Supporting Information

α-Selective Allylation of Isatin Imines Using Metallic Barium

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Experimental Section

General Methods. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 using ATR. NMR spectra were recorded on a JEOL JNM ECS-400 (400 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR, Center for Analytical Instrumentation, Chiba University) or ECA-500 spectrometer (500 MHz for $^1$H NMR and 125.65 MHz for $^{13}$C NMR, Center for Analytical Instrumentation, Chiba University). Chemical shifts were reported in ppm on the δ scale relative to Me$_4$Si (δ = 0 for $^1$H NMR), CDCl$_3$ (δ = 77.0 for $^{13}$C NMR) as an internal reference. ESI mass spectra were measured on a Thermo Scientific Exactive (Center for Analytical Instrumentation, Chiba University). Column chromatography was conducted with silica gel 60 N (KANTO CHEMICAL, spherical, neutral, 63-230 µm). Analytical TLC was done on precoated (0.25 mm) silica-gel plates. HPLC analysis was performed on JASCO HPLC systems consisting of the following instruments: pump, PU-2080; detector, UV-2075, measured at 254 nm; column, Daicel Chiralpak AD-H. All experiments were carried out in Schlenk tube under atmosphere of standard grade argon gas. THF was freshly distilled over sodium benzophenone ketyl under argon gas. Lithium wire (>99.9%) and biphenyl (ReagentPlus®, 99.5%) was purchased from Sigma-Aldrich. BaI$_2$ · 2H$_2$O was purchased from KANTO CHEMICAL. Barium rod (>99%) was purchased from Aldrich. Allylic chlorides were purchased from TCI or prepared from the corresponding alcohols by Appel reaction.$^1$ Isatin (98%) was purchased from Alfa Aesar. N-Protected isatins and isatin imines were prepared by the following methods.$^2$

General Experimental Procedure for Preparation of N-Protected Isatins:

\[
\begin{align*}
\text{Isatin} & \xrightarrow{R},\text{Br},\text{NaH} \quad \text{DMF, } 0^\circ\text{C} \rightarrow r.t. \quad \text{N-Protected Isatin}
\end{align*}
\]
To a solution of isatin (10 mmol) in DMF (10 mL), NaH (10 mmol) was added slowly at 0 °C. After the suspension turned dark purple, the corresponding alkyl bromide (10 mmol) was added and stirred at room temperature until the isatin disappeared (~1 h). This reaction mixture was added to water (10 mL) and the precipitate was filtrated, which was further purified by recrystallization from CHCl₃. Thus, the target N-protected isatin was obtained as orange solids.

**General Experimental Procedure for Preparation of Isatin Imines:**

![Diagram of reaction](image)

To a solution of N-protected isatin (10 mmol) in EtOH (50 mL), the corresponding aniline (10 mmol) and MgSO₄ (3 g) were added. Then, the mixture was stirred at room temperature until the starting materials disappeared (~12 h), and the suspension turned yellow. MgSO₄ was removed by filtration through celite. The residue was concentrated in vacuo, which was further purified by recrystallization from CHCl₃. Thus, the target isatin imine was obtained as yellow solids.

**General Experimental Procedure for Preparation of Allylic Chlorides:**

![Diagram of reaction](image)

Into a two-necked flask (300 mL), the corresponding alcohol (100 mmol) was placed and diluted with CCl₄ (60 mL). To the solution, PPh₃ (120 mmol) was added, and the mixture was heated at 85 °C for 3 h. After the completion of reaction, the resulting white suspension was cooled to room temperature and then hexane (50 mL) was added. The mixture was filtered and the precipitate was washed with hexane (10 mL) three times. The combined organic layer was concentrated in vacuo followed by distillation under reduced pressure affording the corresponding allylic chloride as a colorless liquid.

**General Experimental Procedure for Allylation of Isatin Imines Using Metallic Barium (Entry 6 in Table 1; Tables 2-4; Entries 1 and 3 in Table 5):**

Freshly cut barium (small pieces, 1.0 mmol) was placed in a Schlenk tube (50 mL)
under an argon atmosphere and covered with dry THF (1 mL). The mixture underwent ultrasonication for 30 min and THF was removed through a cannula under an argon stream. The resulting barium pieces were vigorously stirred under reduced pressure until they turned to powder. Then, a solution of allylic chloride (2, 1.0 mmol) and isatin imine 1 (0.25 mmol) in THF (4 mL) was added to the resulting barium powder at room temperature under an argon atmosphere. After being heated to 70 °C, the mixture was stirred for 12 h at this temperature and concentrated in vacuo after filtration through a celite pad. The residual crude product was purified by column chromatography on silica gel (hexane-EtOAc, 9:1) to afford 3-allylated 3-amino-2-oxindole 3. The chemical yield was determined by 1H NMR using 1,4-bis(trimethylsilyl)benzene as an internal standard.

General Experimental Procedure for Generation of Reactive Barium (Entries 2 and 4 in Table 5):
To a solution of biphenyl (370 mg, 2.4 mmol) in dry THF (5 mL) was added freshly cut lithium (16.7 mg, 2.4 mmol). Stirring the mixture at room temperature for 2 h gave dark blue lithium biphenyldi solution. Anhydrous BaI$_2$ (470 mg, 1.2 mmol) was placed in a separate flask, and this was covered with dry THF (5 mL) and stirred for 20 min at room temperature. To the solution of BaI$_2$ in THF was added at room temperature a solution of lithium biphenyldi in THF under an argon stream. The reaction mixture was stirred for 20 min at room temperature, and the resulting dark brown suspension of reactive barium thus prepared was ready to use.

General Experimental Procedure for Reactive Barium-Promoted Prenylation of Isatin Imine 1a or 1h (Entries 2 and 4 in Table 5):
To the resulting dark brown suspension of reactive barium (1.2 mmol) in THF (10 mL) was added a solution of prenyl chloride (2a, 1.0 mmol) and isatin imine 1a or 1h (0.25 mmol) in THF (4 mL) at -78 °C with syringe pump (slow addition 6 mL/h) and the mixture was stirred for 2 h at this temperature. To the mixture was added a saturated NH$_4$Cl aq. (5 mL), and the aqueous layer was extracted with CH$_2$Cl$_2$ (10 mL) three times. The combined organic extracts were washed with sodium thiosulfate (10% (w/v)) and brine, dried over Na$_2$SO$_4$, and concentrated in vacuo after filtration. The residual crude product was purified by column chromatography on silica gel (9:1 hexane-ethyl acetate as eluant) to afford the 3-prenylated 3-amino-2-oxindole 3aa or 3ha. The chemical yield was determined by 1H NMR using CH$_3$CN as an internal standard.
1-Benzyl-3-((4-bromophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one  (3aa, Entry 6 in Table 1; Entry 8 in Table 4; Entry 1 in Table 5):

![Chemical structure](image)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.19-7.31 (m, 7H, Ar-H), 6.98-7.04 (m, 3H, Ar-H), 6.78 (d, 1H, $J = 7.9$ Hz, Ar-H), 6.05-6.08 (m, 2H, Ar-H), 5.05 (tt, 1H, $J = 1.1, 5.7$ Hz, CH), 4.96 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.87 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.40 (br, 1H, NH), 2.62-2.73 (m, 2H, CH$_2$), 1.67 (s, 3H, CH$_3$), 1.57 (s, 3H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.5, 144.3, 141.9, 138.1, 135.6, 131.7 (2C), 129.5, 129.0, 128.7 (2C), 127.7, 127.6 (2C), 123.8, 122.9, 117.0 (2C), 115.4, 111.1, 109.6, 64.4, 44.1, 39.0, 26.0, 18.1; IR (neat) 3328, 2917, 1700, 1592, 1486, 1369, 1320, 812, 754, 731 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{26}$H$_{25}$ON$_2$BrNa]$^+$ ([M+Na]$^+$): 483.1042, found: 483.1036; mp 136-137 °C.

1-Benzyl-3-(3-methylbut-2-en-1-yl)-3-(phenylamino)indolin-2-one (3ba, Entry 1 in Table 2):

![Chemical structure](image)

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.25-7.31 (m, 6H, Ar-H), 7.20 (td, 1H, $J = 0.8, 7.8$ Hz, Ar-H), 7.01 (t, 1H, $J = 7.4$ Hz, Ar-H), 6.93 (dd, 2H, $J = 0.8, 7.8$ Hz, Ar-H), 6.76 (d, 1H, $J = 7.8$ Hz, Ar-H), 6.66 (t, 1H, $J = 7.4$ Hz, Ar-H), 6.20 (d, 2H, $J = 7.8$ Hz, Ar-H), 5.07 (t, 1H, $J = 7.4$ Hz, CH), 4.96 (d, 1H, $J = 15.7$ Hz, one proton of CH$_2$), 4.90 (d, 1H, $J = 15.7$ Hz, one proton of CH$_2$), 4.40 (br, 1H, NH), 2.64-2.75 (m, 2H, CH$_2$), 1.67 (s, 3H, CH$_3$), 1.58 (s, 3H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.9, 145.3, 141.9, 137.8, 135.8, 130.0, 129.0 (2C), 128.8, 128.7 (2C), 127.6 (2C), 127.6 123.8, 122.8, 119.1, 115.6, 115.3 (2C), 109.4, 64.5, 44.0, 39.2, 26.0, 18.1; IR (neat) 3352, 2916, 1714, 1604, 1464, 1356, 1326, 1173, 746, 730, 692 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{26}$H$_{25}$ON$_2$Na]$^+$
([M+Na]⁺): 405.1937, found: 405.1930; mp 62-64 °C.

1-Benzyl-3-(3-methylbut-2-en-1-yl)-3-(p-tolylamino)indolin-2-one (3ca, Entry 2 in Table 2):

1H NMR (400 MHz, CDCl₃) δ 7.15-7.33 (m, 7H, Ar-H), 7.00 (t, 1H, J = 7.6 Hz, Ar-H), 6.70-6.75 (m, 3H, Ar-H), 6.16 (d, 2H, J = 8.2 Hz, Ar-H), 5.04 (t, 1H, J = 7.4 Hz, CH), 4.93 (d, 1H, J = 15.7 Hz, one proton of CH₃), 4.86 (d, 1H, J = 15.5 Hz, one proton of CH₃), 4.28 (br, 1H, NH), 2.74-2.64 (m, 2H, CH₂), 2.13 (s, 3H, CH₃), 1.65 (s, 3H, CH₃), 1.56 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 178.0, 142.8, 142.0, 137.5, 135.7, 130.1, 129.4 (2C), 128.64, 128.57 (3C), 127.4 (3C), 123.8, 122.7, 116.0 (2C), 115.7, 109.3, 64.9, 43.9, 39.0, 26.0, 20.4, 18.0; IR (neat) 3323, 2919, 1701, 1612, 1484, 1464, 1310, 1167, 745, 691 cm⁻¹; MS (ESI) Exact Mass Calcd for [C₂₇H₂₅ON₂]⁺ ([M+H]⁺): 397.2274, found: 397.2267; mp 69-72 °C.

1-Benzyl-3-((4-isopropylphenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3da, Entry 3 in Table 2):

1H NMR (400 MHz, CDCl₃) δ 7.23-7.33 (m, 6H, Ar-H), 7.18 (td, 1H, J = 1.1, 7.7 Hz, Ar-H), 7.00 (t, 1H, J = 7.5 Hz, Ar-H), 6.79 (d, 2H, J = 8.4 Hz, Ar-H), 6.74 (d, 1H, J = 7.9 Hz, Ar-H), 6.15 (d, 2H, J = 8.4 Hz, Ar-H), 5.05 (t, 1H, J = 7.0 Hz, CH), 4.95 (d, 1H, J = 15.4 Hz, one proton of CH₃), 4.89 (d, 1H, J = 15.4 Hz, one proton of CH₃), 4.31 (br, 1H, NH), 2.63-2.75 (m, 3H, CH₂ and CH), 1.65 (s, 3H, CH₃), 1.56 (s, 3H, CH₃), 1.114 (d, 3H, J = 7.1 Hz, CH₃), 1.108 (d, 3H, J = 7.1 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 178.1, 143.2, 142.0, 139.4, 137.5, 135.8, 130.3, 128.65, 128.61 (2C), 127.6 (2C), 127.5, 126.8 (2C), 123.8, 122.7, 115.7, 115.3 (2C), 109.4, 64.6, 44.0, 39.2, 33.0, 26.0,
24.1, 24.0, 18.0; IR (neat) 3369, 2928, 1705, 1612, 1524, 1465, 1324, 1172, 752, 705 cm⁻¹; MS (ESI) Exact Mass Calcd for [C_{29}H_{33}ON_{2}]⁺ ([M+H]⁺): 425.2587, found: 425.2580; mp 102-107 °C.

1-Benzyl-3-((4-methoxyphenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3ea, Entry 4 in Table 2):

![Structural formula](image)

^1^H NMR (400 MHz, CDCl₃) δ 7.38 (dd, 1H, J = 0.7, 7.5 Hz, Ar-H), 7.20-7.23 (m, 2H, Ar-H), 7.16 (td, 1H, J = 1.4, 7.7 Hz, Ar-H), 7.01-7.07 (m, 3H, Ar-H), 6.65 (d, 1H, J = 7.7 Hz, Ar-H), 6.50-6.53 (m, 2H, Ar-H), 6.29-6.32 (m, 2H, Ar-H), 5.03 (tt, 1H, J = 1.4, 7.0 Hz, CH), 4.93 (d, 1H, J = 15.6 Hz, one proton of CH₂), 4.77 (d, 1H, J = 15.6 Hz, one proton of CH₂), 4.17 (br, 1H, NH), 3.65 (s, 3H, CH₃), 2.66-2.73 (m, 2H, CH₂), 1.64 (s, 3H, CH₃), 1.57 (s, 3H, CH₃); ^1^C NMR (100 MHz, CDCl₃) δ 178.1, 153.9, 142.3, 138.8, 137.3, 135.6, 130.1, 128.8, 128.6 (2C), 127.4, 127.3(2C), 124.1, 122.7, 119.4 (2C), 115.9, 114.2 (2C), 109.4, 66.0, 55.4, 43.8, 38.6, 26.0, 18.1; IR (neat) 3367, 2911, 1709, 1613, 1509, 1465, 1237, 1171, 1034, 819, 750, 697 cm⁻¹; MS (ESI) Exact Mass Calcd for [C_{29}H_{32}O_{2}N_{2}]⁺ ([M+H]⁺): 413.2224, found: 413.2215; mp 65-69 °C.

1-Benzyl-3-((4-fluorophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3fa, Entry 5 in Table 2):

![Structural formula](image)

^1^H NMR (400 MHz, CDCl₃) δ 7.33 (dd, 1H, J = 0.9, 7.3 Hz, Ar-H), 7.16-7.23 (m, 6H, Ar-H), 7.03 (dt, 1H, J = 0.7, 6.8 Hz, Ar-H), 6.73 (d, 1H, J = 7.9 Hz, Ar-H), 6.59-6.66 (m, 2H, Ar-H), 6.18-6.23 (m, 2H, Ar-H), 5.04 (tt, 1H, J = 1.1, 7.3 Hz, CH), 4.95 (d, 1H, J = 15.4 Hz, one proton of CH₂), 4.82 (d, 1H, J = 15.6 Hz, one proton of CH₂), 4.29 (br, 1H, NH), 2.60-2.74 (m, 2H, CH₂), 1.65 (s, 3H, CH₃), 1.57 (s, 3H, CH₃); ^1^C NMR (100 MHz, CDCl₃) δ 177.7, 157.0 (d, ^1^J = 238.4 Hz (C-F)), 142.1, 141.4, 137.7, 135.6, 129.7,
128.9, 128.6 (2C), 127.6, 127.4 (2C), 123.9, 122.8, 117.8 (d, 2C, \(^3J = 7.6\) Hz (C-F)), 115.5, 115.4 (d, 2C, \(^2J = 36.2\) Hz (C-F)), 109.5, 65.3, 43.9, 38.8, 26.0, 18.0; IR (neat) 3324, 2967, 1699, 1614, 1505, 1312, 1221, 1168, 820, 749, 693 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{20}\)H\(_{15}\)ON\(_2\)FNa\(^+\)]\(^+\) ([M+Na\(^+\)]: 423.1842, found: 423.1833; mp 82-86 °C.

1-Benzyl-3-((4-chlorophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one  (3ga, Entry 6 in Table 2):

\[\includegraphics[width=0.2\textwidth]{image} \]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.19-7.31 (m, 7H, Ar-H), 7.02 (dt, 1H, \(J = 0.9, 7.5\) Hz, Ar-H), 6.84-6.88 (m, 2H, Ar-H), 6.78 (d, 1H, \(J = 7.9\) Hz, Ar-H), 6.10-6.14 (m, 2H, Ar-H), 5.06 (tt, 1H, \(J = 1.1, 7.3\) Hz, CH), 4.96 (d, 1H, \(J = 15.4\) Hz, one proton of CH\(_2\)), 4.87 (d, 1H, \(J = 15.6\) Hz, one proton of CH\(_2\)), 4.39 (br, 1H, NH), 2.62-2.73 (m, 2H, CH\(_2\)), 1.67 (s, 3H, CH\(_3\)), 1.57 (s, 3H, CH\(_3\)); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.6, 143.9, 142.0, 138.0, 135.6, 129.6, 129.0, 128.8 (2C), 128.7 (2C), 127.7, 127.6 (2C), 124.0, 123.8, 122.9, 116.7 (2C), 115.4, 109.6, 64.6, 44.1, 39.0, 26.0, 18.1; IR (neat) 3319, 2912, 1697, 1600, 1490, 1467, 1372, 1354, 1308, 1178, 817, 761 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{26}\)H\(_{23}\)ON\(_2\)ClNa\(^+\)]\(^+\) ([M+Na\(^+\)]: 439.1547, found: 439.1538; mp 112-116 °C.

1-Benzyl-3-((4-iodophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one  (3ha, Entry 7 in Table 2; Entry 3 in Table 5):

\[\includegraphics[width=0.2\textwidth]{image} \]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.25-7.33 (m, 6H, Ar-H), 7.21 (td, 1H, \(J = 1.4, 7.7\) Hz, Ar-H), 7.15-7.19 (m, 2H, Ar-H), 7.01 (dt, 1H, \(J = 0.7, 6.8\) Hz, Ar-H), 6.78 (d, 1H, \(J = 7.7\) Hz, Ar-H), 5.94-5.98 (m, 2H, Ar-H), 5.05 (tt, 1H, \(J = 1.4, 8.2\) Hz, CH), 4.95 (d, 1H, \(J = 15.4\) Hz, one proton of CH\(_2\)), 4.88 (d, 1H, \(J = 15.4\) Hz, one proton of CH\(_2\)), 4.42 (br,
1H, NH), 2.62-2.73 (m, 2H, CH₂), 1.66 (s, 3H, CH₃), 1.57 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 177.5, 144.9, 141.9, 138.1, 137.6 (2C), 135.6, 129.5, 129.0, 128.7 (2C), 127.7, 127.6 (2C), 123.7, 122.9, 117.3 (2C), 115.3, 109.5, 80.5, 64.2, 44.1, 39.0, 26.0, 18.1; IR (neat) 3327, 2917, 1702, 1588, 1484, 1462, 1366, 1347, 1319, 1173, 755, 731, 690 cm⁻¹; MS (ESI) Exact Mass Calcd for [C₂₆H₂₅ON₂Na⁺] (Na⁺): 531.0904, found: 531.0897; mp 126-129 °C.

**1-Benzyl-3-((3-methylbut-2-en-1-yl)-3-(4-(trifluoromethyl)phenyl)amino)indolin-2-one (3ia, Entry 8 in Table 2):**

![Structure 3ia](image)

¹H NMR (400 MHz, CDCl₃) δ 7.22-7.40 (m, 7H, Ar-H), 7.14 (d, 2H, J = 8.6 Hz, Ar-H), 7.02 (t, 1H, J = 7.3 Hz, Ar-H), 6.85 (d, 1H, J = 7.9 Hz, Ar-H), 6.15 (d, 2H, J = 8.6 Hz, Ar-H), 5.08 (t, 1H, J = 7.5 Hz, CH), 4.98 (d, 1H, J = 15.4 Hz, one proton of CH₂), 4.93 (d, 1H, J = 15.4 Hz, one proton of CH₂), 4.71 (br, 1H, NH), 2.64-2.76 (m, 2H, CH₂), 1.68 (s, 3H, CH₃), 1.58 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 177.2, 147.9, 141.8, 138.4, 135.7, 129.3, 129.1, 128.8 (2C), 127.9, 127.8 (2C), 126.3 (q, 2C, J = 3.8 Hz, (C-F)), 124.6 (q, 1J = 270.6 Hz, (C-F)), 123.7, 123.0, 120.3 (q, 2J = 32.0 Hz, (C-F)), 115.2, 113.8 (2C), 109.7, 63.8, 44.2, 39.2, 26.0, 18.1; IR (neat) 3317, 2911, 1691, 1614, 1319, 1155, 1098, 1065, 825, 758, 702 cm⁻¹; MS (ESI) Exact Mass Calcd for [C₂₆H₂₅ON₂Na⁺] (Na⁺): 473.1811, found: 473.1801; mp 124-128 °C.

**1-Benzyl-3-((3,5-dimethylphenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3ja, Entry 9 in Table 2):**

![Structure 3ja](image)

¹H NMR (400 MHz, CDCl₃) δ 7.24-7.30 (m, 6H, Ar-H), 7.19 (t, 1H, J = 7.7 Hz, Ar-H), 7.01 (t, 1H, J = 7.5 Hz, Ar-H), 6.73 (d, 1H, J = 7.7 Hz, Ar-H), 6.31 (s, 1H, Ar-H), 5.84
(s, 2H, Ar-H), 5.07 (t, 1H, J = 6.8 Hz, CH), 5.00 (d, 1H, J = 15.6 Hz, one proton of CH₂), 4.83 (d, 1H, J = 15.6 Hz, one proton of CH₂), 4.30 (br, 1H, NH), 2.61-2.73 (m, 2H, CH₂), 1.99 (s, 6H, 2 CH₃), 1.67 (s, 3H, CH₃), 1.58 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 178.0, 145.3, 142.0, 138.4 (2C), 137.7, 135.8, 130.3, 128.8 (2C), 128.6, 127.5, 127.4 (2C), 123.8, 122.8, 121.0, 115.7, 113.1 (2C), 109.3, 64.4, 44.0, 39.2, 26.0, 21.3 (2C), 18.1; IR (neat) 3333, 2916, 1706, 1601, 1467, 1348, 1190, 1175, 821, 748 cm⁻¹; MS (ESI) Exact Mass Calcd for [C₂₈H₃₁ON₂]⁺ ([M+H]⁺): 411.2431, found: 411.2422; mp 170-172 °C.

1-Benzyl-3-((2,4-difluorophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3ka, Entry 10 in Table 2):

\[ \text{\includegraphics[width=0.2\textwidth]{image.png}} \]

¹H NMR (400 MHz, CDCl₃) δ 7.27-7.32 (m, 6H, Ar-H), 7.22 (dt, 1H, J = 1.4, 6.3 Hz, Ar-H), 7.02 (dt, 1H, J = 0.9, 6.6 Hz, Ar-H), 6.81 (d, 1H, J = 7.7 Hz, Ar-H), 6.69-6.75 (m, 1H, Ar-H), 6.23-6.28 (m, 1H, Ar-H), 5.65-5.71 (m, 1H, Ar-H), 5.08 (tt, 1H, J = 0.9, 7.3 Hz, CH), 4.96 (d, 1H, J = 15.4 Hz, one proton of CH₂), 4.89 (d, 1H, J = 15.4 Hz, one proton of CH₂), 4.55 (br, 1H, NH), 2.65-2.77 (m, 2H, CH₂), 1.68 (s, 3H, CH₃), 1.61 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 177.4, 155.1 (dd, J = 11.3, 239.6 Hz, (C-F)), 151.6 (dd, J = 11.3, 242.4 Hz, (C-F)), 141.9, 138.4, 135.6, 130.2 (dd, J = 2.8, 11.3 Hz, (C-F)), 129.5, 129.0, 128.7 (2C), 127.74, 127.68 (2C), 123.8, 122.9, 115.3, 114.7 (dd, J = 3.8, 8.5 Hz, (C-F)), 110.3 (dd, J = 3.8, 21.6 Hz, (C-F)), 109.5, 103.5 (dd, J = 24.4, 26.3 Hz, (C-F)), 64.2, 44.0, 38.8, 26.0, 18.0; IR (neat) 3426, 2925, 1708, 1611, 1523, 1483, 1465, 1341, 1271, 1093, 747, 735 cm⁻¹; MS (ESI) Exact Mass Calcd for [C₂₆H₂₆ON₂F₂Na⁺]⁺ ([M+Na⁺]): 441.1749, found: 441.1740; mp 77-82 °C.

1-Benzyl-6-bromo-3-((4-bromophenyl)amino)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3la, Entry 1 in Table 3):

\[ \text{\includegraphics[width=0.2\textwidth]{image.png}} \]
\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.27-7.31 (m, 3H, Ar-H), 6.96-7.07 (m, 5H, Ar-H), 6.01-6.05 (m, 2H, Ar-H), 5.13 (d, 1H, \(J = 15.3\) Hz, one proton of CH\(_2\)), 5.01 (t, 1H, \(J = 7.2\) Hz, CH), 4.97 (d, 1H, \(J = 15.3\) Hz, one proton of CH\(_3\)), 4.39 (br, 1H, NH), 2.58-2.70 (m, 2H, CH\(_2\)), 1.65 (s, 3H, CH\(_3\)), 1.55 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.4, 147.6 (d, \(J = 245.2\) Hz, (C-F)), 144.0, 138.6, 136.7, 132.8, 131.8 (2C), 128.5 (2C), 128.4, 128.0 (2C), 127.7, 123.6 (d, \(J = 5.6\) Hz, (C-F)), 119.6, 117.2 (d, \(J = 18.8\) Hz, (C-F)), 116.9 (2C), 114.9, 111.3, 64.6, 45.7, 39.2, 26.0, 18.0; IR (neat) 3351, 2965, 1708, 1631, 1592, 1485, 1469, 1316, 1240, 1162, 1053, 803, 729, 698 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{26}\)H\(_{32}\)O\(_2\)N\(_2\)Br\(_2\)Na\(^+\): 501.0948, found: 501.0944; mp 122-125 °C.

1-Benzyl-3-((4-bromophenyl)amino)-7-fluoro-3-(3-methylbut-2-en-1-yl)indolin-2-one (3ma, Entry 2 in Table 3):

\[ \text{\begin{figure}[h]
\centering
\includegraphics[width=0.3\textwidth]{image}
\caption{1-Benzyl-3-((4-bromophenyl)amino)-7-fluoro-3-(3-methylbut-2-en-1-yl)indolin-2-one (3ma, Entry 2 in Table 3)}
\end{figure}} \]

\(\text{\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.27-7.31 (m, 5H, Ar-H), 6.96-7.07 (m, 5H, Ar-H), 6.01-6.05 (m, 2H, Ar-H), 5.13 (d, 1H, \(J = 15.3\) Hz, one proton of CH\(_2\)), 5.01 (t, 1H, \(J = 7.2\) Hz, CH), 4.97 (d, 1H, \(J = 15.3\) Hz, one proton of CH\(_3\)), 4.39 (br, 1H, NH), 2.58-2.70 (m, 2H, CH\(_2\)), 1.65 (s, 3H, CH\(_3\)), 1.55 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.4, 147.6 (d, \(J = 245.2\) Hz, (C-F)), 144.0, 138.6, 136.7, 132.8, 131.8 (2C), 128.5 (2C), 128.4, 128.0 (2C), 127.7, 123.6 (d, \(J = 5.6\) Hz, (C-F)), 119.6, 117.2 (d, \(J = 18.8\) Hz, (C-F)), 116.9 (2C), 114.9, 111.3, 64.6, 45.7, 39.2, 26.0, 18.0; IR (neat) 3351, 2965, 1708, 1631, 1592, 1485, 1469, 1316, 1240, 1162, 1053, 803, 729, 698 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{26}\)H\(_{32}\)O\(_2\)N\(_2\)Br\(_2\)Na\(^+\): 501.0948, found: 501.0944; mp 122-125 °C.

3-((4-bromophenyl)amino)-3-(3-methylbut-2-en-1-yl)-1-tritylindolin-2-one (3na, Entry 3 in Table 3):

\[ \text{\begin{figure}[h]
\centering
\includegraphics[width=0.3\textwidth]{image}
\caption{3-((4-bromophenyl)amino)-3-(3-methylbut-2-en-1-yl)-1-tritylindolin-2-one (3na, Entry 3 in Table 3)}
\end{figure}} \]
1H NMR (400 MHz, CDCl₃) δ 7.37-7.40 (m, 6H, Ar-H), 7.17-7.24 (m, 10H, Ar-H), 6.90-6.98 (m, 2H, Ar-H), 6.79 (d, J = 8.8 Hz, 2H, Ar-H), 6.41-6.43 (m, 1H, Ar-H), 5.68 (d, 2H, J = 8.8 Hz, Ar-H), 5.18 (t, 1H, J = 7.6 Hz, CH), 4.24 (br, 1H, NH), 2.73-2.85 (m, 2H, CH₂), 1.79 (s, 3H, CH₃), 1.68 (s, 3H, CH₃); 13C NMR (100 MHz, CDCl₃) δ 179.4, 144.1, 142.7, 141.9 (3C), 137.7, 131.4 (2C), 129.9, 129.2 (6C), 127.6 (6C), 127.4, 126.7 (3C), 123.1, 122.3, 117.4 (2C), 116.3, 116.2, 110.7, 74.6, 64.6, 39.8, 26.3, 18.3; IR (neat) 3344, 2973, 1714, 1590, 1487, 1306, 1262, 1155, 1073, 707 cm⁻¹; MS (ESI) Exact Mass Calced for \([C_{38}H_{34}O_{3}N_{2}Br]^+\) ([M+H]+): 613.1849, found: 613.1843; mp 226-230 °C.

3-((4-Bromophenyl)amino)-1-(4-methoxybenzyl)-3-(3-methylbut-2-en-1-yl)indolin-2-one (3oa, Entry 4 in Table 3):

1H NMR (400 MHz, CDCl₃) δ 7.25-7.32 (m, 1H, Ar-H), 7.21 (dt, 1H, J = 1.4, 6.5 Hz, Ar-H), 7.16 (d, 2H, J = 8.5 Hz, Ar-H), 6.97-7.04 (m, 3H, Ar-H), 6.79-6.85 (m, 3H, Ar-H), 6.03-6.07 (m, 2H, Ar-H), 5.05 (t, 1H, J = 8.1 Hz, CH), 4.94 (d, 1H, J = 15.3 Hz, one proton of CH₂), 4.76 (d, 1H, J = 15.3 Hz, one proton of CH₂), 4.41 (br, 1H, NH), 3.79 (s, 3H, CH₃), 2.60-2.72 (m, 2H, CH₂), 1.66 (s, 3H, CH₃), 1.57 (s, 3H, CH₃); 13C NMR (100 MHz, CDCl₃) δ 177.5, 159.1, 144.3, 141.9, 138.0, 131.7 (2C), 129.5, 129.0 (2C), 128.9, 127.6, 123.7, 122.9, 117.1 (2C), 115.4, 114.0 (2C) 111.1, 109.6, 64.4, 55.3, 43.5, 38.9, 26.0, 18.0; IR (neat) 3350, 2928, 1707, 1610, 1514, 1487, 1464, 1254, 1167, 1037, 820, 748, 731 cm⁻¹; MS (ESI) Exact Mass Calced for \([C_{27}H_{28}O_{2}N_{2}Br]^+\) ([M+H]+): 491.1329, found: 491.1319; mp 109-113 °C.
3-((4-Bromophenyl)amino)-1-methyl-3-(3-methylbut-2-en-1-yl)indolin-2-one  (3pa, Entry 5 in Table 3):

![Chemical Structure]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.34 (dt, 1H, $J = 1.1$, 6.5 Hz, Ar-H), 7.24 (dd, 1H, $J = 0.9$, 6.5 Hz, Ar-H), 7.01-7.08 (m, 3H, Ar-H), 6.91 (d, 1H, $J = 7.6$ Hz, Ar-H), 6.01-6.05 (m, 2H, Ar-H), 5.08 (tt, 1H, $J = 1.4$, 7.2 Hz, CH), 4.40 (br, 1H, NH), 3.26 (s, 3H, CH$_3$), 2.51-2.67 (m, 2H, CH$_2$), 1.69 (s, 3H, CH$_3$), 1.56 (s, 3H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.6, 144.3, 142.6, 138.2, 131.7 (2C), 129.5, 129.1, 123.6, 123.0, 116.1 (2C), 115.3, 110.6, 108.5, 64.1, 39.0, 26.4, 26.0, 18.0; IR (neat) 3321, 2911, 1714, 1686, 1614, 1594, 1488, 1469, 1375, 1310, 754, 730, cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{20}$H$_{22}$ON$_2$Br]$^+$ ([M+H]$^+$): 385.0910, found: 385.0905; mp 158-160 °C.

(E)-1-Benzyl-3-((4-bromophenyl)amino)-3-(3,7-dimethylocta-2,6-dien-1-yl)indolin-2-one  (3ab, Entry 1 in Table 4):

![Chemical Structure]

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.18-7.33 (m, 7H, Ar-H), 6.97-7.03 (m, 3H, Ar-H), 6.79 (d, 1H, $J = 7.9$ Hz, Ar-H), 6.04-6.08 (m, 2H, Ar-H), 5.02-5.10 (m, 3H, CH and one proton of CH$_3$), 4.79 (d, 1H, $J = 15.3$ Hz, one proton of CH$_3$), 4.43 (br, 1H, NH), 2.60-2.77 (m, 2H, CH$_2$), 1.93-2.04 (m, 4H, 2 CH$_2$), 1.66 (s, 3H, CH$_3$), 1.57 (s, 6H, 2 CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.6, 144.3, 141.9, 141.7, 135.6, 131.7, 131.7 (2C), 129.5, 129.0, 128.7 (2C), 127.8, 127.7 (2C), 123.8, 123.8, 122.9, 117.1 (2C), 115.3, 111.2, 109.5, 64.5, 44.1, 39.9, 38.8, 26.6, 25.7, 17.7, 16.4; IR (neat) 3309, 2917, 1698, 1595, 1486, 1464, 1317, 1174, 811, 758 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{33}$H$_{32}$O$_2$N$_2$Br]$^+$ ([M+H]$^+$): 529.1849, found: 529.1845; HPLC (Daicel Chiralpak AD-3, hexane/i-PrOH = 9/1, flow rate = 1.0 mL/min) $t_1$ = 12.2 min (minor), $t_2$ = 14.7 min (major); mp 73-77 °C.
(Z)-1-benzyl-3-((4-bromophenyl)amino)-3-(3,7-dimethylocta-2,6-dien-1-yl)indolin-2-one (3ac, Entry 2 in Table 4):

\[ \text{Chemical structure image} \]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.19-7.33 (m, 7H, Ar-H), 6.98-7.05 (m, 3H, Ar-H), 6.78 (d, 1H, $J = 7.9$ Hz, Ar-H), 6.04-6.08 (m, 2H, Ar-H), 5.07-5.12 (m, 2H, 2 CH), 4.96 (d, 1H, $J = 15.5$ Hz, one proton of CH$_2$), 4.88 (d, 1H, $J = 15.5$ Hz, one proton of CH$_2$), 4.40 (br, 1H, NH), 2.63-2.73 (m, 2H, CH$_2$), 1.97-2.06 (m, 4H, 2 CH$_2$), 1.69 (s, 3H, CH$_3$), 1.67 (s, 3H, CH$_3$), 1.59 (s, 3H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 177.5, 144.3, 141.9, 141.8, 135.6, 132.0, 131.7 (2C), 129.6, 129.0, 128.7 (2C), 127.7, 127.6 (2C), 123.8 (2C), 123.0, 117.0 (2C), 115.9, 111.1, 109.6, 64.3, 44.1, 38.7, 32.0, 26.4, 25.7, 23.7, 17.7; IR (neat) 3323, 2920, 1694, 1592, 1486, 1466, 1311, 1172, 1077, 816, 758, 697 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{33}$H$_{34}$ON$_3$Br]$^+$ ([M+H]$^+$): 529.1849, found: 529.1848; HPLC (Daicel Chiralpak AD-3, hexane/i-PrOH = 9/1, flow rate = 1.0 mL/min) $t_1$ = 12.1 min (major), $t_2$ = 14.7 min (minor); mp 105-108 $^\circ$C.

(E)-1-Benzyl-3-((4-bromophenyl)amino)-3-(non-2-en-1-yl)indolin-2-one (3ad, Entry 3 in Table 4):

\[ \text{Chemical structure image} \]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18-7.32 (m, 7H, Ar-H), 6.97-7.03 (m, 3H, Ar-H), 6.80 (d, 1H, $J = 7.7$ Hz, Ar-H), 6.05 (m, 2H, Ar-H), 5.56-5.63 (m, 1H, CH), 5.28-5.36 (m, 1H, CH), 5.03 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.79 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.48 (br, 1H, NH), 2.53-2.70 (m, 2H, CH$_2$), 1.90-2.02 (m, 2H, CH$_2$), 1.19-1.33 (m, 8H, 4 CH$_2$), 0.88 (t, 3H, $J = 6.8$ Hz, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 177.4, 144.2, 141.8, 138.0, 135.6, 131.7 (2C), 129.5, 129.0, 128.7 (2C), 127.8, 127.7 (2C), 123.8, 123.0, 121.1, 116.9 (2C), 111.1, 109.6, 64.0, 44.1, 43.6, 32.6, 31.7, 29.2, 28.8, 22.6, 14.1; IR (neat) 3335, 2921, 2850, 1703, 1596, 1486, 1466, 1310, 1078, 816, 759, 699 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{33}$H$_{34}$ON$_3$Br]$^+$ ([M+H]$^+$): 517.1849, found: 517.1848; HPLC (Daicel Chiralpak AD-3, hexane/i-PrOH = 9/1, flow rate = 1.0 mL/min) $t_1$ = 12.1 min (major), $t_2$ = 14.7 min (minor); mp 105-108 $^\circ$C.
mL/min) $t_1 = 13.5$ min (minor), $t_2 = 19.3$ min (major); mp 82-84 °C.

**(Z)-1-Benzyl-3-((4-bromophenyl)amino)-3-(non-2-en-1-yl)indolin-2-one (3ae, Entry 4 in Table 4):**

1H NMR (400 MHz, CDCl$_3$) δ 7.20-7.33 (m, 7H, Ar-H), 6.99-7.04 (m, 3H, Ar-H), 6.80 (d, 1H, $J = 7.7$ Hz, Ar-H), 6.05-6.09 (m, 2H, $J = 8.6$ Hz, Ar-H), 5.56-5.62 (m, 1H, CH), 5.26-5.32 (m, 1H, CH), 5.04 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.79 (d, 1H, $J = 15.4$ Hz, one proton of CH$_2$), 4.39 (br, 1H, NH), 2.65-2.78 (m, 2H, CH$_2$), 2.01 (br, 1H, CH$_3$), 1.22-1.32 (m, 8H, 4 CH$_2$), 0.88 (t, 3H, $J = 7.0$ Hz, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.4, 144.2, 141.9, 136.2, 135.6, 131.7 (2C), 129.3, 129.0, 128.7 (2C), 127.8, 127.7 (2C), 123.8, 123.0, 120.2, 117.2 (2C), 111.3, 109.6, 64.2, 44.1, 37.9, 31.7, 29.4, 29.0, 27.4, 22.6, 14.1; IR (neat) 3330, 2922, 1700, 1595, 1487, 1365, 1346, 1310, 1078, 815, 759, 698 cm$^{-1}$; MS (ESI) Exact Mass Calcd for [C$_{39}$H$_{30}$ON$_2$Br]$^+$ ([M+H]$^+$): 517.1849, found: 517.1847; HPLC (Daicel Chiralpak AD-3, hexane/i-PrOH = 9/1, flow rate = 1.0 mL/min) $t_1 = 13.5$ min (major), $t_2 = 19.3$ min (minor); mp 86-89 °C.

**1-Benzyl-3-((4-bromophenyl)amino)-3-cinnamylindolin-2-one (3af, Entry 5 in Table 4):**

1H NMR (400 MHz, CDCl$_3$) δ 7.14-7.37 (m, 12H, Ar-H), 7.07 (t, 1H, $J = 7.4$ Hz, Ar-H), 7.01 (d, 2H, $J = 8.8$ Hz, Ar-H), 6.78 (d, 1H, $J = 7.9$ Hz, Ar-H), 6.54 (d, 1H, $J = 15.7$ Hz, CH), 6.03-6.11 (m, 3H, 3 CH), 4.95 (d, 1H, $J = 15.5$ Hz, one proton of CH$_2$), 4.86 (d, 1H, $J = 15.5$ Hz, one proton of CH$_2$), 4.45 (br, 1H, NH), 2.77-2.95 (m, 2H, CH$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 177.2, 144.1, 141.9, 136.5, 135.9, 135.4, 131.8 (2C), 129.3, 129.3, 128.7 (2C), 128.6 (2C), 127.8, 127.7, 127.5 (2C), 126.4 (2C), 123.8, 123.2, 121.2, 117.2 (2C), 111.5, 109.8, 64.4, 44.2, 43.9; IR (neat) 3338, 2973, 1734, 1706, 1608,
1595, 1486, 1464, 1343, 1317, 731, 692 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{30}\)H\(_{26}\)ON\(_{2}\)Br\(^+\)] ([M+H]\(^+\)): 509.1223, found: 509.1219; mp 139-144 °C.

\((E)-1\)-Benzyl-3-((4-bromophenyl)amino)-3-(but-2-en-1-yl)indolin-2-one [3ag (= 4ah), Entries 6 and 7 in Table 4]:

\[\text{HN} \quad \text{O} \quad \text{Br} \]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.20-7.34 (m, 7H, Ar-H), 6.98-7.06 (m, 3H, Ar-H), 6.80 (d, 1H, \(J = 7.9\) Hz, Ar-H), 6.04-6.09 (m, 2H, Ar-H), 5.61-5.70 (m, 1H, CH), 5.31-5.39 (m, 1H, CH), 4.99 (d, 1H, \(J = 15.5\) Hz, one proton of CH\(_2\)), 4.86 (d, 1H, \(J = 15.3\) Hz, one proton of CH\(_2\)), 4.41 (br, 1H, NH), 2.52-2.75 (m, 2H, CH\(_2\)), 1.66 (d, 3H, \(J = 6.3\) Hz, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.4, 144.2, 141.8, 135.6, 132.3, 131.7 (2C), 129.5, 129.0, 128.8 (2C), 127.8, 127.7 (2C), 123.7, 123.0, 122.4, 116.9 (2C), 111.1, 109.7, 64.0, 44.1, 43.6, 18.1; IR (neat) 3360, 2921, 1712, 1613, 1597, 1487, 1466, 1322, 1174, 1076, 811, 752, 734, 694 cm\(^{-1}\); MS (ESI) Exact Mass Calcd for [C\(_{25}\)H\(_{24}\)ON\(_{2}\)Br\(^+\)] ([M+H]\(^+\)): 447.1067, found: 447.1060; mp 118-121 °C.

References