Supporting Information

for

Fates of imine intermediates in radical cyclizations of *N*-sulfonylindoles and enesulfonamides

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Experimental procedures, compound characterization data, and copies of NMR spectra

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General Remarks: Chemicals and solvents were purchased from commercial suppliers and used as received, except as follows. Dichloromethane, THF, ether, and toluene were dried by passing through an activated alumina column. All reactions were carried out under an inert atmosphere of dry argon, unless otherwise indicated.

All reactions were followed by TLC or ¹H NMR spectroscopy. TLC visualizations were performed by illumination with a UV lamp (254 nm) or staining with a phosphomolybdic acid solution in ethanol and heating. Flash chromatographies were performed with a automated flash chromatography instrument and prepacked columns containing 230-400 mesh silica gel.

¹H NMR spectra were recorded at 300, 400, 500 and 600 MHz in CDCl₃, and chemical shifts were measured relative to tetramethylsilane (δ 0.00 ppm) or residual solvent peak (δ 7.26 ppm). ¹³C NMR spectra were recorded at 75, 100, 125, 150 MHz in CDCl₃, and chemical shifts were measured relative to residual solvent peak (δ 77.0 ppm). Unless otherwise noted, NMR spectra were recorded at 293 K. The following abbreviations were used to describe coupling: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded as thin films (CHCl₃) or neat on NaCl plates on an FTIR spectrometer.

Aldehyde **6** was prepared using published procedures, and the spectral data matched the reported ones.¹ 1-(Phenylsulfonyl)-2,3-dihydro-1*H*-pyrrole **20** was prepared using published procedures.²

Experimental Procedures and Compound Characterization



N-Benzyl-2,2,2-trichloro-*N*-((1-tosyl-1*H*-indol-3-yl)methyl)acetamide (3): The title compound was prepared as a mixture of 2.5:1 rotamers: ¹H NMR (300 MHz, CDCl₃) δ major rotamer: 4.87 (s, 2H), 4.73 (s, 2H); minor rotamer: 4.99 (s, 2H), 4.66 (s, 2H); overlapping signals: 8.04 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.45–7.12 (m, 10H), 2.37 (s, 3H). The above spectral data were identical to those reported.³



1'-Benzyl-4'-chlorospiro[indoline-3,3'-pyrrolidin]-5'-one (5b): A mixture of tin hydride (110 μ L, 0.411 mmol), AIBN (17 mg, 0.102 mmol), and trichloroacetamide **3** (110 mg, 0.205 mmol) in benzene (10 mL) was refluxed for 30 min. The solvent was evaporated and the residue was purified by flash chromatography (silica gel, 30% EtOAc/hexanes) to provide the title compound (33 mg, 51%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.39–7.26 (m, 5H), 7.18–7.10 (m, 2H), 6.74 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.68 (d, *J* = 7.5 Hz, 1H), 4.63 (d, *J* = 14.4 Hz, 1H), 4.53 (d, *J* = 14.4 Hz, 1H), 4.45 (s, 1H), 3.77 (brs, 1H), 3.75 (d, *J* = 10.2 Hz, 1H), 3.63 (d, *J* = 9.6 Hz, 1H), 3.25 (d, *J* = 10.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ

169.3, 151.6, 135.4, 129.5, 128.9, 128.3, 128.1, 126.6, 125.6, 118.8, 110.1, 61.5, 58.6, 55.0, 52.2, 47.2; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3334, 3030, 2922, 2856, 1701, 1607, 1486, 1465, 1257, 742; HRMS (TOF ES) *m/z* cald for C₁₈H₁₇N₂ONaCl, 335.0927 [M+Na]⁺, found: 335.0916.



1'-Benzylspiro[indoline-3,3'-pyrrolidin]-5'-one (5c): A mixture of tin hydride (150 µL, 0.560 mmol), AIBN (4 mg, 0.023 mmol), and trichloroacetamide **3** (50 mg, 0.093 mmol) in benzene (10 mL) was refluxed for 30 min. The solvent was evaporated and the residue was purified by flash chromatography (silica gel, 75% EtOAc/hexanes) to provide the title compound (20 mg, 78%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.37–7.25 (m, 5H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.75 (t, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 4.62 (d, *J* = 14.4 Hz, 1H), 4.41 (d, *J* = 14.4 Hz, 1H), 3.75 (brs, 1H), 3.50 (d, *J* = 14.4 Hz, 1H), 3.48 (d, *J* = 14.4 Hz, 1H), 3.39 (d, *J* = 13.8 Hz, 1H), 3.36 (d, *J* = 13.8 Hz, 1H), 2.87 (d, *J* = 16.8 Hz, 1H), 2.65 (d, *J* = 16.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 173.0, 150.7, 136.2, 132.5, 128.8, 128.6, 128.3, 127.8, 122.1, 119.3, 110.0, 60.6, 58.3, 46.7, 45.8, 44.0; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3336, 2920, 2855, 1680, 1608, 1488, 1256, 745, 702; HRMS (TOF ES) *m/z* cald for C₁₈H₁₈N₂ONa, 301.1317 [M+Na]⁺, found: 301.1304.



2-Iodo-*N***-((1-tosyl-1***H***-indol-3-yl)methyl)aniline (S1)**: 2-Iodoaniline (241 mg, 1.10 mmol), acetic acid (60 mg, 1.00 mmol), and sodium triacetoxyborohydride (637 mg, 3.00 mmol) were added to a stirred solution of 1-tosyl-1*H*-indole-3-carbaldehyde **6** (300 mg, 1.00 mmol) in 1,2-dichloroethane (8 mL). After 12 h, the reaction was quenched with a saturated NaHCO₃ solution and the aqueous layer was extracted with 1,2-dichloroethane. The combined organic layer was washed with brine, dried with MgSO₄, and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, 15% EtOAc/hexanes) to give the title compound (330 mg, 66%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 8.01 (d, *J* = 8.1 Hz, 1H), 7.73–7.69 (m, 3H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.51 (s, 1H), 7.36 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.27 (m, 1H), 7.22–7.14 (m, 3H), 6.58 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 6.50 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 4.54–4.47 (m, 3H), 2.35 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 146.9, 145.0, 139.1, 135.6, 135.1, 129.9, 129.6, 126.9, 125.1, 124.2, 123.4, 119.9, 119.6, 119.2, 114.0, 111.1, 85.6, 40.2, 21.6; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3394, 3061, 2921, 1589, 1502, 1448, 1367, 1277, 1173, 1121, 1005, 970, 810, 744; HRMS (EI) *m/z* cald for C₂₂H₁₉N₂O₂SI, 502.0212 [M]⁺, found: 502.0198.



2-Iodo-N-methyl-N-((1-tosyl-1H-indol-3-yl)methyl)aniline (7): A NaHMDS solution (450 µL, 1M in THF) was added dropwise to a solution of aniline S1 (150 mg, 0.30 mmol) in THF (5 mL) at -78 °C. After 30 min, iodomethane (46 µL, 0.75 mmol) was added dropwise at this temperature. The reaction mixture was then stirred at room temperature for 12 h. A saturated aqueous NaHCO₃ solution was added, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with brine, dried over MgSO₄, and concentrated in *vacuo*. The residue was purified by flash chromatography (silica gel, 20% EtOAc/hexanes) to afford the title compound (140 mg, 91%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.97 (d, J = 8.1 Hz, 1H), 7.88 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.60-7.54 (m, 10.10 Hz)2H), 7.32-7.17 (m, 5H), 7.02 (dd, J = 8.1 Hz, 1.2 Hz, 1H), 6.80 (t, J = 7.8 Hz, 1H), 4.24 (s, 2H), 2.67 (s, 3H), 2.33 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 153.8, 144.8, 140.3, 135.4, 135.3, 130.6, 129.9, 129.1, 126.8, 125.7, 125.4, 124.8, 123.1, 122.2, 120.6, 119.5, 113.7, 98.6, 51.7, 42.4, 21.7; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3053, 2947, 1596, 1470, 1446, 1367, 1173, 1119, 1093, 978, 812, 747, 702; HRMS (TOF ES) m/z cald for C₂₃H₂₂N₂O₂SI, 517.0447 [M+H]⁺, found: 517.0460.



1-Methyl-3,3'-spirobi[indoline] (8): A mixture of aryl iodide **7** (70 mg, 0.136 mmol), tributyltin hydride (91 μL, 0.340 mmol) and AIBN (7 mg, 0.040 mmol) in benzene (13 mL) was refluxed for 20 min. TLC suggested the starting material was not completely consumed. Tin hydride (163 μL, 0.610 mmol) was added in two portions with a catalytic amount of AIBN. After 20 min, the solvent was evaporated, and the residue was purified by flash chromatography (silica gel, 20% EtOAc/hexanes) to provide the title compound (15 mg, 47%) as a colorless oil: ¹H NMR (600 MHz, CDCl₃) δ 7.18 (t, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 3.78 (d, *J* = 9.0 Hz, 1H), 3.63 (d, *J* = 9.0 Hz, 1H), 3.62 (d, *J* = 9.0 Hz, 1H), 3.27 (d, *J* = 9.0 Hz, 1H), 2.82 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 153.1, 151.4, 135.3, 134.1, 128.4, 128.2, 124.1, 123.6, 119.3, 118.6, 109.7, 107.5, 68.9, 60.3, 54.5, 36.1; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3374, 3046, 2949, 2853, 2805, 1606, 1487, 1463, 1295, 1252, 1151, 1121, 1021, 745; HRMS (EI) *m/z* cald for C₁₆H₁₆N₂, 236.1313 [M]⁺, found: 236.1313.



Ethyl 3-formyl-1-tosyl-1*H*-indole-2-carboxylate (9): Ethyl 3-formyl-1*H*-indole-2-carboxylate (150 mg, 0.69 mmol) and tosyl chloride (197 mg, 1.04 mmol) were added to a stirred suspension of Cs_2CO_3 (675 mg, 2.07 mmol) in DMF (4 mL). After 30 min, the reaction was quenched with a

saturated aqueous NH₄Cl solution, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography (silica gel, 15% EtOAc/hexanes) to afford the title compound (75 mg, 29%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 10.16 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 8.02–7.98 (m, 3H), 7.46 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.38 (td, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.61 (q, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.50 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 185.3, 161.1, 146.4, 139.3, 135.3, 134.4, 130.2, 127.9, 127.8, 127.4, 125.7, 125.3, 123.1, 120.9, 114.2, 63.7, 21.9, 14.2; FTIR (thin film, CH₂Cl₂, cm⁻¹) 2924, 2360, 1734, 1680, 1545, 1380, 1321, 1268, 1206, 1179, 1141, 1111, 1086, 1015, 986, 817, 749; HRMS (TOF ES) *m/z* cald for C₁₉H₁₇NO₅NaS, 394.0725 [M+Na]⁺, found: 394.0699.



Ethyl 3-((2-iodophenylamino)methyl)-1-tosyl-1*H*-indole-2-carboxylate (S2): A mixture of aldehyde 9 (66 mg, 0.178 mmol), 2-iodoaniline (43 mg, 0.195 mmol), anhydrous MgSO₄ (64 mg, 0.533 mmol), and pyridinium *p*-toluenesulfonate (13 mg, 0.053 mmol) in CH₂Cl₂ (2 mL) was stirred for 12 h. The reaction was quenched with a saturated aqueous NaHCO₃ solution, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layer was washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The resulting crude imine was dissolved in EtOH (3 mL), and NaBH₄ (20 mg, 0.533 mmol) was added in one portion. After 3 h, the reaction

was quenched with a saturated aqueous NaHCO₃ solution, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography (silica gel, 15% EtOAc/Hexane) to afford the title compound (65 mg, 64%) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 8.07 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H), 7.81 (m, 2H), 7.67 (m, 2H), 7.43 (td, *J* = 7.5 Hz, 1.5 Hz, 1H), 7.30 (m, 1H), 7.21 (m, 3H), 6.72 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 6.49 (td, *J* = 7.5 Hz, 1.5 Hz, 1H), 4.53 (s, 1H), 4.48 (q, *J* = 7.0 Hz, 1H), 2.34 (s, 3H), 1.39 (t, *J* = 7.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 162.4, 146.8, 145.1, 139.1, 136.8, 134.4, 129.7, 129.6, 129.5, 128.9, 127.2, 126.9, 124.4, 124.3, 120.8, 119.3, 115.5, 110.9, 85.5, 62.6, 39.0, 21.6, 14.0; FTIR (thin film, CH₂Cl₂, cm⁻¹) 3395, 2982, 1724, 1590, 1503, 1451, 1371, 1312, 1266, 1177, 1006, 814, 746; HRMS (EI) cald for C₂₅H₂₃N₂O₄SI, 574.0423 [M]⁺, found: 574.0408.



Ethyl 3-((*N*-(2-iodophenyl)acetamido)methyl)-1-tosyl-1*H*-indole-2-carboxylate (10): DMAP (4 mg, 0.03 mmol), pyridine (19 μ L, 0.23 mmol), and acetyl chloride (8 μ L, 0.11 mmol) were added to a stirred solution of aniline S2 (33 mg, 0.057 mmol) in CH₂Cl₂ (2 mL) at 0 °C. The reaction mixture was then stirred at room temperature for 12 h. It was diluted with CH₂Cl₂ and a saturated aqueous NaHCO₃ solution was added. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography (silica gel, 25%)

EtOAc/hexanes) to afford the title compound (29 mg, 80%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, J = 8.0 Hz, 1H), 7.91 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 8.0 Hz, 1H), 7.30-7.27 (m, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.10 (td, J = 7.6 Hz, 1.2 Hz, 1H), 7.02 (td, J = 7.6 Hz, 1.2 Hz, 1H), 6.40 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 5.74 (d, J = 14.4 Hz, 1H), 4.52 (d, J = 14.4 Hz, 1H), 4.17–4.01 (m, 2H), 2.35 (s, 3H), 1.78 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ major rotamer: 62.3, 21.6, 13.9; minor rotamer: 60.4, 21.1, 14.2; overlapping signals: 169.9, 161.4, 145.0, 143.0, 140.1, 136.5, 134.5, 131.3, 130.6, 130.0, 129.6, 129.5, 129.0, 127.3, 126.9, 124.6, 122.6, 121.9, 115.1, 100.0, 39.4, 22.8; FTIR (thin film, CH₂Cl₂, cm⁻¹) 2982, 1723, 1664, 1469, 1372, 1313, 1267, 1177, 1017, 762; HRMS (TOF ES) *m/z* cald for C₂₇H₂₅N₂O₅NaSI, 639.0427 [M+Na]⁺, found: 639.0479.



Ethyl 1'-acetylspiro[indole-3,3'-indoline]-2-carboxylate (11): In a sealed tube, a mixture of tin hydride (28 µL, 0.11 mmol), AIBN (1 mg, 0.0060 mmol), and aryl iodide 10 (13 mg, 0.021 mmol) in benzene (2 mL) was refluxed for 30 min. The solvent was evaporated and the residue was purified by flash chromatography (silica gel, 60% EtOAc/hexanes) to provide the title compound (5 mg, 71%) as a colorless oil, in a 5:1 ratio of rotamers: ¹H NMR (400 MHz, CDCl₃) δ major rotamer: 4.73 (d, *J* = 12.0 Hz, 1H), 2.28 (s, 3H); minor rotamer: 4.80 (d, *J* = 12.0 Hz, 1H), 2.59 (s, 3H); overlapping signals: 8.36 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.32–7.27 (m, 2 H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.42 (d, *J* = 7.6 Hz, 1H), 4.31–4.29 (m, 3H), 1.26 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.3, 168.2, 160.7, 152.6, 145.2, 144.2, 129.8, 129.5, 128.9, 124.0, 123.9, 122.7, 122.3, 118.1, 64.2, 62.3, 55.4, 24.4. 14.0; FTIR (thin film, CH₂Cl₂, cm⁻¹) 2923, 1722, 1665, 1593, 1482, 1402, 1339, 1267, 1146, 1106, 1021, 754; HRMS (TOF ES) *m/z* cald for C₂₀H₁₈N₂O₃Na, 357.1215 [M+Na]⁺, found: 357.1239.



1-(Phenylsulfonyl)-4,5-dihydro-1*H***-pyrrole-3-carbaldehyde (S3)**: Phosphorous oxychloride (1.21 mL, 12.9 mmol) was added to a solution of DMF (8.4 mL, 10.8 mmol) in CH₂Cl₂ (8.4 mL) at 0 °C. The solution as stirred at 0 °C for 10 min, then ene-sulfonamide **20** (2.50 g, 10.8 mmol) in CH₂Cl₂ (10 mL) was added. After 10 min, the solution was poured into saturated aqueous K₂CO₃ (100 mL) and the mixture was stirred vigorously for 1 h. The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂. The combined extracts were dried over MgSO₄ and concentrated. The residue was purification by flash chromatography (20% EtOAc in hexanes) to give the title compound (2.40 g, 94%) as a crystalline solid: mp 76–79 °C. ¹H NMR (500 MHz, CDCl₃) δ 9.55 (s, 1H), 7.82 (d, *J* = 7.5 Hz, 2H), 7.66 (t, *J* = 7.0 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.39 (s, 1H), 3.73 (t, *J* = 9.5 Hz, 2H), 2.78 (t, *J* = 9.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 185.4, 147.1, 136.1, 133.9, 129.6, 127.2, 125.8, 48.6, 25.9; HRMS (APCl) *m/z* calcd for C₁₁H₁₂NO₃S [M+H]⁺ 238.0538, found 238.0552.



1-(Phenylsulfonyl)-4,5-dihydro-1*H*-pyrrole-3-carboxylic acid (21): NaClO₂ (0.97 g, 8.60 mmol) was added in one portion to a mixture of aldehyde S3 (3.00 g, 12.6 mmol), 2-methyl-2butene (25.3 mL, 2M in THF), and NaH₂PO₄ (7.59 g, 63.22 mmol) in 1,4-dioxane/H₂O (3:1; 80 mL). The reaction mixture was stirred for 1 h at room temperature. A saturated NaHCO₃ solution (50 mL) was added with precaution to the solution and the final mixture was stirred vigorously for 30 min. The mixture was concentrated and the residue was dissolved in EtOAc. The organic mixture was washed with 10% HCl and H₂O, then evaporated under vacuum. The residue was purified by flash chromatography (50% EtOAc in hexanes) to give the title compound (3.02 g, 95%) as a white crystalline solid: mp 145–147 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 2H), 7.46 (s, 1H), 3.72 (t, *J* = 9.6 Hz, 2H), 2.79 (t, *J* = 9.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 142.7, 136.2, 133.8, 129.5, 127.4, 113.5, 48.7, 27.8; HRMS (APCI) *m/z* calcd for C₁₁H₁₂NO₄S [M+H]⁺ 254.0487, found 254.0510.



2-Iodo-*N*-(**4-methoxylbenzyl)aniline (S4):** NaBH(OAc)₃ (9.67 g, 45.6 mmol) was added to a solution of *p*-anisaldehyde (1.53 mL, 12.6 mmol), 2-iodoaniline (2.5 g, 11.4 mmol) and AcOH (0.11 mL, 0.11 mmol) in 1,2-DCE (60 mL). The mixture was stirred 24 h, then saturated aqueous KHCO₃ (30 mL) was slowly added while stirring vigorously. The aqueous layer was extracted with EtOAc, the combined organic layer was washed with brine, dried over MgSO₄, and volatile compounds were removed under vacuum. The residue was subjected to flash chromatography (20% EtOAc in hexanes) to give the title compound (3.53 g, 91%). ¹H NMR (400 MHz, CDCl₃) δ 7.68 (dd, *J* = 8.0 Hz, 1.2. Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.17 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.56 (dd, *J* = 8.4 Hz, 1.2 Hz, 1H), 6.45 (td, *J* = 8.0 Hz, 1.2 Hz, 1H), 4.54 (s, 1H), 4.33 (s, 2H), 3.81 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 158.9, 147.1, 139.0, 130.5, 129.4, 128.8, 118.7, 114.1, 110.1, 85.3, 55.3, 47.8; HRMS (APCI) *m/z* calcd for C₁₄H₁₃INO [M–H]⁺ 338.0084, found 338.0070.



N-(2-Iodophenyl)-N-(4-methoxybenzyl)-1-(phenylsulfonyl)-4,5-dihydro-1H-pyrrole-3-

carboxamide (22): Ghosez reagent (0.15 mL, 1.25 mmol) was added to a suspension of carboxylic acid 21 (317 mg, 1.25 mmol) in toluene (12.5 mL), the mixture was stirred for 1 h. NaHMDS (0.93 mL, 1M in THF) was added to a solution of aniline S4 (315 mg, 0.93 mmol) in THF (9 mL) at -78 °C. The mixture was stirred 30 minutes then cannulated into the stirring acid chloride solution. The mixture was stirred to rt for 3 h. The reaction was guenched with aqueous KHCO₃, the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over MgSO₄, volatile compounds were removed under vacuum. The residue was subjected to flash chromatography (20% EtOAc in hexanes) to give the title compound (320 mg, 60%) as a colorless solid: mp 53–56 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.94 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.60–7.57 (m, 1H), 7.49–7.48 (m, 4H), 7.28 (td, J = 8.0 Hz, 1.5 Hz, 1H), 7.18–7.09 (m, 2H), 6.79–6.76 (m, 3H), 5.83 (s, 1H), 5.49 (d, J = 14.0 Hz, 1H), 4.02 (d, J = 14.0 Hz, 1H), 3.75 (s, 3H), 3.45–3.41 (m, 1H), 3.29–3.29 (m, 1H), 2.65 (m, 1H), 2.55 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 164.0, 159.0, 144.1, 140.2, 136.7, 135.7, 133.2, 131.1, 130.8, 128.0, 129.3, 129.2, 128.6, 118.1, 113.6, 101.0, 55.1, 52.0, 47.0, 30.8; HRMS (ESI) m/z calcd for $C_{25}H_{25}IN_2O_4S [M+H]^+ 575.2502$, found 575.0508.



2-Bromo-4-methoxy-*N***-(4-methoxybenzyl)aniline (S5):** NaBH(OAc)₃ (5.10 g, 24.1 mmol) was added to a solution of *p*-anisaldehyde (0.41 mL, 6.63 mmol), 2-bromo-4-methoxyaniline⁴ (1.5 g, 6.02 mmol) and AcOH (0.11 mL, 1.91 mmol) in 1,2-DCE (30 mL). The mixture was stirred 24 h, then saturated aqueous KHCO₃ (15 mL) was slowly added while stirring vigorously. The aqueous layer was extracted with EtOAc, the combined organic layer was washed with brine, dried over MgSO₄, and volatile compounds were removed under vacuum. The residue was subjected to flash chromatography (20% EtOAc in hexanes) to give the title compound (2.14 g, 91%) as a white solid: mp 63–64 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, *J* = 6.8 Hz, 2H), 7.08 (d, *J* = 2.4 Hz, 1H), 6.89 (d, *J* = 6.8 Hz 2H), 6.77 (dd, *J* = 7.2 Hz, 2.4 Hz, 1H), 6.58 (d, *J* = 7.2 Hz, 1H), 4.33 (s, 1H), 4.28 (s, 2H), 3.81 (s, 3H), 3.73 (s, 3H).



N-(2-Bromo-4-methoxyphenyl)-*N*-(4-methoxybenzyl)-1-(phenylsulfonyl)-4,5-dihydro-1*H*pyrrole-3-carboxamide (23): Ghosez reagent (75 μ L, 0.57 mmol) was added to a suspension of carboxylic acid 21 (144 mg, 0.57 mmol) in toluene (5.7 mL), the mixture was stirred for 1 h. NaHMDS (0.38 mL, 1M in THF) was added to a solution of protected aniline S5 (140 mg, 0.38 mmol) at -78 °C. The mixture was stirred 30 minutes, then cannulated into the stirring acid

chloride solution, the mixture was stirred to r.t. for 3 h. The reaction was quenched with KHCO₃, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine, dried over MgSO₄, volatile compounds were removed under vacuum. Flash chromatography (20% EtOAc in hexanes) gave the title compound (158 mg, 69%). ¹H NMR (500 MHz, CDCl₃) δ 7.61 (tt, *J* = 7.0 Hz, 1.8 Hz, 1H) 7.54–7.48 (m, 4H) 7.19 (d, *J* = 3.0 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2 H), 6.74 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 6.02 (s, 1H), 5.47 (d, *J* = 14.0 Hz, 1H), 4.02 (d, *J* = 14.0 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.38 (ddd, *J* = 50.0 Hz, 10.0 Hz, 7.5 Hz, 2H), 2.67–2.48 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 164.7, 159.8, 159.0, 136.7, 135.9, 133.6, 133.3, 132.0, 130.8, 129.2, 129.0, 127.3, 124.6, 119.0, 118.2, 113.8, 113.7, 55.9, 55.2, 47.3, 30.7; HRMS (ESI) *m/z* calcd for C₂₆H₂₅BrNaN₂O₅S [M+Na]⁺ 579.0565, found 579.0604.



2-Iodo-5-methoxy-*N***-(4-methoxybenzyl)aniline (S6):** NaBH(OAc)₃ (5.10 g, 24.1 mmol) was added to a solution of *p*-anisaldehyde (0.41 mL, 6.63 mmol), 2-iodo-5-methoxyaniline⁵ (1.5 g, 6.02 mmol) and AcOH (0.11 mL, 0.11 mmol) in 1,2-DCE (30 mL). The mixture was stirred 24 h, then saturated aq. KHCO₃ (15 mL) was slowly added while stirring vigorously. The aqueous layer was extracted with EtOAc, the combined organic layer was washed with brine, dried over MgSO₄, and volatile compounds were removed under vacuum. The residue was subjected to flash chromatography (20% EtOAc in hexanes) to give the title compound (1.80 g, 81%). ¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, *J* = 8.6 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.14 (d, *J* = 2.8 Hz, 1H), 6.07 (dd, *J* = 8.6 Hz, 2.8 Hz, 1H), 4.49 (s, 1H), 4.27 (s, 1H), 4.26

(s, 1H), 3.78 (s, 3H), 3.69 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.2, 158.8, 147.9, 138.9, 130.3, 128.5, 114.0, 104.0, 97.9, 74.5, 55.2, 47.8.



N-(2-Iodo-5-methoxyphenyl)-N-(4-methoxybenzyl)-1-(phenylsulfonyl)-4,5-dihydro-1H-

pyrrole-3-carboxamide (24): Ghosez reagent (0.12 mL, 0.93 mmol) was added to a suspension of carboxylic acid **21** (236 mg, 0.93 mmol) in toluene (7 mL), the mixture was stirred for 1 h. NaHMDS (0.72 mL, 1M in THF) was added to a solution of aniline S6 (265 mg, 0.72 mmol) in THF (7 mL) at -78 °C. The mixture was stirred 30 minutes, then added by cannula into the stirring acid chloride solution, the mixture was warmed to room temperature and stirred for 3 h. The reaction was quenched with KHCO₃, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with brine and dried over MgSO4; volatiles were removed under vacuum. The residue was purified by flash chromatography (20% EtOAc in hexanes) to give the title compound (235 mg, 54%) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 7.79 (d, J = 9.0 Hz, 1H), 7.61 (tt, J = 6.5 Hz, 2.0 Hz, 1H), 7.53–7.50 (m, 3H), 7.13 (d, J = 8.5 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 6.74 (dd, J = 9.0 Hz, 3.0 Hz, 1H), 6.29 (d, J = 3.0 Hz, 1H), 5.92 (s, 1H),5.52 (d, J = 14.5 Hz, 1H), 3.98 (d, J = 14.5 Hz, 1H), 3.77 (s, 3H), 3.61 (s, 3H), 3.42 (td, J = 10.0 Hz, 7.5 Hz, 1H), 3.34 (td, J = 10.0 Hz, 7.5 Hz, 1H), 2.72–2.58 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) § 163.9, 160.5, 159.1, 144.9, 140.2, 136.9, 135.3, 133.3, 130.9, 129.3, 128.9, 127.3, 118.1, 117.0, 116.6, 113.7, 89.0, 55.6, 55.2, 52.0, 57.1, 30.9; HRMS (ESI) m/z calcd for $C_{26}H_{26}IN_2O_5S[M+H]^+$ 605.0607, found 605.0616.



N-(2-(1-(4-Methoxybenzyl)-2-oxoindolin-3-yl)ethyl)formamide (25): A solution of Bu₃SnH (0.24 mL, 0.83 mmol) and AIBN (14 mg, 0.014 mmol) in degassed benzene (4 mL) were added via syringe pump to a refluxing solution of iodoaniline 22 (98 mg, 0.17 mmol) in degassed benzene (8 mL) to afford the title compound (34 mg, 65%) as a colorless solid: mp >220 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.14 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 2H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.52 (s, 1H), 4.84 (s, 2H), 3.77 (s, 3H), 3.59–3.54 (m, 3H), 2.32 (dq, *J* = 14.0 Hz, 6.0 Hz, 1H), 2.03 (hex, *J* = 7.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 178.0, 161.3, 159.1, 143.0, 128.7, 128.6, 128.4, 128.2, 127.7, 123.9, 122.9, 114.2, 109.2, 55.3, 44.1, 43.3, 36.0, 30.1; HRMS (TOF ES) *m/z* calcd for C₁₉H₂₁N₂O₃ [M+H]⁺ 325.1552, found 325.1562.



N-(2-(5-Methoxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)ethyl)formamide (26): A solution of Bu₃SnH (0.24 mL, 0.83 mmol) and AIBN (14 mg, 0.014 mmol) in degassed benzene (4 mL) were added via syringe pump to a refluxing solution of bromoaniline 23 (100 mg, 0.17 mmol) in degassed benzene (8 mL). After 2 h, the mixture was cooled to r.t. and the volatile compounds were removed under vacuum. Flash chromatography (0–5 % MeOH in CH_2Cl_2) gives the title

compound (25 mg, 42%) as a white solid, mp >220 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.15 (s, 1H), 7.21 (dt, *J* = 10.0 Hz, 2.5 Hz, 2H), 6.91 (dd, *J* = 2.5 Hz, 0.9 Hz, 1H), 6.84 (dt, *J* = 10.0 Hz, 2.5 Hz, 2H), 6.71 (dd, *J* = 8.0 Hz, 2.5 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 4.82 (s, 2H), 3.77 (s, 3H), 3.76 (S, 3H), 3.58–3.53 (m, 2H), 2.31 (dq, *J* = 15.0 Hz, 6.0 Hz, 1H), 2.06–1.98 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 177.6, 161.3, 159.1, 156.2, 136.4, 129.7, 128.6, 127.7, 114.2, 112.6, 111.2, 109.6, 55.7, 55.2, 44.4, 43.3, 35.9, 30.1; HRMS (ESI) *m/z* calcd for C₂₀H₂₁N₂O₃ [M+H]⁺ 337.1552, found 337.1558.



N-(2-(6-Methoxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)ethyl)formamide (27): A solution of Bu₃SnH (0.06 mL, 0.40 mmol) and AIBN (3 mg, 0.003 mmol) in degassed benzene (1 mL) were added via syringe pump to a refluxing solution of iodoanilide 24 (20 mg, 0.03 mmol) in degassed benzene (1.5 mL). After heating an additional 2 h, the mixture was cooled to room temperature and volatile compounds were removed under vacuum. The residue was purified by flash chromatography (5% MeOH in CH₂Cl₂) to give the title compound (6 mg, 54%) as a white solid: mp >220 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.13 (s, 1H), 7.22 (dt, *J* = 10.0 Hz, 2.5 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.84 (dt, *J* = 10.0 Hz, 2.5 Hz, 2H), 6.54 (dd, *J* = 8.0 Hz, 2.5 Hz, 1H), 6.37 (d, *J* = 2.5 Hz, 1H), 4.81 (s, 2H), 3.77 (s, 3H), 3.75 (S, 3H), 3.56–3.49 (m, 2H), 2.26 (dq, *J* = 14.5 Hz, 6.0 Hz, 1H), 2.04–1.97 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 178.7, 161.3, 160.1, 159.2, 144.2, 128.7, 127.7, 124.4, 120.2, 114.3, 106.4, 97.6, 55.5, 55.3, 43.5, 43.3, 36.0, 30.3; HRMS (ESI) *m/z* calcd for C₂₀H₂₁N₂O₃ [M+H]⁺ 337.1552, found 337.1558.

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