Palladium-Catalyzed Regioselective Hydrodebromination of Dibromoindoles: Application to the Enantioselective Synthesis of Indolodioxane U86192A

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Supporting Information

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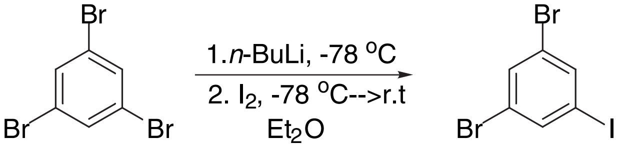
I.General Consideration

Reagents: Toluene, THF, diethyl ether, and dichloromethane were purchased from J. T. Baker in CYCLE-TAINER® solvent delivery kegs, which were vigorously purged with argon for 2 h, and further purified by passing the solvent through two packed columns of neutral alumina and copper (II) oxide under argon pressure. $Pd(OAc)_2$, copper (I) iodide (fine powder), and *rac*-BINAP (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl) were purchased from Strem Chemical Co. and used without further purification. The ligand, 2-(*N,N*-dimethylamino)-2′-di-*tert*-butylphosphinobiphenyl was prepared as previously reported.[1] The Co-Salen oligomer was obtained from Professor Eric N. Jacobsen and Mr. David White (Harvard University). All other reagents were purchased from commercial sources and used without further purification.

Analytical methods: All nonaqueous reactions were carried out in oven-dried glassware under argon, unless otherwise stated. Flash chromatography was performed on silica gel (230-400 mesh). ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on 300 NMR spectrometer with chemical shifts reported in ppm relative to the residual deuterated solvent peaks or to TMS as the internal standard. IR spectra were obtained by placing neat samples directly on the DiComp probe. Mass spectra (HRMS-ESI) were recorded with electrospray (ESI) as ionization sources. HPLC were conducted using Daicel OD column (0.46 cm x 25 cm). Optical rotations were measured using a sodium lamp. Melting points were uncorrected. Yields refer to isolated yields of compounds greater than 95 % pure as determined by ^{1}H NMR and/or combustion analyses. Yields reported in this section refer to a single experiment whereas those reported in Table 1 and 2 are an average of two runs. All compounds were characterized by ^{1}H NMR and ^{13}C NMR. Previously unknown compounds were further characterized by elemental analysis, IR, melting point and optical rotation, if applicable.

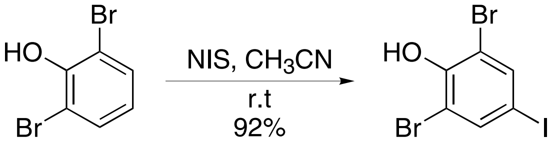
II. Preparation of dibromoaryliodides

1,3-Dibromo-5-iodobenzene



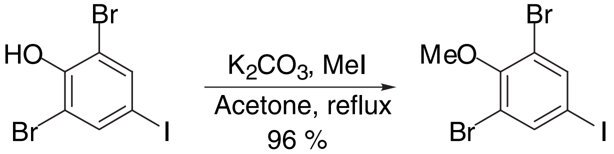
1,3-Dibromo 5-iodobenzene was prepared from 1,3,5-tribromobenzene according to the literature procedure.[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 1.5 Hz, 2H), 7.61(t, *J* = 1.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 133.7, 123.5, 94.7.

2,6-Dibromo-4-iodophenol[3]



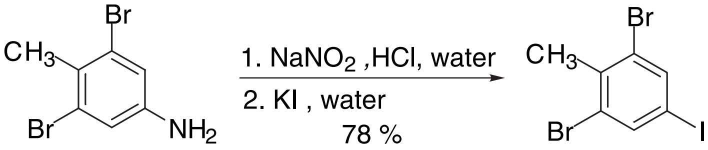
To a solution of 2,6-dibromophenol (10.1 g, 40.0 mmol) in anhydrous acetonitrile (250 mL), N-iodosuccinimide (10.8 g, 48.0 mmol) was added in small portions over 1 h and the reaction was stirred at room temperature for 3 h. Acetonitrile was removed under vacuum and ether (~500 mL) was added. The ethereal layer was washed with aq. $Na_2S_2O_3$ solution, water, and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography (5% EtOAc /hexane) to afford the product as a white solid (14.0 g, 92%). Mp: 99-101 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 2H), 5.87(s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 139.8, 110.9, 81.9. IR (neat, cm^{-1}) 3404 (broad), 1453, 1318, 1233, 1158, 857. Anal. Calcd. for $C_6H_3Br_2IO$: C, 19.92 ; H, 0.84. Found: C, 19.55; H, 0.87.

2,6-Dibromo-4-iodoanisole



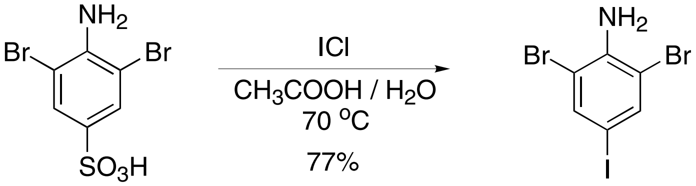
A 3-neck round bottom flask equipped with a reflux condenser was charged with 2,4-dibromo-4-iodophenol (14.0 g, 37.0 mmol) and K_2CO_3 (7.70 g, 55.5 mmol). The flask was evacuated and backfilled with Ar. Acetone (300 mL) was added and the reaction was stirred at room temperature for 30 min. To the reaction suspension, MeI (2.80 mL, 55.5 mmol) was added and then the reaction mixture was refluxed at 65 °C (preheated oil bath) for 3 h. After the reaction mixture was allowed to reach room temperature, acetone was removed under vacuum and ether (~ 400 mL) was added. Ethereal layer was washed with water and brine and dried over $MgSO_4$. Recrystallization of the concentrated crude product from hot MeOH afforded the product as a white solid (13.5 g, 93%). Recrystallization of the concentrated mother liquor gave additional product (435 mg, 3%). The products were combined to give 13.9 g (96% total yield) of the title product. Mp: 84-86 ºC. ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 2H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 140.7, 119.3, 87.8, 60.9. IR (neat, cm^{-1}) 1459, 1410, 1250, 980, 860, 735. Anal. Calcd. for $C_7H_5Br_2IO$: C, 21.46; H, 1.29. Found: C, 21.72; H, 1.29.

2,6-Dibromo-4-iodotoluene[4]



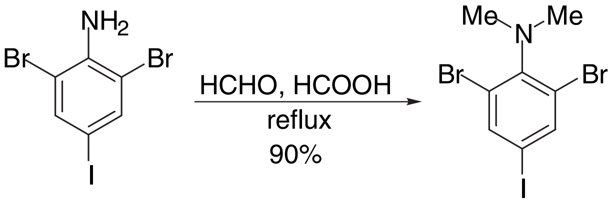
To a stirred solution of 3,5-dibromo-4-methylaniline (2.65 g, 10.0 mmol) in HCl (20.0 mL, 37% solution), and water (20 mL) was added dropwise a solution of $NaNO_2$ (760 mg, 11.0 mmol) in water (15 mL) over 30 min at 0 ºC (ice-water bath) and stirred for 30 min. A solution of KI (1.74 g, 10.5 mmol) in water (15 mL) was added dropwise for 30 min at 0 ºC and the reaction mixture was stirred at room temperature for 3 h. After neutralization with saturated *aq.* $NaHCO_3$, the mixture was extracted with EtOAc (~100 mL x 3). The combined organic layers were washed with *aq.* $Na_2S_2O_3$ solution, water, and brine, and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (hexane only) afforded the title product as a white solid (2.95 g, 78%). Mp: 68-70 ºC. ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 2H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 137.4, 125.9, 90.5, 23.8. IR (neat, cm^{-1}) 1561, 1428, 1374, 1210, 986, 855, 727. Anal. Calcd. for $C_7H_5Br_2I$: C, 22.37; H, 1.34. Found: C, 22.48; H, 1.36.

2,6-Dibromo-4-iodoaniline



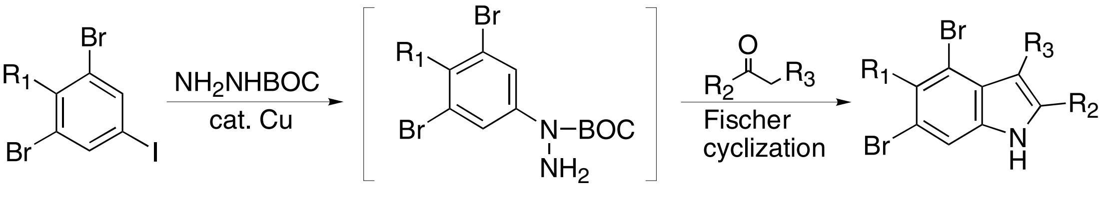
2,6-Dibromo-4-iodoaniline was prepared from 3,5-dibromosulfanilic acid according to the literature procedure.[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 2H), 4.58(s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 139.3, 109.3, 99.9.

(2,6-Dibromo-4-iodophenyl)-dimethylamine



2,6-Dibromo-4-iodoaniline (4.05 g, 10.7 mmol) was added to a 100 mL round bottom flask. Formic acid (40.0 mL) was added followed by formaldehyde (10.0 mL, 37% solution). The reaction mixture was refluxed at 100 °C (preheated oil bath) for 2 h. After the reaction was allowed to reach to room temperature, it was neutralized with 6 N NaOH solution. The aqueous phase was extracted with EtOAc (~70 mL x 3). The combined organic layers were washed with water and brine and dried over $MgSO_4$. The concentrated crude product was purified by column chromatography (5% EtOAc/hexane) to afford the title product as a colorless oil (3.90 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 2H), 2.83 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 140.9, 126.7, 89.2, 42.0. IR (neat, cm^{-1}) 3085, 2971, 2910, 2867, 2794, 1519, 1484, 1412, 1364, 1167, 949, 855, 772, 724. Anal. Calcd. for $C_8H_8Br_2NI$: C, 23.73; H, 1.99. Found: C, 23.91; H, 1.87.

III. One-pot preparation of 4,6-dibromoindoles



Symmetric Aryl hydrazide

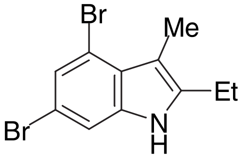
Procedure A [7]: An oven-dried resealable Schlenk tube was charged with the dibromoaryl iodide (1.00 mmol), *t*-butylcarbazate (158 mg, 1.20 mmol), CuI (14.3 mg, 9.50 mmol), and Cs_2CO_3 (455 mg, 1.40 mmol). The Schlenk tube was evacuated and backfilled with Ar. Anhydrous DMF (4 mL) was added and the reaction mixture was stirred at room temperature for 10 min and heated at 80 °C (preheated oil bath) until the dibromoaryliodide was consumed as determined by GC analysis. The reaction mixture was allowed to cool to room temperature and diluted with ether (~20 mL) and water (~40 mL). The aqueous phase was extracted with ether (~20 mL x 2) and the combined ethereal layers were washed with water and brine and dried over Na_2SO_4. The solvent was removed in vacuo and the crude aryl hydrazide was used directly for the Fischer indole cyclization without purification.

The crude aryl hydrazide, ketone (1.00 mmol), and *p*-TsOH•H_2O (304 mg, 1.60 mmol) were dissolved in EtOH (8 mL) and the solution was stirred at 90 °C (preheated oil bath) until the aryl hydrazide was consumed as determined by TLC analysis. After the reaction mixture was allowed to cool to room temperature, EtOH was removed under vacuum. The reaction mixture was diluted with EtOAc (~ 30 mL) and neutralized with sat. $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (~25 mL x 2) and the combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by column chromatography afforded the analytically pure indole product.

Procedure B [8]: An oven-dried resealable Schlenk tube was charged with the dibromoaryl iodide (1.50 mmol), *t*-butyl carbazate (238 mg, 1.80 mmol), CuI (14.3 mg, 0.0750 mmol), and Cs_2CO_3 (683 mg, 2.10 mmol), evacuated and backfilled with Ar. Anhydrous DMF (6 mL) was added and the reaction mixture was stirred at room temperature for 10 min and heated at 80 °C (preheated oil bath) until the dibromoaryl iodide was consumed as determined by GC analysis. The reaction mixture was allowed to cool to room temperature and diluted with ether (~20 mL) and water (~40 mL). The aqueous phase was extracted with ether (~20 mL x 2). The combined ethereal layers were washed with water and brine and dried over Na_2SO_4. The concentrated crude product (aryl hydrazide) was used for Fischer indole cyclization without further purification.

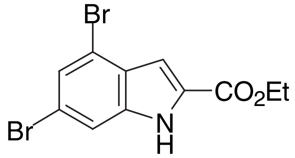
The crude aryl hydrazide was dissolved in anhydrous CH_2Cl_2 (10 mL) and transferred into an Ar-purged Schlenk flask. Ketone (1.50 mmol) was added followed by slow addition of Eaton's reagent (10% P_2O_5 in $MeSO_3H$, 2.00 mL). The reaction mixture was stirred at room temperature for 20 min and heated at 45 °C (preheated oil bath) until the aryl hydrazide was consumed as determined by TLC analysis. At this point the reaction mixture was allowed to cool to room temperature, the reaction mixture was diluted with EtOAc (~ 30 mL) and neutralized with sat. $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (~25 mL x 2) and the combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by recrystallization afforded the analytically pure indole product.

4,6-Dibromo-2-ethyl-3-methyl-1*H*-indole (Table 1, entry 1)



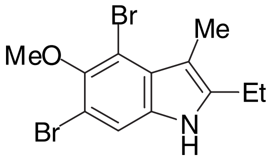
Using procedure A, 1,5-dibromo-3-iodobenzene (362 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and 3-pentanone (105 μL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (7% EtOAc/Hexane) gave the title indole as a yellow solid (189 mg, 60% yield for two steps). Mp: 89-91 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (bs, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.27 (d, *J* = 1.8 Hz, 1H), 2.69 (q, *J* = 7.5 Hz, 2H), 2.42 (s, 3H), 1.24 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 136.7, 126.4, 126.0, 114.3, 113.6, 112.6, 107.7, 19.6, 14.1, 10.9. IR (neat, cm^{-1}) 3415, 2968, 2925,1441, 934, 836, 764. Anal. Calcd. for $C_{11}H_{11}Br_2N$: C, 41.67; H, 3.50. Found: C, 41.58; H, 3.47.

4,6-Dibromo-1*H*-indole-2-carboxylic acid ethyl ester (Table 1, entry 2)



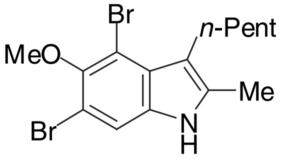
Using procedure B, 1,5-dibromo-3-iodobenzene (543 mg, 1.50 mmol) was coupled with *t*-butyl carbazate (238 mg, 1.80 mmol) and the resulting aryl hydrazide and ethyl pyruvate (164 µL, 1.50 mmol) were converted to the tilted indole. Recrystallization of the crude product from hot EtOH gave the title indole as a yellow solid (209 mg, 40%). The mother liquor was concentrated and purified by column chromatography (7% EtOAc / hexane) to afford additional product (67 mg, 13%). The two crops were combined to give 276 mg (53% total yield for two steps) of the title indole. Mp: 207-209 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (bs, 1H), 7.52 (dd, *J* = 1.0, 1.5 Hz, 1H), 7.45 (d, *J* = 1.5 Hz, 1H), 7.20 (dd, *J* = 1.0, 2.3 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.3, 137.4, 128.8, 126.3, 125.0, 116.8, 115.7, 114.6, 106.8, 61.0, 14.3. IR (neat, cm^{-1}) 3309, 1694, 1320, 1235, 834, 770. Anal. Calcd. for $C_{11}H_9Br_2NO_2$: C, 38.07; H, 2.61. Found: C, 38.24; H, 2.67.

4,6-Dibromo-2-ethyl-5-methoxy-3-methyl-1*H*-indole (Table 1, entry 3)



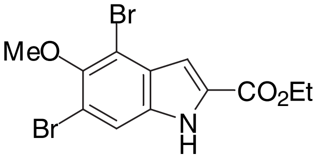
Using procedure A, 2,6-dibromo-4-iodoanisole (392 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and 3-pentanone (105 µL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (7% EtOAc / hexane) gave the title indole as a yellow solid (208 mg, 60% yield for two steps). Mp: 112-114 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (bs, 1H), 7.35 (s, 1H), 3.86 (s, 3H), 2.69 (q, *J* = 7.5 Hz, 2H), 2.4 (s, 3H), 1.24 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 139.7, 133.1, 127.7, 113.7, 109.9, 108.9, 108.2, 61.2, 19.7, 14.1, 11.0. IR (neat, cm^{-1}) 3309, 2968, 1449, 1409, 1218, 1013, 772. Anal. Calcd. for $C_{12}H_{13}Br_2NO$: C, 41.53; H, 3.78. Found: C, 41.62; H, 3.77.

4,6-Dibromo-5-methoxy-2-methyl-3-pentyl-1*H*-indole (Table 1, entry 4)



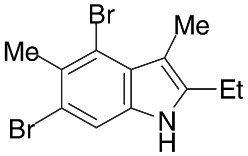
Using procedure A, 2,6-dibromo-4-iodoanisole (392 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and 2-octanone (157 µL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (7% EtOAc / hexane) gave the title indole as a yellow solid (193 mg, 50% yield for two steps). Mp: 131-133 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (bs, 1H), 7.35 (s, 1H), 3.87 (s, 3H), 2.87-2.79 (m, 2H), 2.32 (s, 3H), 1.68-1.53 (m, 2H), 1.42-1.30 (m, 4H), 0.94-0.86 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 134.1, 133.3, 127.1, 114.4, 113.5, 109.8, 108.5, 61.2, 32.7, 32.1, 24.5, 23.0, 14.6, 12.2. IR (neat, cm^{-1}) 3280, 2925, 2858, 1407, 1245, 1038, 853, 772, 614. Anal. Calcd. for $C_{15}H_{19}Br_2NO$: C, 46.30; H, 4.92. Found: C, 46.53; H, 4.86.

4,6-Dibromo-5-methoxy-1*H*-indole-2-carboxylic acid ethyl ester (Table 1, entry 5)



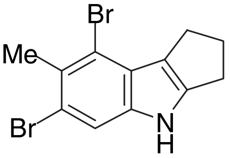
Using procedure B, 1,5-dibromo-3-iodoanisole (588 mg, 1.50 mmol) was coupled with *t*-butyl carbazate (238 mg, 1.80 mmol) and the resulting aryl hydrazide and ethyl pyruvate (164 µL, 1.50 mmol) were converted to the title indole. Recrystallization of the crude product from hot EtOH gave the title indole as a yellow solid (201 mg, 36%). The mother liquor was concentrated and the residue was purified by column chromatography (7% EtOAc / hexane) to afford additional product (74 mg, 13%). The products were combined to give 276 mg (49% total yield for two steps) of the title indole. Mp: 200-202 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (bs, 1H), 7.59 (d, J = 1.0 Hz, 1H), 7.19 (dd, J = 1.0, 2.4 Hz, 1H), 4.43 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 148.3, 133.6, 129.1, 129.0, 116.0, 115.5, 110.5, 109.1, 61.8, 61.4, 14.7. IR (neat, cm^{-1}) 3319, 1694, 1250, 770. Anal. Calcd. for $C_{12}H_{11}Br_2NO_3$: C, 38.23; H, 2.94. Found: C, 37.97; H, 2.89.

4,6-Dibromo-2-ethyl-3,5-dimethyl-1*H*-indole (Table 1, entry 6)



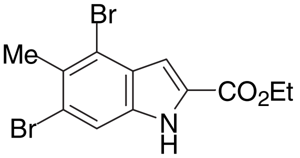
Using procedure A, 2,6-dibromo-4-iodotoluene (376 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and 3-pentanone (105 μL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (7% EtOAc / hexane) gave the title indole as a yellow solid (207 mg, 64% yield for two steps). Mp: 87-90 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (bs, 1H), 7.33 (s, 1H), 2.65 (q, *J* = 7.5 Hz, 2H), 2.61 (s, 3H), 2.43 (s, 3H), 1.21 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 134.7, 127.6, 127.2, 116.8, 116.3, 113.6, 107.7, 23.5, 19.7, 14.1, 11.6. IR (neat, cm^{-1}) 3467, 2973, 2929, 1611, 1465, 1422, 1302, 967, 901, 843. Anal. Calcd. for $C_{12}H_{13}Br_2N$: C, 43.54; H, 3.96. Found: C, 43.56; H, 3.92.

6,8-Dibromo-7-methyl-1,2,3,4-tetrahydro-cyclopenta[*b*]indole (Table 1, entry 7)



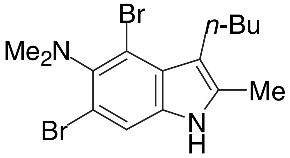
Using procedure A, 2,6-dibromo-4-iodotoluene (376 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and cyclopentanone (88.0 μL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (7% EtOAc / hexane) gave the title indole as a white solid (195 mg, 59% yield for two steps). Mp: 167-169 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (bs, 1H), 7.37 (s, 1H), 3.07-2.98 (m, 2H), 2.82-2.73 (m, 2H), 2.59 (s, 3H), 2.55-2.42 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 139.2, 127.1, 125.8, 120.7, 116.3, 115.4, 114.5, 28.7, 26.2, 26.1, 23.1. IR (neat, cm^{-1}) 3388, 2916,2858, 1416, 1333, 1094, 847. Anal. Calcd. for $C_{12}H_{11}Br_2N$: C, 43.80; H, 3.37. Found: C, 43.65; H, 3.39.

4,6-Dibromo-5-methyl-1*H*-indole-2-carboxylic acid ethyl ester (Table 1, entry 8)



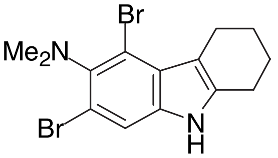
Using procedure B, 1,5-dibromo-3-iodotoluene (564 mg, 1.50 mmol) was coupled with *t*-butyl carbazate (238 mg, 1.80 mmol) and the resulting aryl hydrazide and ethyl pyruvate (164 µL, 1.50 mmol) were converted to the title indole. Recrystallization of the crude product from hot EtOH gave the title indole as a yellow solid (263 mg, 49%). The mother liquor was concentrated and the residue was purified by column chromatography (7% EtOAc / hexane) to afford additional product (28 mg, 5%). The two crops were combined to give 291 mg (54% total yield for two steps) of the title indole. Mp: 237-239 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (bs, 1H), 7.62 (s, 1H), 7.17 (dd, *J* = 0.9, 2.4 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 2.65 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 160.4, 135.4, 128.6, 127.5, 127.0, 120.1, 116.6, 115.5, 107.2, 60.9, 22.7, 14.3. 26.2, 26.1, 23.1. IR (neat, cm^{-1}) 3315, 3135, 2973, 1692, 1522, 1335, 1235, 1021, 847, 770. Anal. Calcd. for $C_{12}H_{11}Br_2NO_2$: C, 39.92; H, 3.07. Found: C, 40.12; H, 3.15.

(4,6-Dibromo-3-butyl-2-methyl-1*H*-indol-5-yl)-dimethyl-amine (Table 1, entry 9)



Using procedure A, (2,6-dibromo-4-iodophenyl)dimethylamine (404 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and 2-heptanone (139 µL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (10% EtOAc / hexane) gave the title indole as a yellow solid (206 mg, 53% yield for two steps). Mp: 98-100 ºC ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (bs, 1H), 7.36 (s, 1H), 2.89 (s, 6H), 2.85 (t, *J* = 7.8 Hz,2H), 2.30 (s, 3H), 1.63-1.53 (m, 2H), 1.46-1.34 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 134.4, 133.4, 127.4, 118.6, 118.2, 114.5, 113.7, 42.3, 35.1, 24.6, 22.9, 14.5, 12.2. IR (neat, cm^{-1}) 3396, 3344, 2952, 2931, 2854, 2788, 1739, 1407, 1218, 938, 727. Anal. Calcd. for $C_{15}H_{20}Br_2N_2$: C, 46.42; H, 5.19. Found: C, 46.57; H, 5.18.

(2,4-Dibromo-6,7,8,9-tetrahydro-5*H*-carbazol-3-yl)-dimethyl-amine (Table 1, entry 10)

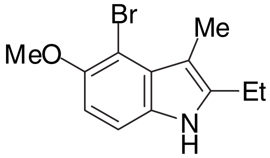


Using procedure A, (2,6-dibromo-4-iodophenyl)-dimethylamine (404 mg, 1.00 mmol) was coupled with *t*-butyl carbazate (158 mg, 1.20 mmol) and the resulting aryl hydrazide and cyclohexanone (104 µL, 1.00 mmol) were converted to the title indole. Purification of the crude product by column chromatography (10% EtOAc / hexane) gave the title indole as a yellow solid (208 mg, 56% yield for two steps). Mp: 163-165 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (bs, 1H), 7.33 (s, 1H), 3.12-3.04 (m, 2H), 2.88 (s, 6H), 2.66-2.59 (m, 2H), 1.89-1.76 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 136.4, 134.5, 127.6, 118.7, 117.8, 113.9, 111.8, 42.3, 23.9, 23.7, 23.6, 22.7. IR (neat, cm^{-1}) 3411, 2931, 2917, 2850, 1739, 1410, 1231, 1127, 936, 857, 727. Anal. Calcd. for $C_{14}H_{16}Br_2N_2$: C, 45.19; H, 4.33. Found: C, 45.24; H, 4.33.

IV. Regioselective hydrodebromination (Table 2)

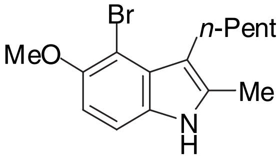
General procedure: An oven-dried Schlenk tube was charged with 4,6-dibromoindole (0.500 mmol), $Pd(OAc)_2$ (5.60 mg, 0.0250 mmol), and *rac*-BINAP (17.0 mg, 0.0275mmol). The schlenk tube was evacuated and backfilled with Ar, and anhydrous THF (1 mL) was added. The reaction mixture was stirred for 20 min at room temperature. TMEDA (113 µL, 0.750 mmol) and additional THF (1 mL) were added and the reaction mixture was stirred for 20 min at room temperature. $NaBH_4$ (0.5 M solution in diglyme, 1.05 mL, 0.525 mmol) was slowly added and the reaction mixture was stirred at room temperature or 50 °C (preheated oil bath) for 24 h. After the reaction mixture was allowed to cool to room temperature, it was diluted with EtOAc (~2 mL). The resulting heterogeneous mixture was then filtered through a pad of silica gel eluting with EtOAc. The filtrate was concentrated and purification of the concentrated filtrate by column chromatography afforded the desired product.

4-Bromo-2-ethyl-5-methoxy-3-methyl-1*H*-indole (Table 2, entry 3)



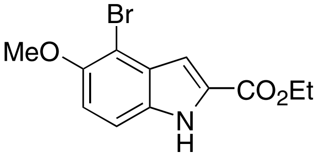
Using the general procedure, 4,6-dibromo-2-ethyl-5-methoxy-3-methyl-1*H*-indole (174 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (15% EtOAc/hexane) afforded the title compound as a yellow solid (115 mg, 86%). Mp: 50-52 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (bs, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 1H), 3.88 (s, 3H), 2.70 (q, *J* = 7.8 Hz, 2H), 2.47 (s, 3H), 1.24 (t, *J* = 7.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 139.3, 131.8, 128.2, 109.7, 108.8, 107.6, 103.3, 58.5, 19.8, 14.2, 11.3. IR (neat, cm^{-1}) 3381, 1422, 1283, 1237, 1054, 783. Anal. Calcd for $C_{12}H_{14}BrNO$: C, 53.75; H, 5.26. Found: C, 54.00; H, 5.21.

4-Bromo-5-methoxy-2-methyl-3-pentyl-1*H*-indole (Table 2, entry 4)



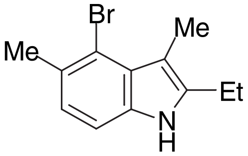
Using the general procedure, 4,6-dibromo-5-methoxy-2-methyl-3-pentyl-1*H*-indole (195 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (7% EtOAc/hexane) afforded the title compound as a yellow solid (131 mg, 85%). Mp: 106-108 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (bs, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 1H), 3.89 (s, 3H), 2.92-2.81 (m, 2H), 2.32 (s, 3H), 1.70-1.54 (m, 2H), 1.44-1.28 (m, 4H), 0.95-0.85 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 133.7, 131.9, 127.6, 113.8, 109.5, 108.4, 102.9, 58.4, 32.8, 32.1, 24.7, 23.0, 14.6, 12.2. IR (neat, cm^{-1}) 3361, 2925, 2858, 1463, 1424, 1239, 1065, 789. Anal. Calcd. for $C_{15}H_{20}BrNO$: C, 58.07; H, 6.50. Found: C, 58.16; H, 6.53.

4-Bromo-5-methoxy-1*H*-indole-2-carboxylic acid ethyl ester (Table 2, entry 5)



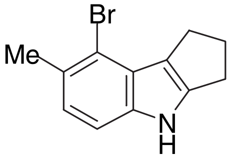
Using the general procedure, 4,6-dibromo-5-methoxy-1*H*-indole-2-carboxylic acid ethyl ester (189 mg, 0.500 mmol) was hydrodebrominated at room temperature. Purification of the crude product by column chromatography (20% EtOAc/hexane) afforded the title compound as a yellow solid (129 mg, 87%). Mp: 167-169 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.19 (bs, 1H), 7.32 (dd, *J* = 0.9, 8.7 Hz, 1H), 7.21 (dd, *J* = 0.9, 2.1 Hz, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 150.7, 132.5, 129.6, 128.8, 113.6, 111.6, 108.4, 103.9, 61.6, 58.2, 14.7. IR (neat, cm^{-1}) 3311, 1739, 1366, 1218, 770. Anal. Calcd. for $C_{12}H_{12}BrNO_3$: C, 48.34; H, 4.06. Found: C, 48.51; H, 4.16

4-Bromo-2-ethyl-3,5-dimethyl-1*H*-indole (Table 2, entry 6)



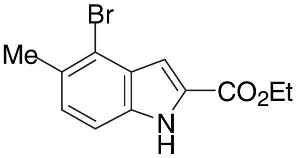
Using the general procedure, 4,6-dibromo-2-ethyl-3,5-dimethyl-1*H*-indole (166 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (7% EtOAc/hexane) afforded the title compound as a yellow solid (99 mg, 79%). Mp: 58-60 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (bs, 1H), 7.06 (d, *J* = 8.1 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 2.69 (q, *J* = 7.5 Hz, 2H), 2.48 (s, 3H), 2.45 (s, 3H), 1.23 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 134.7, 128.5, 127.8, 123.6, 116.1, 109.3, 107.3, 23.1, 19.8, 14.2, 11.6. IR (neat, cm^{-1}) 3413, 2970, 2929, 1451, 1318, 1283, 1088, 895, 795. Anal. Calcd. for $C_{12}H_{14}BrN$: C, 57.16: H, 5.60. Found: C, 57.12; H, 5.70.

8-Bromo-7-methyl-1,2,3,4-tetrahydro-cyclopenta[*b*]indole (Table 2, entry 7)



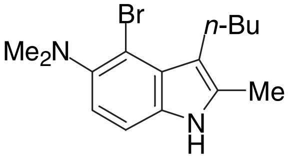
Using the general procedure, 6,8-dibromo-7-methyl-1,2,3,4-tetrahydro-cyclopenta[*b*]indole (165 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (10% EtOAc/hexane) afforded the title compound as a yellow solid (101 mg, 81%). Mp: 89-91 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (bs, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.78 (d, J = 7.8 Hz, 1H), 3.12-3.02 (m, 2H), 2.84-2.75 (m, 2H), 2.55-2.43 (m, 2H) 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 139.3, 128.1, 123.0, 120.3, 115.2, 110.2, 28.9, 26.3, 26.2, 22.5. IR (neat, cm^{-1}) 3475, 2956, 2854, 1434, 1295, 1090. Anal. Calcd. for $C_{12}H_{12}BrN$: C, 57.62; H, 4.84. Found: C, 57.56; H, 4.82.

4-Bromo-5-methyl-1*H*-indole-2-carboxylic acid ethyl ester (Table 2, entry 8)



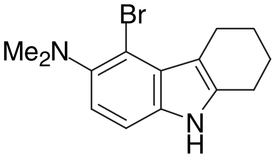
Using the general procedure, 4,6-dibromo-5-methyl-1*H*-indole-2-carboxylic acid ethyl ester (181 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (15% EtOAc/hexane) afforded the title compound as a yellow solid (118 mg, 84%). Mp: 179-181 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (bs, 1H), 7.25 (dd, J = 0.4, 8.1 Hz, 1H), 7.22 (dd, J = 0.4, 2.4 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 4.41 (q, J = 7.5 Hz, 2H), 2.49 (s, 3H), 1.43 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 135.3, 129.7, 129.1, 128.2, 127.8, 117.7, 110.8, 108.9, 61.5, 22.4, 14.7. IR (neat, cm^{-1}) 3299, 1683, 1526, 1250, 1218, 1019, 770. Anal. Calcd. for $C_{12}H_{12}BrNO_2$: C, 51.09; H, 4.29. Found: C, 50.99; H, 4.26.

(4-Bromo-3-butyl-2-methyl-1*H*-indol-5-yl)-dimethyl-amine (Table 2, entry 9)



Using the general procedure, (4,6-dibromo-3-butyl-2-methyl-1*H*-indol-5-yl)-dimethyl-amine (194 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (15% EtOAc/hexane) afforded the title compound as a yellow solid (116 mg, 75%). Mp: 83-85 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (bs, 1H), 7.12 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 2.90 (t, J = 7.8 Hz, 2H), 2.76 (s, 6H), 2.31 (s, 3H), 1.66-1.56 (m, 2H), 1.47-1.35 (m, 2H), 0.94 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 133.4 133.2 127.6, 114.3, 114.0, 111.6, 109.7, 45.9, 35.3, 24.7, 23.0, 14.5, 12.2. IR (neat, cm^{-1}) 3224, 2931, 2856, 1449, 1422, 1245, 1098, 797. Anal. Calcd. for $C_{15}H_{21}BrN_2$: C, 58.26; H, 6.84. Found: C, 58.00; H, 6.76.

(4-Bromo-6,7,8,9-tetrahydro-5*H*-carbazol-3-yl)-dimethyl-amine (Table 2, entry 10)



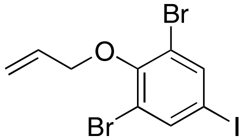
Using the general procedure, (2,4-dibromo-6,7,8,9-tetrahydro-5 *H*-carbazol-3-yl)-dimethyl-amine (186 mg, 0.500 mmol) was hydrodebrominated at 50 °C. Purification of the crude product by column chromatography (10% EtOAc/hexane) afforded the title compound as a yellow solid 108 mg, 74%). Mp: 141-143 ºC. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.72 (bs, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 3.17-3.10 (m, 2H), 2.75 (s, 6H), 2.69-2.61 (m, 2H), 1.88-1.78 (m, 4H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 144.3, 136.1, 133.5, 127.8, 114.4, 111.5, 111.3, 109.8, 45.8, 24.0, 23.9, 23.8, 22.8. IR (neat, cm^{-1}) 3421, 2933, 2852, 2788, 1434, 1410, 1233, 1125. Anal. Calcd. for $C_{14}H_{17}BrN_2$: C, 57.35; H, 5.84. Found: C, 57.16; H, 5.79.

V. Synthesis of U86192A (Scheme 3 and 4)

2,6-Dibromo-4-iodophenol (Scheme 3)

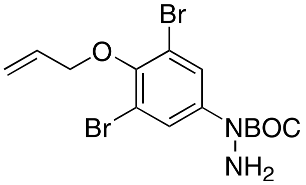
See the procedure for preparation of the dibromoaryl iodides.

2-Allyloxy-1,3-dibromo-5-iodo-benzene (Scheme 3, compound 7)



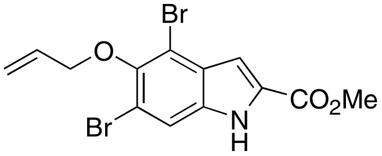
A 3-neck round bottom flask equipped with a reflux condenser was charged with 2,4-dibromo-4-iodophenol (14.0 g, 37.0 mmol) and K_2CO_3 (7.70 g, 55.5 mmol). The flask was evacuated and backfilled with Ar. Acetone (300 mL) was added and the reaction was stirred at room temperature for 30 min. To the resulting suspension, allyl bromide (4.80 mL, 55.5 mmol) was added and then the reaction mixture was heated to reflux (65 °C, preheated oil bath) for 3 h. After the reaction mixture was allowed to reach room temperature, acetone was removed under vacuum and ether (~ 400 mL) was added. The ethereal layer was washed with water and brine and dried over MgSO$_4$. Recrystallization of the concentrated crude product from hot MeOH afforded the product as a white solid (14.8 g, 96%). Mp: 84-86 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 2H), 6.13 (ddt, *J* = 17.1, 10.3, 6.0 Hz, 1H), 5.43 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.29 (dq, *J* = 10.3, 1.5 Hz, 1H), 4.51 (dt, *J* = 6.0, 1.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3, 140.7, 132.6, 119.6, 119.2, 87.8, 74.4. IR (neat, cm^{-1}) 2364, 1441, 1414, 1239, 967, 934, 857, 735. Anal. Calcd. for $C_9H_7Br_2IO$: C, 25.87; H, 1.69. Found: C, 26.06; H, 1.70.

N-(4-Allyloxy-3,5-dibromo-phenyl)-hydrazinecarboxylic acid *tert*-butyl ester (Scheme 3, compound 8)



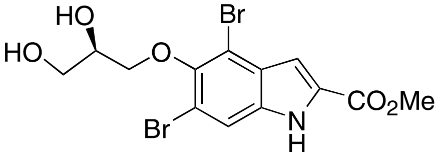
An oven-dried Schlenk flask was charged with 2-Allyloxy-1,3-dibromo-5-iodo-benzene (13.37 g, 32.0 mmol), *t*-butylcarbazate (5.07 g, 38.4 mmol), CuI (304 mg, 1.6 mmol), and Cs_2CO_3 (14.57 g, 44.8 mmol). DMF (130 mL) was added and the reaction mixture was stirred at room temperature for 10 min and heated at 80 °C (preheated oil bath) until the dibromoaryl iodide was consumed as determined by GC analysis. The reaction mixture was allowed to cool to room temperature and diluted with ether (~200 mL) and water (~200 mL). The aqueous phase was extracted with ether (~150 mL x 2) and the combined ethereal layers were washed with water and brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (5% EtOAc/Hexane) afforded the title compound as a yellow solid (9.39 g, 70%). Mp: 60-63 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 2H), 6.15 (ddt, *J* = 17.1, 10.2, 6.0 Hz, 1H), 5.44 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.28 (dq, *J* = 10.2, 1.5 Hz, 1H), 4.50 (dt, *J* = 6.0, 1.5 Hz, 2H), 4.36 (s, 2H), 1.52 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 149.1, 140.5, 133.0, 126.5, 118.7, 117.2, 82.9, 74.3, 28.5. IR (neat, cm^{-1}) 2364, 1740, 1686, 1466, 1320, 1241, 1150, 978, 922, 743. Anal. Calcd. for $C_{14}H_{18}Br_2N_2O_3$: C, 39.84; H, 4.30. Found: C, 40.11; H, 4.27.

5-Allyloxy-4,6-dibromo-1*H*-indole-2-carboxylic acid methyl ester (Scheme 3, compound 9)



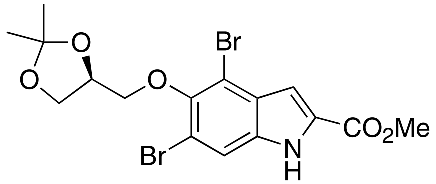
A solution of *N*-(4-Allyloxy-3,5-dibromo-phenyl)-hydrazinecarboxylic acid *tert*-butyl ester (4.22 g, 10.0 mmol), methyl pyruvate (992 µL, 11.0 mmol), HCl (2 mL, 37% solution) and MeOH (150 mL) was refluxed at 100 ºC for 6 h. After the reaction mixture was allowed to cool to room temperature, the solvent was removed under vacuum. The crude product was further dried under vacuum and dissolved in anhydrous CH_2Cl_2 (100 mL). Eaton's reagent (10% P_2O_5 in $MeSO_3H$, 2.84 mL) was slowly added and the reaction mixture was stirred at 45 ºC for 24 h. The reaction mixture was then allowed to cool to room temperature and neutralized with 3 N NaOH solution. The aqueous phase was extracted with EtOAc (~100 mL x 3). The combined organic layers were washed with water, brine and dried over $MgSO_4$. Recrystallization of the concentrated crude product from hot MeOH gave 2.16 g of the title indole as a yellow solid (56%). The mother liquor was concentrated and the residue was purified by column chromatography (15% EtOAc / hexane) to afford additional product (595 mg, 15%). The products were combined to give 2.74 g (71% total yield) of the title indole. Mp: 173-174 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (bs, 1H), 7.59 (d, *J* = 0.9 Hz, 1H), 7.19 (dd, *J* = 0.9, 2.1 Hz, 1H), 6.15 (ddt, *J* = 17.1, 10.2, 6.0 Hz, 1H), 5.48 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.30 (dq, *J* = 10.2, 1.5, 1H), 4.55 (dt, *J* = 6.0, 1.5 Hz, 2H), 3.96 (s, 3H). ^{13}C NMR (75 MHz, Acetone-d_6) δ 161.7, 147.4, 134.9, 134.4, 130.3, 129.2, 118.0, 116.9, 115.9, 110.4, 108.4, 75.1, 52.5. IR (neat, cm^{-1}) 3325, 2368, 1694, 1439, 1256, 988, 930, 855, 766. Anal. Calcd. for $C_{13}H_{11}Br_2NO_3$: C, 40.13; H, 2.85. Found: C, 40.18; H, 2.85.

4,6-Dibromo-5-(2,3-dihydroxy-propoxy)-1*H*-indole-2-carboxylic acid methyl ester (Scheme 3, compound 10)



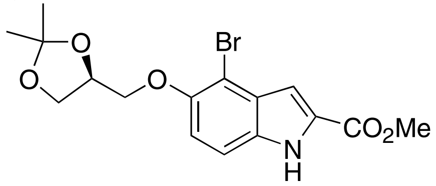
A 100 mL round bottom flask was charged with $K_2OsO_2(OH)_4$ (10.6 mg, 0.03 mmol), $(DHQD)_2PYR$ (264 mg, 0.30 mmol), $K_3Fe(CN)_6$ (2.96 g, 9.00 mmol), and K_2CO_3 (1.24 g, 9.00 mmol). *t*-BuOH (15 mL) and H_2O (15 mL) were added to the reaction flask and the reaction solution was vigorously stirred at room temperature for 40 min. 5-Allyloxy-4,6-dibromo-1*H*-indole-2-carboxylic acid methyl ester (1.17 g, 3.00 mmol) was added to the reaction flask at 0 ºC (ice-water bath) and the reaction mixture was stirred at 4 ºC for 3 days. After the reaction mixture was warmed up to room temperature, water (150 mL) was added. The aqueous phase was extracted with EtOAc (~100 mL x 3). The combined organic layers were washed with water, brine and dried over $MgSO_4$. After concentration, purification of the crude product by column chromatography (EtoAc : Hexane = 3 : 2) afforded the title product as a pale yellow solid (1.12 g, 88%) with 78% ee as determined by chiral HPLC analysis (Chiracel, OD, 2% isopropanol/ hexane, 0.7 mL/min, 280 nm, t_R (major)= 64.3 min, t_R (minor)= 78.4 min). $[\alpha]_D^{22}$= -1.71° (c=0.5, MeOH). Mp: 191-193 ºC. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.4 (bs, 1H), 7.66 (s, 1H), 6.99 (s, 1H), 4.97 (d, *J* = 4.8 Hz, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 3.99-3.86 (m, 3H), 3.88 (s, 3H), 3.62-3.41(m, 2H).^{13}C NMR (75 MHz, DMSO-d_6) δ 160.8, 146.1, 133.8, 128.9, 127.6, 115.9, 114.3, 108.9, 107.2, 75.4, 70.6, 63.2, 52.2. IR (neat, cm^{-1}) 3317, 2366, 1696, 1437, 1266, 1254, 1036, 770. Anal. Calcd. for $C_{13}H_{13}Br_2NO_5$: C, 36.91; H, 3.10. Found: C, 36.97; H, 3.05.

4,6-Dibromo-5-(2,2-dimethyl-[1,3]dioxolan-4-ylmethoxy)-1*H*-indole-2-carboxylic acid methyl ester (Scheme 3, compound 11)



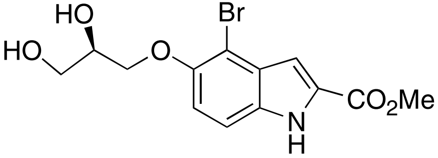
An oven-dried 100 mL one arm round bottom flask equipped with Dean-Stark apparatus and reflux condenser was charged with 4,6-Dibromo-5-(2,3-dihydroxy-propoxy)-1*H*-indole-2-carboxylic acid methyl ester (1.06 g, 2.50 mmol) and PPTS (pyridinium *p*-toluenesulfonate) (64 mg, 0.13 mmol). Dimethoxy propane (370 µL, 3.00 mmol) was added to the reaction mixture followed by benzene (40 mL). The reaction mixture was then heated to refluxed (65 ºC, preheated oil bath) overnight. After the reaction mixture was allowed to cool down to room temperature, water (~50 mL) was added. The aqueous layer was extracted with EtoAc (~50 mL x 2). The combined organic layers were washed with water, brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (EtoAc : Hexane = 3 : 7) afforded the title product as a white solid (1.13 g, 98%). $[\alpha]_D^{22}$= +0.84° (c=0.5, $CHCl_3$). Mp: 180-182 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.11 (bs, 1H), 7.59 (d, *J* = 0.6 Hz, 1H), 7.19 (dd, *J* = 0.9, 2.4 Hz, 1H), 4.66-4.58 (m, 1H), 4.27-4.09 (m, 3H), 4.12-3.96 (m, 1H), 3.96 (s, 3H), 1.48 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 146.7, 133.8, 128.9, 128.7, 115.9, 115.6, 110.5, 109.7, 109.4, 74.3, 73.9, 67.3, 52.7, 27.2, 25.6. IR (neat, cm^{-1}) 3313, 2368, 1698, 1437, 1258, 1214, 1032, 849, 766, 627. Anal. Calcd. for $C_{16}H_{17}Br_2NO_5$: C, 41.50; H, 3.70. Found: C, 41.51; H, 3.67.

4-Bromo-5-(2,2-dimethyl-[1,3]dioxolan-4-ylmethoxy)-1*H*-indole-2-carboxylic acid methyl ester (Scheme 3, compound 12)



Using the general procedure for the regioselective hydrodebromination, 4,6-dibromo-5-(2,2-dimethyl-[1,3]dioxolan-4-ylmethoxy)-1*H*-indole-2-carboxylic acid methyl ester (232 mg, 0.500 mmol) was hydrodebrominated at room temperature. Purification of the crude product by column chromatography (25% EtOAc/hexane) afforded the title compound as a pale yellow solid (167 mg, 87%). $[\alpha]_D^{22}$= -9.22° (c=0.5, $CHCl_3$). Mp: 151-153 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (bs, 1H), 7.30 (dd, J = 0.9, 9.0 Hz, 1H), 7.21 (dd, *J* = 0.9, 2.4 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 1H), 4.54-4.47 (m, 1H), 4.24-4.13 (m, 2H), 4.11-3.98 (m, 2H), 3.95 (s, 3H), 1.47 (s, 3H), 1.41 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 150.0, 132.8, 129.5, 128.5, 116.3, 111.7, 109.8, 108.9, 105.6, 74.3, 72.2, 67.2, 52.5, 27.1, 25.8. IR (neat, cm^{-1}) 3313, 1740, 1694, 1526, 1447, 1372, 1260, 1229, 1208, 1075, 772. Anal. Calcd. for $C_{16}H_{18}BrNO_5$: C, 50.02; H, 4.72. Found: C, 50.38; H, 4.77.

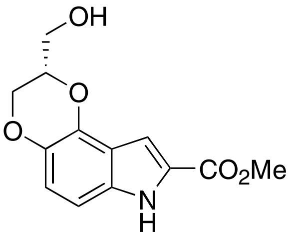
4-Bromo-5-(2,3-dihydroxy-propoxy)-1*H*-indole-2-carboxylic acid methyl ester (Scheme 3)



A 50 mL round bottom flask was charged with 4-Bromo-5-(2,2-dimethyl-[1,3]dioxolan-4-ylmethoxy)-1*H*-indole-2-carboxylic acid methyl ester (384 mg, 1.00 mmol) and Dowex-H$^+$ (50 mg). MeOH (10 mL) was added and the reaction mixture was stirred at room temperature for 4 h. Dowex-H$^+$ was removed by filtration on a pad of silica gel and the concentrated crude product was purified by column chromatography (EtoAc : MeOH = 9 : 1) to afford the title compound as white solid (327 mg, 95%). $[\alpha]_D^{22}$= -1.55° (c=0.5, MeOH). Mp: 152-155 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.19 (bs, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.97 (d, *J* = 1.5

Hz, 1H), 4.96 (d, *J* = 5.1 Hz, 1H), 4.67 (t, J = 6.0 Hz, 1H), 4.07-3.94 (m, 2H), 3.88 (s, 3H), 3.88-3.78 (m, 1H), 3.60-3.44 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 149.7, 133.0, 128.5, 128.3, 115.0, 112.7, 106.7, 102.6, 72.3, 70.2, 62.9, 52.1. IR (neat, cm^{-1}) 3440, 3290, 3205, 1702, 1526, 1443, 1260, 1237, 2323, 2079, 2054, 772. Anal. Calcd. for $C_{13}H_{14}BrNO_5$: C, 45.37; H, 4.10. Found: C, 45.64; H, 4.09.

2,3-Dihydro-2-(hydroxymethyl)-7*H*-1,4-dioxino[2,3-e]-indole-8-carboxylic acid methyl ester (Scheme 3, compound 2)

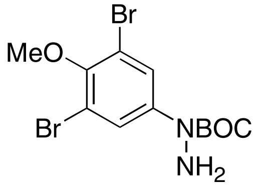


An oven-dried Schlenk tube was charged with 4-Bromo-5-(2,3-dihydroxy-propoxy)-1 *H*-indole-2-carboxylic acid methyl ester (172 mg, 0.500 mmol), $Pd(OAc)_2$ (5.600 mg, 0.025mmol), ligand (2-(*N,N*-dimethylamino)-2'-di-*t*-butylphosphinobiphenyl)(10 mg, 0.030 mmol) and Cs_2CO_3 (244 mg, 0.825 mmol). The Schlenk tube was evacuated and backfilled with Ar. Toluene (4 mL) was added and the reaction mixture was stirred at room temperature for 10 min and heated at 50 ºC (preheated oil bath) for 48 h. The reaction mixture was allowed to cool to room temperature and then filtered through a pad of silica gel eluting with EtOAc. Purification of the concentrated crude product by column chromatography (15% EtOAc/Hexane) afforded the title compound as a pale yellow solid (82 mg, 62%). $[\alpha]_D^{22}$= -6.44º (c=0.5, MeOH), ^{1}H NMR (300 MHz, $CDCl_3$) 8.84 (bs, 1H), 7.22 (dd, *J* = 0.6, 2.1 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.88 (dd, *J* = 0.6, 8.4 Hz, 1H), 4.43-4.36 (m, 1H), 4.34 (dd, *J* = 2.4, 11.4 Hz, 1H), 4.16 (dd, *J* = 6.9, 11.4 Hz, 1H), 4.04-3.87 (m, 2H), 3.92 (s, 3H), 2.04 (t, *J* = 6.3 Hz, 1H).

2,6-Dibromo-4-iodoanisole (Scheme 4, compound 13)

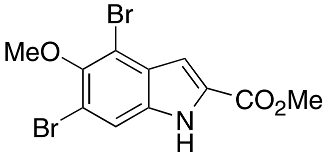
See the procedure for preparation of the dibromoaryl iodides.

N-(3,5-Dibromo-4-methoxy-phenyl)-hydrazinecarboxylic acid t-butyl ester (Scheme 4, compound 14)



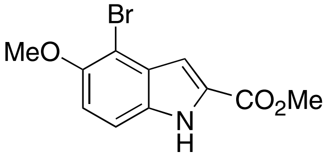
An oven-dried Schlenk flask was charged with 2,6-Dibromo-4-iodoanisole (3.92 g, 10.0 mmol), *t*-butylcarbazate (1.58 g, 12.0 mmol), CuI (95 mg, 0.5 mmol), and Cs_2CO_3 (4.56 g, 14.0 mmol). DMF (40 mL) was added and the reaction mixture was stirred at room temperature for 10 min and heated at 80 °C (preheated oil bath) until the dibromoaryl iodide was consumed as determined by GC analysis. The reaction mixture was allowed to cool to room temperature and diluted with ether (~100 mL) and water (~100 mL). The aqueous phase was extracted with ether (~100 mL x 2) and the combined ethereal layers were washed with water and brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (7% EtOAc/Hexane) afforded the title compound as a yellow oil (2.92 g, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 2H), 4.37 (s, 2H), 3.86 (s, 3H), 1.53 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.6, 150.5, 140.7, 126.8, 117.1, 83.1, 60.9, 28.4. IR (neat, cm^{-1}) 3354, 2975, 2933, 1698, 1472, 1291, 1252, 1241, 1148, 992, 866, 741. Anal. Calcd. for $C_{12}H_{16}Br_2N_2O_3$: C, 36.39; H, 4.07. Found: C, 36.51; H, 4.00.

4,6-Dibromo-5-methoxy-1H-indole-2-carboxylic acid methyl ester (Scheme 4, compound 15)



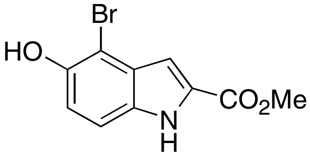
A solution of *N*-(3,5-dibromo-4-methoxy-phenyl)-hydrazinecarboxylic acid *t*-butyl ester (7.91 g, 20.0 mmol), methyl pyruvate (1.98 mL, 22.0 mmol), HCl (4 mL, 37% solution) and MeOH (150 mL) was heated to reflux (65 ºC, preheated oil bath) for 6 h. After the reaction mixture was allowed to cool to room temperature, the solvent was removed under vacuum. The crude product was further dried under vacuum and dissolved in anhydrous CH_2Cl_2 (150 mL). Eaton's reagent (10% P_2O_5 in $MeSO_3H$, 15 mL) was slowly added and the reaction mixture was stirred at 45 ºC for 24 h. The reaction mixture was then allowed to cool to room temperature and neutralized with 3 N NaOH solution. The aqueous phase was extracted with EtOAc (~150 mL x 3). The combined organic layers were washed with water, brine and dried over $MgSO_4$. Recrystallization of the concentrated crude product from hot MeOH gave 4.49 g of the title indole as a yellow solid (62%). The mother liquor was concentrated and the residue was purified by column chromatography (7% EtOAc / hexane) to afford additional product (586 mg, 8%). The products were combined to give 5.08 g (70% total yield) of the title indole. Mp: 202-204 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (bs, 1H), 7.59 (d, *J* = 0.9Hz, 1H), 7.19 (dd, *J* = 0.9, 2.4Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 148.4, 133.5, 129.0, 128.8, 116.2, 115.4, 110.6, 109.4, 61.4, 52.6. IR (neat, cm^{-1}) 3311, 1696, 1519, 1250, 978, 851, 766. Anal. Calcd. for $C_{11}H_9Br_2NO_3$: C, 36.40; H, 2.50. Found: C, 36.42; H, 2.46.

4-Bromo-5-methoxy-1*H*-indole-2-carboxylic acid methyl ester (Scheme 4, compound 16)



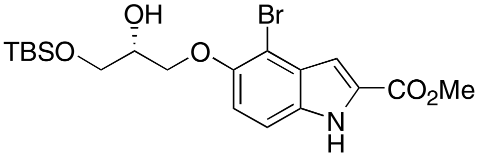
An oven-dried round bottom flask was charged with 4,6-dibromo-5-methoxy-1*H*-indole-2-carboxylic acid methyl ester (4.00 g, 11.0 mmol), $Pd(OAc)_2$ (123 mg, 0.55 mmol), and *rac*-BINAP (377 mg, 0.605 mmol). The flask was evacuated and backfilled with Ar and anhydrous THF (10 mL) was added. The reaction mixture was stirred for 20 min at room temperature. TMEDA (2.50 mL, 16.5 mmol) was added and the reaction mixture was stirred for an additional 20 min at room temperature. Additional THF (30 mL) was added and $NaBH_4$ (0.5 M solution in diglyme, 33.0 mL, 16.5 mmol) was slowly added and the reaction mixture was stirred at room temperature until the dibromoindole was consumed as determined by TLC analysis. The reaction mixture was quenched with water (~150 mL) and the aqueous layer was extracted with EtOAc (~120 mL x 3). The combined organic layers were washed with water, brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (25% EtOAc/Hexane) afforded the title compound as a yellow solid (2.66 g, 85%). Mp: 181-183 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (bs, 1H), 7.32 (dd, *J* = 0.9, 8.7 Hz, 1H), 7.21 (dd, *J* = 0.9, 2.4 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 150.7, 132.5, 129.6, 128.4, 113.7, 111.6, 108.6, 103.9, 58.2, 52.5. IR (neat, cm^{-1}) 3334, 1698, 1522, 1252, 766. Anal. Calcd. for $C_{11}H_{10}BrNO_3$: C, 46.50; H, 3.55. Found: C, 46.68; H, 3.51.

4-Bromo-5-hydroxy-1*H*-indole-2-carboxylic acid methyl ester (Scheme 4, compound 17)



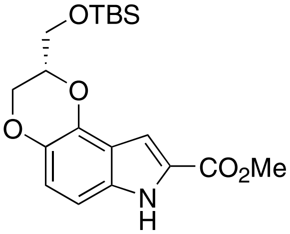
An oven-dried round bottom flask was charged with 4-bromo-5-methoxy-1*H*-indole-2-carboxylic acid methyl ester (2.27 g, 8.00 mmol) and the flask was evacuated and backfilled with Ar. CH_2Cl_2 (150 mL) was added and BBr_3 was slowly added at −78 ºC. The reaction mixture was allowed to warm up to room temperature and stirred for 12 h. The reaction mixture was poured into cold water in an ice-bath and stirred for 30 min. The aqueous layer was then extracted with CH_2Cl_2 (~100 mL x 2). The combined organic layers were washed with sat. $NaHCO_3$ solution, water and brine, and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (35% EtOAc/Hexane) afforded the title indole as a yellow solid (1.50 g, 69%). Mp: 152-154 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.15 (bs, 1H), 7.27 (dd, *J* = 0.6, 9.0 Hz, 1H), 7.12 (dd, *J* = 0.6, 2.4 Hz, 1H), 7.05 (d, *J* = 9.0 Hz, 1H), 5.40 (s, 1H), 3.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 147.2, 131.9, 128.3, 128.1, 115.9, 112.4, 108.0, 100.8, 52.5. IR (neat, cm^{-1}) 3319, 2971, 1739, 1706, 1366, 1229, 1208, 764. Anal. Calcd. for $C_{10}H_8BrNO_3$: C, 44.47; H, 2.99. Found: C, 44.62; H, 2.93.

4-Bromo-5-[3-(*tert*-butyl-dimethyl-silanyloxy)-2-hydroxy-propoxy]-1*H*-indole-carboxylic acid methyl ester (Scheme 4, compound 18)



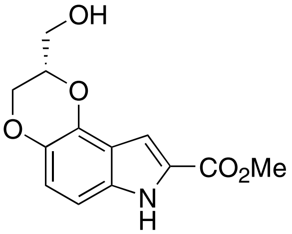
An oven-dried round bottom flask was charged with 4-bromo-5-hydroxy-1*H*-indole-2-carboxylic acid methyl ester (945 mg, 3.50 mmol), Co-salen oligomer **19** (28.0 mg, 0.0350 mmol)[9] and 3 Å molecular sieves (155 mg, 44.4 mg/mmol of the indole). The flask was evacuated and backfilled with Ar. CH_3CN (310 µL) was added followed by (±)-(*tert*-butyldimethylsilyl) gylcidyl ether (1.65 g, 8.75 mmol) and the reaction mixture was stirred at room temperature for 22 h. PPTS (54.0 mg, 0.105 mmol) and ether (8 mL) were added and the resulting solution was stirred for 10 min. The reaction mixture was filtered through a pad of silica gel, eluting with ether. After concentration *in vacuo*, purification of the crude product by column chromatography (5% EtOAc/CH_2Cl_2) afforded the title product as a pale yellow solid (1.17 g, 73%) with >99% ee as determined by chiral HPLC analysis (Chiracel, OD, 7% isopropanol/ hexane, 0.6 mL/min, 280 nm, t_R (major)= 24.9 min, t_R (minor)= 28.4 min). $[\alpha]_D^{22}$=-3.2° (*c*=1, $CHCl_3$). Mp: 104-106 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 9.45 (bs, 1H), 7.29 (dd, *J*=0.9, 8.7 Hz, 1H), 7.19 (dd, *J* = 0.9, 2.4 Hz, 1H) 7.04 (d, *J* = 8.7 Hz, 1H), 4.14-4.02 (m, 3H), 3.95 (s, 3H), 3.85 (d, *J* = 5.1 Hz, 2H), 2.83 (d, *J* = 5.1 Hz, 1H), 0.90 (s, 9H), 0.084 (s, 3H), 0.080 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 162.3, 149.8, 132.8, 129.4, 128.4, 115,6, 111.8, 108.7, 105.1, 72.0, 70.6, 63.9, 52.5, 26.2, 18.6, -5.0.IR (neat, cm^{-1}) 3323, 3018, 2971, 2950, 1739, 1374, 1218, 764. Anal. Calcd. for $C_{19}H_{28}BrNO_5Si$: C, 49.78; H, 6.16. Found: C, 49.80; H, 6.28.

8-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7,8-dihydro-3*H*-6,9-dioxa-3-aza cyclopenta[*a*]naphthalene-2-carboxylic acid methyl ester



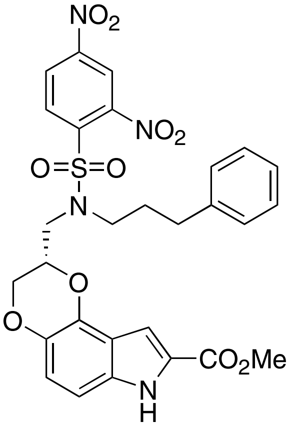
An oven-dried Schlenk tube was charged with 4-bromo-5-[3-(*tert*-butyl-dimethyl-silanyloxy)-2-hydroxy-propoxy]-1*H*-indole-carboxylic acid methyl ester (320 mg, 0.700 mmol), $Pd(OAc)_2$ (8.00 mg, 0.0350 mmol), 2-(*N,N*-dimethylamino)-2'-di-*t*-butylphosphinobiphenyl (14.5 mg, 0.0420 mmol) and Cs_2CO_3 (342 mg, 1.05 mmol). The Schlenk tube was evacuated and backfilled with Ar. Toluene was added and the reaction mixture was stirred at room temperature for 10 min and heated at 70 ºC (preheated oil bath) for 40 h. The reaction mixture was allowed to cool to room temperature and then filtered through a pad of silica gel eluting with EtOAc. Purification of the concentrated crude product by column chromatography (15% EtOAc/Hexane) afforded the title compound as a pale yellow solid (201 mg, 76%). $[\alpha]^D_{22}$=+10.0º (*c*=1, $CHCl_3$). Mp: 129-131 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 8.76 (bs, 1H), 7.20 (d, *J* = 1.8 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 4.38-4.26 (m, 2H), 4.12 (dd, *J* = 11.7, 7.2 Hz, 1H), 4.00-3.82 (m, 2H), 3.92 (s, 3H), 0.91 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 162.4, 136.2, 135.8, 133.5, 126.8, 119.1, 117.5, 105.5, 104.4, 74.1, 65.8, 62.2, 52.2, 26.1, 18.6, -5.0. IR (neat, cm^{-1}) 3336, 3018, 2971, 2948, 1739, 1441, 1366, 1229, 1218, 1102, 836, 778. Anal. Calcd. for $C_{19}H_{27}NO_5Si$: C, 60.45; H, 7.21. Found: C, 60.40; H, 7.19.

2,3-Dihydro-2-(hydroxymethyl)-7*H*-1,4-dioxino[2,3-e]-indole-8-carboxylic acid methyl ester (Scheme 4, compound 2)

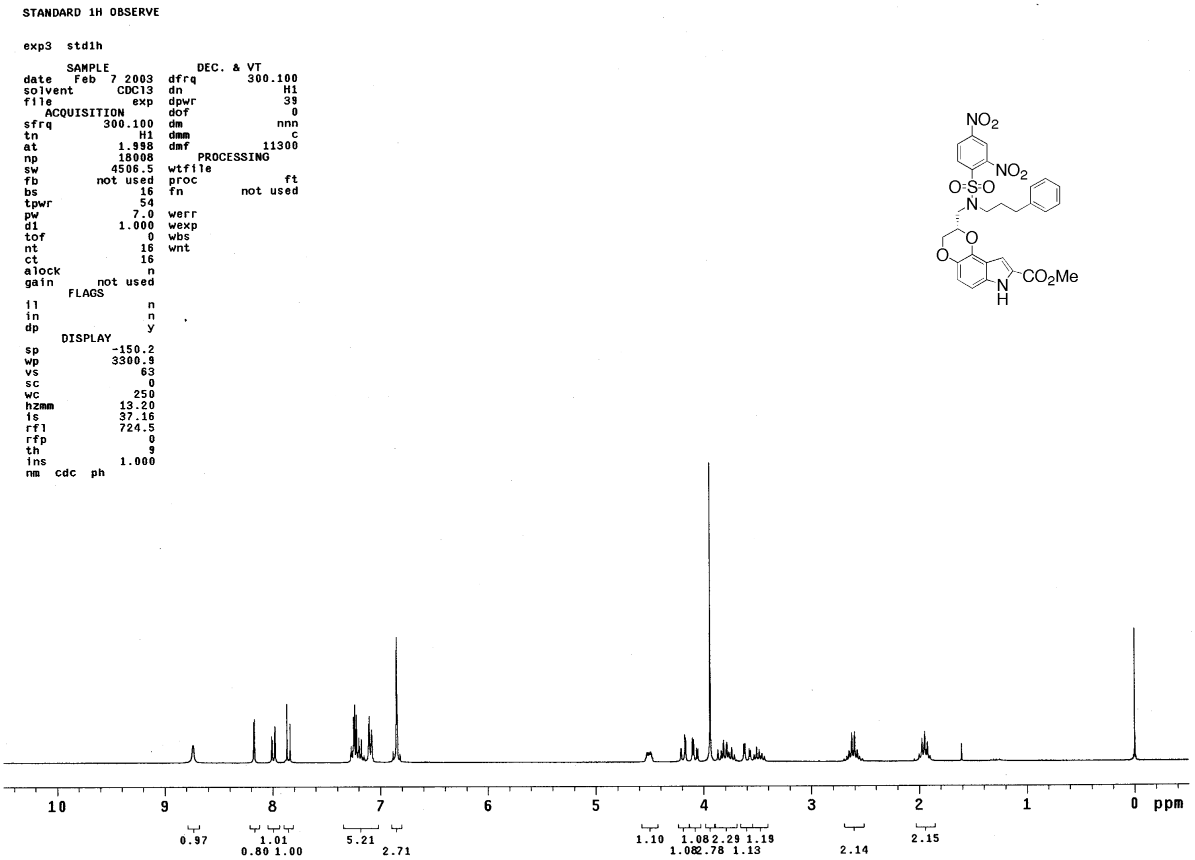


To a solution of 8-(*tert*-butyl-dimethyl-silanyloxymethyl)-7,8-dihydro-3*H*-6,9-dioxa-3-aza cyclopenta[*a*]naphthalene-2-carboxylic acid methyl ester (227 mg, 0.600 mmol) in anhydrous THF (5 mL) was added TBAF (1M solution in THF, 720 µL, 0.720 mmol). The reaction mixture was stirred at room temperature for 2 h and then filtered through a pad of silica gel eluting with EtOAc. Purification of the concentrated crude product by column chromatography (EtOAc/ hexane=1/1) afforded the title compound as a white solid (151 mg, 96%). $[\alpha]_D^{22}$=-7.1 ° (*c*=0.5, MeOH). Mp: 158-160 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 8.84 (bs, 1H), 7.22 (dd, *J* = 0.6, 2.1 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.88 (dd, *J* = 0.6, 8.4 Hz, 1H), 4.43-4.36 (m, 1H), 4.34 (dd, *J* = 2.4, 11.4 Hz, 1H), 4.16 (dd, *J* = 6.9, 11.4 Hz, 1H), 4.04-3.87 (m, 2H), 3.92 (s, 3H), 2.04 (t, *J* = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 162.3, 135.8, 135.7, 133.4, 126.9, 119.1, 117.4, 105.3, 104.8, 74.1, 65.4, 62.1, 52.3. IR (neat, cm^{-1}) 1698, 1526, 1250, 1206, 1046, 1003, 770, 739. Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.62; H, 5.18.

8-{[(2,4-Dinitro-benzenesulfonyl)-(3-phenyl-propyl)-amino]-methyl}-7,8-dihydro-3*H*-6,9-dioxa-3-aza-cyclopenta[*a*]naphthalene-2-carboxylic acid methyl ester



An oven-dried round bottom flask was charged with 8-hydroxymethyl-7,8-dihydro-3*H*-6,9-dioxa-3-aza-cyclopenta[*a*]naphthalene-2-carboxylic acid methyl ester (79.0 mg, 0.300 mmol), 2,4-dinitro-*N*-(3-phenyl-propyl)-benzenesulfonamide (164 mg, 0.450 mmol) and PPh_3 (118 mg, 0.450 mmol). The flask was evacuated and backfilled with Ar. Anhydrous THF (3 mL) was added followed by slow addition of DEAD (78.0 mg, 0.450 mmol) dissolved in THF (2 mL) and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with water (~30 mL) and the aqueous layer was extracted with EtOAc (~ 25 mL x 3). The combined organic layers were washed with water and brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (EtOAc/hexane=2/5) afforded the title compound as a orange solid (169 mg, 92%). $[\alpha]_D^{22}$=+64.5 ° (*c*=0.5, $CHCl_3$). Mp: 170-172 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 8.74 (bs, 1H), 8.17 (d, *J* = 2.1 Hz, 1H), 7.99 (dd, *J* = 2.1, 8.7 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.28-7.06 (m, 6H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.83 (dd, *J* = 0.6, 8.7 Hz, 1H), 4.55-4.47 (m, 1H), 4.19 (dd, *J* = 2.7, 12.0 Hz, 1H), 4.08 (dd, *J* = 4.2, 12 Hz, 1H), 3.94 (s, 3H), 3.88-3.70 (m, 2H), 3.60 (dd, *J* = 3.6, 15.3 Hz, 1H), 3.55-3.42 (m, 1H), 2.71-2.52 (m, 2H), 1.95 (quint, *J* = 7.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 161.8, 148.6, 147.5, 140.7, 138.4, 135.4, 134.5, 133.3, 132.2, 128.6, 128.4, 127.0, 126.3, 125.6, 119.6, 118.5, 117.5, 105.0, 104.8, 70.9, 65.1, 52.5, 47.4, 46.4, 32.9, 29.4. IR (neat, cm^{-1}) 1702, 1538, 1349, 1248, 1208, 1164, 1000, 770, 743. HRMS (ESI) calcd for $C_{29}H_{26}N_4O_{10}S$ $[M+Na]^+$: 633.1262 Found 633.1277.



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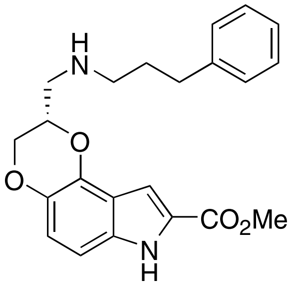
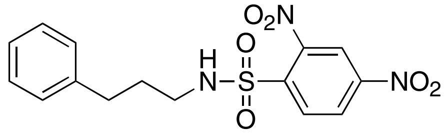
2,3-Dihydro-2-{[(3-phenylpropyl)amino]methyl}-7*H*-1,4-dioxino[2,3-*e*]indole-8-carboxylic acid methyl ester (Scheme 4, compound 1)



To a solution of 8-{[(2,4-dinitro-benzenesulfonyl)-(3-phenyl-propyl)-amino]-methyl}-7,8-dihydro-3*H*-6,9-dioxa-3-aza-cyclopenta[*a*]naphthalene-2-carboxylic acid methyl ester (122 mg, 0.200 mmol) in CH_2Cl_2 (3 mL) was added mercaptoacetic acid (21.0 µL, 0.300 mmol) followed by Et_3N (56.0 µL, 0.400 mmol). The reaction mixture was stirred at room temperature for 15 min. The reaction mixcture was then neutralized with sat. $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (~20 mL x 3). The combined organic layers were washed with water and brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (MeOH/EtOAc=1/9) afforded the title compound as a white solid (72 mg, 95%). $[\alpha]_D^{22}$=-9.1 ° (*c*=0.5, CH_3Cl). Mp: 98-100 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 8.87 (bs, 1H), 7.30-7.13 (m, 6H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.86 (dd, *J* = 0.6, 9.0 Hz, 1H), 4.45-4.36 (m, 1H), 4.29 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.06 (dd, *J* = 6.9, 11.4 Hz, 1H), 3.92 (s, 3H), 2.99 (dd, *J* = 7.2, 12.6 Hz, 1H), 2.90 (dd, *J* = 4.8, 12.6 Hz, 1H), 2.78-2.63 (m, 4H), 1,85 (quint, *J* = 7.5 Hz, 2H), 1.64 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 162.3, 142.0, 135.8, 135.7, 133.5, 128.5, 128.4, 126.8, 125.9, 119.1, 117.4, 105.4, 104.6, 73.3, 66.8, 52.2, 50.1, 49.7, 33.8, 31.9. IR (neat, cm^{-1}) 3315, 2929, 1737, 1686, 1526, 1441, 1351, 1256, 1235, 1218, 1034, 770. Anal. Calcd. for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36. Found: C, 69.22; H, 6.39.

2,4-Dinitro-*N*-(3-phenyl-propyl)-benzenesulfonamide



An oven-dried round bottom flask was charged with 2,4-dinitrobenzenesulfonylchloride (1.33 g, 5.00 mmol). The flask was evacuated and backfilled with Ar. Anhydrous CH_2Cl_2 (50 mL) was added followed by 3-phenylpropylamine (711 µL, 5.00 mmol) and pyridine (606 µL, 7.5 mmol). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 (~50 mL) and the organic layer was washed with water and brine and dried over $MgSO_4$. Purification of the concentrated crude product by column chromatography (20% EtOAc/ hexane) afforded the title compound as a white solid (1.70g, 93%). Mp: 101-103 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) 8.64 (d, *J* = 2.1 Hz, 1H), 8.54 (dd, *J* = 2.1, 8.7 Hz, 1H), 8.27 (d, *J* = 8.7 Hz, 1H), 7.28-7.04 (m, 5H), 5.32 (t, *J* = 6.0 Hz, 1H), 3.15 (dt, *J* = 6.0, 6.9 Hz, 2H), 2.65 (t, *J* = 7.5 Hz, 2H), 1.88 (quint, *J* = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 149.7, 148.1, 140.3, 139.1, 132.6, 128.6, 128.3, 127.2, 126.3, 120.8, 43.5, 32.7, 31.3. IR (neat, cm^{-1}) 1740, 1540, 1345, 1218, 1160, 747, 737, 702. Anal. Calcd. for $C_{15}H_{15}N_3O_6S$: C, 49.31; H, 4.14 Found: C,49.40; H, 4.21.

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9. Calculation of the amount of the catalyst used was based on the molecular weight (798.71/Co).