Supporting Information for:

Fluorous-tagged indolylboron for the diversity-oriented synthesis of biologically-attractive bisindole derivatives
Experimental Section

General Comments. Toluene, benzene and dioxane were distilled from sodium benzenophenone ketyl. DMF was distilled from CaH₂. CH₂Cl₂ was distilled from P₂O₅. MeOH was distilled from magnesium methoxide. Other dry solvents and reagents were purchased from commercial sources and used without further purification. Perfluorinated silica gel (FluoroFlash® Fluorous SPE Cartridges) was purchased from FLUOROUS Technologies Incorporated.

Sulfonyl chloride 1b. A mixture of PhI (3.95 ml, 35.3 mmol), C₆F₅I (9.5 ml, 35.5 mmol) and Cu powder (10.2 g, 160.5 mmol) in DMSO (50ml) was stirred for 22 h at 120 °C. The mixture was filtered by Celite® and washed with Et₂O and H₂O. The aqueous layer was extracted with Et₂O (1×15 ml). The organic layer was washed with H₂O and brine, and the organic layer was dried over MgSO₄. The evaporation of the organic phase gave the crude product, and the crude product was purified by short-path silica gel column chromatography with hexane to afford 17.30 g (98%) of perfluoroctylbenzene.

CISO₂H (30 ml) was added to perfluoroctylbenzene (15.30 g, 30.8 mmol) at rt. The mixture was stirred for 2.5 h at 120 °C, and cooled to rt. The mixture was pipetted cautiously onto ice. The aqueous layer was extracted with AcOEt (3×10 ml). The organic layer was washed with saturated NaHCO₃ and brine, and the organic layer was dried over MgSO₄. The evaporation of the organic phase gave 3-iodoindole. The evaporation of the organic phase gave the crude product, and the crude product was purified by silica gel column chromatography with hexane to afford 17.30 g (98%) of perfluoroctylbenzene.

**Sulphonate 2b.** Et₃N (1.1 ml, 7.8 mmol) was added to a stirred solution of 1b (2.90 g, 4.88 mmol), 4-iodophenol (1.33 g, 6.03 mmol), DMAP (122.3 mg, 1.00 mmol) and CH₂Cl₂ (30ml) at 0 °C. The mixture was stirred for 12 h at rt, and the reaction was monitored by silica gel TLC. The mixture was quenched with H₂O and evaporated. The mixture was purified by F-SPE (80% MeOH/H₂O-AcOEt) using perfluorinated silica gel to afford 3.30 g (87%) of 3-iodoindole as a solid; 1H NMR (CDCl₃, 500 MHz) δ 8.31 (1H, d, J = 8.0 Hz), 8.28 (1H, s), 8.01 (1H, d, J = 8.0 Hz), 7.87 (1H, t, J = 8.0 Hz); EIMS m/z (rel intensity) 578 (M⁺, 100%); HRMS calcd. for C₁₆H₈O₃F₉SI 777.8967, found 777.8981.

Sulfonyl chloride 1a. Starting with PhI and C₆F₅I and following the procedure for the preparation of 1b gave 1a (2 steps 27%) as an oil; 1H NMR (CDCl₃, 400 MHz) δ 8.31 (1H, d, J = 8.0 Hz), 8.28 (1H, s), 8.01 (1H, d, J = 8.0 Hz), 7.87 (1H, t, J = 8.0 Hz); EIMS m/z (rel intensity) 394 (M⁺, 10%), 359 (100).

Sulphonate 2a. Starting with 1a and following the procedure for the preparation of 2b gave 2a (85%) as an oil; 1H NMR (CDCl₃, 400 MHz) δ 8.06 (1H, d, J = 8.0 Hz), 8.02 (1H, d, J = 8.0 Hz), 7.91 (1H, d, J = 8.0 Hz), 7.74 (1H, t, J = 8.0 Hz), 7.62 (2H, d, J = 9.0 Hz), 6.72 (2H, d, J = 9.0 Hz); EIMS m/z (rel intensity) 578 (M⁺, 100%); HRMS calcd. for C₁₆H₁₆O₂F₅SI 577.9095, found 577.9091.

Sulfonyl chloride 1c. Starting with 1,3-diiodobenzene and C₆F₅I and following the procedure for the preparation of 1b gave crude 1c as a solid (chlorosulfonylation condition: MW irradiation, 300 W, 120 °C, 10 min). Further purification was not performed, because the title compound was decomposed by silica gel column chromatography.

Sulfonyl chloride 2c. Starting with 1c and following the procedure for the preparation of 2b gave 2c (3 steps 44%) as a solid; 1H NMR (CDCl₃, 400 MHz) δ 8.24 (2H, s), 8.08 (1H, s), 7.64 (2H, d, J = 9.0 Hz), 6.72 (2H, d, J = 9.0 Hz); EIMS m/z (rel intensity) 1195 (M⁺, 25%), 219 (100); HRMS calcd. for C₁₆H₁₆O₂F₅SI 1195.8618, found 1195.8610.

Boronate 3. A mixture of indole (2.34 g, 20.0 mmol) and KOH (4.30 g, 76.6 mmol) in DMF (30 ml) was stirred for 10 min. Then the DMF (20 ml) solution of iodine (5.26 g, 20.7 mmol) was added, and the mixture was stirred for 30 min. The mixture was poured into the solution (H₂O 400 ml, 25% aqueous NH₃ 8 ml, Na₂S₂O₅ 400 mg), and the precipitation was filtrated with H₂O. The precipitation was dissolved with CHCl₃, and the organic layer was washed with brine and dried over MgSO₄. The evaporation of the organic phase gave 3-iodoindole.

Et₃N (3.2 ml, 22.8 mmol) was added to a stirred solution of 3-iodoindole, 1b (8.91g, 15.0 mmol), DMAP (366.3 mg, 3.00 mmol) and CH₂Cl₂ (50 ml) at 0 °C. The mixture was stirred for 12 h at rt, and the reaction was monitored by silica gel TLC. The mixture was quenched with H₂O and evaporated. The mixture was purifed by F-SPE (80% MeOH/H₂O-AcOEt) using perfluorinated silica gel to afford 10.54 g (88%) of 3-iodoindole protected by BsRF₆ as a solid; 1H NMR (CDCl₃, 400 MHz)
In a sealed tube, Et3N (0.45 ml, 3.2 mmol) and pinacolborane (0.22 ml, 1.5 mmol) were added into a mixture of 3-iodoindole protected by Br2SiC6 (801.0 mg, 1.00 mmol), PdCl2(dppf) complex with dichloromethane (1:1) (24.5 mg 0.03 mmol), and dioxane (5 ml), and the mixture was heated at 80 °C for 10 h. The evaporation of the reaction mixture gave the crude product, and the crude product was purified by F-SPE (80% MeOH/H2O-AcOEt) using perfluorinated silica gel to afford 250.1 mg (2 steps 88%) of 

\[ \text{C}_{23}\text{H}_{38}\text{NO}_2\text{SiB} \ 399.2765, \text{found} 399.2757. \]

**Dibromobenzoquinone 4.** AcCl (1.2 ml, 16.8 mmol) was added to a mixture of 2,5-dihydroxybenzoquinone (7.00 g, 50 mmol) and MeOH (150 ml), and the mixture was stirred for 24 h at 80 °C. The precipitation was filtration and washed with cold MeOH. The precipitation was dried in vacuo to afford 681.1 g (81%) of 2,5-dimetoxybenzoquinone.

NBS (7.20 g, 40.4 mmol) was slowly added to the mixture of 2,5-dimetoxybenzoquinone (3.36 g, 20.0 mmol) and DMF (100 ml). The mixture was stirred for 15 h at rt. H2O was added to the reaction mixture, the aqueous layer was extracted with AcOEt (3×10 ml). The organic layer was washed with H2O (two times) and brine (two times), and dried over MgSO4. The evaporation of the mixture gave the crude product, and the crude product was purified by silica gel column chromatography with hexane/CHCl3 (50:50)-(0:100) to afford 5.36 g (82%) of 

\[ \text{C}_{22}\text{H}_{21}\text{NO}_2\text{F}_{17}\text{SI} \ 801.9127, \text{found} 801.9136. \]

**Monoidolylbenzoquinone 5.** In a sealed tube, A mixture of 3 (641.1 mg, 0.800 mmol), 4 (1.00 g, 3.08 mmol), TiCl3 (1.121 g, 2.39 mmol), Pd[PPh3]4 (91.1 mg, 0.298 mmol) in benzene (7 ml) was stirred for 24 h at 80 °C. The mixture was filtered by Celite® and washed with AcOEt. The evaporation of the organic phase gave the crude product. The crude product was purified by F-SPE (80% MeOH/H2O–AcOEt) using perfluorinated silica gel to afford 6.81 g (81%) of 2,5-dimetoxybenzoquinone.

In a sealed tube, A mixture of 2,5-dimetoxybenzoquinone (3.36 g, 20.0 mmol), PdCl2(dppf) complex with dichloromethane (1:1) (24.5 mg 0.03 mmol), and dioxane (5 ml), and the mixture was heated at 80 °C for 10 h. The evaporation of the reaction mixture gave the crude product, and the crude product was purified by F-SPE (80% MeOH/H2O–AcOEt) using perfluorinated silica gel to afford 250.1 mg (2 steps 88%) of 

\[ \text{C}_{23}\text{H}_{38}\text{NO}_2\text{SiB} \ 399.2765, \text{found} 399.2757. \]

**Boronate 6.** This was synthesized according to the reported procedure\(^3\). \(^1\)H NMR (CDCl3, 400 MHz) δ 7.96-8.00 (1H, m), 7.59 (1H, s), 7.40-7.43 (1H, m), 1.65 (3H, sept, J = 7.6 Hz), 1.28 (12H, s), 1.05 (18H, d, J = 7.6 Hz); \(^13\)C NMR (CDCl3, 100 MHz) δ 141.73, 141.07, 135.03, 122.28, 121.41, 120.33, 113.63, 82.63 (2C), 25.01 (2C), 18.18 (6C), 12.79 (3C); IR (neat) 1534, 1449, 1387, 1136 cm\(^{-1}\); EIMS m/z (rel intensity) 399 (M\(^+\), 100%), HRMS calcd. for C\(_{38}\)H\(_{21}\)N\(_2\)O\(_6\)F\(_{17}\)S 918.9532, found 918.9527.

**Bisindolylbenzoquinone 7.** In a sealed tube, A mixture of 5 (274.3 mg, 0.298 mmol), 6 (359.0 mg, 0.898 mmol), TiCl3 (420.9 mg, 0.898 mmol), Pd[PPh3]4 (34.4 mg, 0.0298 mmol) in benzene (5 ml) was heated at 80 °C for 24 h. The mixture was filtered by Celite\(^5\) and washed with AcOEt. The evaporation of the organic phase gave the crude product. The mixture was washed with saturated NH\(_4\)Cl and evaporated. The mixture was purified by F-SPE (80% MeOH/H2O–AcOEt) using perfluorinated silica gel to afford 250.1 mg (2 steps 88%) of 

\[ \text{C}_{23}\text{H}_{38}\text{NO}_2\text{SiB} \ 399.2765, \text{found} 399.2757. \]

**Cleaved bisindolylbenzoquinone 8.** Mel (0.020 ml, 0.320 mmol) was added to the mixture of 7 (31.4 mg, 0.0328 mmol), Cs\(_2\)CO\(_3\) (48.7 mg, 0.150 mmol) and DMF (1 ml). The mixture was stirred for 1.5 h at rt. The mixture was quenched with saturated NH\(_4\)Cl and evaporated. The mixture was purified by F-SPE (80% MeOH/H2O–AcOEt) using perfluorinated silica gel to afford 250.1 mg (2 steps 88%) of 

\[ \text{C}_{23}\text{H}_{38}\text{NO}_2\text{SiB} \ 399.2765, \text{found} 399.2757. \]
gel to afford alkylated product 30.5 mg (96%) as a solid; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) 8.22 (1H, s), 8.16 (1H, d, \(J = 8.0\) Hz), 8.00 (1H, d, \(J = 8.0\) Hz), 7.86 (1H, s), 7.78 (1H, d, \(J = 8.0\) Hz), 7.66 (1H, t, \(J = 8.0\) Hz), 7.55 (1H, d, \(J = 8.0\) Hz), 7.50 (1H, s), 7.42 (1H, d, \(J = 8.0\) Hz), 7.27-7.39 (4H, m), 7.19 (1H, t, \(J = 8.0\) Hz), 3.90 (3H, s), 3.85 (3H, s), 3.78 (3H, s); EIMS \(m/z\) (rel intensity) 970 (M\(^-\), 100%); HRMS calced. for C\(_{30}\)H\(_{20}\)N\(_2\)O\(_4\) 970.1005, found 970.1021.

The mixture of above product (8.4 mg, 0.00865 mmol), Mg (2.0 mg, 0.0823 mmol), NH\(_4\)Cl (4.7 mg, 0.0879 mmol), MeOH (1 ml), and THF (1 ml) was stirred for 2 h at rt. The mixture was quenched with saturated NH\(_4\)Cl, and the aqueous layer was extracted with AcOEt (3×5 ml). The organic layer was washed with brine, and dried over MgSO\(_4\). The evaporation

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10.0 Hz), 5.17 (1H, dd, J = 1.0, 17.0 Hz), 4.75 (2H, dt, J = 5.5, 1.0 Hz); EIMS m/z (rel intensity) 930 (M+, 44%), 371 (100); HRMS calcd. for C17H19NO2F18S2 930.0679, found 930.0668.

Ester 17. A mixture of Ethyl 4-iodobenzoate (3.30 ml, 19.6 mmol), C6F4I (5.40 ml, 20.2 mmol) and Cu powder (5.08 g, 80.0 mmol) in DMSO (15ml) was stirred for 24 h at 120 °C. The mixture was filtered by Celite® and washed with AcOEt and H2O. The aqueous layer was extracted with AcOEt (2×15 ml). The organic layer was washed with H2O (two times) and brine, and the organic layer was dried over MgSO4. The evaporation of the organic phase gave the crude product, and the crude product was purified by short-path column chromatography over silica gel with hexane/AcOEt (50:50) to afford 8.23 g (95%) of Ethyl 4-perfluorooctylbenzoate. 1H NMR (CDCl3, 400 MHz) δ 8.18 (2H, d, J = 8.0 Hz), 7.67 (2H, d, J = 8.0 Hz), 4.43 (2H, q, J = 7.0 Hz), 1.42 (3H, t, J = 7.0 Hz); EIMS m/z (rel intensity) 568 (M+, 20%); HRMS calcd. for C17H17F18O2S 568.0331, found 568.0349.

Bnzylbromide 18. The THF (10 ml) solution of 17 (5.21 g, 9.20 mmol) was slowly added to a solution of LiAlH4 (570.1 mg, 15.0 mmol) and THF (30 ml) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and the reaction was monitored by gel TLC. The mixture was quenched with aqueous THF, and 1M HCl was added. The aqueous layer was extracted with AcOEt (3×10 ml). The organic layer was washed with saturated NaHCO3 and brine and dried over MgSO4. The evaporation of the organic phase gave the crude product, and the crude product was purified by short-path column chromatography over silica gel with hexane/AcOEt (70:30)-(50:50) to afford 4.18 g (87%) of benzyl alcohol; 1H NMR (CDCl3, 400 MHz) δ 7.56 (2H, d, J = 8.0 Hz), 7.46 (2H, d, J = 8.0 Hz), 4.72 (2H, s); EIMS m/z (rel intensity) 526 (M+, 72%); HRMS calcd. for C13H15OF17S 526.0225, found 526.0217.

Monoindolylpyrazine 19. Starting with 3 and dihalo pyrazine3 and following the procedure for the preparation of 5 gave 21. 1H NMR (CDCl3, 500 MHz) δ 8.62 (1H, d, J = 8.0 Hz), 8.45 (1H, s), 8.33 (1H, s), 8.22 (1H, s), 8.07 (1H, t, J = 8.0 Hz), 8.02 (1H, d, J = 8.0 Hz), 7.75 (1H, t, J = 8.0 Hz), 7.59 (1H, t, J = 8.0 Hz), 7.31-7.41 (2H, m), 4.19 (3H, s); 13C NMR (CDCl3, 125 MHz) δ 156.31, 138.95, 137.32, 136.71, 134.80, 132.63, 132.18, 130.56, 130.15, 129.22, 128.42, 125.67 (2C), 124.52, 123.86, 117.18, 113.07, 54.93, the other C of perfluoroalkyl unit were not assigned.; IR (neat) 1526, 1478, 1200, 1152, 1142 cm−1; EIMS m/z (rel intensity) 863 (M2+, 100%), 861 (M+, 93%), HRMS calcd. for C27H13N3O3BrF17S 860.9590, found 860.9570.

Boronate 20. In a sealed tube, A mixture of Product 22 (49.9 mg, 0.0606 mmol), Pd(PPh3)4 (5.8 mg, 0.005 mmol) in benzene (2.5 ml) was heated at 80 °C for 24 h. The mixture was filtered with Celite® and washed with AcOEt. The evaporation of the organic phase gave the crude product. The crude product was purified by F-SPE (80% MeOH/H2O-MeCN-THF) using perfluorinated silica gel. The MeCN eluent contained 72.1 mg (98%) of boronate 20.

Double tagged compound 21. In a sealed tube, A mixture of Product 22 (10.0 mg, 0.0067 mmol) and THF (1 ml), and the mixture was stirred for 1 h at rt. The reaction was monitored by TLC and quenched with saturated NH4Cl. The mixture was extracted with AcOEt and H2O, and the organic layer was washed with saturated NaHCO3 and brine, and the organic layer was dried over MgSO4. The evaporation of the organic phase gave the crude product, and the crude product was purified by short-path column chromatography over silica gel with hexane/AcOEt (50:50) to afford 10.5 g (95%) of Ethyl 4-perfluorooctylbenzoate. 1H NMR (CDCl3, 400 MHz) δ 8.18 (2H, d, J = 8.0 Hz), 7.67 (2H, d, J = 8.0 Hz), 4.43 (2H, q, J = 7.0 Hz), 1.42 (3H, t, J = 7.0 Hz); EIMS m/z (rel intensity) 1478 (M+, 100%); HRMS calcd. for C27H29N4O4F18S2 1478.1238, found 1478.1244. The THF eluent contained the trace amount of unreacted 19 and excess 20.

Product 22. TBAF (30.1 mg, 0.115 mmol) was added to the mixture of 21 (10.0 mg, 0.0067 mmol) and THF (1 ml), and the mixture was stirred for 1 h at rt. The reaction was monitored by TLC and quenched with saturated NH4Cl. The mixture was evaporated, and purified by F-SPE (80% MeOH/H2O-AcOEt) using perfluorinated silica gel. The 80% MeOH/H2O
eluent contained the hydrolyzed BsRf. The AcOEt eluent contained 6.1 mg (98%) of deprotected compound as a solid; 1H NMR (CDCl3, 400 MHz) δ 8.85-8.87 (1H, m), 8.53 (1H, s), 8.50 (1H, s), 8.30 (1H, d, J = 3.0 Hz), 7.99 (1H, d, J = 8.0 Hz), 7.53 (2H, d, J = 3.0 Hz), 7.45-7.47 (1H, m), 7.34-7.39 (2H, m), 7.26-7.31 (5H, m), 5.86 (2H, s), 4.21 (2H, t, J = 7.0 Hz), 4.18 (3H, s), 1.05 (3H, q, J = 7.0 Hz); EIMS m/z (rel intensity) 920 (M+, 100%); HRMS calcd. for C39H25N4O3F17 920.1655, found 920.1642.

MeI (5 µl, 0.08 mmol) was added to the mixture of the above deprotected product (6.1 mg, 6.6×10^-3 mmol), Cs2CO3 (16.0 mg, 0.049 mmol) and DMF (0.5 ml). The mixture was stirred for 1.5 h at rt. The mixture was quenched with saturated NH4Cl and the organic solvent was evaporated. The mixture was purified by F-SPE (80% MeOH/H2O-AcOEt) using perfluorinated silica gel to afford 6.0 mg (97%) of 22 as a solid; 1H NMR (CDCl3, 500 MHz) δ 8.86 (1H, d, J = 8.0 Hz), 8.51 (1H, s), 8.14 (1H, s), 8.00 (1H, d, J = 8.0 Hz), 7.52 (2H, d, J = 8.4 Hz), 7.26-7.30 (8H, m), 5.86 (2H, s), 4.20 (2H, q, J = 7.0 Hz), 4.19 (3H, s), 1.04 (3H, q, J = 7.0 Hz); EIMS m/z (rel intensity) 934 (M+, 100%); HRMS calcd. for C40H27N4O3F17 934.1812, found 934.1832.

Product 23. PhCOCl (5 µl, 0.045 mmol) was added to the mixture of the above deprotected product (13.5 mg, 0.0147 mmol), DMAP (0.4 mg, 0.003 mmol), Et3N (10 µl, 0.070 mmol), and CH2Cl2 (0.5 ml) at 0 °C. The mixture was stirred for 2 h at rt. The reaction was quenched with H2O, and the organic solvent was evaporated. The mixture was purified by F-SPE (80% MeOH/H2O-AcOEt) using perfluorinated silica gel to afford 13.8 mg (92%) of 23 as a solid; 1H NMR (CDCl3, 500 MHz) δ 8.42-8.60 (1H, m), 8.57 (1H, s), 8.43-8.45 (1H, s), 8.39 (1H, s), 7.96 (1H, d, J = 8.0 Hz), 7.86-7.88 (2H, m), 7.68 (1H, t, J = 8.0 Hz), 7.58-7.61 (2H, m), 7.52-7.55 (3H, m), 7.45-7.47 (2H, m), 7.38-7.40 (2H, m), 7.26-7.29 (2H, m), 5.86 (2H, s), 4.21 (2H, q, J = 7.0 Hz), 4.05 (3H, s), 1.05 (3H, s); EIMS m/z (rel intensity) 1024 (M+, 100%); HRMS calcd. for C46H29N4O4F17 1024.1917, found 1024.1924.

References
