Tert-butyl 3-{5-[(2-chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(2,4,6-trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate. *R*t 1.53 min (System B), $[M+H]^+$ 528.0

Tert-butyl 3-{5-[(2-chloro-6-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate. *R*t 1.50 min (System B), $[M+H]^+$ 472.1

<u>Compound 19.</u> **3-(5-{[2-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.** Tert-butyl 3-(5-{[2-(trifluoromethyl)phenyl]-methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl}propanoate (0.21 g; 0.43 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (3.2 mL; 12.82 mmol) and stirred overnight at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (0.17 g). ^1H NMR (400 MHz, DMSO/TFA- d_6) δ ppm 9.5 (bs, 1H), 7.75 (d, J =8.2 Hz, 2H), 7.68 (t, J =8.2 Hz, 1H), 7.53 (t, J =7.7 Hz, 1H), 6.69 – 6.82 (m, 3H), 5.15 (s, 2H), 4.42 (bs, 2H), 3.45 – 3.60 (m, 2H), 3.29 – 3.41 (m, 2H), 2.98 – 3.18 (m, 2H), 2.78 (t, J =7.4 Hz, 2H), 2.02 – 2.18 (m, 2H), 1.80 – 1.91(m, 2H). *R*t 1.36 min (System B), $[M+H]^+$ 436.1

The following compounds were obtained according to a similar manner:

<u>Compound 20.</u> **3-[5-(Cyclohexylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.**

*R*t 1.40 min (System B), $[M+H]^+$ 374.2

<u>Compound 21.</u> **3-(5-{[3-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.**

*R*t 1.77 min (System B), $[M+H]^+$ 436.1

(m, 1H), 7.04 – 6.95 (m, 1H), 6.56 – 6.62 (m, 2H), 5.18 (s, 2H), 4.48 (bs, 2H), 3.42 – 3.56 (m, 2H), 3.24 – 3.41 (m, 2H), 2.96 – 3.18 (m, 2H), 2.86 (t, J =8.0 Hz, 2H), 2.10 – 2.30 (m, 2H), 1.80 – 1.91(m, 2H). Rt 1.57 min (System B), $[M+H]^+$ 436.0

The following compounds were obtained according to a similar manner:

Compound 30. 3-{6-[(4-Phenylpentyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

Rt 1.46 min (System B), $[M+H]^+$ 424.1

Compound 31. 3-{6-[(3-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.20 (bs, 1H) 11.30 (bs, 1H) 7.37 - 7.51 (m, 4H), 6.94 - 7.08 (m, 1H), 6.50 - 6.58 (m, 2H), 5.09 (s, 2H), 4.46 (s, 2H), 3.24 – 3.49 (m, 4H), 2.97 - 3.13 (m, 2H), 2.87 (t, J =7.8 Hz, 2H), 2.13 – 2.26 (m, 2H), 1.79 – 1.89 (m, 2H).

Compound 32. 3-[6-(Cyclohexylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.

Rt 1.42 min (System B), $[M+H]^+$ 374.2

Compound 33. 3-[6-(Oxan-2ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.

Rt 1.13 min (System B), $[M+H]^+$ 376.2

Compound 34. 3-{6-[(2,5-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

Rt 1.40 min (System B), $[M+H]^+$ 436.1

Compound 35. 3-(6-{[3-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO/TFA- d_6) δ ppm 10.0 (bs, 1H), 7.69 – 7.78 (m, 2H), 7.56 – 7.66 (m, 2H), 7.00 (d, J = 8.4 Hz, 1H), 6.49 – 6.58 (m, 2H), 5.15 (s, 2H), 4.50 (bs, 2H), 3.45 – 3.60 (m, 2H), 3.29 – 3.41 (m, 2H), 2.95 – 3.18 (m, 2H), 2.86 (t, J = 7.4 Hz, 2H), 2.18 – 2.33 (m, 2H), 1.85 – 1.94 (m, 2H). Rt 1.38 min (System B), $[M+H]^+$ 436.1

Compound 36. **3-(6-{[2-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.**
*R*t 1.37 min (System B), $[M+H]^+$ 436.1

Compound 37. **3-{6-[(2,3-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.**
*R*t 1.40 min (System B), $[M+H]^+$ 436.0

Compound 38. **3-{6-[(2-Chloro-6-fluorphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** ^1H NMR (400 MHz, DMSO/TFA- d_6) δ ppm 9.80 (bs, 1H), 7.40 – 7.48 (m, 1H), 7.34 (d, J = 8.9 Hz, 1H), 7.20 (t, J =.8.9 Hz, 1H), 7.01 (d, J = 8.Hz, 1H), 6.52 – 6.58 (m, 2H), 5.15 (s, 2 H), 4.51 (bs, 1H), 3.35 – 3.63 (m, 4H), 3.06 – 3.20 (m, 2H), 2.84 (t, J =7.5 Hz, 2H), 2.18 – 2.28 (m, 2H), 1.85 – 1.93 (m, 2H). *R*t 1.31 min (System B), $[M+H]^+$ 420.1

Compound 39. **3-[6-(Benzyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-propanoic acid hydrochloride.**
*R*t 1.57 min (System B), $[M+H]^+$ 368.1

Compound 40. **3-{6-[(2,4-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.**
*R*t 1.42 min (System B), $[M+H]^+$ 436.1

Compound 41. **3-(6-{[2-Chloro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.**
*R*t 1.37 min (System B), $[M+H]^+$ 470.1

Compound 42. **3-[6-(Cyclohex-3-en-1ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.**
*R*t 1.38 min (System B), $[M+H]^+$ 372.2

Compound 43. **3-{6-[(3,5-Dichloropyridin-4-yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.**
*R*t 1.23 min (System B), $[M+H]^+$ 437.0

Compound 51. 3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs., 1H) 10.55 (bs, 1H), 7.43 (d, J = 2.2 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.24 (dd, J = 8.2 and 2.2 Hz, 1H), 6.94 – 7.03 (m, 1H), 6.51 – 6.61 (m, 2H), 5.06 (s, 2 H), 4.47 (bs., 2H), 3.22 - 3.55 (m, 4H), 2.95 - 3.15 (m, 2H), 2.86 (t, J =7.6 Hz, 2H), 2.61 (q, J =7.6 Hz, 2H), 2.10 - 2.30 (m, 2H), 1.79 – 1.91 (m, 2H), 1.16 (t, J =7.6 Hz, 3H). *R*t 1.45 min (System B), $[M+H]^+$ 430.1.

Compound 52. 3-{6-[(2-Chloro-5-proylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.52 min (System B), $[M+H]^+$ 444.1

Compound 53. 3-{6-[3-(2-Fluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (600 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.70 (bs, 1H), 7.27 - 7.32 (m, 1H), 7.20 - 7.27 (m, 1H), 7.09 - 7.15 (m, 2H), 6.88 – 6.98 (m, 1H), 6.44 (d, J =7.6 Hz, 1H), 6.38 (d, J =2.2 Hz, 1 H), 4.45 (bs., 2H), 3.91 (t, J =6.2 Hz, 2H), 3.19 - 3.52 (m, H), 3.01 (m, 2H), 2.85 (t, J =7.7 Hz, 2H), 2.74 (t, J =7.6 Hz, 2H), 2.14 – 2.28 (m, 2H), 1.91 - 1.99 (m, 2H), 1.73 – 1.88 (m, 2H).

Compound 54. 3-{6-[3-(2-Chlorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.44 min (System B), $[M+H]^+$ 430.1

Compound 55. 3-[6-(3-Phenylpropoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl]propanoic acid hydrochloride. *R*t 1.45 min (System B), $[M+H]^+$ 396.2

Compound 56. 3-{6-[2-(2,4-Dichlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.47 min (System B), $[M+H]^+$ 450.0

Compound 57. 3-{6-[2-(2-Chlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.39 min (System B), $[M+H]^+$ 416.0

Compound 58. 3-(6-{[2,6-Dichloro-4-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. *R*t 1.49 min (System B), $[M+H]^+$ 504.0

Compound 59. 3-{6-[(2,6-Dichloro-4-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.64 (bs, 1H), 9.90 (bs, 1H), 7.42 (s, 2H), 7.01 (bs, 1H), 6.56-6.61 (m, 2H), 5.14 (s, 2H), 4.49 (br s, 2H), 3.31-3.53 (m, 4H), 3.01-3.11 (m, 2H), 2.81-2.87 (m, 2H), 2.35 (s, 3H), 2.09-2.19 (m, 2H), 1.84-1.92 (m, 2H). *R*t 1.43 min (System B), $[M+H]^+$ 450.0

Compound 60. 3-{6-[(5-Bromo-2-chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.52 min (System B), $[M+H]^+$ 480.0

Compound 61. 3-{6-[(2-Chloro-6-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.42 min (System B), $[M+H]^+$ 416.1

Compound 62. 3-(6-{3-[2-(Trifluoromethyl)phenyl]propoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. *R*t 1.48 min (System B), $[M+H]^+$ 464.1

Compound 63. 3-{6-[3-(2,3-Difluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.42 min (System B), $[M+H]^+$ 432.1

Compound 64. 3-{6-[3-(2-Chloro-6-fluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.42 min (System B), $[M+H]^+$ 432.1

Compound 65. 3-{6-[3-(2,6-Dichlorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs., 1H), 10.70 (bs., 1H), 7.46 (d, J =8.3 Hz, 2H), 7.27 (dd, J =8.3 and 7.6 Hz, 1H), 6.95 (d, J =8.0 Hz, 1H), 6.46 (dd, J =8.0 and 2.0 Hz, 1H), 6.40 (d, J =2.0 Hz, 1H), 4.47 (bs., 2H), 3.99 (t, J =6.1 Hz, 2H), 3.46 (m, 2H), 3.29 (m, 2H), 2.98 - 3.10 (m, 4H), 2.87 (t, J =7.7 Hz,

Compound 71. **3-{6-[(2-Chloro-5-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.**

*R*t 1.68 min (System B), $[M+H]^+$ 442.1

Compound 72. **3-[6-({2-Chloro-5-[2-phenylcyclopropyl]phenyl}methoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.**

*R*t 1.72 min (System B), $[M+H]^+$ 518.0

Compound 73. **3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.80 (bs, 1H), 10.30 (bs, 1H), 7.35 – 7.37 (m, 2H), 7.26 – 7.30 (m, 1H), 6.95 – 7.40 (m, 1H), 6.56 – 6.63 (m, 2H), 5.10 (s, 2H), 4.49 (bs, 2H) 3.24 – 3.54 (m, 4H), 2.96 – 3.14 (m, 2H), 2.87 (t, *J* =8.2Hz, 2 H), 2.71 (q, *J* =7,6 Hz, 2H), 2.18 – 2.33 (m, 2H), 1.80 -1.90 (m, 2H), 1.17 (t, *J*=7.6 Hz, 3 H). *R*t 1.40 min (System B), $[M+H]^+$ 430.0

Compound 74. **3-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.** ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.80 (bs, 1H), 10.90 (bs, 1H), 7.33 – 7.41 (m, 3H), 6.94 – 7.04 (m, 1H), 6.56 – 6.63 (m, 2H), 5.15 (s, 2H), 4.49 (bs, 2H), 3.24 – 3.54 (m, 4H), 3.14 – 3.22 (m, 1H), 2.95 - 3.14 (m, 2H), 2.88 (t, *J* = 8.0 Hz, 2H), 2.14 – 2.33 (m, 2H), 1.80 -1.90(m, 2H), 1.19 (d, *J* = 6.7Hz, 6H). *R*t 1.40 min (System B), $[M+H]^+$ 430.0.

Compound 75. **3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.90 (bs,1H), 10.10 (bs, 1H), 7.29 – 7.37 (m, 2H), 6.94 – 7.09 (m,2H), 6.56 – 6.62 (m, 2H), 5.26 (s, 2H), 4.49 (bs, 2H), 3.42 – 3.56 (m, 2H), 3.24 – 3.41 (m, 2H), 2.96 – 3.18 (m, 2H), 2.84 (t, *J* =7.7 Hz, 2H) , 2.00 – 2.23 (m, 3H), 1.80 – 1.91 (m, 2H), 0.88 – 0.96 (m, 2H), 0.73 – 0.65 (m, 2H). *R*t 1.43 min (System B), $[M+H]^+$ 442.0

was stirred for 3 hours at 50°C and subsequently cooled to 0°C. To this reaction mixture was added aqueous HCl (10 mL; 1mol/l), dropwise, after which it was concentrated in vacuo. The residue was treated with saturated brine and dichloromethane. The water layer was washed with dichloromethane (twice). Subsequently, the organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo, followed by treated with iPr_2O. The formed precipitate was collected by filtration, washed with iPr_2O and dried in vacuo to yield the product (209 mg; 81.8%). ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.25 (s, 1H) ,7.19 (s, 1H), 7.06 (d, *J* =8.2 Hz, 1H), 6.53 (dd, *J* =8.2 and 2.1 Hz, 1H), 6.47 (d, *J* =2.1 Hz, 1H), 5.70 (d, *J* =5.1 Hz, 1H), 4.40 (s, 2H), 3.14 - 3.28 (m, 3H), 2.84 - 2.98 (m, 3H), 2.60 (t, *J*=5.9 Hz, 2H), 2.27 - 2.46 (m, 4H), 2.09 (t, *J* =11.4 Hz, 2H), 1.89 (bd, *J*=13.8 Hz, 2 H). *R*t 1.47 min (System B), $[M+H]^+$ 462.0

The following compounds were obtained according to a similar manner:

Compound 80. 3-{6-[(5,7-Difluoro-2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.
*R*t 1.39 min (System B), $[M+H]^+$ 430.1

Compound 81. 3-{6-[(1R)-(2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.
*R*t 1.34 min (System B), $[M+H]^+$ 394.1

Compound 82. 3-{6-[(1S)-(2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.42 (d, *J* =7.3 Hz, 1H), 7.21 - 7.34 (m, 3H), 7.05 (d, *J* =8.2 Hz, 1H), 6.57 (dd, *J* =8.2 and 2.0 Hz, 1H), 6.51 (d, *J* =2.0 Hz, 1H), 5.71 (dd, *J* =6.5 and 4.4 Hz, 1H), 4.40 (s, 2H), 3.08 - 3.19 (m, 3H), 2.87 - 2.97 (m, 1H), 2.84 (t, *J* =6.1 Hz, 2H), 2.50 - 2.62 (m, 3H), 2.30 - 2.46 (m, 2H), 2.15 - 2.25 (m, 1H), 2.00 - 2.11 (m, 2H), 1.84 - 1.93 (m, 2H). *R*t 1.34 min (System B), $[M+H]^+$ 394.1

Compound 83. 3-(6-{[(2E)-3-(4-Chlorophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.
*R*t 1.48 min (System B), $[M+H]^+$ 428.0

Compound 84. **3-{6-{[(3-Phenyl)prop-2-yn-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.**

*R*t 1.37 min (System B), $[M+H]^+$ 392.1

Compound 85. **3-[6-(2,3-Dihydro-1-benzofuran-3-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid.**

*R*t 1.95 min (System B), $[M+H]^+$ 396.1

Compound 86. **3-(6-{[(2E)-3-(2,6-dichlorophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.48 - 7.52 (m, 2H), 7.32 (t, *J* =8.1Hz, 1H), 7.10 (d, *J* =8.1Hz, 1H), 6.72 - 6.60 (m, 1H), 6.53 - 6.46 (m, 2H), 6.31 - 6.39 (m, 1H), 4.75 (dd, *J* =5.1 and 2.0Hz, 2H), 4.37 (s, 2H), 2.87 - 2.95 (m, 2H), 2.64 - 2.71 (m, 2H) 2.40 - 2.46 (m, 2H), 2.12 - 2.22 (m, 2H), 1.78 - 1.88 (m, 2H), 1.59 - 1.67 (m, 2H).

*R*t 1.51 min (System B), $[M+H]^+$ 462.1

Compound 87. **3-(6-{[(2E)-3-phenylprop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.**

*R*t 1.37 min (System B), $[M+H]^+$ 394.1

Compound 88. **3-{6-[(7-Chloro-2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.**

*R*t 1.37 min (System B), $[M+H]^+$ 428.0

Compound 89. **3-(6-{[3-(4-Chlorophenyl)prop-2-yn-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.**

*R*t 1.43 min (System B), $[M+H]^+$ 426.0

Compound 90. **3-(6-{[(2E)-3-(2-fluororophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.**

*R*t 1.41 min (System B), $[M+H]^+$ 412.1

Compound 91. **3-{6-[(4-Bromothiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.**

*R*t 1.57 min (System B), $[M+H]^+$ 452.0

Compound 92. **3-{6-[(4-Butylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.**

*R*t 1.67 min (System B), $[M+H]^+$ 430.1

Compound 93. 3-(6-{[4-(2-Fluorophenyl)thiophen-2yl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid.

*R*t 1.68 min (System B), $[M+H]^+$ 468.0

Compound 94. 3-{6-[(4-Phenylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.

*R*t 1.99 min (System B), $[M+H]^+$ 450.0

Compound 95. 3-{6-[(4-Bromo-3-methylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.60 (bs., 1H), 7.68 (s, 1H), 7.08 - 7.13 (m, 1H), 6.45 - 6.51 (m, 2H), 5.18 (s, 2H), 4.36 (s, 2H), 2.81 – 2.89 (m, 2H), 2.61 (t, *J*=7.2 Hz, 2H), 2.39 (t, *J*= 7.2 Hz, 2H), 2.17 (s, 3H), 2.02 - 2.12 (m, 2H), 1.74 - 1.86 (m, 2H), 1.56 – 1.64 (m, 2H). *R*t 1.72 min (System B), $[M+H]^+$ 467.9

Compound 96. 3-{6-[(4-Cyclopropylmethylthiophen-2yl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.06 - 7.10 (m, 2H), 6.91 (d, *J*=1.2 Hz, 1H), 6.44 - 6.49 (m, 2H), 5.12 (s, 2H), 4.35 (s, 2H), 2.89 – 2.83 (m, 2H), 2.63 (t, *J* =7.0 Hz, 2H), 2.40 (t, *J* =7.0 Hz, 2H), 2.04 – 2.14 (m, 2H), 1.90 (dt, *J*=8.4, 5.0 Hz, 1H), 1.74 – 1.85 (m, 2H), 1.57 – 1.64 (m, 2H), 0.82 - 0.89 (m, 2H), 0.56 - 0.61 (m, 2H). *R*t 1.69 min (System B), $[M+H]^+$ 414.1.

Compound 97. 3-{6-[(3-Methyl-4-phenylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.

*R*t 1.69 min (System B), $[M+H]^+$ 464.0

Compound 98. 3-{6-[(4-Butyl-3-methylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.

*R*t 1.82 min (System B), $[M+H]^+$ 444.1

Compound 252. 3-(6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.37 - 7.46 (m, 1H), 7.23 (d, *J*=7.8 Hz, 1H), 7.03 - 7.14 (m, 2H), 6.47 - 6.54 (m, 2H), 5.05 (s, 2H), 4.37 (s, 2H), 3.12 – 3.22 (d, 1H), 2.82

– 2.91 (m, 2H), 2.63 (t, *J*=7.1 Hz, 2H), 2.40 (t, *J*=7.1 Hz, 2H), 2.10 (t, *J*=11.1 Hz, 1H), 1.76 - 1.88 (m, 2H), 1.62 (d, *J*=13.1 Hz, 2H), 1.20 (d, *J*=6.8 Hz, 6H). *R*t 1.45 min (System B), $[M+H]^+$ 429.3

Compound 253. 3-{6-[(2-cyclopropyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.29 - 7.37 (m, 1H), 7.02 - 7.14 (m, 2H), 6.85 (d, *J*=7.8 Hz, 1H), 6.50 - 6.56 (m, 2H), 5.16 (s, 2H), 4.37 (s, 2H), 2.86 – 2.92 (m, 2H), 2.64 (t, *J*=7.2 Hz, 2H), 2.41 (t, *J*=7.2 Hz, 2H), 2.00 - 2.18 (m, 3H), 1.77 - 1.88 (m, 2H), 1.62 (d, *J*=12.6 Hz, 2H), 0.89 - 0.98 (m, 2H), 0.66 - 0.72 (m, 2H). *R*t 1.40 min (System B), $[M+H]^+$ 426.2

Compound 254. 3-{6-[(2-ethyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.33 - 7.42 (m, 1H), 7.04 - 7.17 (m, 3H), 6.48 - 6.56 (m, 2H), 5.02 (s, 2H), 4.37 (s, 2H), 2.87 – 2.97 (m, 2H), 2.62 - 2.74 (m, 5H), 2.45 (t, *J*=7.2 Hz, 2H), 2.11 - 2.23 (m, 2H), 1.80 - 1.92 (m, 2H), 1.64 (d, *J*=12.4 Hz, 2H), 1.16 (t, *J*=7.5 Hz, 3H). *R*t 1.41 min (System B), $[M+H]^+$ 414.3

Compound 255. 3-(6-{[2-fluoro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.63 - 7.75 (m, 3H), 7.12 (d, *J*=8.0 Hz, 1H), 6.47 - 6.53 (m, 2H), 5.09 (s, 2H), 4.37 (s, 2H), 2.86 (d, *J*=11.7 Hz, 2H), 2.62 (t, *J*=7.2 Hz, 2H), 2.40 (t, *J*=7.2 Hz, 2H), 2.04 - 2.13 (m, 2H), 1.77 - 1.86 (m, 2H), 1.62 (d, *J*=13.1 Hz, 2H). *R*t 1.50 min (System B), $[M+H]^+$ 454.2

Compound 256. 3-{6-[(4-chloro-2,6-difluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.43 - 7.49 (m, 2H), 7.07 - 7.12 (m, 1H), 6.47 (s, 2H), 5.01 (s, 2H), 4.34 (s, 2H), 2.73 - 2.79 (m, 2H), 2.40 - 2.47 (m, 2H), 1.85 - 1.98 (m, 4H), 1.74 - 1.84 (m, 2H), 1.51 - 1.58 (m, 2H). *R*t 1.36 min (System B), $[M+H]^+$ 439.2

Compound 257. 3-{6-[1-(2,6-dichlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-

d_6) δ 7.45 (d, J=8.1 Hz, 2H), 7.28 - 7.34 (m, 1H), 7.02 (d, J=8.1 Hz, 1H), 6.29 (dd, J=8.1, 2.1 Hz, 1H), 6.21 (d, J=2.1 Hz, 1H), 5.93 (q, J=6.6 Hz, 1H), 4.30 (s, 2H), 2.81 (d, J=11.9 Hz, 2H), 2.57 (t, J=7.2 Hz, 2H), 2.37 (t, J=7.2 Hz, 2H), 2.02 (t, J=11.2 Hz, 2H), 1.69 - 1.78 (m, 2H), 1.67 (d, J=6.6 Hz, 3H), 1.55 (d, J=11.9 Hz, 2H). Rt 1.41 min (System B), $[M+H]^+$ 450.1

Compound 258. 3-{6-[(2,6-diethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.22 - 7.27 (m, 1H), 7.07 - 7.15 (m, 3H), 6.49 - 6.55 (m, 2H), 4.96 (s, 2H), 4.37 (s, 2H), 2.85 (d, J=11.7 Hz, 2H), 2.56 - 2.69 (m, 6H), 2.36 (t, J=7.0 Hz, 2H), 2.01 - 2.10 (m, 2H), 1.77 - 1.86 (m, 2H), 1.62 (d, J=12.9 Hz, 2H), 1.14 (t, J=7.5 Hz, 6H). Rt 1.47 min (System B), $[M+H]^+$ 424.2

Compound 259. 3-(6-{[2-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.30 - 7.40 (m, 3H), 7.15 - 7.22 (m, 1H), 7.08 (d, J=8.0 Hz, 1H), 6.47 - 6.54 (m, 2H), 5.04 (s, 2H), 4.39 (s, 2H), 3.10 - 3.19 (m, 1H), 3.02 (d, J=11.9 Hz, 2H), 2.81 (t, J=7.0 Hz, 2H), 2.54 (t, J=7.0 Hz, 2H), 2.32 - 2.43 (m, 2H), 1.89 - 2.00 (m, 2H), 1.68 (d, J=13.3 Hz, 2H), 1.16 - 1.22 (m, 6H). Rt 1.45 min (System B), $[M+H]^+$ 410.7

Compound 260. 3-(6-{[2-ethyl-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.61 - 7.67 (m, 2H), 7.53 - 7.60 (m, 1H), 7.12 (d, J=7.8 Hz, 1H), 6.48 - 6.55 (m, 2H), 5.04 (s, 2H), 4.35 (s, 2H), 2.79 (d, J=11.2 Hz, 2H), 2.73 (q, J=7.5 Hz, 2H), 2.45 - 2.5 (m, 2H), 2.05 (t, J=7.6 Hz, 2H), 1.87 - 1.97 (m, 2H), 1.77 - 1.86 (m, 2H), 1.58 (d, J=12.1 Hz, 2H), 1.17 - 1.23 (m, 3H). Rt 1.47 min (System B), $[M+H]^+$ 464.2

Compound 261. 3-(6-{[2-Chloro-6-(difluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.43 - 7.56 (m, 2H), 7.27 - 7.32 (m, 1H), 7.06 - 7.13 (m, 1H), 6.49 - 6.57 (m, 2H), 5.06 (s, 2H), 4.40 (s, 2H), 3.04 (d, J=11.7 Hz, 2H),

Compound 107. 3-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.9 (bs, 1H), 9.8 (bs, 1H), 7.58 – 7.65 (m, 2H), 7.47 – 7.52 (m, 1H), 7.06 – 6.97 (m, 1H), 6.56 – 6.62 (m, 2H), 5.10 (s, 2H), 4.47 (bs, 2H), 3.28 – 3.54 (m, 4H), 2.95 – 3.18 (m, 3H), 2.11 – 2.25 (m, 2 H), 1.80 – 1.91(m, 2H), 1.22 (d, J =7.6 Hz ,3H).

Compound 108. 3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid hydrochloride.

Rt 1.54 min (System B), $[M+H]^+$ 444.1.

Compound 263. 3-{6-[(2-ethyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid hydrochloride. The required [2-ethyl-6-fluorophenyl]-methanol was obtained analogous to the the sequence described for compound **273**. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.88 (br. s., 1H), 10.29 (br. s., 1H), 7.34 - 7.42 (m, 1H), 6.98 - 7.16 (m, 3H), 6.53 - 6.60 (m, 2H), 5.04 (s, 2H), 4.47 (br. s., 2H), 3.29 - 3.54 (m, 4H), 2.95 - 3.22 (m, 3H), 2.70 (q, J=7.5 Hz, 2H), 2.24 - 2.38 (m, 2H), 1.80 - 1.89 (m, 2H), 1.26 (d, J=7.1 Hz, 3H), 1.17 (t, J=7.5 Hz, 3H). Rt 1.44 min (System B), $[M+H]^+$ 428.8.

Compound 264. 3-{6-[(2-cyclopropyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 12.92 (br. s., 1H), 10.07 (br. s., 1H), 7.30 - 7.37 (m, 1H), 6.95 - 7.09 (m, 2H), 6.86 (d, J=7.8 Hz, 1H),, 6.55 - 6.62 (m, 2H), 5.17 (s, 2H), 4.47 (br. s., 2H), 3.39 - 3.49 (m, 4H), 2.98 - 3.18 (m, 3H), 2.18 - 2.34 (m, 2H), 2.00 - 2.09 (m, 1H), 1.78 - 1.88 (m, 2H), 1.25 (d, J=7.1 Hz, 3H), 0.90 - 0.98 (m, 2H), 0.64 - 0.73 (m, 2H). Rt 1.42 min (System B), $[M+H]^+$ 440.7.

Compound 265. 3-(6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid

(400 MHz, DMSO- d_6) δ ppm 13.9 (bs, 1H) 10.90 (bs, 1H) 7.34 – 7.39 (m, 2H), 7.25 – 7.31 (m, 1H), 7.17 – 7.20 (m, 1H), 6.56 – 6.62 (m, 2H), 5.10 (s, 2H), 4.47 (bs, 2H), 4.17 (bs, 2H), 3.46 – 3.58 (m, 2H), 3.15 – 3.28 (m, 2H), 2.71 (q, *J*=7.4 Hz, 2H), 2.13 – 2.28 (m, 2H), 1.83 – 1.91(m, 2H), 1.16 (t, *J*=7.4Hz, 3H). *R*t 1.65 min (System B), $[M+H]^+$ 416.0

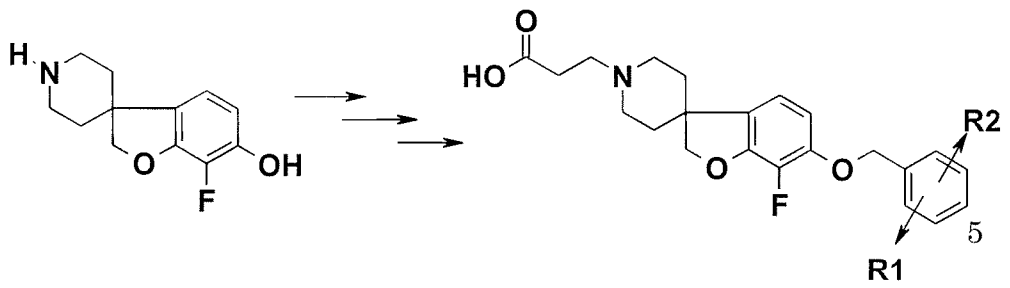
Compound 112. 2-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl} acetic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 13.80 (bs, 1H), 10.40 (bs, 1H), 7.28 – 7.38 (m, 2H), 7.08 – 7.23 (m, 1H) 7.04 (dd, *J*=7.0 and 2.0 Hz ,1H), 6.56 – 6.62 (m, 2H), 5.27 (s, 2H), 4.47 (bs, 2H) 4.13 (bs, 2H), 3.06 – 3.56 (m, 4H), 2.13 – 2.28 (m, 2H), 2.00 – 2.10 (m, 1H), 1.83 – 1.91(m, 2H), 0.95 – 0.87 (m, 2H), 0.73 – 0.65 (m, 2H). *R*t 1.67 min (System B), $[M+H]^+$ 428.0.

Compound 113. 2-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid hydrochloride.
*R*t 1.99 min (System B), $[M+H]^+$ 478.0

Compound 114. 2-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid hydrochloride.
*R*t 1.71 min (System B), $[M+H]^+$ 416.1

Compound 115. 2-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)acetic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 14.0 (bs, 1H), 10.30 (bs, 1H), 7.31 – 7.42 (m, 3H), 7.18 – 7.05 (m, 1H), 6.56 – 6.62 (m, 2H), 5.15 (s, 2H), 4.45 (bs, 2H), 4.15 (bs, 2H), 3.45 – 3.56 (m, 2H), 3.12 – 3.27 (m, 3H), 2.15 – 2.27 (m, 2H), 1.80 – 1.91(m, 2H), 1.20 (d, *J*=7.2Hz, 6H). *R*t 1.72 min (System B), $[M+H]^+$ 430.1

Compound 116. 2-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 13.9 (bs, 1H), 10.40 (bs, 1H), 7.50 (d, *J* =8.4 Hz, 1H), 7.45 (d, *J* =8.4 Hz, 1H), 7.19 – 7.03 (m, 1H), 6.56 – 6.62 (m, 2H), 5.20 (s, 2H), 4.47 (bs, 2H), 4.17 (bs, 2H), 3.08 – 3.56 (m, 4H), 2,75 (q, *J* =7.2Hz, 2H),



Compound 130. 3-{6-[(2,6-Dichlorophenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs, 1H), 10.50 (bs, 1H), 7.56 - 7.61 (m, 2H), 7.46 - 7.52 (m, 1H), 6.81 – 6.94 (m, 2H), 5.26 (s, 2H), 4.60 (bs, 2H), 3.43 - 3.53 (m, 2H), 3.25 – 3.37 (m, 2H), 3.00 - 3.11 (m, 2H), 2.86 (t, J =7.5 Hz, 2H), 2.13 - 2.29 (m, 2H), 1.89 – 2.96 (m, 2H). *R*t 1.37 min (System B), $[M+H]^+$ 454.0

Compound 131. 3-{6-[(2,6-Dichloro-4-methylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.50 (bs, 1H), 10.90 (bs, 1H), 7.42 (s, 2H), 6.85 – 6.93 (m, 2H), 5.21 (s, 2H), 4.59 (s, 2H), 3.41 – 3.52 (m, 2H), 3.37 - 3.26 (m, 2H), 3.00 – 3.15 (m, 2H), 2.86 (t, J =7.6 Hz, 2H), 2.34 (s, 3H), 2.16 - 2.29 (m, 2H), 1.88 - 1.96 (m, 2H). *R*t 1.44 min (System B), $[M+H]^+$ 468.1

Compound 132. 3-{7-Fluoro-6-[(2,4,6-trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.90 (bs., 1H), 10.40 (bs., 1H), 7.81 (s, 2H), 6.85 - 6.93 (m, 2H), 5.23 (s, 2H), 4.60 (bs., 2H), 3.40 - 3.55 (m, 2H), 3.25 – 3.37 (m, 2H), 2.96 - 3.15 (m, 2H), 2.85 (t, J =7.3 Hz, 2H), 2.12 – 2.25 (m, 2H), 1.88 – 1.97 (m, 2H). *R*t 1.44 min (System B), $[M+H]^+$ 490.0.

Compound 133. 3-{6-[(2,6-Dichloro-3-methoxyphenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.50 (bs., 1H), 7.54 (d, J =9.0 Hz, 1H), 7.28 (d, J =9.0 Hz, 1H), 6.84 - 6.94 (m, 2H),

5.25 (s, 2H), 4.60 (bs, 2H), 3.90 (s, 3H), 3.41 - 3.54 (m, 2H), 3.25 – 3.35 (m, 2H), 2.97 - 3.16 (m, 2H), 2.86 (t, *J* =7.6 Hz, 2H), 2.13 - 2.28 (m, 2H), 1.94 (m, 2H). *R*t 1.36 min (System B), $[M+H]^+$ 484.1

Compound 134. 3-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.70 (bs, 1H), 7.43 (s, 2H), 6.81 – 6.93 (m, 2H), 5.21 (s, 2H), 4.60 (bs, H), 3.42 - 3.54 (m, 2H), 3.26 – 3.35(m, 2H), 2.98 - 3.12, (m, 2H), 2.87 (t, *J* =7.6 Hz, 2H), 2.62 (t, *J* =7.6 Hz, 2H), 2.18 - 2.30 (m, 2H), 1.92 (d, *J* =13.7 Hz, 2H), 1.51 - 1.62 (m, 2H), 1.24 - 1.35 (m, 2H), 0.90 (t, *J* =7.4 Hz, 3H). *R*t 1.67 min (System B), $[M+H]^+$ 510.1. *R*t 0.97 min (System B), $[M+H]^+$ 448.0

Compound 135. 3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

Compound 136. 3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 11.80 (bs, 1H), 7.35 - 7.40 (m, 2H), 7.29 – 7.32 (m, 1H), 6.82 - 6.96 (m, 2H), 5.19 (s, 2H), 4.60 (bs, 2H), 3.43 - 3.54 (m, 2H), 3.24 - 3.34 (m, 2H), 2.98 - 3.12 (m, 2H), 2.87 (t, *J* =7.6 Hz, 2H), 2.73 (q, *J* =7.8 Hz, 2H), 2.15 - 2.30 (m, 2H), 1.88 - 1.97 (m, 2H), 1.17 (t, *J* =7.8 Hz, 3H). *R*t 1.47 min (System B), $[M+H]^+$ 448.1

Compound 137. 3-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

*R*t 1.44 min (System B), $[M+H]^+$ 504.0.

Compound 269. 3-{6-[(2-Chloro-6-ethylophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (br. s., 1H), 10.60 (br. s., 1H), 7.35 - 7.41 (m, 2H), 7.27 - 7.33 (m, 1H), 6.80 - 6.97 (m, 2H), 5.19 (s, 2H) 4.60 (br. s., 2H), 3.25 - 3.55 (m, 4H), 3.00 - 3.12 (m, 2H), 2.87 (t, *J*=7.5 Hz,

2H), 2.73 (q, *J*=7.5 Hz, 2H), 2.18 - 2.30 (m, 2H), 1.88 - 1.97 (m, 2H), 1.17 (t, *J*=7.5 Hz, 3H). *R*t 1.47 min (System B), $[M+H]^+$ 448.1.

Compound 270. 3-{6-[(2-Chloro-6-fluorophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. A mixture of tert-butyl 3-{6-[(2-Chloro-6-fluorophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate (178 mg; 0.36 mmol), 2M aqueous NaOH (5 mL; 10 mmol) and ethanol (40 mL) was stirred for 3 hours at 50°C and subsequently cooled to 0°C. To this reaction mixture was added aqueous HCl (10 mL; 1mol/l), dropwise, after which it was concentrated in vacuo. The residue was treated with saturated brine and dichloromethane. The water layer was washed with dichloromethane (twice). Subsequently, the organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo, followed by treated with iPr_2O. The formed precipitate was collected by filtration, washed with iPr_2O and dried in vacuo to yield the product (142 mg; 85.5%). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.49 - 7.56 (m, 1H), 7.43 (d, *J*=8.0 Hz, 1H), 7.33 (t, *J*=8.8 Hz, 1H), 7.00 (d, *J*=8.0 Hz, 1H), 6.80 (t, *J*=7.6 Hz, 1H), 5.16 (d, *J*=1.4 Hz, 2H), 4.48 (s, 2H), 2.86 (d, *J*=11.7 Hz, 2H), 2.61 (t, *J*=7.0 Hz, 2H), 2.41 (t, *J*=7.0 Hz, 2H), 2.06 (t, *J*=11.7 Hz, 2H), 1.78 - 1.88 (m, 2H) 1.67 (d, *J*=12.5 Hz, 2H). *R*t 1.34 min (System B), $[M+H]^+$ 438.1.

The following compounds were obtained according to a similar manner:

Compound 271. 3-{6-[(2-Chloro-6-(propan-2-yl)phenyl]methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.35 - 7.45 (m, 3H), 7.01 (d, *J*=8.5 Hz, 1H), 6.84 (t, *J*=7.4 Hz, 1H), 5.22 (s, 2H), 4.48 (s, 2H), 3.16 - 3.25 (m, 1H), 2.84 - 2.89 (m, 2H), 2.61 (t, *J*=7.0 Hz, 2H), 2.40 (t, *J*=7.0 Hz, 2H), 2.02 - 2.11 (m, 2H), 1.80 - 1.89 (m, 2H), 1.67 (d, *J*=12.9 Hz, 2H), 1.20 (d, *J*=6.8 Hz, 6H). *R*t 1.49 min (System B), $[M+H]^+$ 462.2.

Compound 272. 3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^1H NMR

Compound 283. **3-{7-fluoro-6-[(5,5,6,6,6-pentafluorohexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.94 (d, J=8.2 Hz, 1H), 6.59 - 6.64 (m, 1H), 4.47 (s, 2H), 4.03 (t, J=6.2 Hz, 2H), 2.86 (d, J=11.8 Hz, 2H), 2.60 (t, J=7.1 Hz, 2H), 2.21 - 2.43 (m, 4H), 2.06 (t, J=11.2 Hz, 2H), 1.76 - 1.87 (m, 4H), 1.60 - 1.72 (m, 4H). Rt 1.44 min (System B), $[M+H]^+$ 470.2.

Compound 284. **3-[7-fluoro-6-(4,4,4-trifluorobutoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.95 (dd, J=8.3, 1.1 Hz, 1H), 6.58 - 6.65 (m, 1H), 4.48 (s, 2H), 4.06 (t, J=6.2 Hz, 2H), 2.85 (d, J=11.9 Hz, 2H), 2.60 (t, J=7.1 Hz, 2H), 2.34 - 2.48 (m, 4H), 2.05 (t, J=11.0 Hz, 2H), 1.88 - 1.98 (m, 2H), 1.81 (td, J=12.6, 3.6 Hz, 2H), 1.65 (d, J=12.8 Hz, 2H). Rt 1.28 min (System B), $[M+H]^+$ 406.2

Compound 285. **3-[6-(Cyclohexylethoxy)-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.93 (d, J=8.1 Hz, 1H), 6.90 - 6.94 (m, 1H), 4.46 (s, 2H), 4.01 (t, J=6.6 Hz, 2H), 2.85 (d, J=11.4 Hz, 2H), 2.60 (t, J=7.0 Hz, 2H), 2.38 (t, J=7.0 Hz, 2H), 2.05 (t, J=11.4 Hz, 2H), 1.55 - 1.86 (m, 12H), 1.38 - 1.50 (m, 1H), 1.07 - 1.27 (m, 2H), 0.87 - 1.00 (m, 2H). Rt 1.51 min (System B), $[M+H]^+$ 406.7

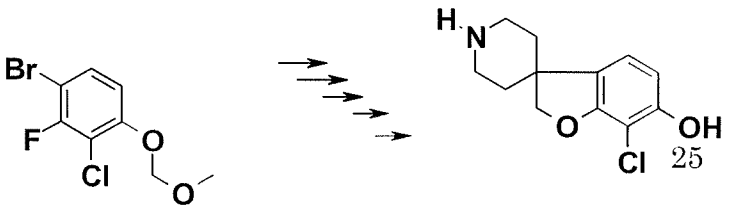
Compound 286. **3-{6-[(2-Ethylhexyl)oxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.93 (d, J=8.2 Hz, 1H), 6.58 - 6.64 (m, 1H), 4.46 (s, 2H), 3.87 (d, J=5.7 Hz, 2H), 2.85 (d, J=11.7 Hz, 2H), 2.60 (t, J=7.0 Hz, 2H), 2.39 (t, J=7.0 Hz, 2H), 2.06 (t, J=11.7 Hz, 2H), 1.75 - 1.87 (m, 2H), 1.59 - 1.71 (m, 3H), 1.22 - 1.49 (m, 8H), 0.82 - 0.92 (m, 6H). Rt 1.57 min (System B), $[M+H]^+$ 408.7.

Compound 287. **3-{7-Fluoro-6-[(3,5,5-trimethylhexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid.** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.93 (d, J=8.2 Hz, 1H), 6.61 (t, J=7.7 Hz, 1H), 4.46 (s, 2H), 4.00 (t, J=6.1 Hz, 2H), 2.85 (d, J=11.9 Hz, 2H), 2.60 (t, J=7.0 Hz, 2H), 2.39 (t, J=7.0 Hz, 2H), 2.01 - 2.11 (m, 2H), 1.75 - 1.86 (m, 2H), 1.60 - 1.74 (m, 3H), 1.55

Compound 289. 3-{6-[(2,6-Dichlorophenyl)methoxy]-5-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.54 - 7.60 (m, 2H), 7.46 - 7.51 (m, 1H), 7.17 (d, *J*=10.7 Hz, 1H), 6.88 (d, *J*=6.9 Hz, 1H), 5.23 (s, 2H), 4.38 (s, 2H), 2.86 (d, *J*=11.8 Hz, 2H), 2.60 (t, *J*=7.1 Hz, 2H), 2.39 (t, *J*=7.1 Hz, 2H), 2.06 (t, *J*=11.8 Hz, 2H), 1.83 (td, *J*=12.7, 3.6 Hz, 2H), 1.62 (d, *J*=12.7 Hz, 2H). *R*t 1.36 min (System B), $[M+H]^+$ 454.1

Compound 290. 3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-5-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.37 (d, *J*=4.4 Hz, 2H) 7.26 - 7.31 (m, 1H) 7.16 (d, *J*=10.7 Hz, 1H) 6.89 (d, *J*=6.9 Hz, 1H) 5.16 (s, 2H) 4.38 (s, 2H) 2.85 (d, *J*=11.7 Hz, 2H) 2.72 (q, *J*=7.5 Hz, 2H) 2.59 (t, *J*=7.0 Hz, 2H) 2.36 (t, *J*=7.0 Hz, 2H) 2.04 (t, *J*=11.7 Hz, 2H) 1.83 (td, *J*=12.6, 3.3 Hz, 2H) 1.61 (d, *J*=12.6 Hz, 2H) 1.16 (t, *J*=7.5 Hz, 3H). *R*t 1.39 min (System B), $[M+H]^+$ 448.6

Compound 336. 3-[5-Fluoro-6-(hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.78 - 7.03 (m, 1H) 6.69 (d, *J*=6.9 Hz, 1H) 4.45 (br. s., 2H) 3.98 (t, *J*=6.4 Hz, 2H) 3.20 - 3.61 (m, 4H) 2.96 - 3.19 (m, 2H) 2.89 (t, *J*=7.7 Hz, H) 2.23 (m, 2H) 1.86 (d, *J*=13.1 Hz, 2H) 1.62 - 1.74 (m, 2H) 1.21 - 1.46 (m, 6H) 0.87 (t, *J*=6.4 Hz , 3H)



7-Chloro-2H-spiro[1-benzofuran-3,4'-piperidine]-6-ol. This compound was synthezised according to the procedure of 5-Fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-6-ol (see compound **289**), starting from 1-bromo-3-

Compound 138. 3-(6-{[(2,6-Dichloro-3-methoxy)phenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. Tert-butyl 3-(6-{[(2,6-dichloro-3-methoxy)phenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate (190 mg, 0.35 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (144 mg, 82%). *R*t 1.45 min (System B), $[M+H]^+$ 482.0

The following compounds were obtained according to a similar manner:

Compound 139. 3-(6-{[(4-Butyl-2,6-dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

*R*t 1.75 min (System B), $[M+H]^+$ 508.0

Compound 140. 3-(6-{[(2-Chloro-6-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.73 (bs, 1H), 10.27 (bs, 1H), 7.19-7.35 (m, 3H), 7.06 (bs, 1H), 6.94 (d, *J* =8Hz, 1H), 6.88 (s, 1H), 4.50 (bs, 2H)m 4.31 (s, 2H), 3.27-3.54 (m, 4H), 2.99-3.15 (m, 2H), 2.85 (t, *J* =8Hz, 2H), 2.66-2.74 (m, 2H), 2.12-2.26 (m, 2H), 1.84-1.94 (m, 2H), 1.18 (t, *J*=8Hz, 3H).

Compound 141. 3-(6-{[(2-Chloro-6-cyclopropylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.82 (bs, 1H), 9.91 (bs, 1H), 7.36 (d, *J* =8Hz, 1H), 7.28 (t, *J* =8Hz, 1H), 7.13 (bs, 1H), 7.03 (t, *J* =8Hz, 2H), 6.96 (d, *J* =2Hz, 1H), 4.56 (bs, 4H), 3.37-3.59 (m, 4H), 3.19-3.25 (m, 2H), 2.88 (t, *J* =8Hz, 2H), 2.17-2.23 (m, 2H), 2.09-2.13 (m, 1H), 1.92-1.99 (m, 2H), 0.96-1.12 (m, 2H), 0.64-0.80 (m, 2H). *R*t 1.52 min (System B), $[M+H]^+$ 458.0.

Compound 142. 3-(6-{[(2,6-Dichloro-3-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

*R*t 1.57 min (System B), $[M+H]^+$ 480.0

Compound 143. 3-(6-{[(2,4,6-Trichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.82 (bs, 1H), 10.09 (bs, 1H), 7.71 (s, 2H), 7.05 (bs, 1H), 6.94 (d, *J* =8Hz, 1H), 6.88 (d, *J* =2Hz, 1H), 4.50 (bs, 2H), 4.34 (s, 2H), 3.26-3.54 (m, 4H), 2.99-3.12 (m, 2H), 2.83 (t, *J* =8Hz, 2H), 2.10-2.22 (m, 2H), 1.85-1.92 (m, 2H). *R*t 1.55 min (System B), $[M+H]^+$ 487.9

Compound 144. 3-(6-{[(2,6-Dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.55 (bs, 1H), 10.18 (bs, 1H), 7.50 (d, *J* =8 Hz, 2H), 7.35 (t, *J* =8 Hz, 1H), 7.06 (bs, 1H), 6.95 (bd, *J* =8 Hz, 1H), 6.89 (s, 1H), 4.50 (bs, 2H), 4.39 (s, 2H), 3.27-3.54 (m, 4H), 2.99-3.12 (m, 2H), 2.84 (t, *J* =8Hz, 2H), 2.09-2.24 (m, 2H), 1.85-1.92 (m, 2H). *R*t 1.44 min (System B), $[M+H]^+$ 451.9

Compound 145. 3-(6-{[(2-Chlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.82 (bs, 1H), 10.00 (bs, 1H), 7.41-7.48 (m, 2H), 7.25-7.33 (m, 2H), 7.03 (bs, 1H), 6.88 (d, *J* =8 Hz, 1H), 6.84 (s, 1H), 4.47 (bs, 2H), 4.28 (s, 2H), 3.18-3.55 (m, 4H), 2.97-3.12 (m, 2H), 2.83 (t, *J* =8 Hz, 2H), 2.06-2.21 (m, 2H), 1.81-1.91 (m, 2H). *R*t 2.31 min (System B), $[M+H]^+$ 418.0.

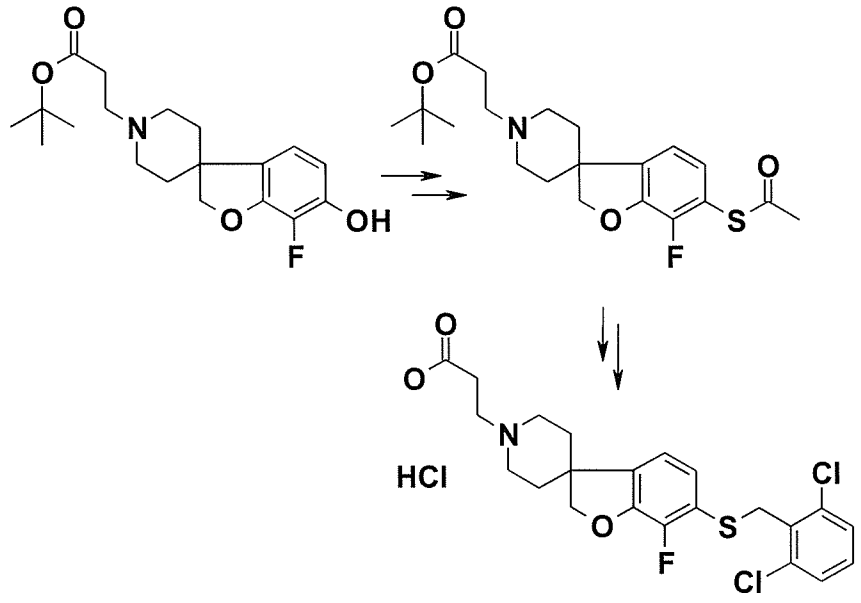
Compound 146. 3-(6-{[(2-Methylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

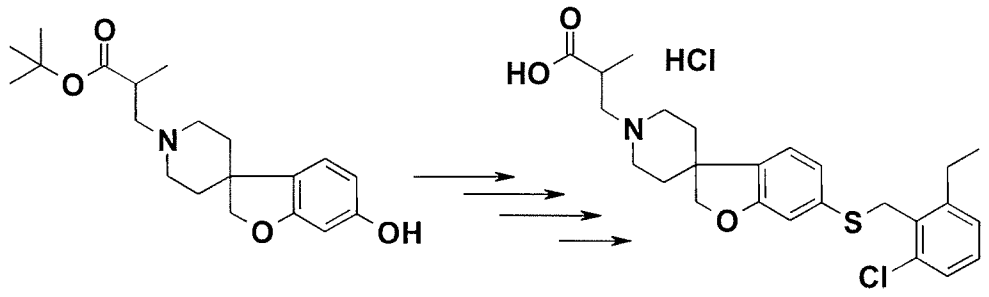
*R*t 1.72 min (System B), $[M+H]^+$ 398.1

Compound 147. 3-[6-(Benzylsulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride. *R*t 1.35 min (System B), $[M+H]^+$ 384.1

Compound 293. 3-(6-{[(2-Cyclopropyl-6-fluorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.73 (br s, 1H), 10.27 (br s, 1H), 7.20-7.25 (m, 1H), 6.97-7.06 (m, 2H), 6.93 (d, *J*=8Hz, 1H), 6.88 (s, 1H), 6.80 (d, *J*=8Hz, 1H), 4.49 (br s, 2H), 4.35 (s, 2H), 3.25-3.53 (m, 4H), 3.01-3.13 (m, 2H), 2.83 (t, *J*=8Hz, 2H), 2.11-2.22 (m, 2H), 2.01-2.08 (m, 1H), 1.87 (d, *J*=8Hz, 2H), 0.91-0.98 (m, 2H), 0.64-0.68 (m, 2H). *R*t 1.47 min (System B), $[M+H]^+$ 442.2.

Compound 294. 3-[6-({[2-Fluoro-6-(propan-2-yl)phenyl]methyl}sulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.27-7.46 (m, 1H), 6.93-7.14 (m, 5H), 4.50 (br s, 2H), 4.22 (br s, 2H), 3.32-3.53 (m, 4H), 3.12-3.17 (m, 2H), 2.81-2.86 (m, 3H), 2.13-2.18 (m, 2H), 1.85-1.91 (m, 2H), 1.16 (d, *J*=8Hz, 6H). *R*t 1.48 min (System B), $[M+H]^+$ 444.3.





The following compounds, starting from tert-butyl 3-{6-hydroxy-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl}-2-methyl-propanoate, were obtained according to the procedure described for compound **138.**

The corresponding benzylic chlorides were obtained from the already described benzylic alcohols:

Compound 148. 2-Methyl-3-(6-{[(2,4,6-trichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 13.00 (bs, 1H), 9.64 (bs, 1H), 7.82 (s, 2H), 7.06 (d, J =8Hz, 1H), 7.18 (bs, 1H), 7.01 (d, J =2 Hz, 1H), 4.61 (bs, 2H), 4.46 (s, 2H), 3.41-3.65 (m, 4H), 3.16-3.27 (m, 2H), 3.07-3.14 (m, 1H), 2.25-2.39 (m, 2H), 1.95-2.05 (m, 2H), 1.35 (d, J =8Hz, 3H). *R*t 1.65 min (System B), $[M+H]^+$ 502.0.

Compound 149. 3-(6-{[(2,6-Dichloro-3-methoxyphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.91 (bs, 1H), 9.82 (bs, 1H), 7.45 (d, J =8 Hz, 1H), 7.14 (d, J =8 Hz, 1H), 7.05 (bs, 1H), 6.95 (d, J =8 Hz, 1H), 6.89 (d, J =2Hz, 1H), 4.49 (bs, 2H), 4.37 (s, 2H), 3.86 (s, 3H), 3.42-3.55 (m, 3H), 2.98 (m, 4H), 2.18-2.29 (m, 2H), 1.83-1.91 (m, 2H), 1.24 (d, J =8Hz, 3H).

Compound 150. 3-(6-{[(2,6-Dichloro-4-methylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydrochloride. *R*t 1.55 min (System B), $[M+H]^+$ 487.9

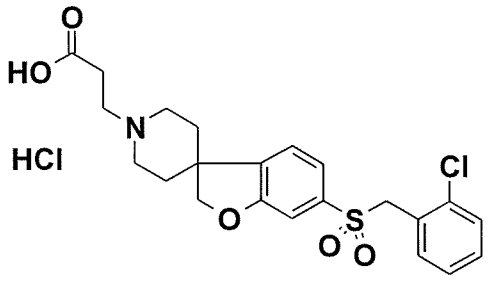
Compound 151. 3-(6-{[(2-Chloro-6-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydrochloride. *R*t 1.57 min (System B), $[M+H]^+$ 460.1

Compound 152. 3-[6-({[2-Chloro-6-(propan-2-yl)phenyl]methyl}sulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-2-methylpropanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.82 (bs, 1H), 9.82 (bs, 1H), 7.27-7.33 (m, 3H), 7.01-7.09 (bs, 1H), 6.94 (d, J =8 Hz, 1H), 6.88 (s, 1H), 4.49 (bs, 2H), 4.34 (s, 2H), 3.31-3.52 (m, 4H), 2.99-3.21 (m, 4H), 2.19-2.33 (m, 2H), 1.82-1.92 (m, 2H), 1.24 (d, J =8 Hz, 3H), 1.16 (d, J =8 Hz, 6H).

Compound 153. 3-(6-{[(2,6-Dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydrochloride.

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.82 (bs, 1H), 9.82 (bs, 1H), 7.49 (d, J =8 Hz, 2H), 7.38 (t, J =8 Hz, 1H), 7.06 (bs, 1H), 6.95 (d, J =8 Hz, 1H), 6.88 (s, 1H), 4.49 (bs, 2H), 4.38 (s, 2H), 3.30-3.53 (m, 4H), 2.98-3.17 (m, 3H), 2.18-2.35 (m, 2H), 1.82-1.93 (m, 2H), 1.24 (d, J =8 Hz, 3H).

Compound 298. 3-(6-{[(2-Chloro-6-cyclopropylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid hydro-chloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm12.87 (br s, 1H), 9.80 (br s, 1H), 7.31 (d, J=4Hz,1H), 7.23 (t, J=4Hz, 1H), 7.04 (br s,1H), 6.98 (t, J=4Hz, 2H), 6.90 (s, 1H), 4.46 (s, 4H), 3.30-3.55 (m, 4H), 3.00-3.15 (m, 3H), 2.20-2.30 (m, 2H), 2.02-2.10 (m, 1H), 1.84-1.91 (m, 2H), 1.23 (d, J=4Hz, 3H), 0.91-0.95 (m, 2H), 0.66-0.70 (m, 2H). *R*t 1.58 min (System B), $[M+H]^+$ 472.1

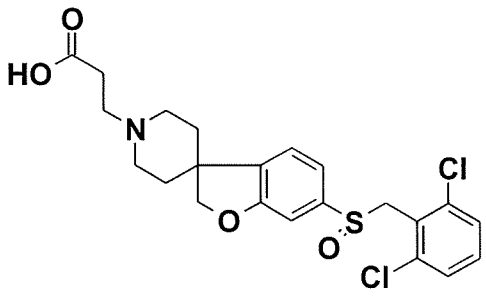


<u>Compound 154.</u> 3-(6-{[(2-Chlorophenyl)methane]sulfonyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. Tert-butyl 3-(6-{[(2-chlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}pro-panoate. (237 mg, 0.50 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 5 minutes at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration. To this HCl salt, dissolved in MeOH (7.50 mL) at 0°C, was added potassium peroxymonosulfate (922 mg; 1.50 mmol) in H_2O (7.50 mL) and the reaction mixture was stirred for 2 hour. Subsequently, the reaction mixture was diluted with dichloromethane and washed with 5% aqueous $NaHCO_3$ and brine. The remaining organic layer was dreid (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, dichloro-methane:acetone 9:1) to afford tert-butyl 3-(6-{[(2-chlorophenyl)methane]sulfonyl}-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl}propanoate (220 mg; 72.5%) which was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (150 mg, 70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.55 (bs, 1H), 10.27 (bs, 1H), 7.24-7.44 (m, 6H), 7.08 (s, 1H),, 4.74 (s, 2H), 4.59 (br s, 2H), 3.24-3.54 (m, 4H), 3.01-3.14 (m, 2H), 2.81-2.89 (t, *J*

=8 Hz, 2H), 2.15-2.28 (m, 2H), 1.89-1.96 (m, 2H). *R*t 1.36 min (System B), $[M+H]^+$ 450.0

The following compound was obtained according to a similar manner:

Compound 299. 3-(6-{[(2,6-Dichlorophenyl)methane]sulfonyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.64 (br s, 1H), 10.27 (br s, 1H), 7.52 (d, *J*=8Hz, 2H), 7.40-7.45 (m, 2H), 7.32-7.39 (m, 2H), 4.87 (s, 2H), 4.63 (s, 2H), 3.26-3.56 (m, 4H), 3.01-3.16 (m, 2H), 2.84 (t, *J*=8Hz, 2H), 2.17-2.28 (m, 2H), 1.91-1.99 (m, 2H). *R*t 1.24 min (System B), $[M+H]^+$ 484.1

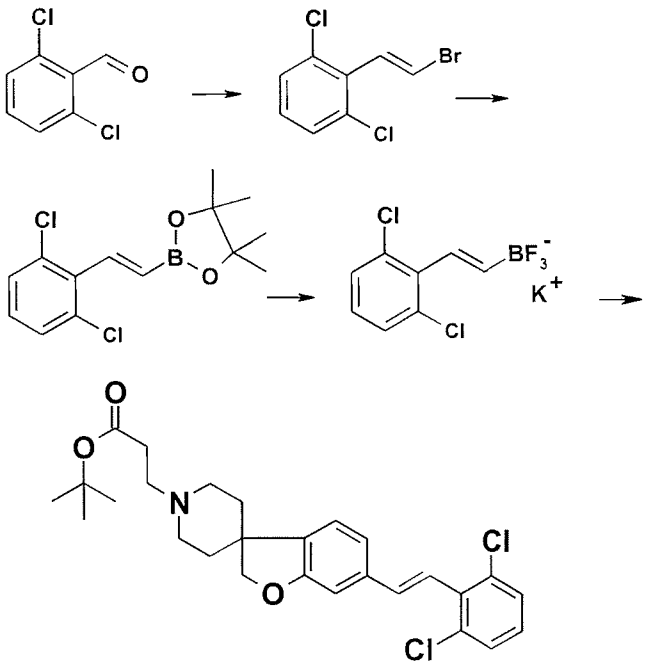


Compound 300. 3-(6-{[(2,6-Dichlorophenyl)methane]sulfinyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. To tert-butyl 3-(6-{[(2,6-dichlorophenyl)-methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoate hydro-chloride. (210 mg, 0.41 mmol), dissolved in MeOH (7.50 mL) at 0°C, was added potassium peroxymonosulfate (254 mg; 0.41 mmol) in H_2O (7.50 mL) and the reaction mixture was stirred for 2 hour. Subsequently, the reaction mixture was diluted with EtOAc and washed with 5% aqueous $NaHCO_3$ and brine. The remaining organic layer was dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, dichloro-methane:acetone 95:5) to afford tert-butyl 3-(6-{[(2,6-dichlorophenyl)methane]sulfinyl}-2H-spiro[1-

Compound 157. 3-{6-[(2-Methylbenzene)sulfonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.21 min (System B), $[M+H]^+$ 416.0

Compound 158. 3-{6-[(2,6-Dichlorobenzene)sulfonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. *R*t 1.63 min (System B), $[M+H]^+$ 469.9

Compound 159. 3-[6-(Benzenesulfonyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride. *R*t 1.40 min (System B), $[M+H]^+$ 384.1



Tert-butyl 3-{6-[(E)-2-(2,6-dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

To a solution (bromomethyl)triphenylphosphonium bromide (23.92 g; 54.85 mmol), dissolved in THF (150 ml) was added a suspension of potassium tert-butoxide (6.16 g; 54.85 mmol) in THF (50 mL), at -78°C (Adv. Synth. Catal., 2006, 348, 851). The reaction mixture was stirred for 2 hours. Subsequently, a

Compound 164. 3-{6-[(E)-2-(2,6-Dichloro-3-ethylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.54 min (System B), $[M+H]^+$ 460.0

Compound 165. 3-{6-[(E)-2-(2,6-Dichloro-4-cyclopropylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.56 min (System B), $[M+H]^+$ 472.0

Compound 166. 3-{6-[(E)-2-(4-Butyl-2,6-dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

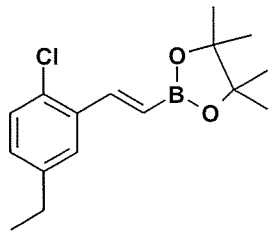
*R*t 1.70 min (System B), $[M+H]^+$ 488.0

Compound 167. 3-{6-[(1Z)-3,3,3-Trifluoro-2-phenylprop-1-en-1-yl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs., 1 H), 9.60 (bs., 1 H), 7.41 - 7.52 (m, 5 H), 7.30 (s, 1 H), 7.15 - 7.25 (m, 1 H), 7.01 (d, *J* =7.7 Hz, 1 H), 6.90 (s, 1 H), 4.53 (s, 2 H), 3.48 – 3.56 (m, 2 H), 3.30 - 3.41 (m, 2 H), 3.02 - 3.20 (m, 2 H), 2.80 (t, *J*=7.4 Hz, 3 H), 2.06 - 2.17 (m, 2 H), 1.94 (bd, J = 14.1 Hz, 2H). *R*t 1.55 min (System B), $[M+H]^+$ 432.0

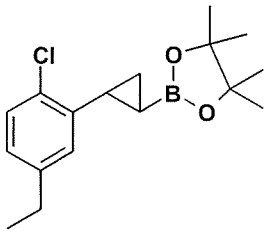
Tert-butyl 3-{6-[2-(2-fluorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[2-(2-chlorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate. ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.30-7.26 (m, 2 H) 7.04 – 7.13 (m, 2H), 6.79 (dd, *J*=7.7 and 1.6Hz, 1H), 6.66 (d, *J*=1.6Hz, 1H), 4.36 (s, 2H), 2.87 – 2.94 (m, 2H), 2.71 (t, *J* =7.6 Hz, 2H), 2.46 (t, *J* =7.6 Hz, 2H), 2.19 – 2.24 (m, 1H), 1.92 – 2.16 (m, 5H), 1.72 – 1.79(m, 2H), 1.54 – 1.61 (m, 1H), 1.46 (s, 9H), 1.37 – 1.41 (m, 1H).

Tert-butyl 3-{6-[2-(2-chloro-5-ethylphenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.



A



B

As an example, NMR data are given for A and B:

A: ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.76 (d, *J*=18.4 Hz, 1H), 7.46 (d, *J*=2.1 Hz, 1H), 7.26 (d, *J*=8.2 Hz, 1H), 7.06 (dd, *J*=8.2, 2.1 Hz, 1H), 6.17 (d, *J*=18.4 Hz, 1H), 2.62 (q, *J*=7.6 Hz, 2H), 1.32 (s, 12H), 1.22 (t, *J*=7.6 Hz, 3H).

B :^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.23 (d, *J*=8.1 Hz, 1 H), 6.93 (dd, *J*=8.1 and 2.0 Hz, 1H), 6.80 (d, *J*=2.0 Hz, 1H), 2.55 (q, *J*=7.6 Hz, 2H), 2.34 (dt, *J*=8.1 and 5.7 Hz, 1H) 1.26 (s, 12H), 1.15 – 1.23 (m, 4H), 1.00 – 1.06 (m, 1H), 0.15 - 0.23 (m, 1H)

Tert-butyl 3-{6-[2-(4-butyl-2,6-dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}propanoate.

Compound 175. **4-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}butanoic acid hydrochloride.** Tert-butyl 4-{6-[2-(2,6-dichlorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoate (268 mg, 0.52 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (239 mg, 92.7%). *R*t 1.44 min (System B), $[M+H]^+$ 460.0.

The following compounds were obtained according to a similar manner:

Compound 176. **2-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}acetic acid hydrochloride.**
*R*t 1.70 min (System B), $[M+H]^+$ 431.9

Compound 177. **3-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid hydrochloride.**
*R*t 1.53 min (System B), $[M+H]^+$ 460.0.

Compound 178. **3-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.20 (bs, 1H), 7.45 (d, *J* =8.1 Hz, 2 H), 7.30 (t, *J* =8.1 Hz, 1, 1H), 6.67 – 7.30 (m, 1H), 6.82 (d, *J* =8.4 Hz, 1, 1H), 6.68 (s, 1H), 4.47 (bs, 2H), 3.42 - 3.55 (m, 2H), 3.21 – 3.42 (m, 2H), 2.95 – 3.14 (m, 2H), 2.86 (t, *J*=8,3Hz, 2H), 2.08 - 2.28 (m, 4H), 1.82 - 1.95 (m, 2H), 1.54 – 1.62 (m, 1H), 1.32 – 1.41 (m, 1H). *R*t 1.45 min (System B), $[M+H]^+$ 446.0.

Compound 179. **3-[6-(2-Phenylcyclopropyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.**
*R*t 1.33 min (System B), $[M+H]^+$ 378.2.

treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (120 mg, 70%). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.55 (br s, 1H), 10.18 (br s, 1H), 7.39-7.45 (m, 2H), 7.28-7.33 (m, 3H), 7.02 (s, 2H), 6.87 (s, 1H), 4.42 (s, 2H), 3.14-3.44 (m, 4H), 2.89-3.01 (m, 2H), 2.73 (t, *J*=8Hz, 2H), 2.05-2.17 (m, 2H), 1.75-1.84 (m, 2H). *R*t 1.37 min (System B), $[M+H]^+$ 363.2.

The following compound was obtained according to a similar manner:

Compound 304. 3-{6-[2-(2-Chlorophenyl)ethynyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.52-7.56 (m, 1H), 7.40-7.44 (m, 1H), 7.22-7.26 (m, 2H), 7.07-7.14 (m, 2H), 6.97 (s, 1H), 4.39 (s, 2H), 2.88-2.95 (m, 2H), 2.70 (t, *J*=8Hz, 2H), 2.45 (t, *J*=8Hz, 2H), 2.03-2.12 (m, 2H), 1.91-2.01 (m, 2H), 1.71-1.78 (m, 2H), 1.46 (s, 9H). *R*t 1.39 min (System B), $[M+H]^+$ 396.2.

Tert-butyl 3-{6-benzyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

To a degassed mixture of B-benzyl-9-BBN (279.3 mg; 1.32 mmol) (0.5 m/l in THF (15 mL) was added potassium phosphate tribasic monohydrate (420 mg; 1.98 mmol) and the reaction mixture was stirred for 15 minutes. Subsequently were added tert-butyl 3-{-{6-[(trifluoromethane)sulfonyloxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoate (307 mg, 0.66 mmol), palladium(II) acetate (6 mg; 0.03 mmol) and 2-dicyclohexylphosphino-2',6'-dimethoxy-1',1'-biphenyl (22 mg; 0.05 mmol). The resulting mixture was heated for 1 hour under reflux. After cooling to RT, the mixture was diluted with EtOAc. The reaction mixture was partitioned between EtOAc and 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, dichloromethane:MeOH 95:1) to afford the product (200 mg; 74.4%). *R*t 1.40 min (System B), $[M+H]^+$ 408.2.

Tert-butyl 3-[6-(2-phenylethyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoate. To a degassed mixture of potassium phenethyltrifluoroboronate (209 mg; 0.99 mmol) in toluene (15 mL) and H2O (1.5 mL), was added potassium phosphate tribasic monohydrate (630 mg; 3 mmol), and the resulting reaction mixture was stirred for 15 minutes. Subsequently was added tert-butyl 3-{-{6-[(trifluoro-methane)sulfonyloxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoate (307 mg, 0.66 mmol), palladium(II) acetate (7 mg; 0.03 mmol) and 2-dicyclohexylphosphino-2',6'-di-isopropoxy-1',1'-biphenyl (30 mg; 0.07 mmol). The resulting mixture was heated for 1 hour in a pre-heated oilbath (100°C). After cooling to RT, the mixture was diluted with EtOAc. The reaction mixture was partitioned between EtOAc and 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by repeated column chromatography (SiO_2, dichloromethane:MeOH 95:5) to afford the product (190 mg; 68.4%). *R*t 1.43 min (System B), $[M+H]^+$ 422.2.

Tert-butyl 3-{6-[(2-(2,6dichlorophenyl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate. To a degassed solution of potassium [2-(2,6-dichlorophenyl)ethyl]trifluoroborate (0.3 g; 1.07 mmol) in toluene (10 mL) and water (1 mL) was added and potassium phosphate tribasic (0.68 g; 3.2 mmol) and the reaction mixture was srtirred for 10 minutes.Subsequently was added tert-butyl 3-{-{6-[(trifluoromethane)sulfonyloxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]pro-panoate (382 mg, 0.82 mmol), palladium(II) acetate (7.3 mg; 0.03 mmol), and 2-dicyclohexylphosphino-2',6'-diisopropoxy-1,1'-biphenyl (30 mg; 0.07 mmol). The resulting mixture was heated under reflux, overnight. After cooling to RT, the mixture was concentrated in vacuo and partitioned between EtOAc and 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by

and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (120 mg, 66.5%). *R*t 1.29 min (System B), $[M+H]^+$ 352.2.

The following compounds were obtained according to a similar manner:

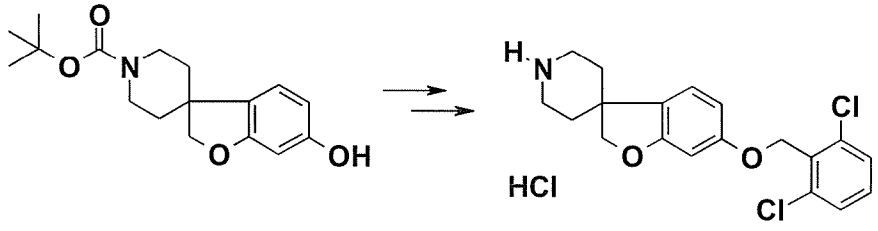
Compound 185. **3-[6-(2-Phenylethyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]**propanoic acid hydrochloride,
*R*t 1.37 min (System B), $[M+H]^+$ 366.2.

Compound 186. **3-{6-[(2-(2-fluorophenyl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}**propanoic acid hydrochloride,
*R*t 1.36 min (System B), $[M+H]^+$ 384.1.

Compound 187. **3-{6-[2-(2-Fluorophenyl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}**propanoic acid hydrochloride, ^1H NMR (400 MHz, DMSO- d_6) δ ppm 12.90 (bs, 1H), 10.20 (bs, 1H) ,7.42-7.48 (m, 2H), 7.27 – 7.32 (m, 1H), 7.04 (bs, 1H), 6.82 (d, *J* =6.2 Hz, 1H), 6,69 (s, 1H), 4.48 (bs, 2H), 3.42 – 3.56 (m, 2H), 3.26 – 3.39 (m, 2H), 3.00 – 3.14 (m, 4H), 2.86 (t, *J* =7.7 Hz, 2H), 2.68 – 2.75 (m, 2H), 2.16 – 2.30 (m, 2H), 1.85 – 1.95 (m, 2H). *R*t 1.42 min (System B), $[M+H]^+$ 433.9.

Compound 188. **3-[6-(Phenoxymethyl)-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl]**propanoic acid hydrochloride, ^1H NMR (400 MHz, DMSO- d_6) δ ppm 12.64 (bs, 1H), 10.18 (bs, 1H), 7.29 (t, *J* =8 Hz, 2H), 7.12 (bs, 1H), 6.88-7.03 (m, 5H), 5.05 (s, 2H), 4.49 (s, 2H), 3.27-3.54 (m, 4H), 3.00-3.16 (m, 2H), 2.84 (t, *J* =8 Hz, 2H), 2.12-2.27 (m, 2H), 1.85-1.94 (m, 2H). *R*t 1.32 min (System B), $[M+H]^+$ 368.2

Compound 189. **3-[6-(Phenylamino)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]**propanoic acid hydrochloride,
*R*t 1.24 min (System B), $[M+H]^+$ 353.2



dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (220 mg; 0.55 mmol) and N-ethyldiisopropylamine (0.19 mL; 1.10 mmol) in MeOH (20 mL), was added formaldehyde (0.08 mL; 1.1 mmol; 37% in H_2O) and sodiumtriacetoxyborohydride (232 mg; 1.1 mmol). Subsequently, the resulting mixture was stirred at RT overnight. Subsequently, the mixture was diluted with EtOAc, washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4), and filtered. The residue was purified by column chromatography (SiO_2, MeOH) to afford the product (160 mg; 67.5%). *R*t 1.36 min (System B), $[M+H]^+$ 378.0.

Compound 192. 3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid hydrochloride. To a mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (0.6 g; 1.5 mmol) in dichloroethane (12 mL), was added tert-butyl acetoacetate (1 mL; 6 mmol), sodiumtriacetoxyborohydride (232 mg; 1.1 mmol) and a drop of acetic acid. Subsequently, the resulting mixture was stirred at RT overnight. Subsequently, the mixture was diluted with EtOAc, washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4), and filtered. The residue was purified by column chromatography (SiO_2, Et_2O:hexanes 1:3) to afford Tert-butyl 3-{6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoate (0.76g; 72.5%). *R*t 1.70 min (System B), $[M+H]^+$ 506.0, which was hydrolyzed using the 4M solution of HCl in 1,4-dioxane conditions, affording the product (90%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.70 (bs, 1H), 7.55-7.59 (m, 2H), 7.46 (dd, *J* =8.1 and 6.2 Hz, 1, 1H) 7.05 (bs, 1 H), 6.55 – 6.62 (m, 2H), 5.18 (s, 2H), 4.52 (bs, 2H), 3.62 – 3.72 (m, 1H), 3.30 – 3.48 (m, 2H), 2.98 – 3.20 (m, 3H), 2.52 – 2.63 (m, 1H) 2.30 – 2.48 (m, 2H). 1.80 – 1.90 (m, 2 H) 1.33 (d, *J* =7.8 Hz, 3H). *R*t 1.70 min (System B), $[M+H]^+$ 450.0.

Compound 193. 3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2,2-difluoropropanoic acid. To a solution of

3.87 (t, J =15.1 Hz, 2H), 3.35 – 3.42 (m, 2H), 3.03 – 3.18 (m, 2H) 2.08 – 2.19 (m, 2H), 1.79 – 1.85 (m, 2H). *R*t 1.77 min (System B), $[M+H]^+$ 472.0.

Compound 194. 3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2,2-dimethylpropanoic acid. To a mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (0.42 g; 1.05 mmol) in dichloroethane (10 mL), was added Tert-butyl 2,2-dimethyl-3-oxopropanoate (0.35 g; 2.1 mmol), sodiumtriacetoxyborohydride (0.6 g; 3 mmol), and the resulting mixture was stirred at RT for 72 hours. Subsequently, the mixture was diluted with EtOAc, washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4), and filtered. The residue was purified by column chromatography (SiO_2, Et_2O:hexanes 1:1) to afford Tert-butyl 3-{6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl-2,2-methylpropanoate (0.54 g). *R*t 1.70 min (System B), $[M+H]^+$ 506.0, which was suspended in THF (11 mL). To this suspension was added lithium hydroxide (82 mg; 3.39 mmol) and the mixture was stirred at 50°C for 48 hours. To this mixture (at RT) were added, 3 mL 1M HCl, 50 mL H_2O and 25 mL phosphate buffer (pH 7). This mixture was washed with dichloromethane (3 times). Subsequently, the organic layer was dried (Na_2SO_4), filtered en concentrated in vacuo and to afford the product (490 mg; 93%).^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 7.36-7.39 (m, 2H) 7.25 (dd, J =8.1 and 6.2Hz, 1H), 7.08 (d, J =8.3 Hz, 1H), 6.60 (dd, J =8.2 and 2.3 Hz , 1H) 6.53 (d, J =2.2 Hz, 1H), 5.23 (s, 2H), 4.39 (s, 2H), 3.08 – 3.18 (m, 2H), 2.45 – 2.62 (m, 4H), 2.01 - 2.11 (m, 2H), 1.80 - 1.88 (m, 2H), 1.27 (s, 6H). *R*t 1.64 min (System B), $[M+H]^+$ 464.0.

Compound 305. 4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-3-methylbutanoic acid. A mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (0.45 g; 1.12 mmol), K_2CO_3 (0.47 g; 3.37 mmol), methyl 4-chloro-3-methylbutanoate and potassium iodide (0.22 g; 1.35 mmol) in CH_3CN (20 mL) was refluxed

chromatography (SiO_2, Et_2O:hexanes 1:1) to afford ethyl 4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}pentanoate (0.14 g; 18.8%). *R*t 1.40 min (System B), $[M+H]^+$ 492.6, which was hydrolyzed to the acid as described for compound **305** (100 mg; 70%). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.54 - 7.59 (m, 2H), 7.44 - 7.50 (m, 1H), 7.07 (d, *J*=8.1 Hz, 1H), 6.53 - 6.60 (m, 2H), 5.17 (s, 2H), 4.41 - 4.48 (m, 2H), 2.97 - 3.10 (m, 2H), 2.72 - 2.82 (m, 1H), 2.58 - 2.69 (m, 1H), 2.25 - 2.41 (m, 2H), 1.91 - 2.13 (m, 4H), 1.75 (d, *J*=12.9 Hz, 2H), 1.52 - 1.63 (m, 1H), 1.12 (d, *J*=6.4 Hz, 3H). *R*t 1.35 min (System B), $[M+H]^+$ 464.6.

Compound 195. 2-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}ethan-1-ol hydrochloride. A mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (1.61 g; 4.02 mmol), 2-(2-chloroethoxy)tetrahydro-2*H*-pyran (0.71mL; 4.82 mmol), K_2CO_3 (1.67 g; 12.05 mmol) and NaI (0.12 g; 0.8 mmol) in DMF 215 mL) was heated to 100°C overnight. After cooling to RT the reaction mixture was partitioned between 5% aqueous $NaHCO_3$ solution and Et_2O. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O) to afford 6-[(2,6-dichlorophenyl)methoxy]-1'-[2-(oxan-3-yloxy)ethyl-2H-spiro[1-benzfuran-3,4'-piperidine] (1 g; 50%), which was dissolved in MeOH (20 mL). To this reaction mixture was aded p-toluenesulfonic acid monohydrate (0.39 g; 2 mmol) and the resulting mixture was stirred at 50°C for 1 hour. The reaction mixture was partitioned between 5% aqueous $NaHCO_3$ solution and EtOAc. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, MeOH) to afford the product (0.46 g), which was converted into its HCl salt by treatment of the product in 1 M HCl in EtOH followed by concentration in vacuo (70 mg; 7.7%).^1H NMR (400 MHz, DMSO-d_6) δ ppm 9.70 (bs., 1H), 7.54 - 7.80 (m, 2H), 7.44 - 7.50 (m, 1H), 7.0 (d, *J* =7.9 Hz, 1H), 6.55 – 6.62 (m, 2H), 5.37 (m, 1H), 5.17 (s, 2H), 4.50 (s,

Compound 197. **6-[(2,6-Dichlorophenyl)methoxy]-1'-[2-(1H-1,2,3,4-tetrazol-5-yl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine].** To a mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (0.51 g; 1.27 mmol) in MeOH (10 mL), was added N-ethyldiisopropylamine (0.27 mL; 1.59 mmol) and acrylonitrile (0.11 mL; 2.8 mmol) and the resulting mixture was stirred at 80°C for 4 hours (in a closed pyrex bottle). Subsequently, the mixture was concentrated in vacuo and the residue was purified by column chromatography (SiO_2, Et_2O) to afford 3-{6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine]-1'-yl}pro-panenitrile (0.31 g; 58%). *R*t 1.80 min (System B), $[M+H]^+$ 417.0, which was dissolved in toluene (10 mL). Subsequently was added azidotrimethyltin (0.39 g; 1.8 mmol) and the reaction mixture was heated for 72 hours at 100°C. Subsequently, the mixture was concentrated in vacuo and the residue was purified by column chromatography (SiO_2, EtOAc:MeOH 9:1, followed by MeOH) to afford the product (0.09 g; 29.3%). *R*t 1.54 min (System B), $[M+H]^+$ 460.0.

Compound 198. **(3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propyl)phosphonic acid.** A mixture of 6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine] (0.59 g; 1.47 mmol), diethyl (3-bromopropyl)phosphonate (0.34 mL; 1.77 mmol), NaI (0.04 g; 0.29 mmol), and K_2CO_3 (0.61 g; 4.42 mmol) in CH_3CN (10 mL) was heated under reflux for 2 hours. After cooling to RT the mixture was partitioned between 5% aqueous $NaHCO_3$ solution and Et_2O. The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, EtOAc:MeOH 90:10) to afford diethyl (3-{6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propyl)phosphonate (0.8 g; 85..1%). *R*t 1.62 min (System B), $[M+H]^+$ 542.0,. To a solution of diethyl (3-{6-[(2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propyl)phosphonate (0.68 g; 1.25 mmol) in CH_2Cl_2 (15 mL) was added bromotrimethylsilane (1.32 ml; 10 mmol)

2.15-2.05 (m, 2H), 1.96-1.86 (m, 2H), 1.70-1.78 (m, 2H), 1.46 (s, 9H). *R*t 1.38 min (System B), $[M+H]^+$ 459.0.

The following compound was obtained in a similar manner:

Tert-butyl 3-{5-[(2,6-dichlorophenyl)methoxy-2H-spiro[furo[2,3-b]pyridine-1,4'-piperidine]-1'-yl]propanoate.

^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 7.21-7.37 (m, 4H), 6.31 (d, *J* =7.8 Hz, 1H), 5.54 (s, 2H), 4.42 (s, 2H), 2.90-2.82 (m, 2H), 2.70 (t, *J* =7.5 Hz, 2H), 2.44 (t, *J* =7.5 Hz, 2H), 2.17-2.06 (m, 2H), 1.97-1.87 (m, 2H), 1.79-1.69 (m, 2H), 1.46 (s, 9H). *R*t 1.40 min (System B), $[M+H]^+$ 493.0.

***Tert*-butyl 3-[5-(2,6-dimethylphenoxy)-2H-spiro[furo[2,3-b]pyridine-1,4'-piperidine]-1'-yl]propanoate.** To a degassed solution of tert-butyl 3-{5-bromo-2H-spiro[furo[2,3-b]pyridine-1,4'-piperidine]-1'-yl}propanoate (250 mg; 0.63 mmol)

In xylene (3 mL), was added subsequently, 2,6-dimethylphenol (76.78 mg; 0.63 mmol), potassium carbonate (173.92 mg; 1.26 mmol), 1-butylimidazole (0.50 mL; 3.8 mmol) and copper(I) iodide (23.97 mg; 0.13 mmol). The reaction mixture was heated at 140 °C and stirred overnight After cooling to RT, the reaction mixture was diluted with EtOAc, filtered and washed with 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O:hexanes:triethylamine 50:49:1) to afford the product (70 mg, 25%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ ppm: 7.33 (d, *J*= 7.8 Hz, 1H), 7.07-7.02 (m, 3H), 6.09 (d, *J*=7.8 Hz, 1H), 4.38 (s, 2H), 2.89-2.81 (m, 2H), 2.69 (t, *J*= 7.5 Hz, 1H), 2.43 (t, *J*=7.5 Hz, 2H), 2.13 (s, 6H), 2.10-2.03 (m, 2H), 1.95-1.85 (m, 2H), 1.78-1.71 (m, 2H), 1.45 (s, 9H). *R*t 1.35 min (System B), $[M+H]^+$ 493.1.

<u>Compound 200.</u> 3-{5-[(2-Chlorophenyl)methoxy-2H-spiro[furo[2,3-b]pyridine-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

Tert-butyl 3-{5-[(2-chlorophenyl)methoxy-2H-spiro[furo[2,3-b]pyridine-1,4'-piperidine]-1'-yl)propanoate (200 mg, 0.44 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (170 mg, 88%). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.08 (bs, 1H), 10.9 (bs, 1H), 7.56-7.48 (m, 3H), 7.41-7.36 (m,, 2H), 6.45 (d, 1H), 5.32 (s, 2H), 4.56-4.55 (m, 2H), 3.5-3.4 (m, 2H), 3.37-3.27 (m, 2H), 3.20-3.01 (m, 2H), 2.87 (t, J = 7.4 Hz, 2H), 2.30-2.10 (m, 2H), 1.96-1.87 (m, 2H). *R*t 1.30 min (System B), $[M+H]^+$ 403.0

In a similar manner were made:

Compound 201. 3-{5-[(2,6-Dichlorophenyl)methoxy-2H-spiro[furo[2,3-b]pyri-dine-3,4'-piperidine]-1'-yl)propanoic acid hydrochloride. ^1H-NMR (DMSO-d_6, 400 MHz) δ ppm: 12.08 (bs, 1H), 10.03 (bs, 1H), 7.58-7.41 (m, 4H), 6.40 – 6.36 (m, 2H), 5.39 (s, 2H), 4.59-4.53 (m, 2H), 3.55-3.4 (m, 2H), 3.34-3.22 (m, 2H), 3.15-2.99 (m, 2H), 2.85 (t, J = 7.3 Hz, 2H), 2.28-2.13 (m, 2H), 1.96-1.87 (m, 2H). *R*t 1.32 min (System B), $[M+H]^+$ 436.9

Compound 202. 3-[5-(2,6-Dimethylphenoxy)-2H-spiro[furo[2,3-b]pyridine-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride. ^1H-NMR (DMSO-d_6, 400 MHz) δ ppm: 12.08 (bs, 1H), 10.03 (bs, 1H), 7.52 (s, 1H), 7.15-7.04 (m, 3H), 6.40 – 6.36 (m, 2H), 4.53-4.40 (m, 2H), 3.52-3.40 (m, 2H), 3.39-3.25 (m, 2H), 3.13-2.93 (m, 2H), 2.84 (t, J = 7.3 Hz, 2H), 2.20-2.08 (m, 2H), 2.03 (s, 6H), 1.97-1.87 (m, 2H). *R*t 1.24 min (System B), $[M+H]^+$ 383.1

1,4'-piperidine]-1'-yl}propanoate (0.26 g; 56.1%). *R*t 1.45 min (System B), $[M+H]^+$ 492.1.

The following compounds were obtained in a similar manner:

Tert-butyl 3-[5-(cyclohexylmethoxy)-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(2-chlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-(5-{[2-(trifluoromethyl)phenyl]methoxy}-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-[5-(oxan-2-ylmethoxy)-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(3-chlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(2,3-dichlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-(5-{[3-(trifluoromethyl)phenyl]methoxy}-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(2,5-dichlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{5-[(3,5-dichlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate.

<u>Compound 203.</u> **3-{5-[(2,6-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** Tert-butyl 3-{5-[(2,6-dichlorophenyl)methoxy]-3-H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoate (260 mg, 0.53 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (8 mL; 4 mol/l; 32 mmol) and stirred for 72 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried

overnight under reduced pressure to afford the product (220 mg, 95.5%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs., 1H), 10.40 (bs, 1H), 7.56 – 7.60 (m, 2H), 7.46 - 7.51 (m, 1H), 7.00 - 7.18 (m, 3H), 5.22 (s, 2H), 5.02 (s, 2H), 3.42 - 3.49 (m, 2H), 3.30 – 3.39 (m, 2H), 3.11 - 3.21 (m, 2H), 2.84 (t, J =7.6 Hz, 2H), 2.21 – 2.31 (m, 2H), 1.78 - 1.86 (m, 2H). *R*t 1.35 min (System B), $[M+H]^+$ 436.1.

The following compounds were obtained in a similar manner:

Compound 204. 3-{5-(Cyclohexylmethoxy)-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.41 min (System B), $[M+H]^+$ 374.2.

Compound 205. 3-{5-[(2-Chlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.35 min (System B), $[M+H]^+$ 402.1.

Compound 206. 3-(5-{[2-(Trifluoromethyl)phenyl]methoxy}-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

*R*t 1.36 min (System B), $[M+H]^+$ 436.1.

Compound 207. 3-{5-(Oxan-2-ylmethoxy)-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.17 min (System B), $[M+H]^+$ 376.2.

Compound 208. 3-{5-[(3-Chlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.34 min (System B), $[M+H]^+$ 402.1.

Compound 209. 3-{5-[(2,3-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs, 1H), 10.40 (bs, 1H), 7.65 – 7.79 (m, 1H), 7.56 - 7.60 (m, 1H), 7.43 (t, J =7.5 Hz, 1H), 6.98 – 7.13 (m, 3H), 5.20 (s, 2H), 5.01 (s, 2H), 3.43 - 3.51 (m, 2H), 3.31 – 3.39 (m, 2H), 3.12 - 3.23 (m, 2H), 2.85 (t, J =7.6 Hz, 2H). 2.21 – 2.31 (m, 2H), 1.78 - 1.86 (m, 2H). *R*t 1.40 min (System B), $[M+H]^+$ 436.1.

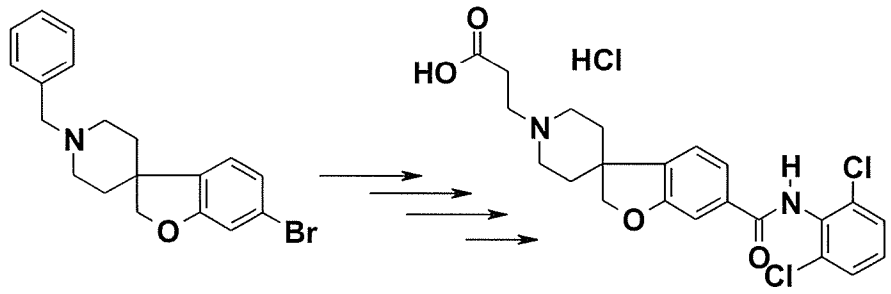
Compound 210. 3-(5-{[3-(Trifluoromethyl)phenyl]methoxy}-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl)propanoic acid hydrochloride.

*R*t 1.40 min (System B), $[M+H]^+$ 436.1.

Compound 211. 3-{5-[(2,5-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

*R*t 1.43 min (System B), $[M+H]^+$ 436.1.

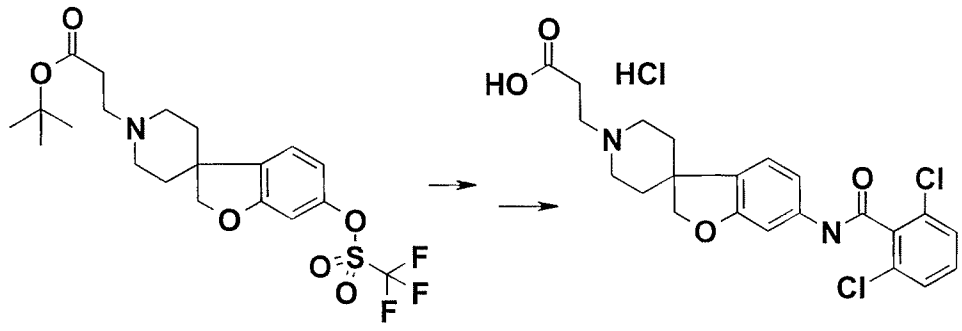
Compound 212. 3-{5-[(3,5-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.80 (bs, 1H), 10.50 (bs, 1H), 7.58 – 7.61 (m, 1H), 7.50 - 7.53 (m, 2H), 6.96 - 7.10 (m, 3H), 5.13 (s, 2H), 4.99 (s, 2H), 3.44 - 3.53 (m, 2H), 3.30 – 3.39 (m, 2H), 3.11 - 3.22 (m, 2H), 2.86 (t, *J* =7.6 Hz, 2H), 2.21 – 2.32 (m, 2H), 1.76 - 1.85 (m, 2H).



Compound 213. 3-{6-[((2,6-Dichlorophenyl)carbamoyl)]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride

To a solution of 1'-benzyl-6-bromo-2H-spiro[1-benzofuran-3,4'-piperidine] (0.51 g; 0.87 mmol) in tetrahydrofuran (50 mL) was cooled to -78 °C and *n*-butyllithium (0.35 mL, 2.5 mol/l in hexane, 0.87 mmol) was added.

(System B), $[M+H]^+$ 505.1, which was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the title compound (140 mg, 80.9%). *R*t 1.09 min (System B), $[M+H]^+$ 449.1.

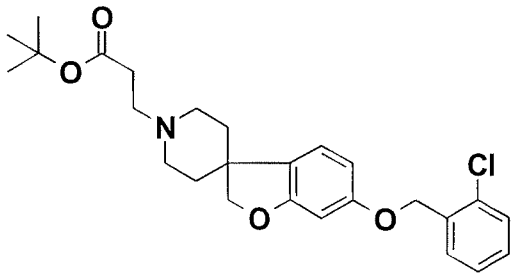


<u>Compound 311.</u> 3-{6-[(2,6-Dichlorobenzene)amido]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.

To a degassed solution of 2,6-dichlorobenzamide (113 mg; 0.6 mmol) and tert-butyl 3-{-{6-[(trifluoromethane)sulfonyloxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-propanoate (232 mg, 0.5 mmol) in tert-butyl alcohol (7.5 mL), was added potassium phosphate tribasic (0.16 g; 0.75 mmol). Subsequently were added tris-(dibenzylidenaceton)-dipalladium(0) (9.1 mg; 0.01 mmol), and 2-di-t-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-tri-i-propylbiphenyl (24 mg; 0.05 mmol). The resulting mixture was heated under reflux, overnight. After cooling to RT, the mixture was concentrated in vacuo and partitioned between EtOAc and 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, dichloromethane:aceton 9:1) to afford the product (0.18

g; 71%). ^{1}H NMR (400 MHz, $CHCl_3$-*d*) δ ppm 7.56 (br s, 1H), 7.38-7.45 (m, 1H), 7.22 (d, *J*=2Hz, 1H), 6.96-7.10 (m, 3H), 5.90 (br s, 1H), 4.39 (s, 2H), 2.87-2.94 (m, 2H), 2,70 (t, *J*=8Hz, 2H), 2.45 (t, *J*=8Hz, 2H), 2.03-2.12 (m, 2H), 1.90-1.99 (m, 2H), 1.71-1.77 (m, 2H), 1.48 (s, 9H), *R*t 1.31 min (System B), $[M+H]^+$ 505.2, which was dissolved in a 4M solution of HCl in 1,4-dioxane (20 mL; 4 mol/l; 80 mmol) and stirred for *3* hours at 65°C. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (80 mg, 49%). ^{1}H NMR (400 MHz, DMSO- d_6) δ ppm 10.73 (s, 1H), 7.46-7.62 (m, 3H), 7.28 (br s, 1H), 7.13-7.18 (m, 2H), 4.49 (br s, 2H), 3.30-3.51 (m, 4H), 3.00-3,20 (m, 2H), 2.81-2.87 (m, 2H), 2.12-2.19 (m, 2H), 1.86-1.92 (m, 2H). *R*t 1.25 min (System B), $[M+H]^+$ 449.2

Compound 312. 3-{6-[(2,6-Difluorobenzene)amido]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.64 (br s, 1H), 10.82 (s, 1H), 10.27 (br s, 1H), 7.56-7.63 (m, 1H), 7.04-7.29 (m, 5H), 4.51 (br s, 2H), 3.29-3.55 (m, 4H), 3.05-3.12 (m, 2H), 2.82-2.89 (m, 2H), 2.15-2.24 (m, 2H), 1.84-1.93 (m, 2H).



Tert-butyl 3-{6-[(2-chlorophenyl)methoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate. Cs_2CO_3 (240 mg; 0.735 mmol) and NaI (4 mg; 0.025 mmol) are placed as solid in a 16x100 mm glass tube reactor fitted with a magnetic stir bar. A solution of tert-butyl 3-{6-hydroxy-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate (81 mg; 0.245 mmol) in CH_3CN/THF/DMF 1.5:1:1.5 (0.061M) is added and the mixture is stirred at RT

Tert-butyl 3-{6-[2-(benzyloxy)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.
Tert-butyl 3-{6-[(4-methanesulfonylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Compound 214. **3-{6-[(2-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** The crude Tert-butyl 3-{6-[(2-chlorophenyl)methoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate was treated with a mixture of TFA/DCM 2:1 and stirred at RT for 2h. Subsequently, the volatiles were removed using a nitrogen flow and subsequently a Genevac HT4 full vacuum at 40°C for 14 hours. The crude product was purified by preparative HPLC to afford the title compound; R_t = 1.38 min. (System A), $[M+H]^+$ Found: 403.21; Calc: 402.14. Conditions for the preparative LC-MS: Injection of the crude product dissolved in 600 □L DMSO/CH_3CN 1:2; column ACQUITY UPLC BEH C18 1.7 μm (50 x 2.1 mm x 1.7 μm) at 45°C. Mobile phase A = water + 0.1% CH_3COOH and B = CH_3CN + 0.1% CH_3COOH, from 5% B to 90% B in 5 minutes. C18 flow rate 0.8 mL/minute, detection with UV 210-260nm.

The following compounds were obtained similarly:

Compound 215. **3-[6-(Benzyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid trifluoroacetic acid.** R_t = 1.28 min. (System A), $[M+H]^+$ Found: 368.23; Calc: 368.18.

Compound 216. **3-{6-[(4-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** R_t = 1.42 min. (System A), $[M+H]^+$ Found: 403.21; Calc: 402.14.

Compound 217. **3-{6-[(6-Cyanohexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** R_t = 1.18 min. (System A), $[M+H]^+$ Found: 387.28; Calc: 387.22.

chromatography (SiO_2, dichloromethane:acetone 9:1) to afford the product (120 mg; 55.7%). *R*t 1.47 min (System B), $[M+H]^+$ 436.2.

The following compounds were obtained in a similar manner:

Tert-butyl 3-{6-benzoyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[(2-chlorophenyl)carbonyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[(2E)-3-phenylprop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[(2E)-3-(2-chlorophenyl)prop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[(1-benzofuran-2-yl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-{6-[(2-phenylcyclopropyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate.

Tert-butyl 3-[6-(3-phenylpropanoyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoate.

<u>Compound 240.</u> **3-{6-[(2-Methylphenyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** Tert-butyl 3-{6-[(2-chlorophenyl)carbonyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate (100 mg, 0.23 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (20 mL; 4 mol/l; 80 mmol) and stirred for 48 hours at RT. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (0.7 g, 73%). *R*t 1.36 min (System B), $[M+H]^+$ 380.1.

The following compounds were obtained obtained in a similar manner:

Compound 241. **3-{6-Benzoyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** *R*t 1.45 min (System B), $[M+H]^+$ 366.2.

Compound 242. **3-{6-[(2-Chlorophenyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** ^1H NMR (400 MHz, DMSO-d_6) δ ppm 12.72 (bs, 1H), 10.20 (bs, 1H), 7.58-7.63 (m, 2H), 7.46-7.52 (m, 2H), 7.39-7.42 (m, 1H), 7.22-7.26 (m, 1H), 7.15 (bs, 1H), 4.59 (bs, 2H), 3.29-3.56 (m, 4H), 3.04-3.13 (m, 2H), 2.81-2.88 (m, 2H), 2.15-2.25 (m, 2H), 1.92-2.01 (m, 2H). *R*t 1.55 min (System B), $[M+H]^+$ 400.0

Compound 243. **3-{6-[(2E)-3-Phenylprop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** Tert- butyl 3-{6-[(2E)-3-phenylprop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoate (200 mg, 0.45 mmol) was dissolved DCM (6 mL) and trifluoroacetic acid was added (2 mL; 25.96 mmol) and stirred at RT overnigth. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (0.21 g; 88.3%). *R*t 1.35 min (System B), $[M+H]^+$ 392.1.

The following compounds were obtained obtained in a similar manner:

Compound 244. **3-{6-[(2E)-3-(2-Chlorophenyl)prop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** *R*t 1.38 min (System B), $[M+H]^+$ 426.0.

Compound 245. **3-{6-[(1-Benzofuran-2-yl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** *R*t 1.26 min (System B), $[M+H]^+$ 406.1.

Compound 246. **3-{6-[(2-Phenylcyclopropyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid trifluoroacetic acid.** *R*t 1.31 min (System B), $[M+H]^+$ 406.1.

RT, the mixture was concentrated in vacuo and partitioned between EtOAc and 5% aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, DCM:MeOH 97:3) to afford the product (150 mg; 51%). *R*t 1.38 min (System B), $[M+H]^+$ 410.2.

The following compound was obtained in a similar manner:
Tert-butyl 3-[6-(2,6-dimethylphenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoate.

<u>Compound 248.</u> **3-[6-(2,6-Dichlorophenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.** Tert-butyl 3-[6-(2,6-dichlorophenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl]propanoate (120 mg, 0.25 mmol) was dissolved in a 4M solution of HCl in 1,4-dioxane (10 mL; 4 mol/l; 40 mmol) and stirred for 2 hours at 50°C. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford the product (0.1 g, 86.9%). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 12.70 (bs, 1H), 10.10 (bs, 1H), 7.64 (d, *J* =8.2 Hz, 2H), 7.38 (t, *J* =8.2 Hz, 1H), 6.97 - 7.06 (m, 1H), 6.24 – 6.33 (m, 2H), 4.51 (bs, 2H), 3.43 – 3.52 (m, 2H), 3.26 - 3.37 (m, 2H), 2.96 – 3.09 (m, 2H), 2.83 (t, *J* =7.5 Hz, 2H), 2.07 – 2.18 (m, 2H), 1.86 - 1.93 (m, 2H) *R*t 1.33 min (System B), $[M+H]^+$ 422.0.

The following compounds were obtained in a similar manner:
<u>Compound 249.</u> **3-{(6-Phenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid hydrochloride.** *R*t 1.27 min (System B), $[M+H]^+$ 354.1.
<u>Compound 250.</u> **3-[6-(2,6-Dimethylphenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid hydrochloride.** *R*t 1.36 min (System B), $[M+H]^+$ 382.2

7.00 (d, *J*=8.0 Hz, 1H), 6.29 (dd, *J*=8.2, 2.1 Hz, 1H), 6.21 (d, *J*=2.1 Hz, 1H), 5.93 (q, *J*=6.6 Hz, 1H), 4.41 (d, *J*=8.8 Hz, 1H), 4.18 (d, *J*=8.8 Hz, 1H), 2.69 - 2.77 (m, 2H), 2.44 - 2.62 (m, 4H), 2.28 - 2.35 (m, 2H), 1.99 - 2.09 (m, 3H), 1.67 (d, *J*=6.6 Hz, 3H), 1.48 - 1.63 (m, 3H), 1.34 - 1.48 (m, 1H). *R*t 1.42 min (System B), $[M+H]^+$ 416.2

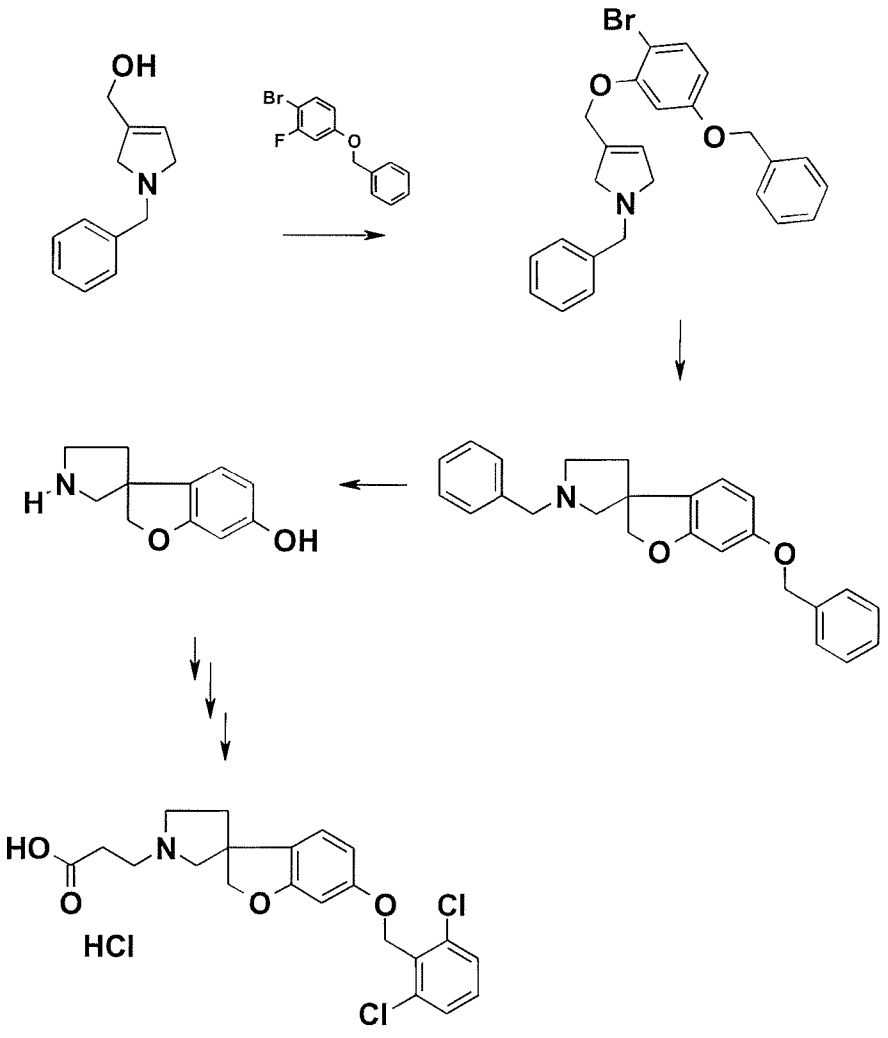
Compound 328. 3-(6-{[2-Fluoro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl)propanoic acid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.62 - 7.77 (m, 3H), 7.11 (d, *J*=8.8 Hz, 1H), 6.45 - 6.53 (m, 2H), 5.09 (s, 2H), 4.48 (d, *J*=9.0 Hz, 1H), 4.25 (d, *J*=9.0 Hz, 1H), 2.71 - 2.81 (m, 1H), 2.52 - 2.66 (m, 3H), 2.35 (t, *J*=6.9 Hz, 2H), 2.05 - 2.18 (m, 2H), 1.53 - 1.70 (m, 3H), 1.37 - 1.52 (m, 1H). *R*t 1.45 min (System B), $[M+H]^+$ 454.2

Compound 329. 3-[6-(Oct-7-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]- 1'-yl]propanoic acid, was prepared from tert-butyl 3-{6-hydroxy-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoate using the method described for compound **275**. ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 12.10 (br. s., 1H), 7.04 (d, *J*=8.1 Hz, 1H), 6.32 - 6.41 (m, 2H), 5.73 – 5.84 (m, 1H), 4.95 (m, 2H), 4.46 (d, *J*=8.8 Hz, 1H), 4.22 (d, *J*=8.8 Hz, 1H), 3.88 (t, *J*=6.5 Hz, 2H), 2.72 - 2.80 (m, 1H), 2.51 - 2.67 (m, 3H), 2.31 - 2.40 (t, *J*=6.9 Hz, 2H), 1.97 - 2.18 (m, 3H), 1.53 - 1.71 (m, 6H), 1.26 - 1.50 (m, 7H). *R*t 1.37 min (System B), $[M+H]^+$ 388.3

The following compounds were obtained according to a similar manner:

Compound 330. 3-[6-(Hept-6-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl]propanoic acid. ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 12.10 (br. s., 1H), 7.04 (d, *J*=8.1 Hz, 1H), 6.32 - 6.40 (m, 2H), 5.80 (ddt, *J*=17.0, 10.3, 6.7, 6.7 Hz, 1H), 4.90 - 5.06 (m, 2H), 4.45 (d, *J*=8.8 Hz, 1H), 4.22 (d, *J*=8.9 Hz, 1H), 3.88 (t, *J*=6.5 Hz, 2H), 2.69 - 2.80 (m, 1H), 2.51 - 2.65 (m, 3H), 2.29 - 2.39 (m, 2H), 1.98 - 2.16 (m, 4H), 1.52 - 1.73 (m, 5H), 1.33 - 1.48 (m, 5H). *R*t 1.53 min (System B), $[M+H]^+$ 374.3

<u>Compound 331.</u> 3-[6-(Hex-5-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]- 1'-yl]propanoic acid. ^{1}H NMR (400 MHz, $CDCl_3$-*d*) δ ppm 12.10 (br. s., 1H), 7.04 (d, *J*=8.1 Hz, 1H), 6.29 - 6.42 (m, 2H), 5.69 - 5.91 (m, 1H), 4.90 - 5.10 (m, 2H), 4.45 (d, *J*=9.4 Hz, 1H), 4.22 (d, *J*=9.4 Hz, 1H), 3.84 - 3.94 (m, 2H), 2.69 – 2.83 (m, 1H), 2.60 – 2.68 (s, 3H), 2.28 - 2.41 (m, 2H), 2.00 - 2.18 (m, 3H), 1.33 - 1.77 (m, 9H). *R*t 1.53 min (System B), $[M+H]^+$ 360.3



2.79 (m, 10H), 2.08 - 2.17 (m, 1H), 1.46 (s, 9H). *R*t 1.04 min (System B), $[M+H]^+$ 334.1

A mixture of tert-butyl 3-{5-hydroxy-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoate (315 mg; 0.94 mmol), K_2CO_3 (0.39 g; 2.83 mmol) and 2,6-dichlorobenzylbromide (250 mg; 1.04 mmol) in CH_3CN (10 mL) was stirred overnight (at RT). The reaction mixture was partitioned between 5% aqueous $NaHCO_3$ solution and Et_2O. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, Et_2O:hexanes 4:6) to afford tert-butyl 3-{5-[(2,6-Dichlorophenyl)methoxy]-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoate (0.387 g; 83%). *R*t 1.68 min (System B), $[M+H]^+$ 492.0., which was dissolved in a 1M solution of HCl in 1,4-dioxane (10 mL) and stirred for 2 hours at 70°C. Subsequently, the solvent was removed in vacuo and the residue treated with iPr_2O, the precipitate was collected by filtration and dried overnight under reduced pressure to afford 3-{5-[(2,6-dichlorophenyl)methoxy]-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid hydrochloride (300 mg, 83%). ^{1}H NMR (400 MHz, DMSO-*d*) δ ppm 12.80 (bs, 1H), 11.20 (bs, 1H), 7.58 (d, *J*=8.0 Hz, 2H), 7.47 (t, *J*=8.0 Hz, 1H), 7.29 (d, *J*=8.8 Hz, 1H), 7.02 (s, 1H), 6.95 (d, *J*=8.8 Hz, 1H), 5.22 (s, 2H), 3.98 (d, *J*=7.5 Hz, 2H), 2.88 – 3.54 (m, 11H), 2.08 – 2.18 (m, 1H). *R*t 1.45 min (System B), $[M+H]^+$ 435.9.

The following compounds were obtained according to a similar manner:

Compound 334. 3-{5-(Octyloxy)-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz, DMSO-*d*) δ ppm 12.80 (bs, 1H), 11.20 (bs, 1H), 7.23 (d, *J*=8.8 Hz, 1H), 6.78 – 6.86 (m, 2H), 3.85 – 4.03 (m, 4H), 3.24 – 3.50 (m, 4H), 3.05 – 3.23 (m, 2H), 2.80 – 3.03 (m, 5H), 2.04 – 2.18 (m, 1H), 1.62 – 1.75 (m, 2H), 1.18 – 1.45 (m, 10 H), 0.85 – 0.95 (m, 3H).

Compound 335. 3-{5-(2,6-Dichlorophenoxy)-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid hydrochloride. ^{1}H NMR (400 MHz,

coelenteramide, CO_2 and light (λ_{max} 469nm). This luminescent response is dependent on the agonist concentration. Luminescence is measured using the MicroBeta Jet (Perkin Elmer). Agonistic effects of compounds are expressed as pEC_{50}. Compounds were tested at a 10 points half log concentration range, and 3 independent experiments were performed in single point's measurements.

***In vitro* functional activity (agonism) on human S1P3 receptors**

The CHO-human-S1P3- Aeqorin assay (CHO/Gα16/AEQ/h-$S1P_3$) was established at Solvay Pharmaceuticals. The plasmid DNA coding for the S1P3 receptor (accession number in GenBank NM_005226 was purchased from UMR cDNA resource Centre (Rolla, MO). The pcDNA3.1/hS1P3 construct carrying the mitochondrially targeted apo-Aeqorin and Gα16 protein was transfected in CHO K1 cell-line.

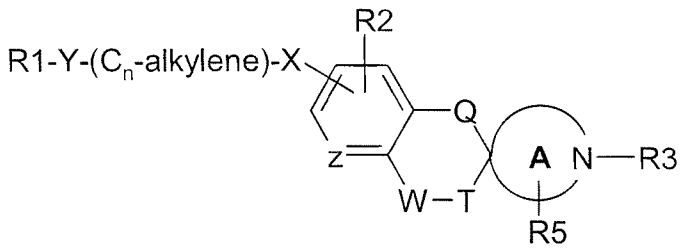
Human-S1P3-Aequorin cells express mitochondrial targeted apo-Aequorin. Cells have to be loaded with coelanterazine, in order to reconstitute active Aequorin. After binding of agonists to the human S1P3 receptor the intracellular calcium concentration increases and binding of calcium to the apo-Aequorin/coelenterazine complex leads to an oxidation reaction of coelenterazine, which results in the production of apo-Aequorin, coelenteramide, CO_2 and light (λ_{max} 469nm). This luminescent response is dependent on the agonist concentration. Luminescence is measured using the MicroBeta Jet (Perkin Elmer). Agonistic effects of compounds are expressed as pEC_{50}. Compounds were tested at a 10 points half log concentration range, and 3 independent experiments were performed in single point's measurements.

***In vitro* functional activity (agonism) on human S1P1 receptors (method A)**

The CHO-K1-human-S1P1-Aeqorin assay was bought from Euroscreen *Fast*, Brussels (Euroscreen, Technical dossier, Human S1P1 (Edg1) receptor, DNA clone and CHO-K1 AequoScreen™ recombinant cell-line, catalog n°: FAST-

Claims

1. A spiro-cyclic amine derivative of the formula (**I**)



(**I**)

wherein
R1 is selected from

cyano,

(2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkyl each optionally substituted with CN or one or more fluoro atoms,

(3-6C)cycloalkyl, (4-6C)cycloalkenyl or a (8-10C)bicyclic group, each optionally substituted with halogen or (1-4C)alkyl,

phenyl, biphenyl, naphthyl, each optionally substituted with one or more substituents independently selected from halogen, cyano, (1-6C)alkyl optionally substituted with one or more fluoro atoms, (1-6C)alkoxy optionally substituted with one or more fluoro atoms, amino, di(1-4C)alkylamino and (3-6C)cycloalkyl optionally substituted with phenyl which may be substituted with (1-4C)alkyl or halogen,

phenyl substituted with phenoxy, benzyl, benzyloxy, phenylethyl or monocyclic heterocycle, each optionally substituted with (1-4C)alkyl optionally substituted with one or more fluoro atoms,

monocyclic heterocycle optionally independently substituted with halogen, (1-6C)alkyl optionally substituted with one or more fluoro atoms, (3-6C)cycloalkyl, or phenyl optionally substituted with (1-4C)alkyl or halogen,

and

bicyclic heterocycle optionally substituted with halogen or (1-4C)alkyl optionally substituted with one or more fluoro atoms;

–Y-(C_n-alkylene)-X- is a linking group wherein

Y is attached to R1 and selected from a bond, -O-, -CO-, -S-, -SO-, -SO_2-, -NH-, -CH=CH-, -C(CF_3)=CH-, -C ≡C-, -CH_2-O-, -O-CO-, -CO-O-, -CO-NH-, -NH-CO-, and trans-cyclopropylene;

n is an integer from 0 to 10; and

X is attached to the phenylene/pyridyl moiety and selected from a bond, -O-, -S-, -SO-, -SO_2-, -NH-, -CO-, -CH=CH-, and trans-cyclopropylene;

R2 is H or independently selected from one or more substituents selected from halogen, (1-4C)alkoxy and (1-4C)alkyl optionally substituted with one or more fluor atoms; and

R3 is (1-4C)alkylene-R4 wherein the alkylene group may be substituted with one or more halogen atoms or with $(CH_2)_2$ to form a cyclopropyl moiety, or R3 is (3-6C)cycloalkylene-R4, -CH_2-(3-6C)cycloalkylene-R4, (3-6C)cycloalkylene-CH_2-R4 or -CO-CH_2-R4, wherein R4 is -PO_3H_2, -OPO_3H_2, -COOH, -COO(1-4C)alkyl or tetrazol-5-yl;

Q is a bond;

-W-T- is selected from -CH=CH-, -CH_2-CH_2-, -CH_2-O-, -O-CH_2-, -O-CH_2-CH_2- and -CO-O-;

R5 is H or independently selected from one or more halogens;

Z is CH, CR2 or N; and

A represents a morpholine ring structure or a 5-, 6- or 7-membered cyclic amine;

or a pharmaceutically acceptable salt, or one or more N-oxides thereof.

2. The compound of claim 1, wherein R3 is selected from -$(CH_2)_2$-OH, -CH_2-COOH, -$(CH_2)_2$-COOH, -$(CH_2)_3$-COOH, -CH_2-$CHCH_3$-COOH, -CH_2-$C(CH_3)_2$-COOH, -$CHCH_3$-CH_2-COOH, -CH_2-CF_2-COOH, -CO-CH_2-COOH, 1,3-cyclobutylene-COOH, -$(CH_2)_2$-PO_3H_2, -$(CH_2)_3$-PO_3H_2, -$(CH_2)_2$-OPO_3H_2, -$(CH_2)_3$-OPO_3H_2, -CH_2-tetrazol-5-yl, -$(CH_2)_2$-tetrazol-5-yl and -$(CH_2)_3$-tetrazol-5-yl.

3. The compound of any one of claims 1 to 2, wherein R2 is H, methyl, chloro or fluoro and Z is CH or CR2.

4. The compound of any one of claims 1 to 3, wherein -W-T- is selected from -CH_2-O-, -O-CH_2-, -O-CH_2-CH_2-, -CO-O-; and R5 is H.

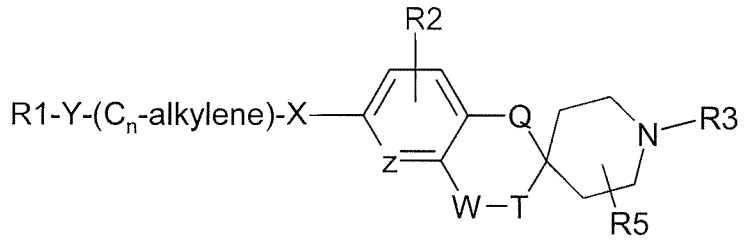
5. The compound of any one of claims 1 to 4, wherein Y is selected from a bond, -O-, -CO-, -CH=CH-, -C(CF_3)=CH-, -C ≡C-, and trans-cyclopropylene; n is an integer from 0 to 6.

6. The compound of any one of claims 1 to 5, wherein R1 is selected from
(1-4C)alkyl, cyclohexyl, cyclohexenyl, biphenyl optionally substituted with halogen,
phenyl optionally substituted with one, two or three substituents independently selected from halogen, (1-4C)alkyl, trifluoromethyl, (1-4C)alkoxy, trifluoromethoxy, and cyclopropyl optionally substituted with phenyl,
thienyl, pyridyl, tetrahydropyranyl, each optionally substituted with halogen, (1-4C)alkyl, cyclopropyl or phenyl optionally substituted with halogen,
and indolyl, dihydrobenzofuranyl and benzdioxanyl, each optionally substituted with halogen or (1-4C)alkyl.

7. The compound of any one of claims 1 to 6, wherein
R1 is selected from phenyl, optionally substituted with one or more substituents independently selected from halogen, (1-4C)alkyl, cyclopropyl and trifluoromethyl;
the group -Y-(C_n-alkylene)-X- is selected from -CH_2-O-, -CH_2-S- and -CH=CH-;
and -W-T- is -O-CH_2-.

8. The compound of any one of claims 1 to 7, wherein **A** represents a piperidine structure.

9. The compound of any one of claims 1 to 8, having the structure (**II**)



(**II**).

10. The compound of any one of claims 1 to 9, wherein R1 is 2,6-dichlorophenyl and R3 is -$(CH_2)_2$-COOH.

11. The compound of claim 1, selected from

2-(6-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(6-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(6-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

2-(6-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(6-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(6-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

2-(6-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(6-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(6-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

2-(5-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(5-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(5-(Hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

2-(5-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(5-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(5-(Heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

2-(5-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)acetic acid,

2-(5-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propanoic acid,

2-(5-(Octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)butanoic acid,

3-(5-{[2-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-[5-(Cyclohexylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-(5-{[3-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{5-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{5-[(3,5-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{5-[(2,6-Difluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{5-[(2-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{5-[(2,4,6-Trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{5-[(2-Chloro-6-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[5-(Phenylamino)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(4-Phenylpentyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(3-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-[6-(Cyclohexylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(Oxan-2ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(2,5-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-(6-{[3-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-(6-{[2-(Trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2,3-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl}-propanoic acid,

3-{6-[(2-Chloro-6-fluorphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl}propanoic acid,

3-[6-(Benzyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-propanoic acid,

3-{6-[(2,4-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-(6-{[2-Chloro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-[6-(Cyclohex-3-en-1ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-propanoic acid,

3-{6-[(3,5-Dichloropyridin-4-yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,4-Dichloropyridin-3-yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,4,6-Trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-4-iodophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Difluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[2-(2,6-Dichlorphenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[2-(2-Fluororphenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2-Chloro-5-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chloro-5-proylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[3-(2-Fluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[3-(2-Chlorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-[6-(3-Phenylpropoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[2-(2,4-Dichlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[2-(2-Chlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-(6-{[2,6-Dichloro-4-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2,6-Dichloro-4-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(5-Bromo-2-chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chloro-6-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{3-[2-(Trifluoromethyl)phenyl]propoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[3-(2,3-Difluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[3-(2-Chloro-6-fluorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[3-(2,6-Dichlorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[3-(4-Chlorophenyl)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2-Chloro-5-phenylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-4-cyclorpropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chloro-5-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-({2-Chloro-5-[2-phenylcyclopropyl]phenyl}methoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-3-methoxyphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-(6-{[2-Chloro-6-(2-methylpropyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(5,7-Dichloro-2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(5,7-Difluoro-2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(1R)-(2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(1S)-(2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{[(2E)-3-(4-Chlorophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(3-Phenyl)prop-2-yn-1-yl]oxy-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-[6-(2,3-Dihydro-1-benzofuran-3-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-(6-{[(2E)-3-(2,6-dichlorophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2E)-3-phenylprop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-{6-[(7-Chloro-2,3-dihydro-1H-inden-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-(6-{[3-(4-Chlorophenyl)prop-2-yn-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2E)-3-(2-fluororophenyl)prop-2-en-1-yl]oxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-{6-[(4-Bromothiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(4-Butylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,
3-(6-{[4-(2-Fluorophenyl)thiophen-2yl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-{6-[(4-Phenylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(4-Bromo-3-methylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(4-Cyclopropylmethylthiophen-2yl)methoxy]-2H-spiro[1-benzfuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(3-Methyl-4-phenylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(4-Butyl-3-methylthiophen-2yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,

2-Methyl- 3-{6-[(2,4,6-trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-Dichloro-4-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
3-{6-[(2,6-Dichloro-3-methoxyphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
3-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
3-(6-{[2-Chloro-6-(2-methylpropyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2- methylpropanoic acid,
3-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,
3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2- methylpropanoic acid,
2-{6-[(2,4,6-Trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
2-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
2-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl} acetic acid,
2-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
2-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
2-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)acetic acid,
2-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
2-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)acetic acid,

2-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,

4-{6-[(2,4,6-Trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(2-Chloro-5-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(2,6-Dichloro-3-methoxyphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

4-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)butanoic acid,

4-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)butanoic acid,

4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

3-{6-[(2,6-Dichlorophenyl)methoxy]-7-methyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichlorophenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-4-methylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{7-Fluoro-6-[(2,4,6-trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2,6-Dichloro-3-methoxyphenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-7-fluor-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-5-ethylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-(6-{[2-Chloro-6-(trifluoromethoxy)phenyl]methoxy}-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,6-Dichloro-3-methoxyphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(4-Butyl-2,6-dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2-Chloro-6-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2-Chloro-6-cyclopropylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,6-Dichloro-3-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,4,6-Trichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,6-Dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2-Chlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2-Methylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-[6-(Benzylsulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
2-Methyl-3-(6-{[(2,4,6-trichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,6-Dichloro-3-methoxyphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,
3-(6-{[(2,6-Dichloro-4-methylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,

3-(6-{[(2-Chloro-6-ethylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,

acid 3-[6-({[2-Chloro-6-(propan-2-yl)phenyl]methyl}sulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]-2-methylpropanoic acid,

3-(6-{[(2,6-Dichlorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,

3-(6-{[(2-Chlorophenyl)methane]sulfonyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2-Methylphenyl)sulfanyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2,6-Dichlorophenyl)sulfanyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Methylbenzene)sulfonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2,6-Dichlorobenzene)sulfonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-[6-(Benzenesulfonyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(E)-2-(2,6-Dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(2-Chlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-Phenylethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(E)-2-(4-Fluorphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(E)-2-(2,6-Dichloro-3-ethylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(2,6-Dichloro-4-cyclopropylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(4-Butyl-2,6-dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(1Z)-3,3,3-Trifluoro-2-phenylprop-1-en-1-yl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(2-Chloro-5-ethylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(2,5-Dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(3-Methylphenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(E)-2-(2-Fluorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

4-{6-[(E)-2-(2,6-Dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,

2-{6-[(E)-2-(2,6-Dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,

3-{6-[(E)-2-(2,6-Dichlorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid,

4-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}butanoic acid,

2-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}acetic acid,

3-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid,

3-{6-[2-(2,6-Dichlorophenyl)cyclopropyl]-2H-spiro[1-benzo-furan-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-(2-Phenylcyclopropyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[2-(2-Fluorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[2-(2-Chlorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[2-(2-Chloro-5-ethylphenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[2-(4-Butyl-2,6-dichlorophenyl)cyclopropyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-Benzyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-[6-(2-Phenylethyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
3-{6-[2-(2,6-Dichlorophenyl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[2-(2-Fluorophenyl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-[6-(Phenoxymethyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
3-[6-(Phenylamino)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-butanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2,2-difluoropropanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2,2-dimethylpropanoic acid,
2-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}ethan-1-ol,
(2-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-ethoxy)phosphonic acid,
6-[(2,6-Dichlorophenyl)methoxy]-1'-[2-(1H-1,2,3,4-tetrazol-5-yl)ethyl]-2H-spiro[1-benzofuran-3,4'-piperidine],
(3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propyl)phosphonic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-3-oxopropanoic acid,
3-{5-[(2-Chlorophenyl)methoxy]-2H-spiro[furo[2,3-b]pyridine-3,4'-piperidine]-1'-yl}-propanoic acid,
3-{5-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[furo[2,3-b]pyridine-3,4'-piperidine]-1'-yl}propanoic acid,
3-[5-(2,6-Dimethylphenoxy)-2H-spiro[furo[2,3-b]pyridine-3,4'-piperidine]-1'-yl]propanoic acid,

3-{5-[(2,6-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{5-(Cyclohexylmethoxy)-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{5-[(2-Chlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-(5-{[2-(Trifluoromethyl)phenyl]methoxy}-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl)propanoic acid,

3-{5-(Oxan-2-ylmethoxy)-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{5-[(3-Chlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{5-[(2,3-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-(5-{[3-(Trifluoromethyl)phenyl]methoxy}-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl)propanoic acid,

3-{5-[(2,5-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{5-[(3,5-Dichlorophenyl)methoxy]-3H-spiro[2-benzofuran-1,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[((2,6-Dichlorophenyl)carbamoyl)]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-(Benzyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(4-Chlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(6-Cyanohexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-(4-Phenylbutoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(2,3-Dihydro-1-benzofuran-2-ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(2-Phenoxyethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(2-Phenoxypropoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(2-Phenoxybutoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

Tert-butyl 3-{6-[3-(Benzyloxy)propoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-(2-,3-Dihydro-1,4-benzodioxin-2-ylmethoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-(6-{[3-(4-Tert-butylphenyl)-1,2,4-oxadiazol-5-yl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-(6-{[4-(5-Methyl-1,2,4-oxadiazol-3-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-(6-{[4-(1H-Pyrazol-1-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-(6-{[4-(1H-1,2,4-Triazol-1-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2-Methyl-1,3-thiazol-4-yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(1-Methyl-1H-pyrazol-3-yl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-({6-Methylimidazol[1,2-a]pyridin-2yl}methoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(Hex-5-yn-1-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(5-Oxohexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[2-(Naphtalen-2-yloxy)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{3-[(2-Propyl-1,3-thiazol-5-yl)oxy]propoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(7-Methoxyheptyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(Phenylcarbamoyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[2-(Benzyloxy)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Methylphenyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-Benzoyl-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chlorophenyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2E)-3-Phenylprop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2E)-3-(2-Chlorophenyl)prop-2-enoyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(1-Benzofuran-2-yl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-{6-[(2-Phenylcyclopropyl)carbonyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-propanoic acid,

3-[6-(3-phenylpropanoyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(2,6-Dichlorophenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{(6-Phenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[6-(2,6-Dimethylphenoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-cyclobutane-1-carboxylic acid,

3-(6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-{6-[(2-cyclopropyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-ethyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(6-{[2-fluoro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-

piperidine]-1'-yl)propanoic acid,
3-{6-[(4-chloro-2,6-difluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[1-(2,6-dichlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-diethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-(6-{[2-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[2-ethyl-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[2-Chloro-6-(difluoromethoxy)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid ,
3-{6-[(2-Fluoro-6-methoxyphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid ,
3-{6-[(2-ethyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid,
3-{6-[(2-cyclopropyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylpropanoic acid,
3-(6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,
2-methyl-3-(6-{[2-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
2-{6-[(2,6-dichloro-3-methoxyphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}acetic acid,
1'-(3-Carboxypropyl)-6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidin]-1'-ium-1'-olate,
3-{6-[(2-Chloro-6-ethylophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-fluorophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-(propan-2-yl)phenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{6-[(2-Cyclopropyl-6-fluorophenyl)methoxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-(7-fluoro-6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,

3-[7-fluoro-6-(hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[7-fluoro-6-(heptyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[7-fluoro-6-(octyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[7-fluoro-6-(hex-5-en-1-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[7-fluoro-6-(oct-7-en-1-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[7-fluoro-6-(hept-6-en-1-yloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{7-fluoro-6-[(5,6,6-trifluorohex-5-en-1-yl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{7-fluoro-6-[(4,4,5,5,5-pentafluoropentyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{7-fluoro-6-[(5,5,6,6,6-pentafluorohexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-[7-fluoro-6-(4,4,4-trifluorobutoxy)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-[6-(Cyclohexylethoxy)-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,

3-{6-[(2-Ethylhexyl)oxy]-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

3-{7-Fluoro-6-[(3,5,5-trimethylhexyl)oxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,

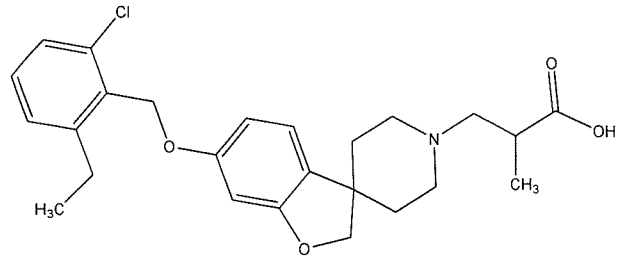
3-[6-(3-Cyclohexylpropoxy)-7-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-

yl]propanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-5-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-5-fluoro-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{7-Chloro-6-[(2-chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-(7-Chloro-6-{[2-fluoro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2-Cyclopropyl-6-fluorophenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-[6-({[2-Fluoro-6-(propan-2-yl)phenyl]methyl}sulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
3-[7-Fluoro-6-(pentylsulfanyl)-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl]propanoic acid,
3-(6-{[(2-Chloro-6-cyclopropylphenyl)methyl]sulfanyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)-2-methylpropanoic acid,
3-(6-{[(2,6-Dichlorophenyl)methane]sulfonyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-(6-{[(2,6-Dichlorophenyl)methane]sulfinyl}-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl)propanoic acid,
3-{6-[(E)-2-(2-Chloro-6-fluorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(E)-2-(2-Cyclopropyl-6-fluorophenyl)ethenyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-[6-(2-Phenylethynyl)-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl]propanoic acid,
3-{6-[2-(2-Chlorophenyl)ethynyl]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-3-methylbutanoic acid,
4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}pentanoic acid,

2-Methyl-4-{6-[(2,4,6-trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}butanoic acid,
4-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylbutanoic acid,
4-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylbutanoic acid,
4-{6-[(2-Chloro-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}-2-methylbutanoic acid,
3-{6-[(2,6-Dichlorobenzene)amido]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-Difluorobenzene)amido]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}propanoic acid,
2-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,4'-piperidine]-1'-yl}cyclopentane-1-carboxylic acid,
3-{6-[(2-Chloro-6-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]- 1'-yl}propanoic acid,
3-{6-[(2-Cyclopropyl-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-(6-{[2-Chloro-6-(propan-2-yl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl)propanoic acid,
3-{6-[(2-Chloro-6-cyclopropylphenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-fluorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-Dichloro-3-ethylphenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(4-Butyl-2,6-dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2,4,6-Trichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(3,5-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-

yl}propanoic acid,
3-{6-[(2,5-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-{6-[(2-Chloro-6-methylphenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-(6-{[2-Chloro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl)propanoic acid,
3-{6-[1-(2,6-Dichlorophenyl)ethoxy]-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl}propanoic acid,
3-(6-{[2-Fluoro-6-(trifluoromethyl)phenyl]methoxy}-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl)propanoic acid,
3-[6-(Oct-7-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl]propanoic acid,
3-[6-(Hept-6-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl]propanoic acid,
3-[6-(Hex-5-en-1-yloxy)-2H-spiro[1-benzofuran-3,3'-piperidine]-1'-yl]propanoic acid,
3-{6-[(2,6-Dichlorophenyl)methoxy]-2H-spiro[1-benzofuran-3,3'-pyrrolidine]-1'-yl}propanoic acid,
3-{5-[(2,6-Dichlorophenyl)methoxy]-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid,
3-{5-(Octyloxy)-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid,
3-{5-(2,6-Dichlorophenoxy)-2,3-dihydrospiro[indene-1,2'-morpholine]-4'-yl}propanoic acid, and
3-[5-Fluoro-6-(hexyloxy)-2H-spiro[1-benzofuran-3,4'-piperidine]- 1'-yl]propanoic acid,
or a pharmaceutically acceptable salt, or one or more N-oxides thereof.

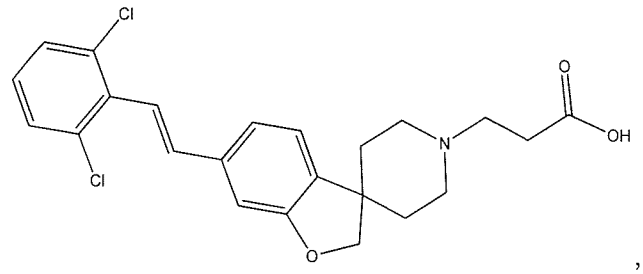
12. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

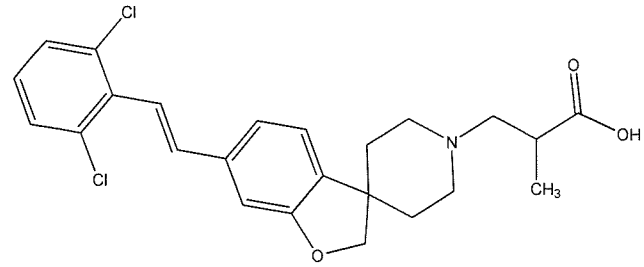
13. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

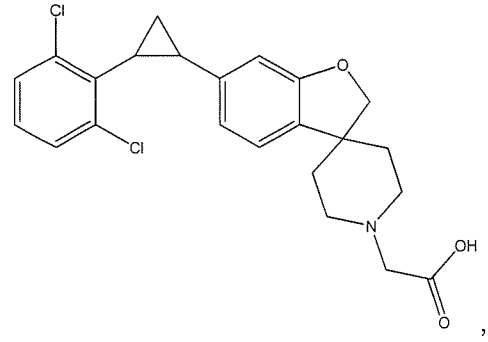
14. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

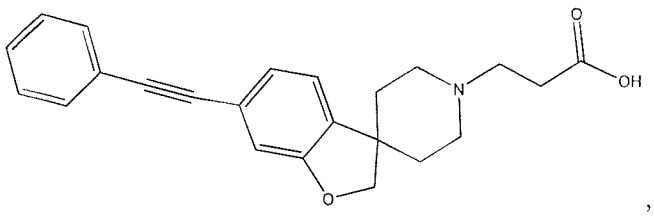
15. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

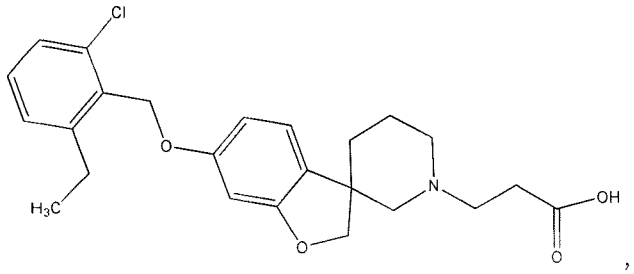
16. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

17. A compound of formula



,

or a pharmaceutically acceptable salt thereof.

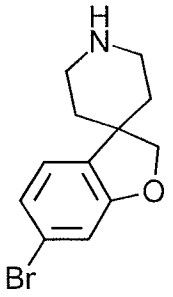
18. The compound of any one of claims 1 to 17 for use in therapy.

19. The compound of any one of claims 1 to 17 for use in the treatment, alleviation or prevention of a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.

20. A pharmaceutical composition comprising the compound of any one of claims 1 to 17 and at least one pharmaceutically acceptable auxiliary.

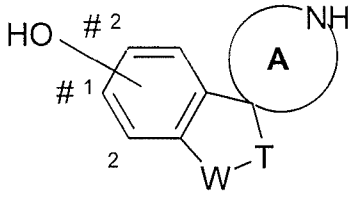
21. Use of the compound of any one of claims 1 to 17 for the manufacture of a medicament for the treatment, alleviation or prevention of a CNS disorder, such as a neurodegenerative disorder, in particular selected from a cognitive disorder, Alzheimer's disease, (vascular) dementia, Nieman's Pick disease, and cognitive deficits in schizophrenia, obsessive-compulsive behavior, major depression, autism, multiple sclerosis and pain, and specifically a cognitive disorder, such as age-related cognitive decline.

22. A compound of the formula



.

23. A compound of the formula (**IV**)



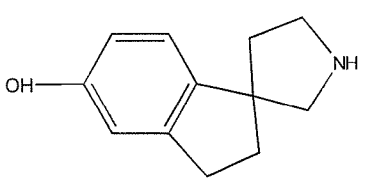
(**IV**),

wherein OH is attached at one of the sites indicated with #, and wherein, if OH is at the position indicated with [1], the compound may be independently substituted with (1-4C)alkyl or halogen selected from F or Cl at one or both positions indicated with [2]; and

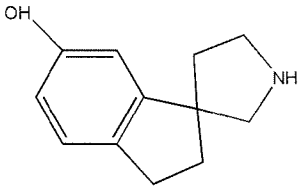
W-T is -O-CH_2- or -CH_2-CH_2-; and

A represents a morpholine ring structure or a 5-, 6- or 7- membered cyclic amine,

with the proviso that the compound of formula (**IV**) is not

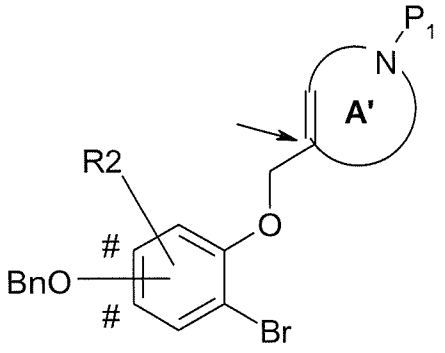


or



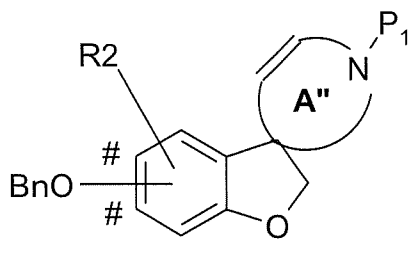
.

24. A process for the preparation of a compound according to claim 1 of formula (**I**) wherein R2 is H or one or two substituents selected from fluoro, (1-4C)alkyl and (1-4C)alkoxy; -W-T- is -O-CH_2- and Z is CH or CR2, comprising an intramolecular Heck cyclization step wherein a compound of formula (**V**),



(**V**),

wherein **A'** represents a 5-, 6- or 7- membered cyclic amine with a double bond at the carbon atom indicated with an arrow, P1 is a protecting group selected from -CO_2-benzyl and -CO_2-(1-4C)alkyl, Bn is benzyl and the BnO-group may be attached at one of the sites indicated with #,
is converted in a suitable solvent at elevated temperature, in the presence of silver carbonate and Herrmann-Beller catalyst, into a compound of formula (**VI**),



(**VI**),

wherein **A"** represents a 5-, 6- or 7- membered cyclic amine with a double bond at a position shifted one or two positions - depending on the position of the nitrogen atom in the ring - with regard to ring **A'**,
whereafter further process steps follow to produce the compound of formula (**I**).