Supporting Information. Experimental Section

General. Melting points were determined with Buchi B-545 apparatus without corrections. NMR data were recorded on a Bruker DPX-300 spectrometer. The ^{1}H NMR chemical shifts are reported as δ values in ppm downfield from TMS, using the solvent peak as an internal reference. The MS spectra were obtained using a Perkin Elmer SCIEX API150 EX equipped with either APCI (heated nebulizer) or ESI sprayer interface by flow injection analysis method (10 μL injected). Flash chromatography was carried out on silica gel 60 (230-400 mesh).

General procedure for the synthesis of compounds 2. (±)-4-Oxiranylmethyl-piperazine-1-carboxylic acid tert-butyl ester (2a). Anhydrous K_2CO_3 (4.12 g, 29.8 mmol) and a solution of Boc-piperazine (5.05 g, 27.1 mmol) of ACN (65 mL) were added to a solution of epibromohydrin (4.27 g, 31.2 mmol) in ACN (40 mL) at 0°C. After 48 hr at rt, the reaction mixture was filtered off and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (Rf = 0.35, EtOAc/MeOH 95:5) to give 5.71 g of the title compound as a colorless oil (87%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.46 (t, 4H, *J* = 5.1 Hz), 3.10 (m, 1H), 2.77 (m, 2H), 2.59-2.46 (m, 5H), 2.27 (dd, 1H, *J* = 13.4, 7.0 Hz), 1.46 (s, 9H). MS (APCI), *m/z*: 243 $[M+H]^+$.

(±)-1-(4-Fluorobenzyl)-4-oxiranylmethyl-piperazine (2b) was prepared with 1-(4-fluorobenzyl)-piperazine as described for compound **2a**. The title compound was obtained as a colorless oil in a 83% yield after purification by flash chromatography (Rf = 0.30, DCM/MeOH 95:5). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (m, 2H), 6.95 (m, 2H), 3.48 (d, 1H, *J* = 13.5 Hz), 3.43 (d, 1H, *J* = 13.5 Hz), 3.07 (m, 1H), 2.70 (dd, 1H, *J* = 13.2, 3.6 Hz), 2.60-2.44 (m, 10H), 2.26 (dd, 1H, *J* = 13.2, 6.7 Hz). MS (APCI), *m/z*: 251 $[M+H]^+$.

(±)-1-(4-Fluorophenyl)-4-oxiranylmethyl-piperazine (2c) was prepared with 1-(4-fluorophenyl)-piperazine as described for compound **2a**. The compound was obtained as a yellow oil in a 75% yield after purification by flash chromatography (DCM/MeOH 95:5). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.97-6.83 (m, 4H), 3.13 (m, 5H), 2.85-2.63 (m, 6H), 2.50 (dd, 1H, *J* = 5.0, 2.7 Hz), 2.30 (dd, 1H, *J* = 13.2, 6.9 Hz). MS (APCI), *m/z*: 237 $[M+H]^+$.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-piperazin-1-yl-propan-2-ol (1). TFA (1.5 mL) was added to a solution of **3** (200 mg, 0.35 mmol) in DCM (6 mL) and the reaction mixture was stirred at rt for 40 min. Concentration in vacuo gave an oily residue which was purified by flash chromatography (ACN/NH_3 (25% aqueous) 5:1). Treatment with excess of TFA in Et_2O gave the TFA salt of the title compound (153 mg, 63%) as a white solid. Mp 133 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.84 (br s, 2H), 8.46 (d, 2H, *J* = 1.7 Hz), 7.67-7.58 (m, 4H), 4.43-4.30 (m, 2H), 4.18 (br s, 1H), 3.18 (br s, 4H), 2.93 (br s, 6H). MS (APCI), *m/z*: 468 $[M+H]^+$. Anal. ($C_{19}H_{21}Br_2N_3O$. 2TFA. 0.13Et_2O) C, H, N.

(±)-4-[3-(3,6-Dibromocarbazol-9-yl)-2-hydroxy-propyl]-piperazine-1-carboxylic *tert*-butyl ester (3). Sodium hydride (265 mg, 55-65% oil suspension) was added to a solution of 3,6-dibromo-9H-carbazole (2.0 g, 6.12 mmol) in anhydrous THF (25 mL) under argon. After 30 min of stirring at rt, a solution of compound 2a (1.0 g, 4.13 mmol) in THF (3 mL) was added. After 16 hr at rt, the reaction mixture was quenched with a saturated aqueous solution of K_2CO_3 (100 mL) and extracted with DCM (500 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (DCM/MeOH 97:3) to give 1.69 g of the title compound as a pale yellow foam (72%). Mp 90-95 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, 2H, *J* = 1.9 Hz), 7.51 (dd, 2H, *J* = 8.7, 1.9 Hz), 7.32 (d, 2H, *J* = 8.7 Hz), 4.33-4.19 (m, 2H), 4.13 (m, 1H), 3.36 (br s, 4H), 2.50 (m, 2H), 2.36 (m, 2H), 2.26 (m, 2H), 1.45 (s, 9H). MS (APCI), *m/z*: 568 $[M+H]^+$.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-[4-(4-methoxybenzyl)-piperazin-1-yl]propan-2-ol (4). A solution of **1** (0.5 g, 1.07 mmol) in TMOF (170 mL) was treated with 4-methoxybenzaldehyde (437 mg, 3.21 mmol) for 4 hr at rt under argon. Then sodium triacetoxy borohydride (680 mg, 3.21 mmol) was added neat. After 2 hr of stirring at rt, the reaction mixture was quenched with water (70 mL), extracted with Et_2O (3 x 400 mL) and dried over $MgSO_4$. Evaporation in vacuo gave an oily residue, which was purified by flash chromatography (DCM/MeOH 95:5). Treatment with excess of HCl (1M in Et_2O) in DCM gave the HCl salt of the title compound (305 mg, 43%) as a white powder. Mp 251 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.45 (d, 2H, *J* = 1.7 Hz), 7.70-7.57 (m, 4H), 7.42 (d, 2H, *J* = 8.2 Hz), 6.98 (d, 2H, *J* = 8.2 Hz), 4.37-4.10 (m, 5H), 3.76 (s, 3H), 3.50-2.90 (m, 10H). MS (APCI), *m/z*: 588 $[M+H]^+$.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-[4-(4-*tert*-butylbenzyl)-piperazin-1-yl]propan-2-ol (5). A solution of **1** (100 mg, 0.21 mmol) in TMOF (5 mL) was treated with 4-*tert*-butylbenzaldehyde (208 mg, 1.28 mmol) for 4 hr under argon. Then sodium triacetoxy borohydride (277 mg, 1.31 mmol) was added neat. After 2 hr of stirring at rt, the reaction mixture was quenched with water (2 mL), extracted with Et_2O (3 x 4 mL) and dried over $MgSO_4$. Evaporation in vacuo gave an oily residue, which was purified by flash chromatography (DCM/MeOH 95:5). Treatment with excess of HCl (1M in Et_2O) in MeOH gave the HCl salt of the title compound (70 mg, 48%) as a white powder. Mp 242 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.46 (d, 2H, *J* = 1.8 Hz), 7.68 (d, 2H, *J* = 8.8 Hz), 7.60 (dd, 2H, *J* = 8.8, 1.8 Hz), 7.47 (br s, 4H), 4.45-4.15 (br s, 5H), 3.52-2.93 (m, 10H), 1.27 (s, 9H). MS (APCI), *m/z*: 614 $[M+H]^+$.

(±)-4-[3-(3,6-Dibromocarbazol-9-yl)-2-hydroxypropyl]-N-(4-fluorophenyl)piperazine-1-carboxamide (6). DIEA (80 μL, 1 equiv.) and 1-fluoro-4-isocyanatobenzene (60 mg, 1 equiv.) were added to a solution of **1** (200 mg, 0.43 mmol) in DCM (10 mL). The reaction mixture was stirred for 4 hr. The solvent was evaporated off. The residue was purified by flash chromatography (Rf = 0.41, DCM/MeOH 95:5). Treatment with excess of HCl (1M in Et_2O) in DCM gave the HCl salt of the title compound (125 mg, 48%) as a white powder. Mp 184 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.40 (br s, 2H), 7.60 (d, 2H, *J* = 8.3 Hz), 7.55 (d, 2H, *J* = 8.3 Hz), 7.34 (m, 2H), 7.01 (m, 2H), 4.33 (br s, 3H), 4.07 (m, 2H), 3.50-2.90 (m, 8H). MS (APCI), *m/z*: 605 $[M + H]^+$, *m/z*: 603 $[M-H]^-$.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-[4-(2-morpholin-4-ethyl)piperazin-1-yl]propan-2-ol (7). A solution of **10** (1.65 g, 4.33 mmol) and 4-(2-piperazin-1-ylethyl)morpholine (2.55 g, 12.8 mmol) in anhydrous THF/absolute EtOH (1:1, 50 mL) was stirred at 60 °C for 18 hr. The solvents were evaporated off. The residue was purified by flash chromatography (EtOAc/MeOH/NH_3 (25% aqueous) 16:3:1) to give 2.45 g (97%) of the title compound as a pale yellow foam. Treatment with excess of HCl (1M in Et_2O, 21.5 mL) in MeOH/DCM (2:1, 150 mL) gave the HCl salt of the title compound as a white powder. Mp 270 °C. ^{1}H NMR (DMSO-d_6 + MeOD-d_4, 300 MHz) δ 8.47 (d, 2H, *J* = 1.9 Hz), 7.72 (d, 2H, *J* = 8.7 Hz), 7.60 (dd, 2H, *J* = 8.7, 1.9 Hz), 4.42 (br s, 3H), 3.88 (br s, 4H), 3.75-2.80 (m, 18H). MS (APCI), *m/z*: 581 $[M+H]^+$. Anal. ($C_{25}H_{32}Br_2N_4O_2$. 3HCl) C, H, N.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-[4-(4-fluorobenzyl)-piperazin-1-yl]-propan-2-ol (8). Sodium hydride (460 mg, 55-65% oil suspension) was added to a solution of 3,6-dibromo-9H-carbazole (3.15 g, 9.68 mmol) in anhydrous THF (50 mL) under argon. After 15 min of stirring at rt, a solution of **2b** (2.20 g, 8.80 mmol) in anhydrous THF (10 mL) was added. After 16 hr at reflux, the reaction mixture was quenched with a saturated aqueous solution of K_2CO_3, extracted with DCM, dried over $MgSO_4$ and concentrated in vacuo. The residue was

purified by flash chromatography (DCM/MeOH 95:5) to give the title compound as an oil. Slow addition of HCl (1M in Et_2O) into a solution of the above compound in MeOH gave the hydrochloride salt of the title compound (3.42 g, 60%) as a white solid. Mp 297 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.44 (d, 2H, *J* = 1.8 Hz), 7.67 (d, 2H, *J* = 8.7 Hz), 7.59 (dd, 2H, *J* = 8.7, 1.8 Hz), 7.54 (m, 2H), 7.27 (m, 2H), 4.45-4.2 (m, 5H), 3.70-3.10 (m, 10H). MS (APCI), *m/z*: 576 $[M+H]^+$. Anal. ($C_{26}H_{26}Br_2FN_3O.2HCl$) C, H, N.

(±)-1-[(4-Fluorophenyl)-piperazin-1-yl]-3-(3,6-dibromo-carbazol-9-yl)-propan-2-ol (9). Sodium hydride (15 mg, 55-65% oil suspension) was added to a solution of 3,6-dibromo-9H-carbazole (98 mg, 0.30 mmol) in anhydrous THF (5 mL) under argon. After 15 min of stirring at rt, a solution of **2c** (60 mg, 0.25 mmol) in anhydrous THF (1 mL) was added. After 16 hr at 60 °C, the reaction mixture was quenched with of a saturated aqueous solution of K_2CO_3, extracted with DCM, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (Rf = 0.4, DCM:MeOH 95:5) to give the title compound as an oil. Slow addition of HCl (1M in Et_2O) into a solution of the above compound in DCM gave the hydrochloride salt of the title compound (89 mg, 56%) as a white solid. Mp 230 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.44 (d, 2H, *J* = 1.8 Hz), 7.66 (d, 2H, *J* = 8.8 Hz), 7.60 (dd, 2H, *J* = 8.8, 1.8 Hz), 7.07 (m, 2H), 6.97 (m, 2H), 4.39 (br s, 3H), 3.69-3.39 (m, 4H), 3.30-2.92 (m, 6H). MS (APCI), *m/z*: 562 $[M+H]^+$. Anal. ($C_{25}H_{24}Br_2FN_3O.2HCl.0.5H_2O$) C, N; H: calcd, 4.23; found, 4.67.

4-[3-(3,6-Dibromocarbazol-9-yl)-2-oxopropyl]-piperazine-1-carboxylic tert-butyl ester (11). Anhydrous DMSO (310 µL, 4.37 mmol) was added to a solution of oxalyl chloride (200 µL, 2.34 mmol) in anhydrous DCM (20 mL) at -78°C. After 15 min of stirring at -78°C, a solution of **3** (1.00 g, 1.76 mmol) in anhydrous DCM (5 mL) was added dropwise. The resulting mixture was stirred for 40 min at -78°C and then TEA (1250 µL, 9.0 mmol) was added neat. After 10 min, the reaction mixture was allowed to warm up to -30°C. After 1 hr of stirring at -30°C, the reaction mixture was quenched with water (50 mL), extracted with DCM (3x100 mL), dried over $MgSO_4$ and evaporated under vacuo. The residue was purified by flash chromatography (Rf = 0.30, Et_2O/MeOH 100:1) to give 804 mg of the title compound as a pale yellow foam (81%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12 (d, 2H, *J* = 1.9 Hz), 7.52 (dd, 2H, *J* = 8.6, 1.9 Hz), 7.12 (d, 2H, *J* = 8.6 Hz), 5.00 (s, 2H), 3.39 (m, 4H), 3.05 (s, 2H), 2.32 (m, 4H), 1.42 (s, 9H). MS (APCI), *m/z*: 566 $[M + H]^+$, *m/z*: 564 $[M-H]^-$.

1-(3,6-Dibromo-carbazol-9-yl)-3-piperazin-1-yl-propan-2-one (12). TFA (250 µL) was added to a solution of **11** (38 mg, 0.067 mmol) in DCM (1 mL). The reaction mixture was stirred at rt for 45 min and then concentrated in vacuo. The residue was purified by flash chromatography (Rf = 0.5, DCM/MeOH/TEA 40:10:1) to give 26 mg (83%) of the title compound as a white solid. Slow addition of HCl (1M in Et_2O) into a solution of the above compound in DCM/MeOH (10:1) gave the hydrochloride salt of the title compound as a white solid. Mp 175 °C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.31 (br s, 2H), 8.48 (d, 2H, *J* = 1.6 Hz), 7.59 (dd, 2H, *J* = 8.8, 1.6 Hz), 7.54 (d, 2H, *J* = 8.8 Hz), 5.52 (s, 2H), 4.18 (m, 2H), 3.25-3.13 (m, 8H). MS (APCI), *m/z*: 466 $[M + H]^+$, *m/z*: 464 $[M-H]^-$.

(±)-3,6-Dibromo-9-(2-fluoro-3-piperazin-1-yl-propyl)-carbazole (13). DAST (5 mL, 40 mmol) was added neat to a solution of **3** (5.07 g, 8.9 mmol) in anhydrous DCM (200 mL) at 0 °C under argon. The reaction mixture was stirred at 0°C for 4 hr and then quenched with a saturated aqueous solution of $NaHCO_3$ (200 mL), extracted with DCM (3 x 500 mL), dried over $MgSO_4$ and evaporated under vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc/Et_2O 1:1:1) to give 1.85 g (37%) of (±)-4-[3-(3,6-dibromo-carbazol-9-yl)-2-fluoro-propyl]-piperazine-1-carboxylic *tert*-butyl ester as a white foam [^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (d, 2H, *J* = 1.9 Hz), 7.50 (dd, 2H, *J* = 8.7, 1.9 Hz), 7.29 (d, 2H, *J* = 8.7 Hz), 4.98 (dm, 1H, *J* = 47.3 Hz), 4.53-4.46 (m, 2H), 3.45 (m, 4H), 2.54 (m, 2H), 2.41 (br s, 4H), 1.44 (s, 9H)]. Then TFA (10 mL) was added to a solution of (±)-4-[3-(3,6-dibromo-carbazol-9-yl)-2-fluoro-propyl]-piperazi-ne-1-carboxylic *tert*-butyl ester (1.85 g, 3.25 mmol) in DCM (40 mL). The reaction mixture was stirred at rt for 60 min and then concentrated under vacuo. The residue was taken up with an aqueous saturated solution of K_2CO_3 (50 mL), extracted with DCM (4 x 100 mL), dried over $MgSO_4$ and the solvent was removed under vacuo to give 1.41 g (93%) the title compound as a pale yellow solid. Slow addition of HCl (1M in Et_2O, 9 mL) into a solution of the above compound in Et_2O (150 mL) gave the hydrochloride salt of the title compound as a white solid. Mp 314 °C. ^{1}H NMR (DMSO-d_6 + D_2O, 300 MHz) δ 8.48 (d, 2H, *J* = 1.8 Hz), 7.68 (d, 2H, *J* = 8.8 Hz), 7.62 (dd, 2H, *J* = 8.8, 1.8 Hz), 5.38 (dm, 1H, *J* = 52.2 Hz), 4.80-4.62 (m, 2H), 3.40-3.25 (m, 10H). MS (APCI), *m/z*: 470 $[M+H]^+$. Anal. ($C_{19}H_{20}Br_2FN_3.2HCl.0.5H_2O$) C, H, N.

3,6-Dibromo-9-(2,2-difluoro-3-piperazin-1-yl-propyl)-9H-carbazole (14). DAST (100 µL, 0.76 mmol) was added neat to a solution of **11** (0.100 g, 0.18 mmol) in anhydrous DCM (4 mL) at rt under argon. The reaction mixture was stirred for 21 hr and then quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL), extracted with DCM (3x40 mL), dried over $MgSO_4$ and evaporated under vacuo. The residue was purified by flash chromatography (DCM/MeOH 100:1.5) to give 19 mg (18%) of (±)-4-[3-(3,6-dibromocarbazol-9-yl)-2,2-difluoropropyl]-piperazine-1-carboxylic *tert*-butyl ester as a yellow oil [^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, 2H, *J* = 1.9 Hz), 7.53 (dd, 2H, *J* = 8.7, 1.9 Hz), 7.42 (d, 2H, *J* = 8.7 Hz), 4.67 (t, 2H, *J* = 13.0 Hz), 3.47 (m, 4H), 2.64 (t, 2H, *J* = 13.0 Hz), 2.49 (m, 4H), 1.46 (s, 9H); MS (APCI), *m/z*: 588 $[M + H]^+$]. Then TFA (250 µL) was added to a solution of (±)-4-[3-(3,6-dibromocarbazol-9-yl)-2,2-difluoropropyl]-piperazine-1-carboxylic *tert*-butyl ester (19 mg, 0.032 mmol) in DCM (1 mL). The resulting mixture was stirred at rt for 60 min and then concentrated in vacuo. The residue was purified by flash chromatography (ACN/25% aqueous NH_3 5:1) to give 13 mg (81%) of the title compound as a yellow oil. [^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (d, 2H, *J* = 1.8 Hz), 7.57 (dd, 2H, *J* = 8.6, 1.8 Hz), 7.46 (d, 2H, *J* = 8.6 Hz), 4.69 (t, 2H, *J* = 13.1 Hz), 3.03 (m, 4H), 2.66 (t, 2H, *J* = 13.0 Hz), 2.62 (m, 4H)]. Slow addition of HCl (1M in Et_2O) into a solution of the above compound in Et_2O gave the hydrochloride salt of the title compound as a beige solid. Mp 305 °C. MS (APCI), *m/z*: 488 $[M+H]^+$.

(±)-1-(3,6-Dibromo-carbazol-9-yl-)-3-piperazin-1-ylpropan-2-amine (15). A solution of **11** (50 mg, 0.088 mmol) and NH_3 0.5M in 1,4-dioxane (1.8 mL) in anhydrous TMOF (1 mL) was stirred at 60°C for 3 hr. The reaction mixture was cooled at 10 °C, then MeOH (2 mL) and $NaBH_4$ (120 mg) were added. After 15 hr of stirring at rt, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (15 mL), extracted with Et_2O (3 x 25 mL), dried over $MgSO_4$ and evaporated under vacuo. The residue was purified by flash chromatography (EtOAc/MeOH/NH_3 (25% aqueous) 80:8:1) to give 29 mg (58%) of (±)-4-[3-(3,6-dibromocarbazol-9-yl)-2-aminopropyl]-piperazine-1-carboxylic *tert*-butyl ester as a pale yellow oil [^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, 2H, *J* = 1.9 Hz), 7.52 (dd, 2H, *J* = 8.7, 1.9 Hz), 7.34 (d, 2H, *J* = 8.7 Hz), 4.25 (dd, 1H, *J* = 14.7, 4.5 Hz), 4.11 (dd, 1H, *J* = 14.7, 7.9 Hz), 3.51 (m, 1H), 3.39 (m, 4H), 2.37 (m, 6H), 1.46 (br s, 2H), 1.43 (s, 9H); MS (APCI), *m/z*: 567 $[M + H]^+$]. Then TFA (1 mL) was added to a solution of (±)-4-[3-(3,6-dibromocarbazol-9-yl)-2-aminopropyl]-piperazine-1-carboxylic *tert*-butyl ester (29 mg, 0.051 mmol) in DCM (4 mL). The reaction mixture was stirred at rt for 40 min and concentrated under vacuo. The residue was purified by flash chromatography (ACN/NH_3 (25% aqueous) 5:1) to give 24 mg (99%) of the title compound as a colorless oil. Slow addition of HCl (1M in Et_2O) into a solution of the above compound in Et_2O gave the hydrochoride salt of the title compound as a white solid. Mp 236 °C. ^{1}H NMR (DMSO-d_6/ MeOD-d_4 35:1, 300 MHz) δ 8.45 (d, 2H, *J* = 1.5 Hz), 7.71 (d, 2H, *J* = 8.7 Hz), 7.59 (dd, 2H, *J* = 8.7, 1.5 Hz), 4.59 (m,

2H), 3.75 (m, 1H), 2.91 (m, 4H), 2.80-2.45 (m, 6H). MS (APCI), m/z: 467 $[M+H]^+$.

(±)-1-(3,6-Dibromocarbazol-9-yl)-3-{[4-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene-8-yl)methyl]pipe-razin-1-yl}propan-2-ol (16). A solution of **1** (14 mg, 0.029 mmol), 8-bromo-methyl-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene (BODIPY 493/503 methyl bromide, B-2103 available from Molecular Probes) (10 mg, 0.029 mmol) and DIEA (4.9 µL, 0.029 mmol) in DMF (1 mL) was stirred at rt for 48 hr in the dark and under argon. The solvent was removed under vacuo and the residue was purified by flash chromatography (Rf = 0.24, DCM/MeOH/25% aqueous NH_3 90/1/0.1) to give 6 mg (29%) of the title compound as a red solid. MS (APCI), m/z: 728 $[M+H]^+$, m/z: 726 $[M-H]^-$.

(±)-4-[({-[3-(3,6-Dibromocarbazol-9-yl)-2-hydroxypropyl]piperazin-1-yl}acetyl)amino]-2-(6-hydroxy-3-oxo-*3H*-xan-then-9-yl)benzoic acid (17). A solution of **1** (45 mg, 0.10 mmol), 5-(iodoacetamido)-fluorescein (5-IAF, I-3 available from Molecular Probes) (52 mg, 0.10 mmol) and DIEA (17 µL, 0.10 mmol) in DMF (2 mL) was stirred at rt for 48 hr in the dark and under argon. The solvent was removed under vacuo and the residue was purified by reverse-phase preparative HPLC (Waters Nova-Pack HR C18 column, ACN/H_2O gradient with 0.1% TFA) to give 40 mg (47%) of the title compound as an orange powder. Mp 107 °C. MS (APCI), m/z: 853 $[M-H]^-$.

Biological Assay.

Mitochondria cytochrome c release assay. The HeLa cells were suspended in buffer A (10 mM Hepes-NaOH, 210 mM mannitol, 70 mM sucrose, 1 mM EDTA, pH 7.4) and disrupted by passage through a 25G1 needle and the mitochondria were isolated by differential centrifugation. The isolated mitochondria were diluted to 0.4 mg/ml in buffer B (10 mM Hepes-NaOH, 125 mM KCl, 4 mM $MgCl_2$, 5 mM NaH_2PO_4, 0.5 mM EGTA, pH 7.4). The compounds were added to 1 ml mitochondria samples and the samples were incubated for 5 min at room temperature. Caspase 8 cut Bid was subsequently added to a final concentration of 10 nM, the samples were incubated at 30°C for 15 min and centrifuged at 13,000 x g for 10 min. The supernatant was removed, recentrifuged at 13,000 x g for 10 min and analyzed on western blot with an in house raised rabbit polyclonal anti-cytochrome c antibody. The western blots were developed with ECL, densitometer scanned and the intensity of the band corresponding to cytochrome c was determined. Each western blot contained a negative (no cut Bid added) and a positive (cut Bid added) control and each sample was analyzed in duplicate. The cytochrome c level in the negative control was substracted from all samples, the positive control was taken as 100% cytochrome c release and % inhibition induced by the compounds was calculated. Values are the mean of two or more separate experiments ±SD.

Liposome channel activity assay. Liposomes containing 20 mM 5,6-carboxyfluorescine in PBS were diluted in PBS to give a suitable fluorescence level. The channel activity assay was performed in 96-well plates on the FLIPER. For the assay 70 µl PBS, 15 µl oligomeric Bax (1 µM) in PBS and 10 µl compound in 8 dilutions (final concentrations 22 nM to 3.8 µM) in 10% DMSO/PBS were mixed in a 96 well plate and incubated at room temperature for 1 minute. At the end of the incubation 20 µl liposomes in PBS was added and the fluorescence monitored in the FLIPER every 3 sec for 3 min. The fluorescence values at 120 sec were used for calculation of the IC_{50} values.