Supporting Information

A General Synthesis of *N*-Hydroxyindoles

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General Procedure for the Preparation of *N*-Hydroxy-Indoles. To a solution containing 1.00 g of the appropriate nitroketone in 10 mL of either MeOH or EtOH was added 4.00 g of lead powder (325 mesh) and 4 mL of HCO₂HNEt₃. The mixture was stirred at 50 °C for 12 h, cooled to rt, and filtered over a pad of Celite. The solvent was removed under reduced pressure and the residue purified by flash silica gel chromatography to give the product.

Preparation of 2-phenyl-*N*-hydroxyindole (5).¹ According to the general procedure, treatment of 1.00 g (0.0041 mol) of ketone **4**² with 4.00 g of lead powder and 4 mL of HCO₂HNEt₃ afforded 0.82 g (94 %) of **5** as a tan solid.

Preparation of 2-pyridin-2-yl-1*H*-indol-1-ol (7).³ According to the general procedure, treatment of 500 mg (2.06 mmol) of ketone **6**³ with 2.00 g of lead powder and 2 mL of HCO₂HNEt₃ yielded 400 mg (92%) of **7**.

Preparation of Ethyl 4-(1-hydroxy-1*H*-indol-2-yl)butanoate (9). According to the general procedure, treatment of 1.00 g (3.58 mmol) of ketone **8**⁴ with 4.00 g of lead powder and 4 mL of HCO₂HNEt₃ provided 850 mg (96%) of **9** as a clear oil: ¹H NMR

(DMSO-*d*₆, 400 MHz) δ 1.15 (t, 3H, *J* = 7.1 Hz), 1.91 (m, 2H), 2.35 (t, 2H, *J* = 7.4 Hz), 2.73 (t, 2H, *J* = 7.4 Hz), 4.02 (q, 2H, *J* = 7.1 Hz), 6.08 (s, 1H), 6.98 (m, 1H), 7.08 (m, 1H), 7.35 (d, 1H, *J* = 8.05 Hz), 7.43 (d, 1H, *J* = 7.8 Hz), 10.80 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 14.1, 23.3, 24.3, 33.0, 59.8, 93.8, 107.9, 118.8, 119.5, 120.4, 123.0, 133.7, 137.7, 172.6.

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Preparation of 1-Hydroxy-5-methoxy-1H-indole-3-carboxaldehyde (11). According to the general procedure, treatment of 1.00 g (4.15 mmol) of 2-(5-methoxy-2-nitrophenyl)malondialdehyde monohydrate **10** with 4.00 g of lead powder and 4.00 mL of $\text{HCO}_2\text{HNEt}_3$ gave 520 mg (66%) of **11** as an off-white solid: mp 183 °C (decomp); ^1H NMR ($\text{DMSO}-d_6$, 400 MHz) δ 3.77 (s, 3H), 6.92 (dd, 1H, $J = 8.9$ and 2.3 Hz), 7.39 (d, 1H, $J = 8.9$ Hz), 7.57 (s, 1H), 8.32 (s, 1H), 9.77 (s, 1H), 12.10 (br s, 1H); ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz) δ 55.4, 102.4, 110.5, 111.9, 113.8, 121.9, 129.3, 135.1, 156.2, 183.8.

Preparation of 2-methyl-6-(trifluoromethoxy)-1H-indol-1-ol (13). According to general procedure, treatment of 460 mg (01.99 mmol) of ketone **12**⁵ with 2.50 g of lead powder and 2 mL of HCO₂HNEt₃ yielded 390 mg (95%) of **13** as a brown solid. mp 48-50°C ¹H NMR (DMSO-*d*₆, 400 MHz) δ 2.34 (s, 3H), 6.12 (s, 1H), 6.88 (m, 1H), 7.20 (s, 1H), 7.45 (d, 1H, *J* = 8.43 Hz), 11.08 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 11.4, 95.1, 101.2, 112.9, 120.9 (q, *J* = 254.4 Hz), 120.9, 122.4, 133.3, 137.0, 143.6 (m); ¹⁹F NMR (DMSO-*d*₆, 376 MHz) δ -57.5. Anal. Calcd for C₁₀H₈F₃NO₂: C, 51.96; H, 3.49; N, 6.06. Found: C, 52.15; H, 3.47; N, 6.06.

To a solution of 6.28 g (0.032 mol) of 4-nitrobenzylacetate⁶ in 120 mL of THF at -15 °C was added dropwise 40 mL (40.0 mmol, 1M in ether) of trimethylsilylmethylmagnesium chloride at such a rate that the internal temperature did not rise above -5 °C. After stirring at -5 °C for 15 min, 8.60 g (39.0 mmol) of DDQ in 30 mL of THF was added and the reaction mixture allowed to warm to 10 °C over 2 h. The reaction mixture was diluted with 150 mL of isopropyl acetate and washed with 150 mL sat. NaHCO₃ (3X), then concentrated under reduced pressure to afford 7.40 g (82%) of the above TMS-nitro compound which was used in the next step without further purification.

To a mixture of 7.30 g (26.0 mmol) of the above crude TMS-nitro compound and 4.90 g (26.0 mmol) of 2-methoxyquinoline-3-carbaldehyde⁷ in 70 mL of isopropyl acetate was added 5.20 mL (5.20 mmol, 1M solution of TBAF in THF). The mixture was stirred at rt for 30 min and quenched with 30 mL of sat. NH_4Cl . The layers were separated and the organic layer washed with 30 mL of water. The solvent was removed under reduced pressure and the residue chromatographed over silica gel to yield 8.90 g, (87%) of the above alcohol as a pale yellow solid. mp 70-71 °C ^1H NMR (CDCl_3 , 400 MHz) δ 2.08 (s, 3H), 2.95 (d, 1H, $J = 6.4$ Hz), 3.46 (m, 2H), 4.15 (s, 3H), 5.10 (s, 2H), 5.24 (m, 1H), 7.31 (d, 1H, $J = 1.6$ Hz), 7.38 (m, 2H), 7.63 (ddd, 1H, $J = 1.6$, 7.2 and 8.4 Hz), 7.73 (dd, 1H, $J = 1.2$ and 8.0 Hz), 7.86 (dd, 1H, $J = 0.8$ and 8.4 Hz), 7.92 (d, 1H, 8.4 Hz), 8.01 (s, 1H) ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.8, 40.0, 53.6, 64.8, 70.7, 124.4, 125.0, 125.2, 126.8, 127.0, 127.2, 127.6, 129.5, 132.4, 133.6, 135.1, 141.0, 145.9, 149.8, 159.4, 170.5. Anal. Calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_6$: C, 63.63; H, 5.09; N, 7.07. Found: C, 63.51; H, 5.01; N, 6.72.

Preparation of 3-[2-(2-methoxyquinolin-3-yl)-2-oxoethyl]-4-nitrobenzyl acetate (14). To a solution of 3.75 g (9.50 mmol) of the above alcohol in 19 mL of isopropyl acetate was added 8.90 g (110.0 mmol) of DMSO followed by 5.80 g (56.8 mmol) of

acetic anhydride. The solution was heated to 80 °C for 4 h, cooled to rt, and was diluted with 30 mL of sat. NaHCO₃ which precipitated the product to give 2.90 g (77%) of ketone **14** as a white solid: mp 133.5-134.5 °C; ¹H NMR (CDCl₃, 400 MHz) δ 2.16 (s, 3H), 4.23 (s, 3H), 4.82 (s, 2H), 5.20 (s, 2H), 7.39 (d, 1H, *J* = 1.6 Hz), 7.45 (m, 2H), 7.73 (ddd, 1H, *J* = 1.6, 6.8 and 8.4 Hz), 7.84 (dd, 1H, *J* = 1.2 and 8.0 Hz), 7.89 (d, 1H, *J* = 8.4 Hz), 8.16 (d, 1H, *J* = 8.4 Hz), 8.59 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.9, 48.8, 53.9, 64.7, 123.0, 124.6, 125.0, 125.6, 127.1, 127.5, 129.3, 131.5, 132.0, 133.0, 141.96, 141.98, 148.1, 148.5, 159.2, 170.6, 195.8; Anal. Calcd for C₂₁H₁₈N₂O₆: C, 63.96; H, 4.60; N, 7.10. Found: C, 63.86; H, 4.38; N, 6.97.

Preparation of 1-hydroxy-2-(2-methoxyquinolin-3-yl)-1H-indol-5-yl]methyl acetate

(15). According to the general procedure, treatment of 50 mg (0.13 mmol) of ketone **14** with 0.20 g of lead powder and 0.20 mL of HCO₂HNEt₃ provided 33 mg of **15** as a pale yellow solid. mp 183-185 °C (decomp) ¹H NMR (CDCl₃, 400 MHz) δ 2.10 (s, 3H), 4.21 (s, 3H), 5.22 (s, 2H), 6.59 (s, 1H), 7.29 (dd, 1H, *J* = 1.2 and 8.4 Hz), 7.46 (ddd, 1H, *J* = 1.2, 7.2 and 8.4 Hz), 7.54 (d, 1H, *J* = 8.43 Hz), 7.62 (d, 1H, *J* = 0.8 Hz), 7.68 (ddd, 1H, *J* = 1.6, 6.8 and 8.4 Hz), 7.80 (dd, 1H, *J* = 1.2 and 8.0 Hz), 7.91 (dd, 1H, *J* = 0.80 and 8.4 Hz), 8.03 (br s, 1H), 8.29 (s, 1H) ¹³C NMR (CDCl₃, 100 MHz) δ 21.2, 54.4, 67.4, 99.5, 109.0, 115.9, 121.3, 123.4, 123.7, 125.1, 125.3, 127.1, 127.66, 127.69, 130.1, 133.9, 134.5, 139.4, 146.0, 158.0, 171.1. Anal. Calcd for C₂₁H₁₈N₂O₄: C, 69.60; H, 5.01; N, 7.73. Found: C, 68.35; H, 4.94; N, 7.03.

Preparation of Ethyl 4-Hydroxy-1,2,3,4-tetrahydrocyclopenta[*b*]indole-6-carboxylate (17). According to the general procedure, treatment of 680 mg (2.45 mmol) of ketone **16**⁴ with 2.72 g of lead powder and 2.72 mL of HCO₂HNEt₃ afforded 580 mg (97%) of **17** as a tan solid: mp 104-105 °C; ¹H NMR (DMSO-*d*₆, 400 MHz) δ 1.33 (t, 3H, *J* = 7.1 Hz), 2.50 (m, 2H), 2.78 (t, 2H, *J* = 6.8 Hz), 2.92 (t, 2H, *J* = 6.8 Hz), 4.29 (q, 2H, *J* = 7.1 Hz), 7.38 (d, 1H, *J* = 8.2 Hz), 7.57 (d, 1H, *J* = 8.2 Hz), 7.91 (s, 1H), 11.20 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 14.8, 24.8, 25.0, 28.3, 60.7, 111.0, 114.0, 118.3, 119.9, 121.5, 123.4, 137.8, 147.2, 167.2; Anal. Calcd For C₁₄H₁₅NO₃: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.29; H, 6.29; N, 6.04.

Preparation of Ethyl 3-nitro-4-(2-oxocyclohexyl)benzoate (18).⁴ A solution of 1.56 g (6.79 mmol) of ethyl 4-chloro-3-nitrophenyl-1-carboxylate, 3.98 g (40.53 mmol) of cyclohexanone, 3.31 g 15.60 mmol) of powdered K₃PO₄, 130 mg (1.38 mmol) of phenol, 110 g (0.280 mmol) of 2-dicyclohexylphosphino-2-dimethylaminobiphenyl, and 62.0 mg (0.068 mmol) of Pd₂(dba)₃ in 20 mL of toluene was heated at 50 °C for 18 h. The reaction mixture was cooled to rt, diluted with 50 mL of EtOAc and 75 mL of water. The organic layer was separated, washed with 50 mL of brine, and dried over MgSO₄. The solvent was removed under reduced pressure and the residue purified by silica gel

chromatography to yield 1.12 g (52%) of **18** as an oil: ^1H NMR (CDCl_3 , 400 MHz) δ 1.40 (t, 3H, $J = 7.1$ Hz), 1.86 (m, 2H), 2.07 (m, 2H), 2.10 (m, 1H), 2.39 (m, 1H), 2.54 (m, 2H), 4.30 (dd, 1H, $J = 12.9$ and 5.2 Hz), 4.45 (q, 2H, $J = 7.1$ Hz), 7.43 (d, 1H, $J = 8.1$ Hz), 8.21 (d, 1H, $J = 8.1$ Hz), 8.60 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.4, 25.5, 27.4, 33.8, 42.3, 53.7, 61.9, 126.0, 130.7, 130.8, 133.6, 138.6, 149.6, 164.6, 207.5.

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Preparation of Ethyl 9-hydroxy-2,3,4,9-tetrahydro-1H-carbazole-7-carboxylate (**19**).

According to the general procedure, treatment of 580 mg (1.84 mmol) of ketone **18** with 2.32 g of lead powder and 2.32 mL of $\text{HCO}_2\text{HNEt}_3$ gave 450 mg (94%) of **19** as a tan

solid: mp 106-107 °C; ^1H NMR (DMSO- d_6 , 400 MHz) δ 1.33 (t, 3H, J = 7.1 Hz), 1.84 (m, 4H), 2.64 (m, 2H), 2.74 (m, 2H), 4.28 (q, 2H, J = 7.1 Hz), 7.43 (d, 1H, J = 8.2 Hz), 7.56 (dd, 1H, J = 8.2 and 1.5 Hz), 7.91 (d, 1H, J = 1.5 Hz), 10.98 (s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ 14.7, 20.8, 21.2, 22.5, 23.1, 60.6, 105.3, 109.9, 117.6, 119.5, 121.9, 126.0, 133.0, 138.1, 167.2; Anal. Calcd For $\text{C}_{15}\text{H}_{17}\text{NO}_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.60; H, 6.72; N, 5.21.

Preparation of 1-hydroxyindole-3-carboxaldehyde (21). According to general procedure, treatment of 1.0 g (0.0052 mol) of dialdehyde **20** with 4.0 g of lead powder and 4 mL of $\text{HCO}_2\text{HNEt}_3$ afforded 0.78 g (94%) of **21** as a dark red solid.

Preparation of 1-methoxyindole-3-carboxaldehyde (22).⁸ 100 mg (0.621 mmol) of **21** was added portion-wise over 15 min to a 0°C solution of CH_2N_2 in ether, which was prepared by treatment of a solution of 320 mg (1.86 mmol) of 60% *N*-nitroso-*N*-methylurea in 5 mL of ether with a solution of 870 mg (13.2 mmol) of KOH pellets in 3 mL water. The mixture was stirred for 30 min at 0°C, and the solvent was removed under reduced pressure to provide 103 mg (95%) of **22** as a brown oil.

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