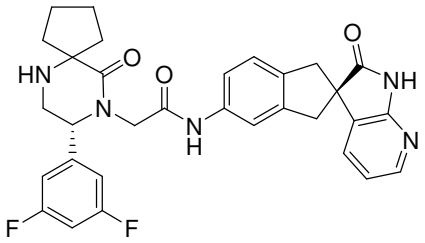
SUPPORTING INFORMATION

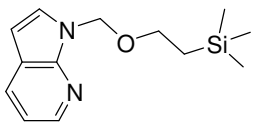
General Experimental Methods

Proton NMR spectra were run at 500 MHz on Varian spectrometers, and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as internal standard. Electrospray mass spectra were recorded on a Micromass ZMD spectrometer. Silica gel chromatography was conducted using Isco CombiFlash instruments and RediSep silica gel cartridges. Analytical HPLC was conducted using either system A or system B as follows. System A: Hewlett Packard 1100 Series instrument and the following conditions: A = H_2O – 0.1% TFA; B = CH_3CN – 0.08% TFA. Gradient: A:B 95:5 to 5:95 over 5 min. Flow rate = 2 mL/min. Column: Zorbax Extend-C18 3.5 µm 4.6 × 75 mm. System B: Waters 2690 separations module and the following conditions: A = 92% H_2O – 8% CH_3CN – 0.05% TFA; B = CH_3CN – 0.0425% TFA. Gradient: A:B 92:8 to 0:100 over 4.2 min. Flow rate = 1.5 mL/min. Column: YMC Pro C18 5 µm 120 Å 3.0 × 50 mm. Reagents and solvents were purchased from commercial vendors and used without further purification. The reported yields represent actual isolated yields of purified material and are not optimized.

Representative Procedures: Synthesis of Compound 4



2-[(8*R*)-8-(3,5-Difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide (4).



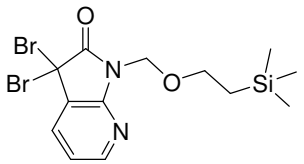
1-{[2-(Trimethylsilyl)ethoxy]methyl}-1*H*-pyrrolo[2,3-b]pyridine (19).

Sodium hydride (60% dispersion in mineral oil; 16.2 g, 0.404 mol) was added in portions over 25 min to a solution of 7-azaindole (39.8 g, 0.337 mol) in *N*,*N*-dimethylformamide

(200 mL) at 0 °C and the mixture was stirred for 1 h. 2-(Trimethylsilyl)ethoxymethyl chloride (71.8 mL, 0.404 mol) was then added slowly over 15 min, keeping the temperature of the reaction mixture below 10 °C. After 1 h, the reaction was quenched with water (500 mL) and the mixture was extracted with dichloromethane (5 × 300 mL). The combined organic layers were washed with saturated brine, dried over magnesium sulfate, filtered, concentrated and dried under high vacuum to provide the title compound (84 g, 100%).

^{1}H NMR ($CDCl_3$) δ 8.35 (1H, dd, *J* = 4.6, 1.5 Hz), 7.93 (1H, dd, *J* = 7.9, 1.5 Hz), 7.37 (1H, d, *J* = 3.7 Hz), 7.11 (1H, dd, *J* = 7.8, 4.6 Hz), 6.53 (1H, d, *J* = 3.4 Hz), 5.71 (2H, s), 3.56 (2H, m), 0.92 (2H, m), -0.06 (9H, s).

MS: *m*/*z* = 249 (M + 1).

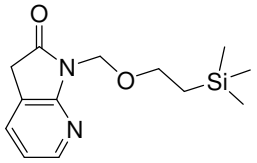


3,3-Dibromo-1-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2*H*-pyrrolo[2,3-b]pyridin-2-one (20).

1-{[2-(Trimethylsilyl)ethoxy]methyl}-1*H*-pyrrolo[2,3-b]pyridine (**19**) (43.1 g, 0.174 mol) in dioxane (300 mL) was added dropwise over 30 min to a clumpy suspension of pyridine hydrobromide perbromide (277 g, 0.868 mol) in dioxane (300 mL). The reaction was stirred at room temperature using an overhead mechanical stirrer to produce two layers. After 60 min, the reaction was quenched with water (300 mL) and extracted with ethyl acetate. The aqueous layer was extracted with ethyl acetate (2 × 300 mL) and the combined organic layers were washed with water (4 × 300 mL, until pH of final wash is approx. 5-6) and brine (300mL), dried over magnesium sulfate, filtered and concentrated. The crude product was immediately dissolved in methylene chloride and the solution filtered through a plug of silica, eluting with dichloromethane until the dark red color had completely eluted from the plug. The filtrate was washed with sat. aq. $NaHCO_3$ (400 mL) and brine (400 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give the title compound (60 g, 82%).

^{1}H NMR ($CDCl_3$) δ 8.35 (1H, d, *J* = 4.4 Hz), 8.00 (1H, d, *J* = 7.3 Hz), 7.28 (1H, m), 5.41 (2H, s), 3.74 (2H, m), 0.98 (2H, m), -0.02 (9H, s).

MS: *m*/*z* = 423 (M + 1).

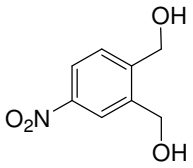


1-{[2-(Trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2*H*-pyrrolo[2,3-b]pyridin-2-one (21).

Zinc (100g, 1.54 mol) was added to a solution of 3,3-dibromo-1-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2*H*-pyrrolo[2,3-b]pyridin-2-one (**20**) (65 g, 0.154 mol) in tetrahydrofuran (880 mL) and saturated aqueous ammonium chloride (220 mL). After 3 h, the reaction was filtered and concentrated. The mixture was partitioned between ethyl acetate and water which resulted in the formation of a white precipitate. Both layers were filtered through Celite and the layers were separated. The aqueous layer was washed with ethyl acetate (2 ×) and the combined organic layers were washed with water, dried over magnesium sulfate, filtered, and concentrated. The crude product was filtered through a plug of silica gel using 10% ethyl acetate/dichloromethane and concentrated to provide the title compound (30 g, 74%).

^{1}H NMR ($CDCl_3$) δ 8.23 (1H, d, J = 5.4 Hz), 7.51 (1H, dd, J = 7.3, 1.2 Hz), 6.98 (1H, dd, J = 7.1, 5.4 Hz), 5.27 (2H, s), 3.70 (2H, m), 0.99 (2H, m), -0.01 (9H, s).

MS: m/z = 265 (M + 1).

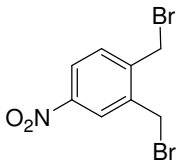


(4-Nitro-1,2-phenylene)dimethanol (22).

4-Nitrophthalic acid (40 g, 189.5 mmol) in tetrahydrofuran (500 mL) was added dropwise over 1.5 h to a solution of borane tetrahydrofuran complex (1 M, 493 mL, 493 mmol) at 0 °C, and the reaction mixture was maintained below 5 °C during the addition. After 2 h, the reaction was allowed to warm to ambient temperature and after 16 h, methanol (20 mL) was added slowly. The mixture was concentrated to ½ volume, cooled to 0 °C, and 10 N aq. sodium hydroxide was added to adjust the pH to 10-11. The solution was extracted with ethyl acetate (3 × 600 mL) and the combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated to give the title compound (35.3 g).

^{1}H NMR ($CDCl_3$) δ 8.29 (1H, d, J = 2.2 Hz), 8.15 (1H, dd, J = 8.5, 2.4 Hz), 7.62 (1H, d, J = 8.3 Hz), 4.76 (2H, s), 4.74 (2H, s), 3.48 (2H, s).

MS: m/z = 207 (M – OH + CH_3CN).

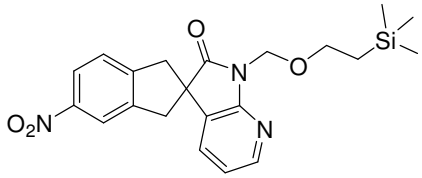


1,2-*Bis*(bromomethyl)-4-nitrobenzene (23).

Phosphorus tribromide (20.1 mL, 212 mmol) in diethyl ether (250 mL) was added dropwise over 1.5 h to a solution of (4-nitro-1,2-phenylene)dimethanol (**22**) (35.3 g, 193 mmol) in diethyl ether (750 mL). After 18 h, the reaction was cooled to 0 °C and quenched with water (100 mL). The layers were separated and the organic layer was washed with water (2 × 200 mL), saturated sodium bicarbonate (100 mL), dried over sodium sulfate, filtered, and concentrated to give the title compound (58.4 g, 100% over 2 steps).

^{1}H NMR ($CDCl_3$) δ 8.26 (1H, d, *J* = 2.4 Hz), 8.16 (1H, dd, *J* = 8.3, 2.4 Hz), 7.56 (1H, d, *J* = 8.3 Hz), 4.68 (2H, s), 4.66 (2H, s).

MS: *m*/*z* = 309 (M + 1).

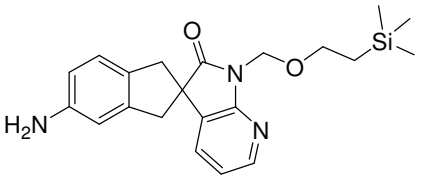


5-Nitro-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'*H*)-one (24).

Cesium carbonate (129 g, 397 mmol) was added portion wise over 5 min to a solution of 1,2-*bis*(bromomethyl)-4-nitrobenzene (**23**) (40.9 g, 132 mmol) and 1-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2*H*-pyrrolo[2,3-b]pyridin-2-one (**21**) (31.5 g, 119 mmol) in DMF (2 L). After 18 h, acetic acid (7.6 mL) was added and the mixture was concentrated to a volume of 500 mL. The mixture was partitioned between ethyl acetate (1.5 L) and water (1L). The organic layer was washed with water (1L), brine (500 mL), dried over sodium sulfate, filtered, and concentrated. Purification by silica gel chromatography, eluting with hexane:EtOAc – 100:0 to 0:100, gave the title compound (37.6 g, 69%).

^{1}H NMR ($CDCl_3$) δ 8.24 (1H, dd, *J* = 5.1, 1.5 Hz), 8.17 (1H, dd, *J* = 8.3, 2.0 Hz), 8.15 (1H, s), 7.43 (1H, d, *J* = 8.3 Hz), 7.07 (1H, dd, *J* = 7.3, 1.5 Hz), 6.88 (1H, dd, *J* = 7.3, 5.1 Hz), 5.31 (2H, s), 3.75-3.70 (4H, m), 3.19 (1H, d, *J* = 16.1 Hz), 3.18 (1H, d, *J* = 16.6 Hz), 1.00 (2H, m), -0.01 (9H, s).

MS: *m*/*z* = 412 (M + 1).

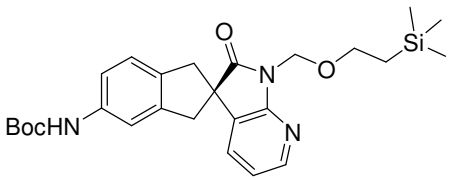


5-Amino-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'*H*)-one (25).

A mixture of 10% Pd/C (3.0 g) and 5-nitro-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'*H*)-one (**24**) (19.1 g, 46.4 mmol) in ethanol (400 mL) was stirred vigorously under an atmosphere of hydrogen (*ca*. 1 atm). After 16 h, methanol (300 mL) was added and the mixture was filtered through Celite, washing exhaustively with methanol, and the filtrate was concentrated to give the title compound (16.9 g, 95%).

^{1}H NMR (DMSO-d_6) δ 8.17 (1H, dd, *J* = 5.1, 1.5 Hz), 7.26 (1H, dd, *J* = 7.3, 1.5 Hz), 6.99 (1H, dd, *J* = 7.3, 5.1 Hz), 6.92 (1H, d, *J* = 8.1 Hz), 6.49 (1H, s), 6.46 (1H, dd, *J* = 7.8, 2.0 Hz), 5.13 (2H, s), 4.98 (2H, br s), 3.61 (1H, t, *J* = 7.9 Hz), 3.27 (1H, d, *J* = 15.6 Hz), 3.24 (1H, d, *J* = 15.1 Hz), 2.96 (1H, d, *J* = 15.1 Hz), 2.93 (1H, d, *J* = 15.6 Hz), 0.86 (1H, t, *J* = 7.9 Hz), -0.06 (9H, s).

MS: *m*/*z* = 382 (M + 1).

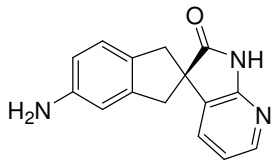


***tert*-Butyl (*R*)-(2'-oxo-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl)carbamate (26).**

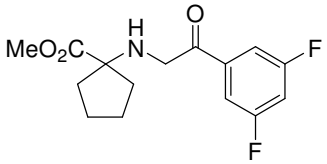
A solution of 5-amino-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'*H*)-one (**25**) (104 g, 273 mmol) and Boc anhydride (71.5 g, 328 mmol) in $CHCl_3$ (1 L) was heated to reflux for 17 h. The cooled mixture was concentrated *in vacuo* and the residue was purified by silica gel chromatography, eluting with hexane:EtOAc – 100:0 to 50:50, to give the title compound (125 g, 95%), which was resolved by HPLC on a ChiralPak AD column, eluting with EtOH, to give the (*R*)-enantiomer, which eluted as the second major peak.

^{1}H NMR (CD_3OD) δ 8.15 (1H, dd, *J* = 5.1, 1.5 Hz), 7.40 (1H, br s), 7.26 (1H, dd, *J* = 8.3, 1.2 Hz), 7.20 (1H, dd, *J* = 7.3, 1.7 Hz), 7.18 (1H, d, *J* = 8.3 Hz), 6.96 (1H, dd, *J* = 7.3, 5.1

Hz), 5.27 (2H, s), 3.73 (1H, m), 3.55-3.49 (2H, m), 3.08-3.03 (2H, m), 0.96 (1H, m), -0.02 (9H, s).
MS: *m*/*z* = 482 (M + 1).



(*R*)-5-Amino-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-2'(1'*H*)-one (18).
A solution of *tert*-butyl (*R*)-(2'-oxo-1'-{[2-(trimethylsilyl)ethoxy]methyl}-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl)carbamate from Step C (13.4 g, 27.8 mmol) in MeOH (300 mL) was saturated with HCl (g). The mixture was resaturated with HCl (g) every 30 min until the starting material was consumed, and then concentrated *in vacuo*. The residue was dissolved in MeOH (150 mL) and treated with ethylenediamine (1.9 mL, 27.8 mmol) and 10 N sodium hydroxide (6 mL, 60 mmol) to adjust the mixture to pH 10. After 30 min, the mixture was diluted with H_2O (400 mL) and extracted with $CHCl_3$ (1 L). The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was triturated with MeOH (35 mL) to give the title compound (5.50 g, 79%).
^{1}H NMR (DMSO-d_6) δ 8.04 (1H, dd, *J* = 5.1, 1.7 Hz), 7.12 (1H, dd, *J* = 7.3, 1.7 Hz), 6.91 (1H, d, *J* = 7.8 Hz), 6.85 (1H, dd, *J* = 7.3, 5.1 Hz), 6.48 (1H, s), 6.46 (1H, dd, *J* = 7.8, 2.0 Hz), 4.94 (2H, br s), 3.25-3.19 (2H, m), 2.92-2.85 (2H, m).
MS: *m*/*z* = 252 (M + 1).

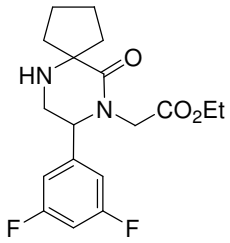


Methyl 1-{[2-(3,5-difluorophenyl)-2-oxoethyl]amino}cyclopentanecarboxylate (15).
A mixture of methyl 1-aminocyclopentanecarboxylate hydrochloride (10.0 g, 55.7 mmol), 3,5-difluorophenacyl bromide (14.4 g, 61.2 mmol), and Na_3PO_4 (22.8 g, 139 mmol) in DMF (100 mL) was stirred at ambient temperature for 3.5 h. The reaction mixture was acidified with 1 N aqueous HCl and the mixture was extracted with EtOAc (200 mL) and this organic extract was discarded. The aqueous layer was adjusted to pH 8-9 by addition of saturated aqueous $NaHCO_3$ and the mixture was extracted with EtOAc (3 × 250 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel

chromatography, eluting with hexane:EtOAc – 90:10 to 50:50, to give the title compound (10.2 g, 62%).

^{1}H NMR ($CDCl_3$) δ 7.46-7.41 (2H, m), 7.03 (1H, tt, *J* = 8.4, 2.3 Hz), 4.02 (2H, s), 3.69 (3H, s), 2.12-2.04 (2H, m), 1.87-1.72 (6H, m).

MS: *m*/*z* = 298 (M + 1).

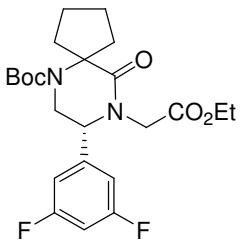


Ethyl [8-(3,5-difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]acetate (27).

A mixture of methyl 1-{[2-(3,5-difluorophenyl)-2-oxoethyl]amino}cyclopentanecarboxylate (**15**) (10.0 g, 33.6 mmol), glycine ethyl ester hydrochloride (46.9 g, 336 mmol), and AcOH (5.78 mL, 101 mmol) in MeOH (300 mL) was stirred at ambient temperature for 10 min. $NaCNBH_3$ (2.54 g, 40.4 mmol) was added and the pH of the mixture was checked and adjusted to pH ~ 5 as necessary. The reaction mixture was heated to 50 °C for 18 h then allowed to cool. The reaction mixture was carefully quenched with saturated aqueous $NaHCO_3$ (250 mL) and then extracted with CH_2Cl_2 (3 × 200 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography, eluting with hexane:EtOAc – 100:0 to 0:100, to give the title compound (6.5 g, 55%).

^{1}H NMR ($CDCl_3$) δ 6.81-6.76 (3H, m), 4.65 (1H, d, *J* = 17.1 Hz), 4.60 (1H, m), 4.18 (2H, q, *J* = 7.1 Hz), 3.51 (1H, dd, *J* = 13.9, 4.6 Hz), 3.17 (1H, d, *J* = 17.3 Hz), 2.93 (1H, dd, *J* = 13.9, 3.9 Hz), 2.33 (1H, m), 2.21 (1H, m), 1.88-1.75 (5H, m), 1.65 (1H, m), 3.69 (3H, s), 2.12-2.04 (2H, m), 1.87-1.72 (6H, m), 1.26 (3H, t, *J* = 7.1 Hz).

MS: *m*/*z* = 353 (M + 1).

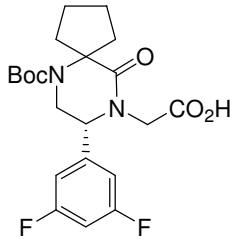


***tert*-Butyl (*R*)-8-(3,5-difluorophenyl)-9-(2-ethoxy-2-oxoethyl)-10-oxo-6,9-diazaspiro[4.5]decane-6-carboxylate (28).**

A solution of ethyl [8-(3,5-difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]acetate (**27**) (22.0 g, 62.4 mmol), *N*,*N*-diisopropylethylamine (5.45 mL, 31.2 mmol), and di-*tert*-butyl dicarbonate (68.1 g, 312 mmol) in acetonitrile (180 mL) was stirred at 60 °C for 6 h, then cooled and concentrated under reduced pressure. The crude product was purified by silica gel chromatography, eluting with hexane:EtOAc – 100:0 to 50:50, to give the title compound (26.5 g, 94%), which was resolved by HPLC on a Chiralcel OD column, eluting with hexane:*i*-PrOH:Et_2NH – 60:40:0.1, to give the (*R*)-enantiomer, which eluted as the second major peak.

^{1}H NMR ($CDCl_3$) δ 6.85-6.81 (2H, m), 6.78 (1H, tt, *J* = 8.7, 2.0 Hz), 4.56 (1H, m), 4.47 (1H, d, *J* = 17.1 Hz), 4.25 (1H, dd, *J* = 13.7, 2.7 Hz), 4.20 (2H, qd, *J* = 7.1, 1.7 Hz), 3.62 (1H, dd, *J* = 13.7, 3.2 Hz), 3.41 (1H, d, *J* = 17.3 Hz), 2.60 (1H, m), 2.43 (1H, m), 2.18 (1H, m), 2.09 (1H, m), 2.00-1.83 (4H, m), 1.27 (3H, m), 1.27 (9H, s).

MS: *m*/*z* = 397 (M – C_4H_7).

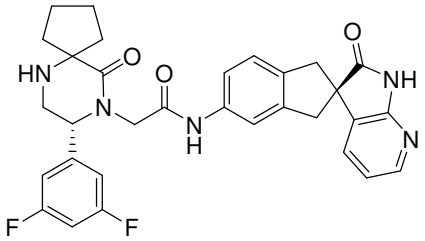


(*R*)-[6-(*tert*-Butoxycarbonyl)-8-(3,5-difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]acetic acid (17).

To a solution of *tert*-butyl (*R*)-8-(3,5-difluorophenyl)-9-(2-ethoxy-2-oxoethyl)-10-oxo-6,9-diazaspiro[4.5]decane-6-carboxylate (**28**) (1.50 g, 3.31 mmol) in THF (8 mL) and H_2O (2 mL) was added 1 N aqueous LiOH (3.31 mL, 3.31 mmol) and the resulting mixture was stirred at ambient temperature for 1 h. The mixture was adjusted to pH 7 by addition of 1 N HCl and concentrated to dryness *in vacuo* to give the title compound (1.42 g, 100%).

^{1}H NMR (CD_3OD) δ 6.98-6.93 (2H, m), 6.91 (1H, tt, *J* = 8.9, 2.2 Hz), 4.75 (1H, m), 4.39 (1H, d, *J* = 16.9 Hz), 4.33 (1H, dd, *J* = 13.8, 2.3 Hz), 3.63 (1H, dd, *J* = 13.9, 3.2 Hz), 3.33 (1H, d, *J* = 16.8 Hz), 2.57 (1H, m), 2.47 (1H, m), 2.14 (1H, m), 2.11 (1H, m), 2.00-1.89 (2H, m), 1.85-1.77 (2H, m), 1.24 (9H, s).

MS: *m*/*z* = 369 (M – C_4H_7).



2-[(8*R*)-8-(3,5-Difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide (4).

A mixture of (*R*)-[6-(*tert*-butoxycarbonyl)-8-(3,5-difluorophenyl)-10-oxo-6,9-diazaspiro[4.5]dec-9-yl]acetic acid (**17**) (9.20 g, 21.4 mmol), (*R*)-5-amino-1,3-dihydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-2'(1'*H*)-one (**18**) (5.91 g, 23.5 mmol), and *N*-methylmorpholine (4.71 mL, 42.8 mmol) was dissolved in degassed DMF (100 mL) and stirred for 15 min. HATU (9.75 g, 25.7 mmol) was added and stirring was continued at ambient temperature for 90 min. The reaction mixture was diluted with EtOAc (1.2 L) and washed successively with 10% citric acid (5 × 200 mL), water (250 mL), sat. aq. $NaHCO_3$ (250 mL), and brine (250 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography, eluting with CH_2Cl_2:MeOH – 100:0 to 90:10, to give the Boc-protected product (12.2 g, 87%). The Boc-protected product (8.5 g, 12.9 mmol) was dissolved in EtOAc (300 mL) and cooled to 0 °C, and HCl (g) was bubbled in for 10 min. After 30 min, HCl (g) was bubbled in for a further 5 min. The mixture was aged at 0 °C for 30 min and the white precipitate was collected by filtration. The solid was dissolved in a minimal volume of MeOH and partitioned between EtOAc (1 L) and sat. aq. $NaHCO_3$ (300 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a white solid which was the title compound (7.0 g, 97%).

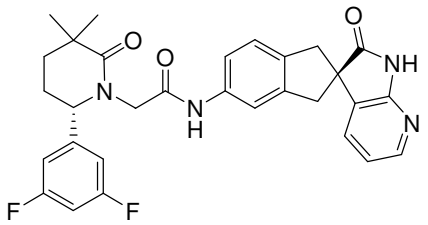
^{1}H NMR (CD_3OD) δ 8.10 (1H, dd, *J* = 5.9, 1.5 Hz), 7.51 (1H, s), 7.47 (1H, dd, *J* = 7.4, 1.3 Hz), 7.40 (1H, d, *J* = 8.3 Hz), 7.25 (1H, d, *J* = 8.1 Hz), 7.16-7.08 (4H, m), 5.18 (1H, dd, *J* = 9.6, 5.0 Hz), 4.57 (1H, d, *J* = 16.4 Hz), 3.90 (1H, dd, *J* = 13.7, 5.1 Hz), 3.62 (1H, dd, *J* = 13.6, 9.6 Hz), 3.57-3.51 (3H, m), 3.19-3.14 (2H, m), 2.68-2.63 (1H, m), 2.50-2.44 (1H, m), 2.23-2.17 (1H, m), 2.04-1.88 (5H, m).

HPLC (system A): r.t. = 3.12 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 558 (M + 1).

HRMS: *m*/*z* = 558.2300; calculated *m*/*z* = 558.2311 for $C_{31}H_{30}F_2N_5O_3$.

Characterization Data for Other Final Compounds



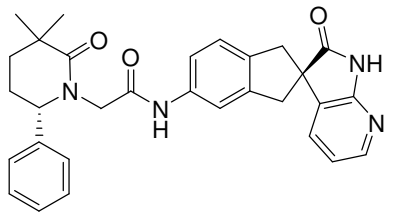
2-[(6*S*)-6-(3,5-Difluorophenyl)-3,3-dimethyl-2-oxopiperidin-1-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-5-yl]acetamide (**5**)

^{1}H NMR ($CDCl_3$) δ 8.69 (1H, s), 8.36 (1H, s), 8.13 (1H, dd, *J* = 5.2, 1.6 Hz), 7.57 (1H, s), 7.21-7.19 (2H, m), 7.07 (1H, dd, *J* = 7.3, 1.5 Hz), 6.83 (1H, dd, *J* = 7.3, 5.2 Hz), 6.81-6.71 (3H, M), 4.85 (1H, t, *J* = 5.0 Hz), 4.57 (1H, d, *J* = 14.7 Hz), 3.63 (2H, dd, *J* = 15.6, 11.5 Hz), 3.37 (1H, d, *J* = 14.4 Hz), 3.06 (2H, dd, *J* = 15.7, 11.1 Hz), 2.40-2.33 (1H, m), 1.90-1.84 (1H, m), 1.75-1.69 (1H, m), 1.59-1.56 (1H, m), 1.38 (3H, s), 1.35 (3H, s).

HPLC (system B): r.t. = 2.60 min, purity = 100% @ 215 nm.

MS: *m*/*z* = 531 (M + 1).

HRMS: *m*/*z* = 531.2188; calculated *m*/*z* = 531.2202 for $C_{30}H_{28}F_2N_4O_3$.



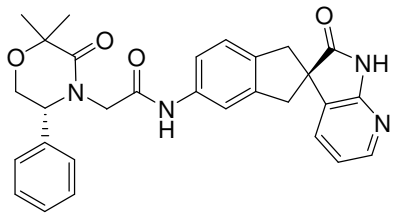
2-[(6*S*)-3,3-Dimethyl-2-oxo-6-phenylpiperidin-1-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-b]pyridin]-5-yl]acetamide (**6**)

^{1}H NMR ($CDCl_3$) δ 11.28 (1H, bs), 8.80 (1H, s), 7.96 (1H, d, *J* = 6.0 Hz), 7.57 (1H, s), 7.39-7.31 (4H, m), 7.21-7.14 (4H, m), 6.99 (1H, t, *J* = 6.7 Hz), 4.83 (1H, t, *J* = 4.7 Hz), 4.54 (1H, d, *J* = 14.6 Hz), 3.64 (2H, dd, *J* = 15.8, 8.4 Hz), 3.35 (1H, d, *J* = 14.6 Hz), 3.02 (2H, dd, *J* = 15.8, 10.0 Hz), 2.36-2.29 (1H, m), 1.90-1.84 (1H, m), 1.77-1.71 (1H, m), 1.55-1.50 (1H, m), 1.35 (3H, s), 1.32 (3H, s).

HPLC (system B): r.t. = 2.47 min, purity = 100% @ 215 nm.

MS: *m*/*z* = 495 (M + 1).

HRMS: *m*/*z* = 495.2408; calculated *m*/*z* = 495.2391 for $C_{30}H_{31}N_4O_3$.



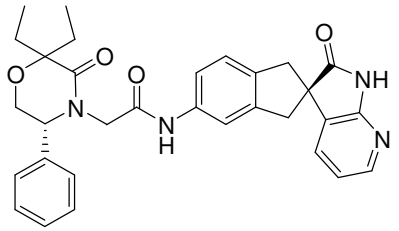
2-[(5*R*)-2,2-Dimethyl-3-oxo-5-phenylmorpholin-4-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide (**7**)

^{1}H NMR ($CDCl_3$) δ 8.54 (1H, s), 7.98 (1H, br s), 8.12 (1H, dd, *J* = 5.3, 1.6 Hz), 7.57 (1H, s), 7.44-7.34 (4H, m) 7.30 (2H, d, *J* = 7.1 Hz), 7.23-7.19 (2H, m), 7.04-7.00 (1H, m), 4.72 (1H, t, *J* = 3.7 Hz), 4.52 (1H, d, *J* = 14.7 Hz), 4.24 (1H, dd, *J* = 12.2, 3.9 Hz), 3.86 (1H, dd, *J* = 12.5, 3.4 Hz), 3.70-3.64 (2H, m), 3.46 (1H, d, *J* = 14.9 Hz), 3.08-3.02 (2H, m), 1.63 (3H, s), 1.58 (3H, s).

HPLC (system A): r.t. = 3.63 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 497 (M + 1).

HRMS: *m*/*z* = 497.2158; calculated *m*/*z* = 497.2184 for $C_{29}H_{27}N_4O_4$.



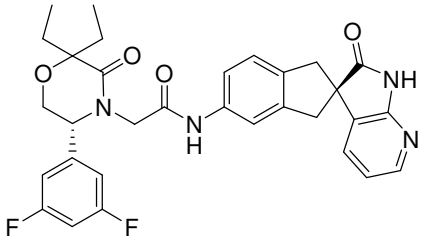
2-[(5*R*)-2,2-Diethyl-3-oxo-5-phenylmorpholin-4-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide (**8**)

^{1}H NMR ($CDCl_3$) δ 8.49 (1H, s), 8.16 (1H, s), 8.12 (1H, dd, *J* = 5.3, 1.6 Hz), 7.50 (1H, s), 7.42-7.35 (3H, m) 7.31 (2H, d, *J* = 8.3 Hz), 7.23-7.17 (2H, m), 7.06 (1H, dd, *J* = 7.3, 1.5 Hz), 6.82 (1H, dd, *J* = 7.3, 5.4 Hz), 4.78 (1H, t, *J* = 5.1 Hz), 4.45 (1H, d, *J* = 14.9 Hz), 4.14 (1H, dd, *J* = 12.6, 4.5 Hz), 3.89 (1H, dd, *J* = 12.5, 5.6 Hz), 3.65-3.59 (2H, m), 3.51 (1H, d, *J* = 14.7 Hz), 3.07-3.02 (2H, m), 2.11-1.99 (2H, m), 1.93-1.80 (2H, m), 1.03 (3H, t, *J* = 7.4 Hz), 0.96 (3H, t, *J* = 7.4 Hz).

HPLC (system A): r.t. = 4.13 min, purity = 95.1% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 525 (M + 1).

HRMS: *m*/*z* = 525.2495; calculated *m*/*z* = 525.2497 for $C_{31}H_{33}N_4O_4$.



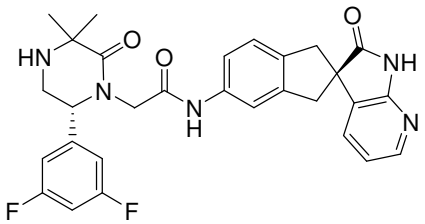
2-[(5*R*)-5-(3,5-Difluorophenyl)-2,2-diethyl-3-oxomorpholin-4-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide (**9**)

^{1}H NMR ($CDCl_3$) δ 8.48 (1H, s), 8.04 (1H, br s), 7.56 (1H, s), 7.22-7.19 (3H, m) 6.92-6.79 (4H, m), 4.74 (1H, t, *J* = 4.2 Hz), 4.50 (1H, d, *J* = 14.9 Hz), 4.21 (1H, dd, *J* = 12.5, 4.54 Hz), 3.84 (1H, dd, *J* = 12.5, 4.2 Hz), 3.67-3.61 (2H, m), 3.54 (1H, d, *J* = 14.6 Hz), 3.07-3.02 (2H, m), 2.06-1.99 (2H, m), 1.90-1.82 (2H, m), 1.02 (3H, t, *J* = 7.4 Hz), 0.95 (3H, t, *J* = 7.4 Hz).

HPLC (system A): r.t. = 4.35 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 561 (M + 1).

HRMS: *m*/*z* = 561.2298; calculated *m*/*z* = 561.2308 for $C_{31}H_{31}F_2N_4O_4$.



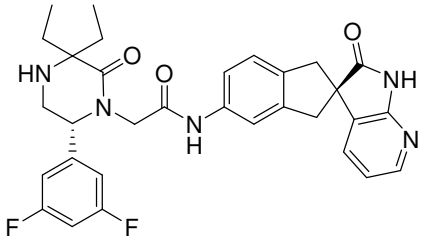
2-[(6*R*)-6-(3,5-Difluorophenyl)-3,3-dimethyl-2-oxopiperazin-1-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide hydrochloride (**10**)

^{1}H NMR (CD_3OD) δ 8.05 (1H, d, *J* = 5.1 Hz), 7.50 (1H, s), 7.37 (1H, d, *J* = 8.3 Hz), 7.23 (1H, d, *J* = 8.1 Hz), 7.15-7.07 (4H, m), 6.88 (1H, dd, *J* = 7.2, 5.5 Hz), 5.16 (1H, dd, *J* = 8.8, 4.9 Hz), 4.60 (1H, d, *J* = 16.6 Hz), 3.88 (1H, dd, *J* = 13.9, 4.9 Hz), 3.67 (1H, dd, *J* = 13.9, 8.8 Hz), 3.54-3.47 (3H, m), 3.09-3.05 (2H, m), 1.75 (3H, s), 1.72 (3H, s).

HPLC (system A): r.t. = 2.99 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 532 (M + 1).

HRMS: *m*/*z* = 532.2166; calculated *m*/*z* = 532.2155 for $C_{29}H_{28}F_2N_5O_3$.



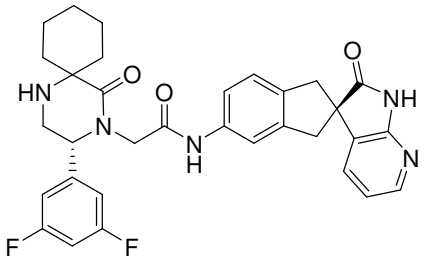
2-[(6*R*)-6-(3,5-Difluorophenyl)-3,3-diethyl-2-oxopiperazin-1-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide hydrochloride (**11**)

^{1}H NMR (CD_3OD) δ 8.11 (1H, dd, *J* = 6.0, 1.3 Hz), 7.53 (1H, s), 7.46 (1H, dd, *J* = 7.5, 1.3 Hz), 7.40 (1H, d, *J* = 8.3 Hz), 7.25 (1H, d, *J* = 8.1 Hz), 7.15-7.09 (4H, m), 5.20 (1H, dd, *J* = 8.8, 4.9 Hz), 4.63 (1H, d, *J* = 16.6 Hz), 3.88 (1H, dd, *J* = 13.7, 4.9 Hz), 3.74 (1H, dd, *J* = 13.7, 8.8 Hz), 3.58-3.51 (3H, m), 3.20-3.15 (2H, m), 2.32-2.23 (1H, m), 2.16 (2H, q, *J* = 7.6 Hz), 2.08-2.00 (1H, m), 1.15 (3H, t, *J* = 7.6 Hz), 1.14 (3H, t, *J* = 7.6 Hz).

HPLC (system A): r.t. = 3.15 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 560 (M + 1).

HRMS: *m*/*z* = 560.2469; calculated *m*/*z* = 560.2468 for $C_{31}H_{32}F_2N_5O_3$.



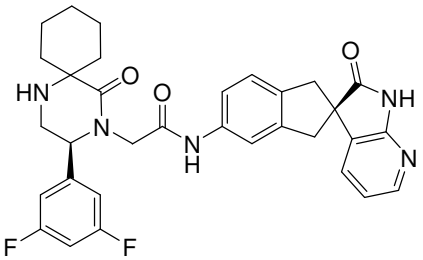
2-[(3*R*)-3-(3,5-Difluorophenyl)-5-oxo-1,4-diazaspiro[5.5]undec-4-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide hydrochloride (**12**)

^{1}H NMR (CD_3OD) δ 8.11 (1H, dd, *J* = 6.0, 1.3 Hz), 7.53-7.50 (2H, m), 7.41 (1H, d, *J* = 8.1 Hz), 7.26 (1H, d, *J* = 8.3 Hz), 7.18-7.09 (4H, m), 5.17 (1H, dd, *J* = 9.3, 5.1 Hz), 4.58 (1H, d, *J* = 16.6 Hz), 3.87 (1H, dd, *J* = 13.8, 5.0 Hz), 3.71 (1H, dd, *J* = 13.9, 9.3 Hz), 3.58-3.52 (3H, m), 3.21-3.16 (2H, m), 2.40-2.34 (1H, m), 2.30-2.24 (1H, m), 2.19-2.14 (1H, m), 2.02-1.95 (2H, m), 1.87-1.82 (1H, m), 1.73-1.55 (4H, m).

HPLC (system A): r.t. = 3.23 min, purity = 100% @ 215 nm; 100% @ 254 nm.

MS: *m*/*z* = 572 (M + 1).

HRMS: *m*/*z* = 572.2478; calculated *m*/*z* = 572.2468 for $C_{32}H_{32}F_2N_5O_3$.



2-[(3*S*)-3-(3,5-Difluorophenyl)-5-oxo-1,4-diazaspiro[5.5]undec-4-yl]-*N*-[(2*R*)-2'-oxo-1,1',2',3-tetrahydrospiro[indene-2,3'-pyrrolo[2,3-*b*]pyridin]-5-yl]acetamide hydrochloride (**13**)

^{1}H NMR (CD_3OD) δ 8.11 (1H, dd, *J* = 6.1, 1.2 Hz), 7.60 (1H, s), 7.52 (1H, dd, *J* = 7.3, 1.5 Hz), 7.34 (1H, d, *J* = 8.1 Hz), 7.26 (1H, d, *J* = 8.3 Hz), 7.18-7.09 (4H, m), 5.16 (1H, dd, *J* = 9.2, 5.0 Hz), 4.59 (1H, d, *J* = 16.4 Hz), 3.87 (1H, dd, *J* = 13.9, 5.1 Hz), 3.71 (1H, dd, *J* = 13.9, 9.3 Hz), 3.65-3.51 (3H, m), 3.22-3.17 (2H, m), 2.40-2.34 (1H, m), 2.30-2.24 (1H, m), 2.19-2.14 (1H, m), 2.03-1.95 (2H, m), 1.87-1.82 (1H, m), 1.73-1.55 (4H, m).

HPLC (system A): r.t. = 3.26 min, purity = 100% @ 215 nm (LC/MS); 100% @ 254 nm.

MS: *m*/*z* = 572 (M + 1).

HRMS: *m*/*z* = 572.2478; calculated *m*/*z* = 572.2468 for $C_{32}H_{32}F_2N_5O_3$.