Supporting Information

Intramolecular palladium-catalysed enolate arylation of 2- and 3-iodoindole derivatives for the synthesis of β-carbolines, γ-carbolines, and pyrrolo[3,4-b]indoles

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**General Methods.** All commercially available reagents were used without further purification. Unless otherwise noted, $^1$H- and $^{13}$C NMR spectra were recorded in CDCl$_3$ solution, using Me$_4$Si as the internal standard, with a Varian Gemini 300 or a Varian Mercury 400 instrument. Chemical shifts are reported in ppm downfield ($\delta$) from Me$_4$Si. TLC was carried out on SiO$_2$ (silica gel 60 F$_{254}$), and the spots were located with UV light, iodoplatinum reagent or 1% aqueous KMnO$_4$. Flash chromatography was carried out on SiO$_2$ (silica gel 60, 230-400 mesh ASTM). Drying of organic extracts during workup of reactions was performed over anhydrous MgSO$_4$. Evaporation of solvents was accomplished with a rotatory evaporator.

**PREPARATION OF THE STARTING MATERIALS**

*2-Iodo-1-methyl-1H-indole-3-carbaldehyde (2)*

POCl$_3$ (1.3 mL, 13.95 mmol) was added slowly to ice-cooled dry DMF (14 mL). The solution was stirred, under Argon, for 15 min at room temperature and then cooled to 0 °C. A solution of 2-iodo-1-methylindole$^1$ (1, 3.36 g, 13.07 mmol) in DMF (14 mL) was then added dropwise. The mixture was stirred at room temperature for 3 h, poured into ice water and made alkaline with 2M NaOH. The resulting mixture was extracted with ether. The organic layer was washed with brine, dried and concentrated. The residue was purified by chromatography (SiO$_2$, from hexanes to 9:1 hexanes-EtOAc) to give 2 (3.20 g, 86%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 3.81 (s, 3H), 7.23-7.34 (m, 3H), 8.31 (m, 1H), 9.83 (s, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 34.6 (CH$_3$), 100.6 (C), 109.9 (CH), 119.1 (C), 120.7 (CH), 122.8 (CH), 124.0 (CH), 126.2 (C), 139.2 (C), 187.6 (CH). ESI-HRMS [M+H]$^+$ calcld for C$_{10}$H$_9$INO 285.9723, found 285.9725.

*N-[(2-Iodo-1-methyl-1H-indol-3-yl)methyl]-N-methylamine (3)*

To a solution of aldehyde 2 (1 g, 3.5 mmol) in CH$_2$Cl$_2$ (5 mL) methylamine (4.4 mL of 8M solution in EtOH, 35.2 mmol) and AcOH (0.2 mL, 3.5 mmol) were added. The mixture was stirred at room temperature for 6 h. The solvent was removed *in vacuo*, the residue was dissolved in MeOH (10 mL), and NaBH$_4$ (0.4 g, 10.5 mmol) was slowly added. The mixture was stirred at room temperature overnight. The solvent was removed *in vacuo* and the residue was partitioned between CH$_2$Cl$_2$ and water. The organic layer was dried and concentrated. The residue was purified by chromatography

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(SiO$_2$, from CH$_2$Cl$_2$ to CH$_2$Cl$_2$-MeOH 10%) to give amine 3 (0.95 g, 90%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.42 (broad s, 1H), 2.46 (s, 3H), 3.76 (s, 3H), 3.93 (s, 2H), 7.09 (ddd, $J$ = 7.6, 7.2, and 0.8 Hz, 1H), 7.17 (ddd, $J$ = 8, 7.2, and 1.2 Hz, 1H), 7.30 (d, $J$ = 8 Hz, 1H), 7.65 (d, $J$ = 7.6 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 34.2 (CH$_3$), 35.6 (CH$_3$), 47.9 (CH$_2$), 88.8 (C), 109.6 (CH), 118.1 (CH), 118.6 (C), 119.6 (CH), 122.0 (CH), 127.8 (C), 138.5 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{11}$H$_{14}$IN$_2$ 301.0202, found 301.0205.

4-{N-[2-Iodo-1-methyl-1H-indol-3-yl]methyl}-N-methylamino}-2-butanone (4)
To a solution of amine 3 (560 mg, 1.87 mmol) in MeOH (16 mL), MVK (0.53 mL, 6.55 mmol) and Et$_3$N (0.65 mL, 4.68 mmol) were added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was partitioned between CH$_2$Cl$_2$ and water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from CH$_2$Cl$_2$ to CH$_2$Cl$_2$-MeOH 1%) to give ketone 4 (450 mg, 65%). $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.10 (s, 3H), 2.22 (s, 3H), 2.66 (m, 2H), 2.77 (m, 2H), 3.64 (s, 2H), 3.76 (s, 3H), 7.07 (ddd, $J$ = 8.1, 6.9, and 1.2 Hz, 1H), 7.16 (ddd, $J$ = 8.4, 6.9, and 1.2 Hz, 1H), 7.29 (d, $J$ = 8.4 Hz, 1H), 7.66 (d, $J$ = 8.1 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 75.5 MHz) $\delta$ 29.9 (CH$_3$), 34.3 (CH$_3$), 41.9 (CH$_3$), 42.0 (CH$_2$), 52.1 (CH$_2$), 55.0 (CH$_2$), 89.6 (C), 109.4 (CH), 117.4 (C), 118.8 (CH), 119.4 (CH), 121.9 (CH), 128.2 (C), 138.6 (C), 208.4 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{15}$H$_{20}$IN$_2$O 371.0614, found 371.0615.

Methyl 3-{N-[2-iodo-1-methyl-1H-indol-3-yl]methyl}-N-methylamino}propanoate (5)
To a solution of amine 3 (430 mg, 1.43 mmol) in MeOH (5 mL), methyl acrylate (0.32 mL, 3.58 mmol) was added. The mixture was stirred at room temperature for 24 h. The solvent was removed in vacuo and the residue was purified by chromatography (SiO$_2$, from hexanes to 7:3 hexanes-EtOAc) to give ester 5 (310 mg, 56%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.25 (s, 3H), 2.58 (t, $J$ = 7.2 Hz, 2H), 2.82 (t, $J$ = 7.2 Hz, 2H), 3.64 (s, 3H), 3.67 (s, 2H), 3.76 (s, 3H), 7.08 (ddd, $J$ = 8, 7.2, and 0.8 Hz, 1H), 7.17 (ddd, $J$ = 8.4, 7.2, and 0.8 Hz, 1H), 7.30 (d, $J$ = 8.4 Hz, 1H), 7.70 (dd, $J$ = 8 and 0.8 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 32.9 (CH$_2$), 34.2 (CH$_3$), 41.8 (CH$_3$), 51.4 (CH$_3$), 52.9 (CH$_2$), 54.9 (CH$_2$), 89.3 (C), 109.4 (CH), 117.6 (C), 119.0 (CH), 119.3 (CH), 121.9 (CH), 128.2 (C), 138.6 (C), 208.4 (C).
128.3 (C), 138.6 (C), 173.1 (C). ESI-HRMS [M+H]^+ calcd for C_{15}H_{20}IN_{2}O_{2} 387.0564, found 387.0562.

1-{(N-[(2-Iodo-1-methyl-1H-indol-3-yl)methyl]-N-methylamino)-2-propanone (6)

To a solution of amine 3 (260 mg, 0.87 mmol) in acetonitrile (5 mL), DIPEA (0.7 mL, 4.0 mmol) and chloroacetone (0.11 mL, 1.39 mmol) were added. After 2.5 h at reflux, the solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO_{3} aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO_{2}, from CH_{2}Cl_{2} to CH_{2}Cl_{2}-MeOH 1%) to give ketone 6 (220 mg, 71%). \textsuperscript{1}H NMR (CDCl_{3}, 300 MHz) \( \delta \) 2.11 (s, 3H), 2.35 (s, 3H), 3.17 (s, 2H), 3.75 (s, 2H), 3.77 (s, 3H), 7.11 (ddd, \( J = 7.6, 7.2, \) and 0.9 Hz, 1H), 7.19 (ddd, \( J = 8.1, 7.2, \) and 1.5 Hz, 1H), 7.31 (dd, \( J = 8.1 \) and 0.9 Hz, 1H), 7.80 (dd, \( J = 7.6 \) and 1.5 Hz, 1H). \textsuperscript{13}C NMR (CDCl_{3}, 75.5 MHz) \( \delta \) 27.5 (CH_{3}), 34.3 (CH_{3}), 43.1 (CH_{3}), 54.8 (CH_{2}), 66.8 (CH_{2}), 89.9 (C), 109.5 (CH), 117.1 (C), 118.9 (CH), 119.5 (CH), 122.0 (CH), 128.2 (C), 138.6 (C), 209.0 (C). ESI-HRMS [M+H]^+ calcd for C_{14}H_{16}IN_{2}O 357.0458, found 357.0460.

Methyl 2-{(N-benzyl-N-[(2-iodo-1-methyl-1H-indol-3-yl)methyl]amino)acetate (7)

To a solution of aldehyde 2 (0.5 g, 1.75 mmol) in DCE (3 mL), glycine methyl ester hydrochloride (0.55 g, 4.38 mmol), AcOH (0.22 mL, 3.85 mmol), and Et\(_3\)N (0.54 mL, 3.85 mmol) were added. After 10 min at room temperature NaBH(OAc)\(_3\) (0.89 g, 4.2 mmol) was slowly added. The resulting mixture was stirred at room temperature for 24 h, poured into 1N NaOH and extracted with CH\(_2\)Cl\(_2\). The organic layer was dried and concentrated. The residue was dissolved in acetonitrile (10 mL) and benzyl bromide (0.25 mL, 2.1 mmol) and K\(_2\)CO\(_3\) (0.48 g, 3.5 mmol) were added. The mixture was stirred at 55 °C for 2.5 h. The solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO\(_3\) aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO\(_2\), from hexanes to 9:1 hexanes-EtOAc) to give ester 7 (0.45 g, 57%). \textsuperscript{1}H NMR (CDCl\(_3\), 400 MHz) \( \delta \) 3.29 (s, 2H), 3.67 (s, 3H), 3.75 (s, 3H), 3.86 (s, 2H), 4.00 (s, 3H), 7.05-7.38 (m, 8H), 7.80 (dd, \( J = 8 \) and 1.2 Hz, 1H). \textsuperscript{13}C NMR (CDCl\(_3\), 100.5 MHz) \( \delta \) 34.2 (CH\(_3\)), 51.1 (CH\(_3\)), 51.4 (CH\(_2\)), 52.8 (CH\(_2\)), 57.6 (CH\(_2\)), 89.5 (C), 109.4 (CH), 117.5 (C), 119.3 (CH), 119.4 (CH), 122.0 (CH), 126.9 (CH), 128.2 (2 CH), 128.3 (C),
129.1 (2 CH), 138.7 (C), 139.4 (C), 172.1 (C). ESI-HRMS [M+H]^+ calcd for C_{20}H_{22}IN_{2}O_{2} 449.0720, found 449.0718.

**3-Iodo-1-methyl-1H-indole-2-carbaldehyde (9)**

To a suspension of NaH (710 mg of 60% dispersion in mineral oil, 17.7 mmol) in THF (70 mL), cooled to 0 °C, a solution of aldehyde 8\(^2\) (2.4 g, 8.85 mmol) in THF (30 mL) was added dropwise. The mixture was stirred at room temperature for 1 h and ICH\(_3\) (1.4 mL, 22.13 mmol) was added. After 24 h at room temperature, the reaction mixture was poured into ice water, was extracted with EtOAc and washed with brine. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO\(_2\), from hexanes to hexanes-EtOAc 1:1) to give aldehyde 9 (2.1 g, 83%). \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 4.08 (s, 3H), 7.24 (ddd, \(J = 7.5, 6.9, \) and 1.2 Hz, 1H), 7.35 (dm, \(J = 7.5\) Hz, 1H), 7.46 (ddd, \(J = 7.5, 6.9, \) and 1.2 Hz, 1H), 7.57 (dm, \(J = 7.5\) Hz, 1H), 9.99 (s, 1H). \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz) \(\delta\) 31.8 (CH\(_3\)), 75.1 (C), 110.6 (CH), 121.7 (CH), 123.6 (CH), 128.0 (CH), 129.7 (C), 131.4 (C), 140.4 (C), 184.6 (CH). ESI-HRMS [M+H]^+ calcd for C\(_{10}\)H\(_9\)INO 285.9723, found 285.9729.

**N-[(3-Iodo-1-methyl-1H-indol-2-yl)methyl]-N-methylamine (10)**

To a solution of aldehyde 9 (1.1 g, 3.86 mmol) in CH\(_2\)Cl\(_2\) (6 mL) methylamine (4.8 mL of 8M solution in EtOH, 38.5 mmol) and AcOH (0.22 mL, 3.86 mmol) were added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo, the residue was dissolved in MeOH (10 mL) and NaBH\(_4\) (0.4 g, 10.5 mmol) was slowly added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was partitioned between CH\(_2\)Cl\(_2\) and water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO\(_2\), from CH\(_2\)Cl\(_2\) to CH\(_2\)Cl\(_2\)-MeOH 10%) to give amine 10 (1.05 g, 91%). \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 2.49 (s, 3H), 3.85 (s, 3H), 3.98 (s, 2H), 7.17 (m, 1H), 7.26 (m, 2H), 7.41 (dm, \(J = 7.5\) Hz, 1H). \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz) \(\delta\) 30.6 (CH\(_3\)), 36.1 (CH\(_3\)), 47.4 (CH\(_2\)), 59.6 (C), 109.4 (CH), 120.2 (CH), 121.1 (CH), 122.7 (CH), 129.6 (C), 137.8 (C), 138.3 (C). ESI-HRMS [M+H]^+ calcd for C\(_{11}\)H\(_{14}\)dIN\(_2\) 301.0202, found 301.0204.

4-\{N-[(3-Iodo-1-methyl-1H-indol-2-yl)methyl]-N-methylamino\}-2-butanone (11)

To a solution of amine 10 (550 mg, 1.83 mmol) in MeOH (15 mL), MVK (0.53 mL, 6.55 mmol) and Et₃N (0.65 mL, 4.68 mmol) were added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was partitioned between CH₂Cl₂ and water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO₂, from CH₂Cl₂ to CH₂Cl₂-MeOH 1%) to give ketone 11 (583 mg, 86%). ¹H NMR (CDCl₃, 400 MHz) δ 2.05 (s, 3H), 2.22 (s, 3H), 2.59 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H), 3.72 (s, 2H), 3.80 (s, 3H), 7.17 (m, 1H), 7.27 (m, 2H), 7.41 (d, J = 8 Hz, 1H). ¹³C NMR (CDCl₃, 100.5 MHz) δ 29.8 (CH₃), 30.5 (CH₃), 41.4 (CH₃), 42.5 (CH₂), 51.9 (CH₂), 53.9 (CH₂), 61.0 (C), 109.3 (CH), 120.2 (CH), 121.2 (CH), 122.7 (CH), 129.6 (C), 136.6 (C), 138.1 (C), 207.9 (C). ESI-HRMS [M+H]⁺ calcd for C₁₅H₂₀IN₂O 371.0614, found 371.0617.

Methyl 3-\{N-[(3-Iodo-1-methyl-1H-indol-2-yl)methyl]-N-methylamino\}propanoate (12)

To a solution of amine 10 (480 mg, 1.6 mmol) in MeOH (5 mL), methyl acrylate (0.36 mL, 4.0 mmol) was added. The mixture was stirred at room temperature for 24 h. The solvent was removed in vacuo and the residue was purified by chromatography (SiO₂, from hexanes to 7:3 hexanes-EtOAc) to give ester 12 (435 mg, 70%). ¹H NMR (CDCl₃, 400 MHz) δ 2.21 (s, 3H), 2.49 (t, J = 6.8 Hz, 2H), 2.79 (t, J = 6.8 Hz, 2H), 3.60 (s, 3H), 3.73 (s, 2H), 3.79 (s, 3H), 7.16 (m, 1H), 7.25 (m, 2H), 7.41 (d, J = 8 Hz, 1H). ¹³C NMR (CDCl₃, 100.5 MHz) δ 30.4 (CH₃), 32.7 (CH₂), 41.2 (CH₃), 51.5 (CH₃), 52.7 (CH₂), 53.9 (CH₂), 60.9 (C), 109.2 (CH), 120.1 (CH), 121.2 (CH), 122.6 (CH), 129.6 (C), 136.6 (C), 138.0 (C), 172.8 (C). ESI-HRMS [M+H]⁺ calcd for C₁₅H₂₀IN₂O 387.0564, found 387.0561.

1-\{N-[(3-Iodo-1-methyl-1H-indol-2-yl)methyl]-N-methylamino\}-2-propanone (13)

To a solution of amine 10 (475 mg, 1.58 mmol) in acetonitrile (10 mL), DIPEA (1.4 mL, 8.0 mmol) and chloroacetone (0.26 mL, 3.32 mmol) were added. After 2.5 h at reflux, the solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO₃ aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO₂, from CH₂Cl₂ to CH₂Cl₂-MeOH 1%) to give ketone 13 (450 mg, 80%). ¹H NMR (CDCl₃, 400 MHz) δ
2.05 (s, 3H), 2.36 (s, 3H), 3.24 (s, 2H), 3.82 (s, 2H), 3.94 (s, 3H), 7.18 (m, 1H), 7.28 (m, 2H), 7.42 (d, J = 7.6 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) δ 27.5 (CH$_3$), 30.7 (CH$_3$), 43.0 (CH$_3$), 53.2 (CH$_2$), 61.5 (CH$_2$), 66.0 (CH$_2$), 109.5 (CH), 120.3 (CH), 121.3 (CH), 122.9 (CH), 129.5 (C), 136.2 (C), 138.1 (C), 206.8 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{14}$H$_{18}$IN$_2$O 357.0458, found 357.0457.

**Methyl 2-{{N-benzyl-}{N}-[(3-iodo-1-methyl-1$H$-indol-2-yl)methyl]amino}acetate (14)**

To a solution of aldehyde 9 (0.35 g, 1.23 mmol) in DCE (3 mL), glycine methyl ester hydrochloride (0.39 g, 3.1 mmol), AcOH (0.16 mL, 2.8 mmol), and Et$_3$N (0.4 mL, 2.8 mmol) were added. After 10 min at room temperature NaBH(OAc)$_3$ (0.63 g, 2.97 mmol) was slowly added. The resulting mixture was stirred at room temperature for 24 h, poured into 1N NaOH and extracted with CH$_2$Cl$_2$. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from hexanes to 1:1 hexanes-EtOAc) to give methyl 2-{{N-}{(3-iodo-1-methyl-1$H$-indol-2-yl)methyl]amino}acetate (0.28 g, 64%). $^1$H NMR (CDCl$_3$, 400 MHz) δ 3.41 (s, 2H), 3.71 (s, 3H), 3.87 (s, 3H), 4.07 (s, 2H), 7.16 (m, 1H), 7.26 (m, 1H), 7.40 (d, J = 8 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) δ 30.6 (CH$_3$), 44.7 (CH$_2$), 49.1 (CH$_2$), 51.8 (CH$_3$), 60.3 (C), 109.4 (CH), 120.3 (CH), 121.2 (CH), 122.8 (CH), 129.5 (C), 137.3 (C), 138.0 (C), 172.8 (C).

To a solution of methyl 2-{{N-}{(3-iodo-1-methyl-1$H$-indol-2-yl)methyl]amino}acetate (0.28 g, 0.78 mmol) in acetonitrile (10 mL), benzyl bromide (0.11 mL, 0.94 mmol) and K$_2$CO$_3$ (0.21 g, 1.56 mmol) were added. The mixture was stirred at 55 ºC for 2.5 h. The solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO$_3$ aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from hexanes to 9:1 hexanes-EtOAc) to give ester 14 (0.32 g, 91%). $^1$H NMR (CDCl$_3$, 400 MHz) δ 3.28 (s, 2H), 3.64 (s, 3H), 3.80 (s, 2H), 3.84 (s, 3H), 4.03 (s, 2H), 7.12-7.42 (m, 9H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) δ 30.7 (CH$_3$), 50.2 (CH$_2$), 51.4 (CH$_3$), 53.3 (CH$_2$), 58.2 (CH$_2$), 61.6 (C), 109.4 (CH), 120.2 (CH), 121.2 (CH), 122.8 (CH), 127.3 (CH), 128.3 (2 CH), 129.1 (2 CH), 129.6 (C), 136.3 (C), 138.2 (C), 138.4 (C), 171.5 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{20}$H$_{22}$IN$_2$O$_2$ 449.0720, found 449.0716.

**N-{(3-Iodo-1-phenylsulfonyl-1$H$-indol-2-yl)methyl]-N-methylamine (16)**}
To a solution of aldehyde 15 (0.6 g, 1.46 mmol) in CH$_2$Cl$_2$ (5 mL), methylamine (1.9 mL of 8M solution in EtOH, 15.2 mmol) and AcOH (0.1 mL, 1.75 mmol) were added. The mixture was stirred overnight at room temperature. The solvent was removed in vacuo, the residue was dissolved in MeOH (10 mL) and NaBH$_4$ (0.22 g, 5.84 mmol) was slowly added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was partitioned between CH$_2$Cl$_2$ and water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from CH$_2$Cl$_2$ to CH$_2$Cl$_2$-MeOH 10%) to give amine 16 (0.55 g, 88%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.43 (s, 4H), 4.27 (s, 2H), 7.30-7.44 (m, 5H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.881 (m, 2H), 8.14 (d, $J = 8.4$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 34.6 (CH$_3$), 48.2 (CH$_2$), 77.2 (C), 114.9 (CH), 122.3 (CH), 124.5 (CH), 126.2 (CH), 126.5 (2 CH), 129.3 (2 CH), 131.4 (C), 134.1 (CH), 136.8 (C), 138.1 (C), 138.2 (C).

4-{$N$-[3-Iodo-1-phenylsulfonyl-1H-indol-2-yl]methyl-}$N$-methylamino}-2-butanone (17)

To a solution of amine 16 (0.54 g, 1.27 mmol) in MeOH (15 mL), MVK (0.4 mL, 4.9 mmol) and Et$_3$N (0.5 mL, 3.6 mmol) were added. The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was partitioned between CH$_2$Cl$_2$ and water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from CH$_2$Cl$_2$ to CH$_2$Cl$_2$-MeOH 3%) to give ketone 17 (0.33 g, 52%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.10 (s, 3H), 2.17 (s, 3H), 2.55 (t, $J = 7.2$ Hz, 2H), 2.78 (t, $J = 7.2$ Hz, 2H), 4.03 (s, 2H), 7.28-7.44 (m, 5H), 7.52 (tt, $J = 8$ and 1.2 Hz, 1H), 8.03-8.10 (m, 3H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 30.0 (CH$_3$), 40.7 (CH$_2$), 41.0 (CH$_3$), 51.5 (CH$_2$), 53.4 (CH$_2$), 76.5 (C), 114.7 (CH), 122.3 (CH), 123.9 (CH), 126.0 (CH), 127.1 (2 CH), 128.8 (2 CH), 130.9 (C), 133.5 (CH), 136.6 (C), 136.9 (C), 139.4 (C), 208.0 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{20}$H$_{22}$IN$_2$O$_3$S 497.0390, found 497.0388.

1-{$N$-[3-Iodo-1-phenylsulfonyl-1H-indol-2-yl]methyl-}$N$-methylamino}-2-propanone (18)

To a solution of amine 16 (0.45 g, 1.06 mmol) in acetonitrile (5 mL), DIPEA (0.7 mL, 4.0 mmol) and chloroacetone (0.2 mL, 2.53 mmol) were added. After 2.5 h at reflux, the solvent was removed in vacuo and the residue was partitioned between dichloromethane...
and saturated NaHCO₃ aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO₂, from CH₂Cl₂ to CH₂Cl₂-MeOH 2%) to give ketone 18 (0.41 g, 81%). ¹H NMR (CDCl₃, 400 MHz) δ 2.04 (s, 3H), 2.40 (s, 3H), 3.39 (s, 2H), 4.25 (s, 2H), 7.27-7.47 (m, 5H), 7.52 (tt, J = 8 and 1.2 Hz, 1H), 8.04 (dd, J = 8.4 and 0.8 Hz, 1H), 8.18 (m, 2H). ¹³C NMR (CDCl₃, 100.5 MHz) δ 27.8 (CH₃), 41.5 (CH₃), 65.8 (CH₂), 76.3 (C), 114.7 (CH), 122.3 (CH), 123.9 (CH), 126.0 (CH), 127.4 (2 CH), 128.9 (2 CH), 130.9 (C), 133.7 (CH), 136.5 (C), 136.9 (C), 138.9 (C), 206.9 (C). ESI-HRMS [M+H]⁺ calcd for C₁₉H₂₀N₂O₃S 483.0234, found 483.0232.

2-(2-Iodo-1-phenylsulfonyl-1H-indol-3-yl)ethyl p-toluenesulfonate (20)
To a cooled (0 ºC) solution of iodotryptophol 19 (0.71 g, 1.66 mmol) in CH₂Cl₂ (10 mL), TsCl (0.35 g, 1.83 mmol), DMAP (10 mg) and Et₃N (0.58 mL, 4.15 mmol) were added. The resulting mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with CH₂Cl₂ and washed with 1N HCl and saturated Na₂CO₃ aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO₂, from hexanes to 1:1 hexanes-EtOAc) to give 20 (0.8 g, 75%). ¹H NMR (CDCl₃, 400 MHz) δ 2.41 (s, 3H), 3.01 (t, J = 7.2 Hz, 2H), 4.17 (t, J = 7.2 Hz, 2H), 7.19-7.58 (m, 10H), 7.83 (m, 2H), 8.25 (d, J = 8 Hz, 1H). ¹³C NMR (CDCl₃, 100.5 MHz) δ 21.6 (CH₃), 27.8 (CH₂), 68.2 (CH₂), 80.1 (C), 115.6 (CH), 118.5 (CH), 123.8 (CH), 125.1 (CH), 126.7 (C), 127.1 (2 CH), 127.4 (2 CH), 129.2 (2 CH), 129.6 (2 CH), 130.1 (C), 132.3 (C), 134.0 (CH), 138.1 (C), 138.8 (C), 144.8 (C). ESI-HRMS [M+NH₄]⁺ calcd for C₂₃H₂₄In₂O₅S₂ 599.0166, found 599.0165.

{N-[2-(2-Iodo-1-phenylsulfonyl-1H-indol-3-yl)ethyl]-N-methylamino}-2-propanone (21)
A mixture of 20 (0.7 g, 1.17 mmol), methylamine (3 mL of 8M solution in EtOH, 24 mmol), and K₂CO₃ (0.34 g, 2.46 mmol) in acetonitrile (7 mL) was stirred at 85 ºC in a sealed tube for 24 h. The solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO₃ aqueous solution. The organic layer was dried and concentrated. The residue was dissolved in acetonitrile (10 mL), and DIPEA (1 mL, 5.7 mmol) and chloroacetone (0.2 mL, 2.46 mmol) were added. After 5

h at reflux, the solvent was removed in vacuo and the residue was partitioned between dichloromethane and saturated NaHCO$_3$ aqueous solution. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO$_2$, from CH$_2$Cl$_2$ to CH$_2$Cl$_2$-MeOH 1%) to give ketone 21 (270 mg, 46%). $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 2.05 (s, 3H), 2.39 (s, 3H), 2.53 (m, 2H), 2.86 (m, 2H), 3.24 (s, 2H), 7.21-7.32 (m, 2H), 7.36-7.46 (m, 3H), 7.53 (tt, $J = 7.2$ and 1.6 Hz, 1H), 7.85 (m, 2H), 8.30 (dm, $J = 7.2$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 75.5 MHz) $\delta$ 26.2 (CH$_3$), 27.5 (CH$_3$), 42.7 (CH$_3$), 56.3 (CH$_2$), 67.5 (CH$_2$), 79.3 (C), 115.9 (CH), 118.5 (CH), 123.8 (CH), 125.1 (CH), 127.1 (2 CH), 129.0 (2 CH), 130.3 (C), 130.4 (C), 133.9 (CH), 138.0 (C), 139.2 (C), 207.3 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{20}$H$_{22}$IN$_2$O$_3$S 497.0396, found 497.0391.

2-\{N-Benzyl-N-\[(3-iodo-1-methyl-1H-indol-2-yl)methyl\]amino\}-N,N-dimethylacetamide (22)
A solution of dimethylamine hydrochloride (296 mg, 3.63 mmol) in toluene (6 mL) was cooled to -30 ºC under argon, and a 2M solution of trimethylaluminum in toluene (1.82 mL, 3.63 mmol) was added dropwise. The solution was stirred at room temperature for 1h.
A solution of ester 14 (0.54 g, 1.20 mmol) in dichloromethane (12 mL) was cooled to 0 ºC. The solution of AlMe$_2$-NMe$_2$ complex prepared above was added dropwise to the ester solution, the temperature being kept below 5 ºC. The mixture was slowly warmed to room temperature. The solution was stirred at 50 ºC for 24 h. The reaction was quenched by slowly adding it to an ice-cold solution containing 10% aqueous KH$_2$PO$_4$ (40 mL), THF (30 mL), and EtOAc (30 mL). The mixture was warmed to 40 ºC and stirred for 1h. The organic layer was then separated, washed with brine, dried, filtered through Celite, and concentrated. The residue was purified by chromatography (SiO$_2$, from hexanes to hexanes-EtOAc 1:1) to give amide 22 (266 mg, 48%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.74 (s, 3H), 2.90 (s, 3H), 3.29 (s, 2H), 3.77 (s, 3H), 3.79 (s, 2H), 3.98 (s, 2H), 7.11-7.42 (m, 9H). $^{13}$C NMR (CDCl$_3$, 100.5 MHz) $\delta$ 30.6 (CH$_3$), 35.4 (CH$_3$), 36.6 (CH$_3$), 50.2 (CH$_2$), 54.5 (CH$_2$), 58.7 (CH$_2$), 61.7 (C), 109.4 (CH), 120.2 (CH), 121.1 (CH), 122.7 (CH), 127.2 (CH), 128.2 (2 CH), 129.4 (2 CH), 129.6 (C), 136.7 (C), 138.0 (C), 138.7 (C), 170.2 (C). ESI-HRMS [M+H]$^+$ calcd for C$_{21}$H$_{25}$IN$_3$O 462.1037, found 462.1036.
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[Chemical structure image]