Synthesis of 3,3-Disubstituted-2-Aminoindolenines by Palladium-Catalyzed Allylic Amidination with Isocyanide

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General Experimental Details

Unless otherwise noted, all reactions were performed under argon. Pd(dba)$_2$ was purchased from Tokyo Chemical Industry Co., Ltd. P(2-furyl)$_3$ was purchased from Sigma Aldrich. THF was purchased from Kanto Chemical Co., Inc. Unless otherwise noted, all other reagents were purchased from commercial suppliers and used as received.

Analytical thin-layer chromatography was performed with Merck Silica gel 60. Silica gel column chromatography was performed with Kanto silica gel 60 (particle size, 63–210 μm). All melting points (m.p.) were determined on YANAGIMOTO micro melting point apparatus. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a JEOL JNM-LA 500 at 500 MHz. Chemical shifts are reported relative to Me$_4$Si (δ 0.00). Multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); sep (septet); m (multiplet); br (broad). Carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on a JEOL JNM-LA 500 at 126 MHz. Chemical shifts are reported relative to CDCl$_3$ (δ 77.0). Infra-red spectra were recorded on a FT/IR-4100 (JASCO). Low and high resolution mass spectra were recorded on JEOL JMS-HX/HX 110A.

Preparation of Starting Materials

(E)-N-(2-(4-Hydroxybut-2-en-2-yl)phenyl)formamide (S1): To formic acid (2.64 mL, 70 mmol) was added acetic anhydride (2.36 mL, 25.0 mmol) and the mixture was stirred at room temperature. After stirring for 10 min, to the mixture was added the solution of 2-iodoaniline (4.38 g, 20.0 mmol) in CH$_2$Cl$_2$ (20 mL) and the mixture was stirred at room temperature. After stirring overnight, the mixture was concentrated under reduced pressure to give N-(2-iodophenyl)formamide$^1$ (4.94 g, quant.) as a white solid.

To a stirred solution of N-(2-iodophenyl)formamide (3.48 g, 14.1 mmol), vinyl borate$^2$ (4.62 g, 14.8 mmol) and aqueous Na$_2$CO$_3$ (1.0 M solution, 42.3 mL, 42.3 mmol) in 1,4-dioxane (94 mL) was added Pd(PPh$_3$)$_2$Cl$_2$ (495 mg, 0.705 mmol) and the mixture was heated to 80 °C. After
stirring for 3 h, to the mixture was added H2O and extracted with EtOAc. The combined extracts were washed with brine, dried over Na2SO4 and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane/EtOAc = 9/1→8/2) to give formanilide. To the solution of the formanilide in THF (50 mL) was added TBAF (1.0 M solution in THF, 16.9 mL, 16.9 mmol) at 0 °C. After stirring for 1.5 h at 0 °C, the reaction mixture was quenched with aqueous NH4Cl, and extracted with EtOAc. The combined extracts were washed with brine, dried over Na2SO4 and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane/EtOAc = 8/2→1/1) to give S1 (2.56 g, 95% in 2 steps) as a colorless oil: 1H NMR (500 MHz, CDCl3) δ 9.13 (d, 0.56H, J = 11.4 Hz), 8.61 (brs, 0.44H), 8.57 (d, 0.56H, J = 7.2 Hz), 8.33 (d, 0.44H, J = 11.4 Hz), 8.14 (d, 0.44H, J = 8.0 Hz), 7.28-7.05 (m, 3.56H), 5.66 (d, 0.56H, J = 6.9 Hz), 5.63 (d, 0.44H, J = 6.9 Hz), 4.41 (brs, 1H), 4.28-4.26 (m, 2H), 1.94 (s, 3H) (Mixture of amide rotamers.); 13C NMR (126 MHz, CDCl3) δ 164.0, 160.2*, 136.7, 136.0*, 135.7, 135.1*, 133.00, 132.98*, 130.6, 129.8*, 129.1, 128.03*, 127.96, 127.5*, 125.5, 124.4*, 121.7, 119.4*, 58.41, 58.35*, 17.9*, 17.6 (* Peaks of the minor rotamer.); IR (ATR) 3330, 1687, 1523, 1449 cm−1; MS (FAB) m/z = 191 ([M]+); HRMS (FAB+) C11H13NO2: ([M]+) 191.0947: Found 191.0948.

(E)-3-(2-isocyanophenyl)but-2-en-1-yl methyl carbonate (1a): To a stirred solution of S1 (669 mg, 3.50 mmol) and pyridine (0.849 mL, 10.5 mmol) in CH2Cl2 (15 mL) was added methyl chloroformate (0.406 mL, 5.25 mmol) at 0 °C and the reaction mixture was warmed to room temperature. After stirring for 2.5 h, the mixture was cooled to 0 °C. To the mixture were added pyridine (0.566 mL, 7.00 mmol) and acetic anhydride (0.270 mL, 3.49 mmol) at the same temperature and the reaction mixture was warmed to room temperature. After stirring for 0.5 h, the mixture was quenched with saturated aqueous NH4Cl and extracted with CHCl3. The combined extracts were dried over Na2SO4 and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane/EtOAc = 7/3) to give formanilide (780 mg, 89%) as a colorless oil.
To the solution of the formanilide (776 mg, 3.11 mmol) and Et₃N (1.30 mL, 9.33 mmol) in THF (20 mL) was added POCl₃ (0.319 mL, 3.42 mmol) at 0 °C. After stirring for 1.5 h at 0 °C, the reaction mixture was quenched with aqueous NaHCO₃, and extracted with EtOAc. The combined extracts were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The obtained residue was purified by alumina column chromatography (hexane/EtOAc = 9/1) to give 1a (452 mg, 63%) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.34 (m, 2H), 7.31-7.24 (m, 2H), 5.72 (t, 1H, J = 6.9 Hz), 4.85 (d, 2H, J = 6.9 Hz), 3.81 (s, 3H), 2.14 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.7, 155.7, 141.3, 138.2, 129.3, 129.0, 128.1, 127.4, 125.4, 124.1, 64.2, 54.8, 17.4; IR (ATR) 2957, 2121, 1748, 1263 cm⁻¹; MS (FAB) m/z = 232 ([M+H]+); HRMS (FAB+) C₁₃H₁₄NO₃: ([M+H]+) 232.0974 Found 232.0963.

(E)-3-(2-Isocyanophenyl)but-2-en-1-yl acetate (1b): To a stirred solution of S₁ (1.14 g, 5.96 mmol) and pyridine (1.45 mL, 17.9 mmol) in CH₂Cl₂ (20 mL) was added acetic anhydride (0.676 mL, 7.15 mmol) at 0 °C and the reaction mixture was warmed to room temperature. After stirring for 2 h, the mixture was cooled to 0 °C. To the mixture were added pyridine (1.45 mL, 17.9 mmol) and acetic anhydride (0.676 mL, 7.15 mmol) at the same temperature and the reaction mixture was warmed to room temperature. After stirring for 1 h, the mixture was quenched with saturated aqueous NH₄Cl and extracted with CHCl₃. The combined extracts were dried over Na₂SO₄ and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane/EtOAc = 8/2→7/3) to give formanilide (1.20 g, 81%) as a colorless oil.

To the solution of the formanilide and Et₃N (2.01 mL, 14.4 mmol) in THF (30 mL) was added POCl₃ (0.560 mL, 6.01 mmol) at 0 °C and stirred at the same temperature. After stirring for 3 h, the reaction mixture was quenched with aqueous NaHCO₃, and extracted with EtOAc. The combined extracts were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The obtained residue was purified by alumina column chromatography (hexane/EtOAc = 9/1) to give 1b (1.03 g, quant.) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 7.39-7.34 (m, 2H), 7.31-7.24 (m, 2H), 5.70 (tq, 1H, J₁ = 6.9 Hz, J₂ = 1.4 Hz), 4.79 (d, 2H, J = 6.9 Hz), 2.12 (d, 3H, J = 1.4 Hz), 2.10 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 170.9, 166.6,
141.5, 137.2, 129.3, 129.0, 128.0, 127.4, 124.2, 61.0, 20.9, 17.4; IR (ATR) 2920, 2121, 1740, 1231 cm$^{-1}$; MS (FAB) $m/z = 216$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{13}$H$_{14}$NO$_2$: ([M+H]$^+$) 216.1024: Found 216.1020.

(E)-3-(2-Isocyano-5-(trifluoromethyl)phenyl)but-2-en-1-yl acetate (1c): The reaction was performed according to the procedure for 1b. A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.58 (dd, 1H, $J_1 = 8.3$ Hz, $J_2 = 1.5$ Hz), 7.53 (d, 1H, $J = 1.5$ Hz), 7.51 (d, 1H, $J = 8.3$ Hz), 5.75 (tq, 1H, $J_1 = 6.9$ Hz, $J_2 = 1.5$ Hz), 4.80 (d, 2H, $J = 6.9$ Hz), 2.14 (d, 3H, $J = 1.5$ Hz), 2.11 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.8, 169.7, 142.3, 136.0, 131.4 (q, $J = 33.7$ Hz), 128.0, 127.7, 126.9, 126.3 (q, $J = 3.6$ Hz), 125.1 (q, $J = 3.6$ Hz), 123.1 (q, $J = 273.5$ Hz), 60.7, 20.9, 17.2; IR (ATR) 2992, 2122, 1743, 1240 cm$^{-1}$; MS (FAB) $m/z = 284$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{14}$H$_{13}$F$_3$NO$_2$: ([M+H]$^+$) 284.0898: Found 284.0901.

(E)-3-(2-Isocyano-5-methoxyphenyl)but-2-en-1-yl acetate (1d): The reaction was performed according to the procedure for 1b. A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.30 (d, 1H, $J = 8.6$ Hz), 6.78 (dd, 1H, $J_1 = 8.6$ Hz, $J_2 = 2.9$ Hz), 6.73 (d, 1H, $J = 2.9$ Hz), 5.70 (tq, 1H, $J_1 = 6.9$ Hz, $J_2 = 1.7$ Hz), 4.78 (d, 2H, $J = 6.9$ Hz), 3.82 (s, 3H), 2.11 (s, 3H), 2.10 (d, 3H, $J = 1.7$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.9, 165.1, 159.6, 143.0, 137.3, 128.7, 126.0, 117.1, 114.1, 113.2, 60.9, 55.5, 20.9, 17.3; IR (ATR) 2944, 2120, 1738, 1229, 1028 cm$^{-1}$; MS (FAB) $m/z = 246$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{14}$H$_{16}$NO$_3$: ([M+H]$^+$) 246.1130: Found 246.1134.
(E)-3-(2-Isocyanophenyl)pent-2-en-1-yl acetate (1e): The reaction was performed according to the procedure for 1b. A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39-7.34 (m, 2H), 7.32-7.28 (m, 1H), 7.23 (dd, 1H, $J_1 = 7.8$ Hz, $J_2 = 1.8$ Hz), 5.60 (t, 1H, $J = 6.9$ Hz), 4.80 (d, 2H, $J = 6.9$ Hz), 2.57 (q, 2H, $J = 7.8$ Hz), 2.09 (s, 3H), 0.94 (t, 3H, $J = 7.8$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.8, 166.3, 143.4, 140.1, 129.6, 129.0, 127.9, 127.2, 125.3, 124.7, 60.6, 24.4, 20.9, 12.8; IR (ATR) 2972, 2122, 1742, 1238 cm$^{-1}$; MS (FAB) $m/z = 230$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{14}$H$_{16}$NO$_2$: ([M+H]$^+$) 230.1181: Found 230.1181.

(E)-3-(2-Isocyanophenyl)hept-2-en-1-yl acetate (1f): The reaction was performed according to the procedure for 1b. A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39-7.34 (m, 2H), 7.29 (ddd, 1H, $J_1 = J_2 = 7.7$ Hz, $J_3 = 1.5$ Hz), 7.23 (dd, 1H, $J_1 = 7.7$ Hz, $J_2 = 1.5$ Hz), 5.63 (t, 1H, $J = 6.9$ Hz), 4.79 (d, 2H, $J = 6.9$ Hz), 2.54 (t, 2H, $J = 7.7$ Hz), 2.09 (s, 3H), 1.35-1.23 (m, 4H), 0.86 (t, 3H, $J = 6.9$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.9, 166.3, 142.1, 140.5, 129.5, 129.1, 127.9, 127.3, 126.0, 124.6, 60.8, 31.0, 30.3, 22.5, 20.9, 13.8; IR (ATR) 2958, 2121, 1739, 1228 cm$^{-1}$; MS (FAB) $m/z = 258$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{16}$H$_{20}$NO$_2$: ([M+H]$^+$) 258.1494: Found 258.1497.

(E)-4-(2-Isocyanophenyl)hex-3-en-2-yl acetate (1i): The reaction was performed according to the procedure for 1b. A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39-7.34 (m, 2H), 7.31-7.27 (m, 1H), 7.23 (dd, 1H, $J_1 = 8.0$ Hz, $J_2 = 1.9$ Hz), 5.82-5.76 (m, 1H), 5.43 (d, 1H, $J = 8.9$ Hz), 2.53 (q, 2H, $J = 7.7$ Hz), 2.09 (s, 3H), 0.94 (t, 3H, $J = 7.8$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 170.9, 166.3, 143.4, 140.1, 129.6, 129.0, 127.9, 127.2, 125.3, 124.7, 60.6, 24.4, 20.9, 12.8; IR (ATR) 2958, 2121, 1739, 1228 cm$^{-1}$; MS (FAB) $m/z = 260$ ([M+H]$^+$); HRMS (FAB$^+$) C$_{17}$H$_{22}$NO$_2$: ([M+H]$^+$) 260.1428: Found 260.1428.
Hz), 2.67-2.59 (m, 1H), 2.57-2.49 (m, 1H), 2.06 (s, 3H), 1.41 (d, 3H, J = 6.3 Hz), 0.93 (t, 3H, J = 7.8 Hz); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 170.3, 166.1, 140.7, 140.1, 131.0, 129.4, 129.0, 127.8, 127.1, 124.9, 67.3, 24.7, 21.3, 20.8, 12.7; IR (ATR) 2975, 2121, 1736, 1242 cm\(^{-1}\); MS (FAB) \(m/z = 243 ([M]^+)\); HRMS (FAB\(^+\)) C\(_{15}\)H\(_{18}\)NO\(_2\): ([M+H]\(^+\)) 244.1337: Found 244.1344.

Procedure for the Synthesis of 3,3-Disubstituted-2-Aminoindolenines

3-Methyl-2-(piperidin-1-yl)-3-vinylindolenine (2a): To a stirred solution of 1b (21.6 mg, 0.100 mmol), piperidine (0.020 mL, 0.202 mmol) and Et\(_3\)N (0.028 mL, 0.201 mmol) in THF (2 mL) were added Pd(dba)\(_2\) (5.8 mg, 0.0101 mmol) and P(2-furyl)\(_3\) (4.6 mg, 0.0198 mmol) at room temperature. After stirring for 12 h at room temperature, the reaction mixture was diluted with toluene and extracted with 2N aqueous HCl. The combined extracts were basified with 2N aqueous NaOH and extracted with EtOAc. The resultant organic layers were washed with brine, dried over Na\(_2\)SO\(_4\) and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane/EtOAc = 8/2\(\rightarrow\)1/1) to give 2a (20.5 mg, 73%) as a colorless block, which was recrystallized from Et\(_2\)O: m.p. 83.0-86.0 \(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.16-7.12 (m, 2H), 6.92 (d, 1H, J = 7.2 Hz), 6.86 (ddd, 1H, \(J_1 = J_2 = 6.6\) Hz, \(J_3 = 1.7\) Hz), 5.90 (dd, 1H, \(J_1 = 17.5\) Hz, \(J_2 = 10.6\) Hz), 5.35 (d, 1H, J = 17.5 Hz), 5.22 (d, 1H, J = 10.6 Hz), 3.71-3.63 (m, 4H), 1.67-1.58 (m, 9H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 176.2, 154.7, 140.6, 138.9, 128.1, 121.2, 120.8, 115.7, 113.6, 55.6, 47.4, 26.0, 24.3, 20.7; IR (ATR) 2934, 1632, 1542, 1458, 1448 cm\(^{-1}\); MS (FAB) \(m/z = 241 ([M+H]^+)\); HRMS (FAB\(^+\)) C\(_{16}\)H\(_{21}\)N\(_2\): ([M+H]\(^+\)) 241.1705: Found 241.1708.

3-Methyl-2-(pyrrolidin-1-yl)-3-vinylindolenine (2b): According to the procedure for 2a, the reaction gave 2b in 58% yield as a white solid: m.p. 94.0-95.5 \(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\),
50 °C) δ 7.19-7.12 (m, 2H), 6.93-6.91 (m, 1H), 6.87-6.84 (m, 1H), 5.85 (dd, 1H, \( J_1 = 17.2 \text{ Hz}, J_2 = 10.6 \text{ Hz} \)), 5.33 (d, 1H, \( J = 17.5 \text{ Hz} \)), 5.24 (d, 1H, \( J = 10.3 \text{ Hz} \)), 3.78-3.77 (m, 2H), 3.63-3.62 (m, 2H), 2.15-1.84 (m, 4H), 1.61 (s, 3H); \(^{13}\text{C} \text{ NMR} (126 \text{ MHz, CDCl}_3, 50 \text{ °C}) \delta 174.7, 155.1, 140.3, 137.9, 128.2, 121.2, 120.9, 115.9, 114.5, 56.1, 48.0, 25.2, 19.0; IR (ATR) 2973, 1540, 1456 \text{ cm}^{-1}; \text{ MS (FAB)} m/z = 227 ([M+H]^+); \text{ HRMS (FAB^+)} \text{ C}_{15}\text{H}_{19}\text{N}_2: ([M+H]^+) 227.1548: \text{ Found 227.1539.}

2-(Azepan-1-yl)-3-methyl-3-vinylindolenine (2c): According to the procedure for 2a, the reaction gave 2c in 50% yield as a colorless oil: \(^1\text{H} \text{ NMR} (500 \text{ MHz, CDCl}_3, 50 \text{ °C}) \delta 7.17-7.11 \text{ (m, 2H), 6.91-6.89 (m, 1H), 6.86-6.83 (m, 1H), 5.88 (dd, 1H, } J_1 = 17.5 \text{ Hz}, J_2 = 10.6 \text{ Hz}), 5.33 \text{ (d, 1H, } J = 17.5 \text{ Hz}), 5.22 \text{ (d, 1H, } J = 10.6 \text{ Hz}), 3.73-3.65 \text{ (m, 4H), 1.80-1.78 \text{ (m, 4H), 1.68-1.52 (m, 7H); } ^{13}\text{C} \text{ NMR} (126 \text{ MHz, CDCl}_3, 50 \text{ °C}) \delta 176.2, 155.2, 140.7, 139.3, 128.1, 121.2, 120.7, 115.8, 113.5, 56.0, 49.2, 28.7, 27.5, 20.8; \text{ IR (ATR) 2931, 1547, 1459 cm}^{-1}; \text{ MS (FAB)} m/z = 255 ([M+H]^+); \text{ HRMS (FAB^+)} \text{ C}_{17}\text{H}_{23}\text{N}_2: ([M+H]^+) 255.1861: \text{ Found 255.1856.}

4-(3-Methyl-3-vinylindolenin-2-yl)morpholine (2d): According to the procedure for 2a, the reaction gave 2d in 62% yield as a white solid: m.p. 102.5-104.0 °C; \(^1\text{H} \text{ NMR} (500 \text{ MHz, CDCl}_3, 50 \text{ °C}) \delta 7.20-7.15 \text{ (m, 2H), 6.96-6.95 (m, 1H), 6.93-6.90 (m, 1H), 5.89 (dd, 1H, } J_1 = 17.5 \text{ Hz}, J_2 = 10.6 \text{ Hz}), 5.37 \text{ (d, 1H, } J = 17.5 \text{ Hz}), 5.26 \text{ (d, 1H, } J = 10.6 \text{ Hz}), 3.79-3.67 \text{ (m, 8H), 1.58 (s, 3H); } ^{13}\text{C} \text{ NMR} (126 \text{ MHz, CDCl}_3) \delta 176.1, 154.3, 140.7, 138.5, 128.2, 121.5, 121.2, 116.2, 114.2, 66.7, 55.6, 46.5, 20.4; \text{ IR (ATR) 2977, 1540, 1542, 1460, 1436 cm}^{-1}; \text{ MS (FAB)} m/z = 243 ([M+H]^+); \text{ HRMS (FAB^+)} \text{ C}_{15}\text{H}_{19}\text{N}_2\text{O}: ([M+H]^+) 243.1498: \text{ Found 243.1499.}
**N,N-Diethyl-3-methyl-3-vinylindolenin-2-amine (2e):** According to the procedure for 2a, the reaction gave 2e in 50% yield as a colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.16-7.14 (m, 2H), 6.93-6.91 (m, 1H), 6.88-6.84 (m, 1H), 5.87 (dd, 1H, $J_1 = 17.2$ Hz, $J_2 = 10.6$ Hz), 5.34 (d, 1H, $J = 17.5$ Hz), 5.22 (d, 1H, $J = 10.6$ Hz), 3.63-3.52 (m, 4H), 1.57 (s, 3H), 1.20 (t, 6H, $J = 7.0$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 176.0, 155.2, 140.6, 139.1, 128.1, 121.1, 120.5, 115.6, 113.4, 55.7, 42.2, 20.7, 13.2; IR (ATR) 2935, 1550, 1458 cm$^{-1}$; MS (FAB) $m/z =$ 229 ([M+H]$^+$); HRMS (FAB$^+$) C$_{15}$H$_{21}$N$_2$: ([M+H]$^+$) 229.1705: Found 229.1709.

![Image of 2e](image)

**N-Benzyl-N,3-dimethyl-3-vinylindolenin-2-amine (2f):** According to the procedure for 2a, the reaction gave 2f in 60% yield as a colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.35-7.16 (m, 7H), 6.96-6.89 (m, 2H), 5.93 (dd, 1H, $J_1 = 17.5$ Hz, $J_2 = 10.6$ Hz), 5.38 (d, 1H, $J = 17.5$ Hz), 5.25 (d, 1H, $J = 10.6$ Hz), 4.84 (d, 1H, $J = 15.5$ Hz), 4.75 (d, 1H, $J = 15.5$ Hz), 3.07 (s, 3H), 1.61 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 177.3, 154.9, 140.8, 138.6, 137.3, 128.7, 128.2, 127.4, 127.2, 121.3, 121.1, 116.1, 114.2, 55.9, 54.2, 36.5, 20.4; IR (ATR) 2935, 1550, 1458 cm$^{-1}$; MS (FAB) $m/z =$ 277 ([M+H]$^+$); HRMS (FAB$^+$) C$_{19}$H$_{21}$N$_2$: ([M+H]$^+$) 277.1705: Found 277.1702.

![Image of 2f](image)

**N-Benzyl-3-methyl-3-vinylindolenin-2-amine (2g):** According to the procedure for 2a, the reaction gave 2g in 13% yield as a white solid: m.p. 128.0-130.0 °C: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.38-7.21 (m, 7H), 7.07 (d, 1H, $J = 6.9$ Hz), 6.96 (t, 1H, $J = 7.4$ Hz), 5.75 (dd, 1H, $J_1 = 17.5$ Hz, $J_2 = 10.6$ Hz), 5.30 (d, 1H, $J = 17.5$ Hz), 5.23 (d, 1H, $J = 10.6$ Hz), 4.71 (d, 1H, $J = 14.3$ Hz), 4.67 (d, 1H, $J = 14.3$ Hz), 1.45 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 175.9, 155.4, 139.9, 138.5, 138.0, 128.8, 128.3, 127.8, 127.7, 121.7, 121.6, 116.8, 115.2, 55.5, 46.9, 21.4; IR (ATR) 3208, 3032, 1558, 1454 cm$^{-1}$; MS (FAB) $m/z =$ 263 ([M+H]$^+$); HRMS (FAB$^+$) C$_{18}$H$_{19}$N$_2$: ([M+H]$^+$) 263.1548: Found 263.1544.
3-Methyl-2-(piperidin-1-yl)-5-(trifluoromethyl)-3-vinylindolenine (2i): According to the procedure for 2a, the reaction gave 2i in 45% yield as a white solid: m.p. 95.0-97.0 °C; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.41 (d, 1H, $J$ = 8.3 Hz), 7.13 (d, 1H, $J$ = 8.3 Hz), 7.12 (s, 1H), 5.88 (dd, 1H, $J_1$ = 17.5 Hz, $J_2$ = 10.6 Hz), 5.39 (d, 1H, $J$ = 17.5 Hz), 5.29 (d, 1H, $J$ = 10.6 Hz), 3.70-3.69 (m, 4H), 1.72-1.59 (m, 9H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 177.5, 158.3, 140.9, 137.8, 125.9 (q, $J$ = 3.6 Hz), 125.0 (q, $J$ = 271.1 Hz), 122.4 (q, $J$ = 32.4 Hz), 118.2 (q, $J$ = 3.6 Hz), 115.2, 114.6, 55.4, 47.5, 26.1, 24.2, 20.6; IR (ATR) 2935, 1545, 1318, 1266, 1155, 1118 cm$^{-1}$; MS (FAB) $m/z$ = 309 ([M+H$^+$]); HRMS (FAB+) C$_{17}$H$_{20}$F$_3$N$_2$: ([M+H$^+$]) 309.1579: Found 309.1581.

5-Methoxy-3-methyl-2-(piperidin-1-yl)-3-vinylindolenine (2j): According to the procedure for 2a, the reaction gave 2j in 69% yield as a colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.05 (d, 1H, $J$ = 8.3 Hz), 6.70 (dd, 1H, $J_1$ = 8.3 Hz, $J_2$ = 2.6 Hz), 6.54 (d, 1H, $J$ = 2.6 Hz), 5.89 (dd, 1H, $J_1$ = 17.5 Hz, $J_2$ = 10.6 Hz), 5.34 (d, 1H, $J$ = 17.5 Hz), 5.22 (d, 1H, $J$ = 10.6 Hz), 3.75 (s, 3H), 3.67-3.58 (m, 4H), 1.68-1.56 (m, 9H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 175.3, 154.9, 148.2, 141.9, 138.9, 115.7, 113.6, 112.3, 108.6, 56.0, 55.7, 47.3, 26.0, 24.4, 20.8; IR (ATR) 2935, 1545, 1318, 1266, 1155, 1118 cm$^{-1}$; MS (FAB) $m/z$ = 271 ([M+H$^+$]); HRMS (FAB+) C$_{17}$H$_{23}$N$_2$O: ([M+H$^+$]) 271.1810: Found 271.1811.

3-Ethyl-2-(piperidin-1-yl)-3-vinylindolenine (2k): According to the procedure for 2a, the reaction gave 2k in 53% yield as a colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.26-7.11 (m, 2H), 6.91-6.85 (m, 2H), 5.94 (dd, 1H, $J_1$ = 17.5 Hz, $J_2$ = 10.6 Hz), 5.27 (d, 1H, $J$ = 17.5 Hz), 5.17 (d, 1H, $J$ = 10.6 Hz), 3.68-3.67 (m, 4H), 2.17-2.04 (m, 2H), 1.69-1.59 (m, 6H), 0.57 (t, 3H, $J$ = 7.2 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 174.2, 155.8, 139.1, 138.7, 128.0, 121.0, 120.7, 115.4,
3-Butyl-2-(piperidin-1-yl)-3-vinylindolenine (2l): According to the procedure for 2a, the reaction gave 2l in 65% yield as a colorless oil: $^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.26-7.11 (m, 2H), 6.91-6.85 (m, 2H), 5.91 (dd, 1H, $J_1 = 17.5$ Hz, $J_2 = 10.6$ Hz), 5.27 (d, 1H, $J = 17.5$ Hz), 5.17 (d, 1H, $J = 10.6$ Hz), 3.69-3.67 (m, 4H), 2.10-1.97 (m, 2H), 1.69-1.59 (m, 6H), 1.29-1.15 (m, 2H), 1.06-0.97 (m, 1H), 0.79 (t, 3H, $J = 7.2$ Hz), 0.75-0.69 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 174.6, 155.6, 139.2, 128.0, 121.0, 120.7, 115.5, 113.5, 60.1, 47.2, 34.2, 26.1, 24.4, 22.9, 13.8 (One carbon peak was missing due to overlapping); IR (ATR) 2934, 1545, 1459 cm$^{-1}$; MS (FAB) $m/z$ = 283 ([M+H]$^+$); HRMS (FAB$^+$) C$_{19}$H$_{27}$N$_2$: ([M+H]$^+$) 282.2096: Found 282.2092.

Methyl (3-methyl-3-vinylindolenin-2-yl)-L-proline (2m) (as a 3:1 inseparable mixture): According to the procedure for 2a, the reaction gave 2m in 44% yield as a colorless oil: $^{1}$H NMR (500 MHz, CDCl$_3$, 50 °C) $\delta$ 7.13-7.11 (m, 2H), 6.94-6.91 (m, 1H), 6.89-6.84 (m, 1H), 5.87 (dd, 0.25H, $J_1 = 17.5$ Hz, $J_2 = 10.3$ Hz), 5.81 (dd, 0.75H, $J_1 = 17.5$ Hz, $J_2 = 10.3$ Hz), 5.41 (d, 0.25H, $J = 17.5$ Hz), 5.36 (d, 0.75H, $J = 17.5$ Hz), 5.25-5.22 (m, 1H), 4.77-4.75 (m, 1H), 4.01-3.96 (m, 0.25H), 3.91-3.86 (m, 0.75H), 3.78-3.66 (m, 4H), 2.29-2.15 (m, 1H), 2.07-1.89 (m, 3H), 1.61 (s, 2.25H), 1.57 (s, 0.75H); $^{13}$C NMR (126 MHz, CDCl$_3$, 50 °C) $\delta$ 174.5, 174.4*, 173.44, 173.36*, 155.2, 155.0*, 140.90*, 140.88, 137.8*, 137.7, 128.00, 127.97*, 121.21, 121.15*, 121.0, 116.52, 116.50*, 114.6, 114.5*, 63.6, 61.0, 59.2*, 56.1, 56.0*, 52.03*, 51.99, 47.3*, 29.5, 24.6*, 19.0 (* Peaks of the minor isomer. Some peaks were missing due to overlapping or broadening); IR (ATR) 2977, 1742, 1540, 1456 cm$^{-1}$; MS (FAB) $m/z$ = 285 ([M+H]$^+$); HRMS (FAB$^+$) C$_{17}$H$_{21}$N$_2$O$_2$: ([M+H]$^+$) 285.1603: Found 285.1600.
(E)- and (Z)-3-Ethyl-2-(piperidin-1-yl)-3-(prop-1-en-1-yl)indolenine (2n) (as a 2:1 inseparable mixture): According to the procedure for 2a, the reaction gave 2n in 31% yield as a colourless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.16-7.11 (m, 2H), 6.94 (d, 0.33H, $J = 7.5$ Hz), 6.90-6.84 (m, 1.67H), 5.71 (dq, 0.33H, $J_1 = 10.9$ Hz, $J_2 = 1.7$ Hz), 5.65 (dq, 0.67H, $J_1 = 15.8$ Hz, $J_2 = 6.0$ Hz), 5.57 (d, 0.67H, $J = 15.8$ Hz), 5.47 (dq, 0.33H, $J_1 = 10.9$ Hz, $J_2 = 7.2$ Hz), 3.69-3.67 (m, 4H), 2.12-1.96 (m, 2H), 1.70-1.61 (m, 6H), 1.69 (d, 2H, $J = 6.0$ Hz), 1.14 (dd, 1H, $J_1 = 7.2$ Hz, $J_2 = 1.7$ Hz), 0.55 (t, 2H, $J = 7.5$ Hz), 0.53 (t, 1H, $J = 7.4$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 175.4*, 174.7, 155.64*, 155.61, 140.2*, 139.6, 131.7, 131.2*, 128.3*, 127.7, 127.4*, 124.4, 120.9, 120.8*, 120.6*, 120.5, 115.3, 115.2*, 60.0, 57.5*, 47.5*, 47.2, 32.6*, 28.2, 26.24*, 26.16, 24.42*, 24.39, 18.1, 13.1*, 8.4, 7.8* (* Peaks of the minor isomer.); IR (ATR) 2934, 1544, 1450 cm$^{-1}$; MS (FAB) $m/z$ = 269 ([M+H]$^+$); HRMS (FAB$^+$) C$_{18}$H$_{25}$N$_2$: ([M+H]$^+$) 269.2018: Found 269.2009.

References
