufficiently pure and used in the next step directly from the crude.

**Scheme S1.** Synthesis of 3-hydroxy-2-oxindoles 1 from isatins 6.
3.0 Synthesis of 2-hydroxyindoxyls 3:

3.0.1 General procedure for the synthesis of 2-hydroxyindoxyls 3a-3b' (GP-1):

To a stirring solution of N-substituted 3-hydroxy-2-oxindoles 1 (1 equiv.) in dry THF, Grignard reagent solution (4 equiv., 1M in THF; for allyl Grignard 3 equiv. was used) was added dropwise at room temperature. The reaction mixture was then stirred at room temperature for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with saturated aqueous NH₄Cl solution and then extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (10/90 to 20/80) to give compounds 3a-3b'.

2-Hydroxy-1-methyl-2-phenylindolin-3-one (3a): Using the general procedure GP-1, compound 1a (200 mg, 1.23 mmol) and phenylmagnesium bromide 2a (5.0 mL, 4.92 mmol) provided compound 3a (218 mg, 74%) as a reddish brown solid; ¹H-NMR (400 MHz, CDCl₃): 7.55-7.51 (2H, m), 7.42-7.39 (2H, m), 7.36-7.33 (3H, m), 6.77-6.74 (2H, m), 3.46 (1H, s), 2.84 (3H, s); ¹³C-NMR (100 MHz, CDCl₃): 200.0, 161.3, 138.9, 136.0, 129.0, 128.9, 126.2, 126.1, 118.2, 117.4, 108.0, 91.0, 27.6; HRMS (ESI) calcd for C₁₅H₁₃NNaO₂ [M+Na]⁺: 262.0844; Found: 262.0844.

2-Hydroxy-1-allyl-2-phenylindolin-3-one (3b): Using the general procedure GP-1, compound 1c (200 mg, 1.06 mmol) and phenylmagnesium bromide 2a (4.2 mL, 4.24 mmol) provided compound 3b (220 mg, 78%) as a brown gummy liquid; ¹H-NMR (500 MHz, CDCl₃): 7.54 (1H, d, J = 7.6 Hz), 7.50 (1H, t, J = 8.4 Hz), 7.43-7.41 (2H, m), 7.35-7.33 (3H, m), 6.78-6.76 (2H, m), 5.84-5.76 (1H, m), 5.22 (1H, dd, J = 15.8, 1.9 Hz), 5.14 (1H, d, J = 10.7 Hz), 3.90 (1H, dd, J = 10.7, 6.3 Hz), 3.82-3.78 (1H, m), 3.44 (1H, d, J = 10.7 Hz); ¹³C-NMR (100 MHz, CDCl₃): 200.0, 160.7, 138.7, 136.6, 134.4, 129.0, 128.9, 126.3, 126.1, 118.4, 117.5, 117.1, 109.0, 91.3, 45.5; HRMS (ESI) calcd for C₁₇H₁₅NNaO₂ [M+Na]⁺: 288.1000; Found: 288.1003.
2-Hydroxy-1-(4-methoxybenzyl)-2-phenylindolin-3-one (3c): Using the general procedure GP-1, compound 1e (200 mg, 0.74 mmol) and phenylmagnesium bromide 2a (3.0 mL, 2.96 mmol) provided compound 3c (195 mg, 76%) as a yellow solid; ^1H-NMR (400 MHz, CDCl₃): 7.57 (1H, d, J = 7.5 Hz), 7.45-7.42 (3H, m), 7.40-7.35 (3H, m), 7.22 (2H, d, J = 8.6 Hz), 6.82 (2H, d, J = 8.6 Hz), 6.77 (1H, t, J = 7.5 Hz), 6.60 (1H, d, J = 8.6 Hz), 4.34 (2H, q, J = 4.3 Hz), 3.77 (3H, s), 3.25 (1H, sbr); ^13C-NMR (100 MHz, CDCl₃): 199.8, 160.8, 159.0, 138.7, 136.7, 129.8, 129.1, 129.0, 128.5, 126.2, 126.1, 118.7, 117.8, 114.2, 109.1, 91.7, 55.4, 46.8; HRMS (ESI) calcd for C₂₂H₂₀NO₃ [M+H]^+: 346.1443; Found: 346.1439.

2-Hydroxy-1-phenyl-2-phenylindolin-3-one (3d): Using the general procedure GP-1, compound 1f (200 mg, 0.89 mmol) and phenylmagnesium bromide 2a (3.5 mL, 3.56 mmol) provided compound 3d (194 mg, 72%) as a deep brown liquid; ^1H-NMR (500 MHz, CDCl₃): 7.65 (1H, d, J = 7.5 Hz), 7.58-7.49 (2H, m), 7.47-7.40 (3H, m), 7.31-7.25 (5H, m), 7.13 (1H, t, J = 7.6 Hz), 7.08 (1H, d, J = 8.4 Hz), 6.89 (1H, t, J = 7.6 Hz), 3.74 (1H, sbr); ^13C-NMR (125 MHz, CDCl₃): 199.7, 159.4, 138.5, 136.9, 130.1, 129.5, 128.9, 128.7, 126.3, 125.0, 119.9, 118.3, 111.0, 91.7; HRMS (ESI) calcd for C₂₀H₁₆NO₂ [M+H]^+: 302.1181; Found: 302.1180.

2-Hydroxy-2-phenyl-1-(4-(trifluoromethyl)phenyl)indolin-3-one (3e): Using the general procedure GP-1, compound 1g (200 mg, 0.68 mmol) and phenylmagnesium bromide 2a (2.7 mL, 2.72 mmol) provided compound 3e (186 mg, 74%) as a greenish liquid; ^1H-NMR (500 MHz, CDCl₃): 7.74 (1H, d, J = 8.2 Hz), 7.66 (1H, s), 7.62-7.54 (2H, m), 7.52-7.50 (1H, m), 7.45-7.43 (2H, m), 7.40-7.38 (2H, m), 7.33-7.29 (2H, m), 7.16 (1H, d, J = 8.2 Hz), 7.01 (1H, t, J = 7.6 Hz), 3.74 (1H, sbr); ^13C-NMR (100 MHz, CDCl₃): 199.2, 158.3, 139.3, 153.7, 136.4, 129.9, 129.2, 128.9, 127.5, 126.5, 126.1, 122.3, 121.1, 121.0, 120.9, 118.7, 110.9, 91.8; HRMS (ESI) calcd for C₂₁H₁₆F₃NNaO₂ [M+Na]^+: 392.0874; Found: 392.0875.
1-(3-Bromopropyl)-2-hydroxy-2-phenylindolin-3-one (3f): Using the general procedure GP-1, compound 1h (200 mg, 0.74 mmol) and phenylmagnesium bromide 2a (3.0 mL, 2.96 mmol) provided compound 3f (180 mg, 70%) as a brown liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.56-7.50 (2H, m), 7.39-7.32 (5H, m), 6.88 (1H, d, $J = 8.3$ Hz), 6.76 (1H, t, $J = 7.8$ Hz), 3.91 (1H, s br), 3.78-3.54 (1H, m), 3.45-3.36 (2H, m), 3.27-3.20 (1H, m), 2.13-2.06 (2H, m); $^{13}$C-NMR (100 MHz, CDCl$_3$): 200.3, 160.9, 139.0, 136.5, 129.0, 128.9, 128.3, 126.3, 126.1, 118.4, 117.3, 108.3, 91.4, 41.2, 31.8, 31.4; HRMS (ESI) calcd for C$_{17}$H$_{17}$BrNO$_2$ [M+H]$^+$: 346.0443; Found: 346.0449.

5-Fluoro-2-hydroxy-1-methyl-2-phenylindolin-3-one (3g): Using the general procedure GP-1, compound 1i (200 mg, 1.10 mmol) and phenylmagnesium bromide 2a (4.4 mL, 4.40 mmol) provided compound 3g (216 mg, 76%) as a red solid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.40-7.35 (5H, m), 7.31-7.25 (1H, m), 7.20-7.18 (1H, m), 6.72-6.69 (1H, m), 3.49 (1H, s br), 2.82 (3H, s); $^{13}$C-NMR (125 MHz, CDCl$_3$): 199.7, 158.1, 157.0, 155.1, 135.7, 129.1, 129.0, 126.1, 126.4, 126.1, 117.6, 117.5, 111.3, 111.1, 107.0, 108.9, 91.6, 27.8; HRMS (ESI) calcd for C$_{15}$H$_{12}$FNNaO$_2$ [M+Na]$^+$: 280.0750; Found: 280.0752.

7-Fluoro-2-hydroxy-1-allyl-2-phenylindolin-3-one (3h): Using the general procedure GP-1, compound 1o (200 mg, 0.97 mmol) and phenylmagnesium bromide 2a (3.9 mL, 3.88 mmol) provided compound 3h (195 mg, 71%) as a brown gummy liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.48-7.46 (2H, m), 7.36-7.32 (4H, m), 7.23 (1H, t, $J = 4.4$ Hz), 6.70-6.65 (1H, m), 5.94-5.84 (1H, m), 5.16 (1H, d, $J = 17.6$ Hz), 5.05 (1H, d, $J = 10.3$ Hz), 4.22 (1H, dd, $J = 10.8$, 5.8 Hz), 3.86 (1H, dd, $J = 11.2$, 4.9 Hz), OH could not be detected; $^{13}$C-NMR (100 MHz, CDCl$_3$): 199.4, 149.7, 148.1, 148.0, 147.3, 136.3, 135.6, 129.3, 128.9, 126.3, 125.1, 124.9, 121.9, 121.8, 121.1, 121.0, 118.5, 118.4, 116.8, 91.5, 46.6, 46.5; HRMS (ESI) calcd for C$_{17}$H$_{15}$FNO$_2$ [M+H]$^+$: 284.1087; Found: 284.1092.
**1-Allyl-4,7-dichloro-2-hydroxy-2-phenylindolin-3-one (3i):** Using the general procedure GP-1, compound 1q (200 mg, 0.77 mmol) and phenylmagnesium bromide 2a (3.1 mL, 3.08 mmol) provided compound 3i (65 mg, 64%) as a brown liquid; \(^1\)H-NMR (400 MHz, CDCl\(_3\)): 7.49-7.46 (1H, m), 7.42 (1H, d, \(J = 8.8\) Hz), 7.39-7.26 (4H, m), 7.02 (1H, d, \(J = 8.8\) Hz), 6.00-5.91 (1H, m), 5.26 (1H, s), 5.23 (1H, d, \(J = 5.4\) Hz), 4.78-4.76 (2H, m); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): 196.5, 157.7, 140.7, 140.3, 136.3, 131.7, 129.5, 129.0, 126.7, 126.5, 126.4, 120.5, 118.0, 91.8, 43.9; HRMS (ESI) calcd for C\(_{17}\)H\(_{14}\)Cl\(_2\)NO\(_2\) [M+H]\(^+\): 334.0402; Found: 334.0399.

**1-Benzyl-5-bromo-2-hydroxy-2-phenylindolin-3-one (3j):** Using the general procedure GP-1, compound 1m (200 mg, 0.63 mmol) and phenylmagnesium bromide 2a (3.1 mL, 2.52 mmol) provided compound 3j (172 mg, 68%) as a brown liquid; \(^1\)H-NMR (400 MHz, CDCl\(_3\)): 7.54 (1H, s), 7.45-7.42 (3H, m), 7.31-7.35 (3H, m), 7.32-7.23 (5H, m), 6.44 (1H, d, \(J = 8.8\) Hz), 4.38 (2H, dd, \(J = 16.6, 8.3\) Hz), 4.16 (1H, s, br); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): 199.0, 159.3, 141.1, 137.3, 136.1, 129.3, 129.1, 128.9, 128.3, 127.5, 127.2, 126.2, 119.3, 110.8, 110.6, 92.1, 47.2; HRMS (ESI) calcd for C\(_{21}\)H\(_{16}\)BrNNaO\(_2\) [M+Na]\(^+\): 416.0262; Found: 416.0264.

**1-Allyl-2-hydroxy-5-iodo-2-phenylindolin-3-one (3k):** Using the general procedure GP-1, compound 1n (200 mg, 0.63 mmol) and phenylmagnesium bromide 2a (2.5 mL, 2.52 mmol) provided compound 3k (174 mg, 70%) as a deep green liquid; \(^1\)H-NMR (500 MHz, CDCl\(_3\)): 7.73 (1H, d, \(J = 1.9\) Hz), 7.70 (1H, dd, \(J = 6.9, 1.9\) Hz), 7.40-7.32 (5H, m), 6.58 (1H, d, \(J = 8.8\) Hz), 5.79-5.71 (1H, m), 5.22 (1H, dd, \(J = 15.8, 1.3\) Hz), 5.14 (1H, dd, \(J = 8.8, 1.3\) Hz), 3.95 (1H, s, br), 3.88 (1H, dd, \(J = 16.4, 6.4\) Hz), 3.81-3.76 (1H, m); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): 198.3, 159.7, 146.6, 136.0, 134.4, 133.9, 129.2, 128.9, 126.2, 119.8, 117.5, 111.3, 91.4, 78.9, 45.4; HRMS (ESI) calcd for C\(_{17}\)H\(_{14}\)INNaO\(_2\) [M+Na]\(^+\): 413.9967; Found: 413.9966.
2-Hydroxy-1-methyl-2-phenyl-5-(trifluoromethoxy)indolin-3-one (3l): Using the general procedure GP-1, compound 1r (200 mg, 0.81 mmol) and phenylmagnesium bromide 2a (3.2 mL, 3.24 mmol) provided compound 3l (178 mg, 68%) as a brown gummy solid; \( ^1H \)-NMR (400 MHz, CDCl\(_3\)): 7.41-7.36 (7H, m), 6.75 (1H, d, \( J = 9.3 \) Hz), 3.33 (1H, s\( _{br} \)), 2.87 (3H, s); \( ^13C \)-NMR (100 MHz, CDCl\(_3\)): 199.1, 159.6, 141.1, 135.4, 132.4, 129.3, 129.1, 126.1, 118.7, 117.6, 108.8, 91.5, 27.7; HRMS (ESI) calcd for C\(_{16}\)H\(_{13}\)F\(_3\)NO\(_3\) [M+H]\(^+\): 324.0848; Found: 324.0855.

1-Benzyl-2-hydroxy-5-methyl-2-phenylindolin-3-one (3m): Using the general procedure GP-1, compound 1t (200 mg, 0.79 mmol) and phenylmagnesium bromide 2a (3.2 mL, 3.16 mmol) provided compound 3m (193 mg, 74%) as a brown gummy solid; \( ^1H \)-NMR (400 MHz, CDCl\(_3\)): 7.46-7.43 (2H, m), 7.38-7.34 (5H, m), 7.31-7.29 (3H, m), 7.27-7.22 (2H, m), 6.48 (1H, d, \( J = 8.5 \) Hz), 4.37 (2H, s), 3.64 (1H, s\( _{br} \)), 2.22 (3H, s); \( ^13C \)-NMR (125 MHz, CDCl\(_3\)): 200.1, 159.3, 139.9, 138.2, 136.9, 128.9, 128.7, 128.1, 127.3, 126.3, 125.6, 117.9, 109.0, 92.1, 47.4, 20.4; HRMS (ESI) calcd for C\(_{22}\)H\(_{19}\)NNaO\(_2\) [M+Na]\(^+\): 352.1313; Found: 352.1314.

1-Allyl-2-hydroxy-5,7-dimethyl-2-phenylindolin-3-one (3n): Using the general procedure GP-1, compound 1u (200 mg, 0.92 mmol) and phenylmagnesium bromide 2a (3.7 mL, 3.68 mmol) provided compound 3n (210 mg, 76%) as a greenish yellow liquid; \( ^1H \)-NMR (500 MHz, CDCl\(_3\)): 7.50-7.46 (2H, m), 7.35-7.30 (3H, m), 7.21 (1H, s), 7.11 (1H, s), 5.98-5.91 (1H, m), 5.18-5.13 (1H, m), 5.10-5.07 (1H, m), 4.34-4.28 (1H, m), 3.90-3.85 (1H, m), 3.32 (1H, s\( _{br} \)), 2.48 (3H, s), 2.22 (3H, s); \( ^13C \)-NMR (100 MHz, CDCl\(_3\)): 200.5, 157.9, 143.3, 137.8, 137.4, 128.9, 128.8, 126.4, 123.4, 120.0, 118.6, 115.7, 91.7, 46.1, 20.2, 19.4; HRMS (ESI) calcd for C\(_{19}\)H\(_{19}\)NNaO\(_2\) [M+Na]\(^+\): 316.1313; Found: 316.1314.
1-Benzyl-2-hydroxy-5-(4-methoxyphenyl)-2-phenylindolin-3-one (3o): Using the general procedure GP-1, compound 1w (200 mg, 0.58 mmol) and allylmagnesium bromide 2c (2.3 mL, 2.32 mmol) provided compound 3o (160 mg, 66%) as a greenish yellow liquid; \(^{1}\)H-NMR (500 MHz, CDCl\(_3\)): 7.75 (1H, d, \(J = 1.9\) Hz), 7.62 (1H, dd, \(J = 6.9, 1.9\) Hz), 7.48 (2H, dd, \(J = 5.7, 2.5\) Hz), 7.40-7.37 (5H, m), 7.35-7.31 (5H, m), 6.92 (2H, d, \(J = 8.8\) Hz), 6.62 (1H, d, \(J = 8.2\) Hz), 4.43 (2H, s), 3.83 (3H, s), 3.54(1H, s); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)): 200.0, 159.8, 159.1, 137.9, 137.6, 136.6, 132.6, 131.9, 129.2, 129.1, 128.8, 127.5, 127.4, 127.3, 126.3, 123.4, 118.3, 114.5, 109.5, 92.2, 55.5, 47.4; HRMS (ESI) calcd for C\(_{28}\)H\(_{33}\)NaO\(_3\) [M+Na]\(^+\): 444.1576; Found: 444.1578.

1,2-Diallyl-2-hydroxy-5-methoxyindolin-3-one (3p): Using the general procedure GP-1, compound 1v (200 mg, 0.91 mmol) and allylmagnesium bromide 2c (2.7 mL, 2.73 mmol) provided compound 3p (164 mg, 69%) as a greenish yellow liquid; \(^{1}\)H-NMR (400 MHz, CDCl\(_3\)): 7.10 (1H, dd, \(J = 6.4, 2.4\) Hz), 6.96 (1H, d, \(J = 2.4\) Hz), 6.64 (1H, d, \(J = 8.8\) Hz), 5.95-5.86 (1H, m), 5.62-5.52 (1H, m), 5.32-5.19 (2H, m), 5.13-5.01 (2H, m), 4.05-3.90 (2H, m), 3.73 (3H, s), 3.18 (1H, s), 2.67-2.59 (2H, m); \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)): 200.1, 156.5, 152.6, 134.9, 130.6, 128.6, 120.1, 117.9, 116.9, 110.6, 105.9, 90.1, 56.0, 44.7, 40.0; HRMS (ESI) calcd for C\(_{15}\)H\(_{18}\)NO\(_3\) [M+H]\(^+\): 260.1287; Found: 260.1289.

2-Allyl-1-ethyl-2-hydroxyindolin-3-one (3q): Using the general procedure GP-1, compound 1b (200 mg, 1.13 mmol) and allylmagnesium bromide 2c (3.4 mL, 3.39 mmol) provided compound 3q (184 mg, 75%) as a yellow liquid; \(^{1}\)H-NMR (400 MHz, CDCl\(_3\)): 7.51 (1H, d, \(J = 7.8\) Hz), 7.45 (1H, t, \(J = 8.3\) Hz), 6.70-6.67 (2H, m), 5.57-5.49 (1H, m), 5.11 (1H, d, \(J = 17.1\) Hz), 5.02 (1H, d, \(J = 10.2\) Hz), 3.54-3.38 (2H, m), 2.71-2.62 (2H, m), 1.30 (3H, t, \(J = 6.8\) Hz); OH could not be detected; \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)): 201.2, 160.1, 138.7, 130.4, 125.5, 120.1, 117.6, 108.3, 89.5, 39.8, 36.1, 14.6; HRMS (ESI) calcd for C\(_{13}\)H\(_{15}\)NaO\(_2\) [M+Na]\(^+\): 240.1001; Found: 240.1004.
1,2-Diallyl-2-hydroxyindolin-3-one (3r): Using the general procedure GP-1, compound 1c (200 mg, 1.05 mmol) and allylmagnesium bromide 2c (3.2 mL, 3.17 mmol) provided compound 3r (194 mg, 80%) as a yellow liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.54 (1H, d, $J = 7.4$ Hz), 7.46-7.42 (1H, m), 6.73 (1H, t, $J = 7.4$ Hz), 6.68 (1H, d, $J = 7.9$ Hz), 5.95-5.88 (1H, m), 5.64-5.56 (1H, m), 5.30 (1H, dd, $J = 15.9, 1.2$ Hz), 5.22 (1H, dd, $J = 9.2, 1.3$ Hz), 5.14 (1H, dd, $J = 15.9, 1.2$ Hz), 5.05 (1H, d, $J = 10.9$ Hz), 4.09-3.96 (2H, m), 2.72 (1H, $s$); $^1$C-NMR (125 MHz, CDCl$_3$): 200.7, 160.4, 138.5, 134.5, 130.4, 125.3, 120.3, 118.2, 117.2, 109.2, 89.3, 44.4, 39.9; HRMS (ESI) calcd for C$_{14}$H$_{15}$NKO$_2$ [M+K]$^+$: 268.0740; Found: 268.0742.

2-Allyl-2-hydroxy-1-(4-methoxybenzyl)indolin-3-one (3s): Using the general procedure GP-1, compound 1e (200 mg, 0.74 mmol) and allylmagnesium bromide 2c (2.2 mL, 2.23 mmol) provided compound 3s (180 mg, 78%) as a yellow liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.55 (1H, d, $J = 7.6$ Hz), 7.35 (1H, t, $J = 7.6$ Hz), 7.28 (2H, t, $J = 8.4$ Hz), 6.86 (2H, d, $J = 8.4$ Hz), 6.71 (1H, t, $J = 7.6$ Hz), 6.51 (1H, d, $J = 8.4$ Hz), 5.59-5.52 (1H, m), 5.06 (2H, dd, $J = 17.6, 16.8$ Hz), 4.62-4.49 (2H, m), 3.79 (3H, s), 3.04 (1H, $s$); $^1$C-NMR (125 MHz, CDCl$_3$): 200.9, 160.6, 159.0, 138.6, 130.3, 129.9, 128.8, 128.4, 125.2, 120.4, 118.3, 114.3, 109.5, 89.5, 55.4, 45.4, 40.3; HRMS (ESI) calcd for C$_{19}$H$_{19}$NNaO$_3$ [M+Na]$^+$: 332.1263; Found: 332.1269.

2-Allyl-2-hydroxy-1-phenylindolin-3-one (3t): Using the general procedure GP-1, compound 1f (200 mg, 0.89 mmol) and allylmagnesium bromide 2c (2.7 mL, 2.66 mmol) provided compound 3t (182 mg, 77%) as a yellow liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.61 (1H, d, $J = 7.6$ Hz), 7.52 (2H, d, $J = 8.4$ Hz), 7.45-7.41 (3H, m), 7.29 (1H, t, $J = 7.6$ Hz), 6.92 (1H, d, $J = 8.4$ Hz), 6.82 (1H, t, $J = 6.7$ Hz), 5.53-5.44 (1H, m), 4.98-4.93 (2H, m), 3.40 (1H, $s$); $^1$C-NMR (125 MHz, CDCl$_3$): 200.6, 159.0, 138.3, 138.2, 129.8, 129.6, 126.6, 126.1, 125.4, 120.6, 119.5, 118.6, 110.6, 90.1, 39.6; HRMS (ESI) calcd for C$_{17}$H$_{16}$NO$_2$ [M+H]$^+$: 266.1181; Found: 266.1194.
2-Allyl-1-benzyl-5-chloro-2-hydroxyindolin-3-one (3u): Using the general procedure GP-1, compound 1j (200 mg, 0.73 mmol) and allylmagnesium bromide 2c (2.2 mL, 2.19 mmol) provided compound 3u (147 mg, 64%) as a brown liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.50 (1H, d, $J = 2.0$ Hz), 7.35-7.27 (6H, m), 6.42 (1H, d, $J = 8.8$ Hz), 5.62-5.51 (1H, m), 5.13-5.05 (2H, m), 4.60 (2H, q, $J = 16.6$ Hz), 2.69-2.66 (2H, m); $^{13}$C-NMR (100 MHz, CDCl$_3$): 199.8, 158.8, 138.2, 137.5, 129.9, 129.0, 127.6, 127.1, 124.5, 123.7, 120.9, 119.4, 110.7, 90.0, 46.0, 40.3; HRMS (ESI) calcd for C$_{18}$H$_{16}$ClNNaO$_2$ [M+Na]$^+$: 336.0767; Found: 336.0778.

2-Hydroxy-2-(4-methoxyphenyl)-1-methylindolin-3-one (3v): Using the general procedure GP-1, compound 1a (200 mg, 1.23 mmol) and $p$-methoxyphenylmagnesium bromide 2b (4.9 mL, 4.92 mmol) provided compound 3v (217 mg, 65%) as a deep green liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.52-7.49 (2H, m), 7.32-7.30 (2H, m), 6.87-6.85 (2H, m), 6.73-6.71 (2H, m), 3.77 (3H, d, $J = 1.7$ Hz), 3.63 (1H, sbr), 2.82 (3H, d, $J = 1.7$ Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$): 200.2, 161.1, 160.1, 138.8, 127.9, 127.6, 126.1, 118.0, 117.4, 114.3, 108.0, 90.8, 55.4, 27.5; HRMS (ESI) calcd for C$_{16}$H$_{16}$NO$_3$ [M+H]$^+$: 270.1130; Found: 270.1135.

1-Benzyl-2-hydroxy-2-(4-methoxyphenyl)indolin-3-one (3w): Using the general procedure GP-1, compound 1d (200 mg, 0.84 mmol) and $p$-methoxyphenylmagnesium bromide 2b (3.3 mL, 3.36 mmol) provided compound 3w (182 mg, 62%) as a yellow liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.89 (1H, d, $J = 8.4$ Hz), 7.52 (1H, d, $J = 7.6$ Hz), 7.38-7.31 (4H, m), 7.24-7.19 (2H, m), 6.92 (1H, d, $J = 9.2$ Hz), 6.83 (2H, d, $J = 8.4$ Hz), 6.71 (1H, dd, $J = 7.6, 7.6$ Hz), 6.51 (1H, d, $J = 8.4$ Hz), 4.36 (2H, s), 3.75 (3H, s), 3.38 (1H, sbr); $^{13}$C-NMR (100 MHz, CDCl$_3$): 200.0, 160.7, 160.3, 138.7, 138.0, 132.6, 128.9, 128.8, 127.6, 127.2, 126.1, 111.6, 114.4, 109.1, 91.6, 55.4, 47.2; HRMS (ESI) calcd for C$_{22}$H$_{20}$NO$_3$ [M+H]$^+$: 346.1443; Found: 346.1447.
1-Allyl-2-hydroxy-5-methoxy-2-(4-methoxyphenyl)indolin-3-one (3x): Using the general procedure GP-1, compound 1v (200 mg, 0.91 mmol) and p-methoxyphenylmagnesium bromide 2b (3.6 mL, 3.64 mmol) provided compound 3x (184 mg, 62%) as a yellowish green liquid; 

\[ ^1H-NMR \] (500 MHz, CDCl\(_3\)): 7.33 (2H, d, \( J = 8.4 \) Hz), 7.16 (1H, dd, \( J = 5.9, 2.5 \) Hz), 7.0 (1H, d, \( J = 2.5 \) Hz), 6.85 (2H, d, \( J = 8.4 \) Hz), 6.73 (1H, d, \( J = 8.4 \) Hz), 5.84-5.77 (1H, m), 5.23 (1H, d, \( J = 16.8 \) Hz), 5.13 (1H, d, \( J = 10.1 \) Hz), 3.87-3.81 (2H, m), 3.78 (3H, s), 3.74 (3H, s); \n
\[ ^13C-NMR \] (125 MHz, CDCl\(_3\)): 200.2, 160.2, 156.7, 152.9, 134.9, 128.6, 128.5, 127.7, 117.4, 116.9, 114.3, 110.4, 106.8, 91.8, 56.1, 55.4, 45.7; HRMS (ESI) calcd for C\(_{19}\)H\(_{26}\)NO\(_4\) [M+H\(^+\)]: 326.1392; Found: 326.1395.

2-Benzyl-2-hydroxy-1-methylindolin-3-one (3y): Using the general procedure GP-1, compound 1a (200 mg, 1.23 mmol) and benzylmagnesium bromide 2d (4.9 mL, 4.92 mmol) provided compound 3y (232 mg, 74%) as a deep brown liquid; 

\[ ^1H-NMR \] (500 MHz, CDCl\(_3\)): 7.41 (1H, d, \( J = 7.5 \) Hz), 7.36 (1H, t, \( J = 8.4 \) Hz), 7.17-7.09 (5H, m), 6.60 (1H, t, \( J = 7.5 \) Hz), 6.55 (1H, d, \( J = 8.4 \) Hz), 3.21 (1H, d, \( J = 13.4 \) Hz), 3.12 (1H, d, \( J = 17.6 \) Hz), 2.97 (3H, s); \n
\[ ^13C-NMR \] (125 MHz, CDCl\(_3\)): 201.3, 161.0, 138.6, 134.0, 130.2, 128.3, 127.0, 125.2, 118.1, 117.7, 108.2, 89.9, 40.9, 27.5; HRMS (ESI) calcd for C\(_{16}\)H\(_{16}\)NO\(_2\) [M+H\(^+\)]: 254.1181; Found: 254.1184.

2-Benzyl-2-hydroxy-1-(4-methoxybenzyl)indolin-3-one (3z): Using the general procedure GP-1, compound 1e (200 mg, 0.74 mmol) and benzylmagnesium bromide 2d (3.0 mL, 2.96 mmol) provided compound 3z (202 mg, 76%) as a deep brown liquid; 

\[ ^1H-NMR \] (500 MHz, CDCl\(_3\)): 7.46 (1H, d, \( J = 7.6 \) Hz), 7.30 (1H, t, \( J = 7.5 \) Hz), 7.22 (2H, d, \( J = 8.4 \) Hz), 7.15-7.08 (4H, m), 6.90-6.82 (3H, m), 6.60 (1H, t, \( J = 7.6 \) Hz), 6.34 (1H, d, \( J = 8.4 \) Hz), 4.62 (1H, d, \( J = 7.6 \) Hz), 4.47 (1H, d, \( J = 15.9 \) Hz), 3.81 (1H, s), 3.78 (3H, s), 3.29 (1H, d, \( J = 14.2 \) Hz), 3.17 (1H, d, \( J = 14.2 \) Hz); \n
\[ ^13C-NMR \] (125 MHz, CDCl\(_3\)): 201.2, 160.3, 158.9, 138.3, 133.8, 130.3, 129.7, 128.8, 128.5, 128.2, 127.1, 125.1, 118.4, 118.0, 114.1, 109.5, 90.4, 55.4, 45.7, 41.9; HRMS (ESI) calcd for C\(_{23}\)H\(_{22}\)NO\(_3\) [M+H\(^+\)]: 360.1600; Found: 360.1614.
1-**Allyl-2-hydroxy-2-methylindolin-3-one (3a’)**: Using the general procedure **GP-1**, compound 1c (200 mg, 1.05 mmol) and methylmagnesium bromide 2e (4.2 mL, 4.20 mmol) provided compound 3a’ (155 mg, 72%) as a yellow liquid; **1H-NMR** (400 MHz, CDCl₃): 7.56 (1H, d, J = 7.3 Hz), 7.47-7.43 (1H, m), 6.74 (1H, t, J = 7.3 Hz), 6.67 (1H, d, J = 8.6 Hz), 5.94-5.86 (1H, m), 5.29-5.20 (2H, m), 4.10-3.94 (2H, m), 1.46 (3H, s); **13C-NMR** (125 MHz, CDCl₃): 200.9, 159.5, 138.6, 134.3, 125.6, 118.1, 117.4, 117.0, 109.3, 88.2, 44.0, 21.2; HRMS (ESI) calcd for C₁₂H₁₄NO₂ [M+H]⁺: 204.1025; Found: 204.1026.

1-**Benzyl-2-hydroxy-2,5-dimethylindolin-3-one (3b’)**: Using the general procedure **GP-1**, compound 1t (200 mg, 0.79 mmol) and methylmagnesium bromide 2e (3.2 mL, 3.16 mmol) provided compound 3b’ (148 mg, 70%) as a yellow liquid; **1H-NMR** (500 MHz, CDCl₃): 7.38 (1H, s), 7.34-7.24 (5H, m), 7.19 (1H, dd, J = 7.4, 1.0 Hz), 6.41 (1H, d, J = 8.3 Hz), 4.57 (2H, s), 3.01 (1H, sbr), 2.23 (3H, s), 1.46 (3H, s); **13C-NMR** (100 MHz, CDCl₃): 201.1, 158.3, 139.9, 138.4, 128.9, 127.9, 127.4, 126.9, 126.6, 126.3, 125.1, 123.2, 117.6, 109.4, 88.6, 45.6, 21.5, 20.5; HRMS (ESI) calcd for C₁₇H₁₈NO₂ [M+H]⁺: 268.1338; Found: 268.1331.

3.0.2 General procedure for the synthesis of 2-hydroxyindoxyls 3c’-3g’ (GP-2):

To a stirring solution of N-substituted 3-hydroxy-2-oxindoles 1 (1 equiv.) in dry THF, Grignard reagent solution (4 equiv.; 1M in THF) was added dropwise at room temperature. The reaction mixture was then refluxed at 70 °C for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was cooled to room temperature and then quenched with saturated aqueous NH₄Cl solution followed by extraction with EtOAc (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (10/90 to 20/80) to give compounds 3c’-3g’.
2-Ethyl-2-hydroxy-1-methylindolin-3-one (3c'): Using the general procedure GP-2, compound 1a (200 mg, 1.23 mmol) and ethylmagnesium bromide 2f (4.9 mL, 4.92 mmol) provided compound 3c' (138 mg, 58%) as a yellow liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.53 (1H, d, $J$ = 7.8 Hz), 7.47 (1H, t, $J$ = 7.8 Hz), 6.72-6.68 (2H, m), 2.96 (3H, s), 2.05-1.96 (1H, m), 1.93-1.84 (1H, m), 1.67 (1H, sbr), 0.68 (3H, t, $J$ = 7.4 Hz); $^{13}$C-NMR (125 MHz, CDCl$_3$): 201.5, 161.0, 138.7, 135.7, 125.2, 117.7, 108.1, 90.5, 27.8, 26.6, 7.7; HRMS (ESI) calcd for C$_{11}$H$_{13}$NKO$_2$ [M+K]$^+$: 230.0583; Found: 230.0597.

1,2-Diethyl-2-hydroxyindolin-3-one (3d'): Using the general procedure GP-2, compound 1b (200 mg, 1.13 mmol) and ethylmagnesium bromide 2f (4.5 mL, 4.52 mmol) provided compound 3d' (130 mg, 56%) as a yellow liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.52 (1H, d, $J$ = 7.8 Hz), 7.46 (1H, t, $J$ = 7.8 Hz), 6.71-6.67 (2H, m), 3.55-3.46 (1H, m), 3.42-3.33 (1H, m), 2.63 (1H, sbr), 2.05-1.96 (1H, m), 1.93-1.85 (1H, m), 1.29 (3H, t, $J$ = 7.3 Hz), 0.69 (3H, t, $J$ = 7.8 Hz); $^{13}$C-NMR (125 MHz, CDCl$_3$): 201.8, 160.5, 138.7, 125.4, 118.2, 117.4, 108.2, 90.9, 35.8, 28.3, 14.6, 7.7; HRMS (ESI) calcd for C$_{12}$H$_{15}$NNaO$_2$ [M+Na]$^+$: 228.1000; Found: 228.1017.

1-Benzyl-2-hydroxy-2-pentylindolin-3-one (3e'): Using the general procedure GP-2, compound 1d (200 mg, 0.84 mmol) and pentylmagnesium bromide 2g (3.4 mL, 3.36 mmol) provided compound 3e' (152 mg, 58%) as a yellow liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.56 (1H, d, $J$ = 7.8 Hz), 7.38-7.29 (6H, m), 6.73 (1H, t, $J$ = 7.3 Hz), 6.55 (1H, d, $J$ = 8.3 Hz), 4.58 (2H, q, $J$ = 16.6 Hz), 2.79 (1H, sbr), 1.98-1.92 (1H, m), 1.87-1.80 (1H, m), 1.11-0.99 (4H, m), 0.90-0.83 (2H, m), 0.78 (3H, t, $J$ = 6.4 Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$): 201.4, 160.8, 138.5, 128.9, 128.0, 127.5, 127.4, 127.2, 125.2, 118.2, 109.2, 90.5, 45.8, 35.7, 31.8, 22.8, 22.4, 14.0; HRMS (ESI) calcd for C$_{20}$H$_{25}$NNaO$_2$ [M+Na]$^+$: 332.1627; Found: 332.1625.
**2-Hydroxy-1-(4-methoxybenzyl)-2-(octan-3-yl)indolin-3-one (3f’):** Using the general procedure GP-2, compound 1e (200 mg, 0.74 mmol) and 2-(ethyl)hexylmagnesium bromide 2h (3.0 mL, 2.96 mmol) provided compound 3f’ (172 mg, 60%) as a yellow liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.50 (1H, d, $J = 7.8$ Hz), 7.35 (1H, t, $J = 8.3$ Hz), 7.28 (2H, d, $J = 8.3$ Hz), 6.85 (2H, d, $J = 8.8$ Hz), 6.71 (1H, t, $J = 6.4$ Hz), 6.50 (1H, dd, $J = 5.4, 3.0$ Hz), 4.57 (1H, d, $J = 17.0$ Hz), 4.42 (1H, d, $J = 16.1$ Hz), 3.79 (3H, s), 2.07-1.82 (2H, m), 1.75-1.58 (3H, m), 1.13-1.04 (3H, m), 0.89-0.81 (5H, m), 0.78-0.74 (3H, m), 0.70 (1H, t, $J = 7.3$ Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$): 201.3, 160.3, 159.0, 138.4, 129.9, 128.6, 127.6, 125.3, 118.1, 114.2, 109.4, 90.6, 55.4, 45.5, 40.1, 31.8, 28.2, 26.2, 23.1, 22.8, 10.8, 9.9; HRMS (ESI) calcd for C$_{24}$H$_{31}$NNaO$_3$ [M+Na]$^+$: 404.2202; Found: 404.2203.

**1-Benzyl-2-cyclohexyl-2-hydroxyindolin-3-one (3g’):** Using the general procedure GP-2, compound 1d (200 mg, 0.84 mmol) and cyclohexylmagnesium bromide 2i (3.4 mL, 3.36 mmol) provided compound 3g’ (174 mg, 64%) as a yellow liquid; $^1$H-NMR (400 MHz, CDCl$_3$): 7.61 (1H, d, $J = 7.3$ Hz), 7.46-7.32 (6H, m), 6.84 (1H, dd, $J = 9.7, 7.3$ Hz), 6.57 (1H, d, $J = 8.3$ Hz), 4.67 (2H, s), 3.71 (1H, sbr), 2.04-1.97 (2H, m), 1.87-1.59 (6H, m), 1.17-1.09 (1H, m), 1.00-0.92 (2H, m); $^{13}$C-NMR (100 MHz, CDCl$_3$): 202.2, 161.2, 138.3, 128.8, 127.3, 129.0, 127.5, 127.2, 124.8, 118.2, 109.5, 91.9, 46.4, 35.7, 27.0, 26.5, 26.2, 25.3, 24.3; HRMS (ESI) calcd for C$_{21}$H$_{23}$NNaO$_2$ [M+Na]$^+$: 344.1626; Found: 344.1628.
4.0 Gram scale experiment:

Preparation of 5-fluoro-2-hydroxy-1-methyl-2-phenylindolin-3-one 3g:

Scheme S2. Gram scale synthesis of 3g.

To a stirring solution of 1i (1.0 g, 5.52 mmol, 1 equiv.) in dry THF (20 mL), phenylmagnesium bromide 2a (22 mL, 22.08 mmol, 4 equiv.) was added dropwise at room temperature. The resulting reaction mixture was then stirred at room temperature for 10 h. After completion of the reaction as monitored by TLC, the mixture was quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with EtOAc–hexane (10/90 to 20/80) to give compound 3g (1.10 g, 70%) as a red solid.

Preparation of 1,2-Diallyl-2-hydroxyindolin-3-one 3r:

Scheme S3. Gram scale synthesis of 3r.

To a stirring solution of 1c (1.0 g, 5.28 mmol, 1 equiv.) in dry THF (20 mL), allylmagnesium bromide 2c (17 mL, 16.84 mmol, 3 equiv) was added dropwise at room temperature. The resulting reaction mixture was then stirred at room temperature for 10 h. After completion of reaction as monitored by TLC, the mixture was quenched with saturated aqueous
NH₄Cl solution and extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with EtOAc–hexane (10/90 to 20/80) to give compound 3r (870 mg, 72%) as a yellow liquid.

5.0 Deuterium labelling experiment:

![Scheme S4](image)

**Scheme S4.** Deuterium labelling experiment for the synthesis of 3b.

To a stirring solution of 1c (50 mg, 0.26 mmol, 1 equiv.) in dry THF (20 mL), phenylmagnesium bromide 2a (1.1 mL, 1.1 mmol, 4 equiv) was added dropwise at room temperature. The resulting reaction mixture was then stirred at room temperature for 6 h. After completion of reaction as monitored by TLC, the mixture was quenched with D₂O and extracted with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with EtOAc–hexane (10/90 to 20/80) to give exclusively compound 3b as a brown gummy liquid.

6.0 Radical quenching experiment:

![Scheme S5](image)

**Scheme S5.** Deuterium labelling experiment for the synthesis of 3b.

To a stirring solution of 1c (50 mg, 0.26 mmol, 1 equiv.) in dry THF (20 mL), phenylmagnesium bromide 2a (1.1 mL, 1.1 mmol, 4 equiv) and radical inhibitor (0.52 mmol, 2 equiv.) were added at room temperature. The resulting reaction mixture was then stirred at room
temperature for 6 h. After completion of reaction as monitored by TLC, the mixture was quenched with saturated aqueous NH$_4$Cl solution and extracted with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with EtOAc–hexane (10/90 to 20/80) to give exclusively compound 3b as a brown gummy liquid (Yield: 76% in presence of TEMPO and 70% in presence of Galvinoxyl).

7.0 General procedure for the synthesis of C2-allyl-2,2-disubstituted oxindoles 6 (GP-3): To a solution of 2-hydroxyindoxyls 3 (1 equiv.) in dry THF (5 mL) was added allylmagnesium bromide solution (2 equiv., 1 M in THF) dropwise and the resulting mixture was stirred at room temperature for 3 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with saturated aqueous NH$_4$Cl solution followed by extraction with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (5/95 to 10/90) to give compounds 6a-b (Scheme S6).

![Scheme S6. Synthesis of C2-allyl-2,2-disubstituted oxindoles 6.](image)

2-Allyl-1-benzyl-5-methyl-2-phenylindolin-3-one (6a): Using the general procedure GP-3, compound 3m (100 mg, 0.30 mmol) and allylmagnesium bromide (0.6 mL, 0.60 mmol) provided compound 6a (82 mg, 76%) as a yellow liquid; $^1$H-NMR (500 MHz, CDCl$_3$): 7.44 (1H, s), 7.35-7.20 (11H, m), 6.62 (1H, d, $J = 8.2$ Hz), 5.59-5.50 (1H, m), 5.00 (1H, dd, $J = 15.2$, 1.9 Hz), 4.93 (1H, dd, $J = 8.8$, 1.3 Hz), 4.55 (1H, d, $J = 17.0$ Hz), 4.30 (1H, d, $J = 16.4$ Hz), 3.19...
(1H, dd, J = 7.6, 6.9 Hz), 2.96 (1H, dd, J = 6.9, 6.9 Hz), 2.31 (3H, s); 13C-NMR (75 MHz; CDCl3): 201.5, 160.5, 139.2, 138.0, 137.8, 131.9, 129.1, 128.6, 128.2, 127.4, 127.3, 126.8, 124.9, 120.2, 119.6, 109.3, 76.8, 48.6, 38.1, 20.5; HRMS (ESI) calcd for C25H24NO [M+H]+: 354.1858; Found: 354.1860.

2-Allyl-2-(4-methoxyphenyl)-1-methylindolin-3-one (6b): Using the general procedure GP-3, compound 3v (100 mg, 0.37 mmol) and allylmagnesium bromide 2d (0.7 mL, 0.74 mmol) provided compound 6b (77 mg, 72%) as a yellow liquid; 1H-NMR (500 MHz, CDCl3): 7.54 (1H, d, J = 7.6 Hz), 7.51-7.48 (1H, m), 7.16-7.12 (2H, m), 6.87-6.84 (2H, m), 6.79 (1H, d, J = 8.2 Hz), 6.69 (1H, t, J = 7.6 Hz), 5.46-5.39 (1H, m), 5.14 (1H, dd, J = 15.8, 1.3 Hz), 4.96 (1H, dd, J = 8.2, 1.9 Hz), 3.77 (3H, s), 3.29-3.25 (1H, m), 2.93 (3H, s), 2.82 (1H, dd, J = 7.6, 6.3 Hz); 13C-NMR (125 MHz; CDCl3): 201.3, 161.4, 159.4, 137.9, 132.0, 129.2, 127.4, 125.5, 119.1, 119.0, 116.9, 114.5, 107.4, 75.1, 55.4, 38.8, 28.4; HRMS (ESI) calcd for C19H20NO2 [M+H]+: 294.1494; Found: 294.1499.

8.0 Synthesis of 3-allyl or aryl-3-hydroxy oxindoles 72

8.0.1 General procedure for the synthesis of 3-allyl-3-hydroxy oxindoles 7a-b from 2-hydroxyindoxyls 3 (GP-4):

To a solution of 2-allyl-2-hydroxyindoxyls 3 (1 equiv.) in dry DMF (5 mL) was added sodium hydride (2 equiv.) portionwise at 0 °C and the resulting mixture was stirred at room temperature for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with water followed by extraction with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na2SO4, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (10/90 to 20/80) to give compounds 7a-b (Scheme S7).
Scheme S7. Synthesis of 3-allyl-3-hydroxy oxindoles 7 from 2-hydroxyindoxyls 3.

1,3-Diallyl-3-hydroxyindolin-2-one (7a): Using the general procedure GP-4, compound 3r (100 mg, 0.44 mmol) and sodium hydride (21 mg, 0.88 mmol) provided compound 7a (82 mg, 82%) as a straw yellow solid; \textsuperscript{1}H-NMR (400 MHz, CDCl\textsubscript{3}): 7.39 (1H, d, J = 7.3 Hz), 7.28-7.24 (1H, m), 7.07 (1H, t, J = 7.9 Hz), 6.79 (1H, d, J = 7.9 Hz), 5.81-5.73 (1H, m), 5.61-5.50 (1H, m), 5.23-5.17 (2H, m), 5.04 (2H, m), 4.42-4.37 (1H, m), 4.18-4.12 (1H, m), 4.03 (1H, s), 2.78 (1H, dd, J = 7.3, 6.1 Hz), 2.65 (1H, dd, J = 8.0, 4.9 Hz); \textsuperscript{13}C-NMR (100 MHz; CDCl\textsubscript{3}): 177.9, 142.5, 131.2, 130.6, 129.9, 129.5, 124.2, 123.1, 120.3, 117.7, 109.3, 76.1, 43.0, 42.4; HRMS (ESI) calcd for C\textsubscript{14}H\textsubscript{15}NKO\textsubscript{2} [M+K]\textsuperscript{+}: 268.0740; Found: 268.0742.

3-Allyl-1-benzyl-5-chloro-3-hydroxyindolin-2-one (7b): Using the general procedure GP-4, compound 3u (100 mg, 0.32 mmol) and allylmagnesium bromide 2d (15 mg, 0.64 mmol) provided compound 7b (86 mg, 86%) as a brown solid; \textsuperscript{1}H-NMR (500 MHz, CDCl\textsubscript{3}): 7.37 (1H, d, J = 1.7 Hz), 7.30-7.22 (5H, m), 7.13 (1H, dd, J = 5.9, 2.6 Hz), 6.57 (1H, d, J = 8.4 Hz), 5.60-5.51 (1H, m), 5.09 (2H, dd, J = 15.9, 9.3 Hz), 4.96 (1H, d, J = 15.9 Hz), 4.67 (1H, d, J = 15.9 Hz), 4.29 (1H, s), 2.81 (1H, dd, J = 6.8, 6.7 Hz), 2.70 (1H, dd, J = 8.4, 8.4 Hz); \textsuperscript{13}C-NMR (125 MHz; CDCl\textsubscript{3}): 178.0, 140.9, 135.0, 131.6, 130.1, 129.5, 128.9, 128.7, 127.9, 127.3, 124.9, 121.0, 110.6, 76.3, 44.0, 42.9; HRMS (ESI) calcd for C\textsubscript{18}H\textsubscript{16}ClNNaO\textsubscript{2} [M+Na]\textsuperscript{+}: 336.0767; Found: 336.0773.
8.0.2 General procedure for the synthesis of 3-aryl or allyl-3-hydroxy oxindoles 7c-e from 3-hydroxyoxindoles 1 (GP-5):

To a solution of 3-hydroxyoxindoles 1 (1 equiv.) in dry THF (10 mL) was added aryl or allyl Grignard solution (4 equiv. for aryl and 3 equiv. for allyl Grignard solution; 1 M in THF) portionwise at 0 °C and the resulting mixture was stirred at room temperature for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with aq. NH₄Cl followed by extraction with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then dissolved in 10 mL of DMF and then sodium hydride (2 equiv.) was added to it portionwise at 0 °C and the reaction mixture was stirred at room temperature for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with water followed by extraction with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (10/90 to 20/80) to give compounds 7c-e (Scheme S8).

Scheme S8. Synthesis of 3-aryl or allyl-3-hydroxy oxindoles 7 from 3-hydroxyoxindoles 1.

1-Allyl-3-hydroxy-3-(4-methoxyphenyl)indolin-2-one (7c): Using the general procedure GP-5, compound 1c (200 mg, 1.05 mmol), p-methoxyphenylmagnesium bromide 2b (4.2 mL, 4.20 mmol) and sodium hydride (48.3 mg, 2.10 mmol) provided compound 7c (217 mg, 70%) as a pale yellow solid; ¹H-NMR (400 MHz, CDCl₃): 7.31-7.25 (4H, m), 7.05 (1H, t, J = 7.4 Hz), 6.87-6.80 (3H, m), 5.87-5.77 (1H, m), 5.26-5.19 (2H, m), 4.43-4.37 (1H,
m), 4.20 (1H, dd, J = 10.8, 5.4 Hz), 4.03 (1H, s), 3.75 (3H, s); \textbf{13C-NMR} (100 MHz; CDCl₃): 177.6, 159.6, 142.6, 132.4, 131.9, 131.2, 129.7, 126.9, 125.0, 123.5, 117.9, 114.1, 109.6, 77.7, 55.3, 42.6; HRMS (ESI) calcd for C₁₈H₁₈NO₃ [M+H⁺]: 296.1287; Found: 296.1279.

\textbf{3- Allyl-5-bromo-3-hydroxy-1-methylindolin-2-one (7d):} Using the general procedure \textbf{GP-5}, compound \textbf{1k} (200 mg, 0.83 mmol), allylmagnesium bromide \textbf{2c} (2.5 mL, 2.49 mmol) and sodium hydride (40 mg, 1.66 mmol) provided compound \textbf{7d} (178 mg, 76%) as a brown solid; \textbf{1H-NMR} (500 MHz, CDCl₃): 7.49 (1H, d, J = 1.7 Hz), 7.45 (1H, dd, J = 5.9, 1.7 Hz), 6.70 (1H, d, J = 8.3 Hz), 5.65-5.57 (1H, m), 5.13 (1H, d, J = 5.0 Hz), 5.10 (1H, s), 3.15 (3H, s), 2.71 (1H, dd, J = 7.5, 5.9 Hz), 2.59 (1H, dd, J = 8.4, 5.1 Hz); \textbf{13C-NMR} (100 MHz; CDCl₃): 177.5, 142.5, 132.6, 131.9, 130.1, 127.6, 121.0, 115.9, 110.0, 76.0, 43.0, 26.4; HRMS (ESI) calcd for C₁₂H₁₂BrNNaO₂ [M+Na⁺]: 303.9949; Found: 303.9947.

\textbf{3- Allyl-1-benzyl-3-hydroxy-5-(trifluoromethoxy)indolin-2-one (7e):} Using the general procedure \textbf{GP-5}, compound \textbf{1s} (200 mg, 0.62 mmol), allylmagnesium bromide \textbf{2c} (2.0 mL, 1.86 mmol) and sodium hydride (30 mg, 1.24 mmol) provided compound \textbf{7e} (162 mg, 72%) as a brown solid; \textbf{1H-NMR} (500 MHz, CDCl₃): 7.32-7.23 (6H, m), 7.04 (1H, dd, J = 6.7, 1.7 Hz), 6.65 (1H, d, J = 8.4 Hz), 5.59-5.54 (1H, m), 5.07 (2H, t, J = 8.4 Hz), 5.00 (1H, d, J = 15.9 Hz), 4.84 (1H, s), 4.66 (1H, d, J = 15.9 Hz), 2.84 (1H, dd, J = 6.8, 6.7 Hz), 2.71 (1H, dd, J = 8.4, 4.2 Hz); \textbf{13C-NMR} (100 MHz; CDCl₃): 178.5, 145.2, 140.9, 135.0, 131.7, 130.1, 128.9, 127.9, 127.4, 124.4, 122.5, 121.9, 120.9, 119.3, 118.4, 116.8 (q, \textit{J} \text{C}-\text{F} = 255.2 Hz), 110.1, 76.4, 44.1, 42.9; HRMS (ESI) calcd for C₁₉H₁₇F₃NO₃ [M+H⁺]: 364.1161; Found: 364.1172.

\textbf{9.0 General procedure for the synthesis of 3-aryl or allyl-3-methoxy oxindoles 8a-b from 2-hydroxyindoxyls 3 (GP-6):}

To a solution of 2-aryl or allyl-2-hydroxyindoxyls 3 (1 equiv.) in dry DMF (5 mL) was added sodium hydride (2 equiv.) portionwise at 0 °C and the resulting mixture was stirred at room temperature for 10 min. Then methyl iodide (1.5 equiv.) was added to the reaction mixture and it
was stirred at room temperature for 6 h. After completion of reaction as monitored by the TLC, the reaction mixture was quenched with water followed by extraction with EtOAc (3 x 5 mL). The combined organic phases were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The crude residue was then purified by column chromatography on silica gel with ethylacetate–hexane (5/95 to 15/85) to give compounds 8a-b (Scheme S9).

![Scheme S9](image)

Scheme S9. Synthesis of 3-aryl or allyl-3-methoxy oxindoles 8 from 2-hydroxyindoxyls 3.

1-Allyl-3-methoxy-3-phenylindolin-2-one (8a): Using the general procedure GP-6, compound 3b (100 mg, 0.38 mmol), sodium hydride (18 mg, 0.76 mmol) and methyl iodide (0.8 mL, 0.57 mmol) provided compound 8a (74 mg, 70%) as a pale yellow solid; $^{1}$H-NMR (400 MHz, CDCl$_3$): 7.40-7.26 (7H, m), 7.13 (1H, t, $J$ = 7.8 Hz), 6.91 (1H, d, $J$ = 7.8 Hz), 5.89-5.79 (1H, m), 5.26-5.21 (2H, m), 4.42-4.31 (2H, m), 3.25 (3H, s); $^{13}$C-NMR (100 MHz; CDCl$_3$): 175.1, 143.9, 138.9, 131.4, 130.2, 128.6, 128.5, 128.2, 126.4, 126.0, 123.4, 118.0, 109.7, 84.1, 53.3, 42.6; HRMS (ESI) calcd for C$_{18}$H$_{17}$NNaO$_2$ [M+Na]$^+$: 302.1157; Found: 302.1156.

1,3-Diallyl-3-methoxyindolin-2-one (8b): Using the general procedure GP-6, compound 3r (100 mg, 0.44 mmol), sodium hydride (21 mg, 0.88 mmol) provided compound 8b (80 mg, 75%) as a brown solid; $^{1}$H-NMR (400 MHz, CDCl$_3$): 7.34-7.27 (2H, m), 7.13-7.08 (1H, m), 6.82 (1H, d, $J$ = 7.8 Hz), 5.85-5.75 (1H, m), 5.58-5.47 (1H, m), 5.24-5.19 (2H, m), 5.05-4.98 (2H, m), 4.43-4.26 (2H, m), 3.05 (3H, s), 2.76 (1H, dd, $J$ = 7.4, 6.4 Hz), 2.64 (1H, dd, $J$ = 8.3, 4.9 Hz); $^{13}$C-NMR (125 MHz; CDCl$_3$):
175.5, 143.3, 131.4, 130.8, 129.8, 128.3, 127.8, 126.8, 124.7, 123.0, 120.0, 117.8, 109.4, 82.6, 53.1, 42.4, 42.2; HRMS (ESI) calcd for C_{15}H_{18}NO_{2} [M+H]^+: 244.1338; Found: 244.1342.

10.0 Synthesis of bis-indoxyl spirofuran derivative 9:³

10.0.1 Synthesis of bis-indoxyl spirofuran 9a-b from 3-hydroxy-2-oxindoles 1:

\[
\text{Bis-indoxyl spirofuran (9a): Using the general procedure GP-1, compound 1c (200 mg, 0.84 mmol) and methylmagnesium bromide 2e (3.4 mL, 3.36 mmol) provided compound 9a (262 mg, 64\%) as a deep green liquid; }^{1}H-NMR (500 MHz, CDCl}_{3}): 7.55 (2H, d, J = 7.6 Hz), 7.36-7.23 (12H, m), 6.72 (2H, t, J = 7.6 Hz), 6.47 (2H, d, J = 8.4 Hz), 5.05 (2H, d, J = 16.8 Hz), 4.68 (2H, d, J = 16.8 Hz), 2.71-2.64 (2H, m), 2.18-2.11 (2H, m); ^{13}C-NMR (125 MHz, CDCl}_{3}): 201.0, 160.7, 138.6, 138.5, 128.8, 127.1, 126.8, 125.3, 118.4, 117.6, 109.4, 97.3, 44.7, 29.6; HRMS (ESI) calcd for C_{32}H_{27}N_{2}O_{3} [M+H]^+: 487.2022; Found: 487.2025.
\]

\[
\text{Bis-indoxyl spirofuran (9b): Using the general procedure GP-1, compound 1i (200 mg, 1.10 mmol) and methylmagnesium bromide 2e (4.4 mL, 4.40 mmol) provided compound 9b (225 mg, 55\%) as a deep green liquid; }^{1}H-NMR (400 MHz, CDCl}_{3}): 7.24-7.19 (4H, m), 6.62 (2H, dd, J = 4.4, 3.9 Hz), 3.03 (6H, s), 2.75-2.72 (2H, m), 2.17-2.13 (2H, m); ^{13}C-NMR (100 MHz, CDCl}_{3}): 200.7, 158.0, 157.0, 126.2, 125.9, 117.8, 110.6, 109.5, 109.4, 97.8, 28.5, 27.2; HRMS (ESI) calcd for C_{20}H_{17}F_{2}N_{2}O_{3} [M+H]^+: 371.1207; Found: 371.1219.
\]
**10.0.2 Transformation of 2-hydroxyindoxyl 3a’ to bis-indoxyl spirofuran 9c:**

The 2-hydroxyindoxyl derivative 3a’, obtained by methylmagnesium bromide 2e addition to 1c converted to the corresponding spiroindoxyl dimer 9c via spontaneous aerial oxidation on standing (Scheme S11).

**Scheme S11. Transformation of 2-hydroxyindoxyl 3a’ to spiroindoxyl dimer 9c.**

**Bis-indoxyl spirofuran (9c):** The 2-hydroxyindoxyl 3a’ (155 mg, 0.76 mmol) provided compound 9c (197 mg, 68%) as a deep green liquid; **1H-NMR** (400 MHz, CDCl₃): 7.53 (2H, d, J = 7.8 Hz), 7.44-7.40 (2H, m), 6.72 (2H, t, J = 7.3 Hz), 6.62 (2H, d, J = 8.3 Hz), 5.95-5.85 (2H, m), 5.26-5.15 (4H, m), 4.46-4.40 (2H, m), 4.05-4.00 (2H, m), 2.80-2.70 (2H, m), 2.18-2.08 (2H, m); **13C-NMR** (125 MHz, CDCl₃): 201.3, 160.0, 138.5, 134.3, 125.2, 118.1, 117.5, 116.3, 109.3, 97.1, 43.3, 29.3; HRMS (ESI) calcd for C₂₄H₂₃N₂O₃ [M+H]+: 387.1709; Found: 387.1723.

**11.0 X-Ray Crystallography of compound 3g and 9c:** Intensity data was collected on a Bruker’s Kappa Apex II CCD Duo diffractometer with graphite monochromated MoKα radiation (0.71073 Å) at the temperature of 296 K. Scaling and multi-scan absorption correction were employed using SADABS. The structure was solved by direct methods and all the non-hydrogen atoms were refined anisotropically while the hydrogen atoms fixed in the predetermined positions by Shelxs-97 and Shelxl-97 packages respectively.
Figure S1. The ORTEP diagram of 3g showing 50% probability thermal ellipsoid.

Crystal Data and Details of the Structure Determination for 3g:

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Data/restraints/parameters | 2221/0/175
Goodness-of-fit on F^2 | 0.942
Final R indexes [I>=2σ (I)] | R_1 = 0.0502, wR_2 = 0.1361
Final R indexes [all data] | R_1 = 0.1049, wR_2 = 0.1747
Largest diff. peak/hole / e Å^{-3} | 0.17/-0.15

Figure S2. The ORTEP diagram of 9c showing 50% probability thermal ellipsoid.

Crystal Data and Details of the Structure Determination for 9c:

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12.0 References.

13.0 $^1$H and $^{13}$C NMR spectra of synthesized compounds:

$^1$H and $^{13}$C NMR spectra of 3a:
$^1$H and $^{13}$C NMR spectra of 3b:
$^{1}H$ and $^{13}C$ NMR spectra of 3c:
$^1$H and $^{13}$C NMR spectra of 3d:

![NMR spectra image]
$^1$H and $^{13}$C NMR spectra of 3e:
$^1$H and $^{13}$C NMR spectra of 3f:
$^1$H and $^{13}$C NMR spectra of 3g:
$^1$H and $^{13}$C NMR spectra of 3h:
$^1$H and $^{13}$C NMR spectra of 3i:
$^1$H and $^{13}$C NMR spectra of 3j:
$^1$H and $^{13}$C NMR spectra of 3k:
$^1$H and $^{13}$C NMR spectra of 3l:
$^1$H and $^{13}$C NMR spectra of 3m:
$^1$H and $^{13}$C NMR spectra of 3n:
$^1$H and $^{13}$C NMR spectra of 3o:
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$^1$H and $^{13}$C NMR spectra of 9a:
$^1$H and $^{13}$C NMR spectra of 9b:
$^{1}H$ and $^{13}C$ NMR spectra of $9c$: 

![NMR Spectra Image]

_X: parts per Million (ppm)_; _Y: Intensities_.