The title compound was prepared by substituting EXAMPLE 156A for EXAMPLE 130C in EXAMPLE 130D. ^{1}H NMR (500MHz, pyridine-d_5) δ 13.05 (s, 1H), 9.29 (s, 1H), 8.62 (t, 1H), 8.43 (d, 1H), 8.32 (dd, 1H), 8.10 (d, 1H), 7.66 (m, 2H), 7.44 (d, 2H), 7.07 (d, 2H), 6.85 (d, 1H), 6.74 (dd, 1H), 6.54 (s, 1H), 6.49 (m, 1H), 4.60 (m, 1H), 3.19 (dd, 2H), 3.06 (m, 4H), 2.77 (s, 2H), 2.70 (m, 1H), 2.26 (t, 2H), 2.20-2.07 (m, 6H), 2.00 (m, 1H), 1.97 (s, 2H), 1.90 (m, 1H), 1.56 (m, 1H), 1.39 (t, 2H), 1.34 (m, 1H), 0.93 (s, 6H).

EXAMPLE 157

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({[(1S,3S)-3-hydroxycyclopentyl]methyl}amino)-3-nitrophenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

EXAMPLE 157A

4-(((1S,3S)-3-hydroxycyclopentyl)methylamino)-3-nitrobenzenesulfonamide

The title compound was prepared by substituting (1S, 3S)-3-hydroxycyclopentyl)methylamine for (tetrahydropyran-4-yl)methylamine in EXAMPLE 1F.

EXAMPLE 157B

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({[(1S,3S)-3-hydroxycyclopentyl]methyl}amino)-3-nitrophenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

The title compound was prepared by substituting EXAMPLE 157A for EXAMPLE 130C in EXAMPLE 130D. ^{1}H NMR (500MHz, pyridine-d_5) δ 13.03 (s, 1H), 9.29 (s, 1H), 8.60 (t, 1H), 8.44 (d, 1H), 8.32 (dd, 1H), 8.14 (d, 1H), 7.66 (m, 2H), 7.44 (d, 2H), 7.07 (d, 2H), 6.83 (d, 1H), 6.75 (dd, 1H), 6.55 (s, 1H), 6.49 (m, 1H), 4.60 (m, 1H), 3.19 (dd, 2H), 3.06 (m, 4H), 2.77 (s, 2H), 2.70 (m, 1H), 2.26 (t, 2H), 2.20-2.07 (m, 6H), 2.00 (m, 1H), 1.97 (s, 2H), 1.90 (m, 1H), 1.56 (m, 1H), 1.39 (t, 2H), 1.34 (m, 1H), 0.93 (s, 6H).

EXAMPLE 158

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({[(1S,3R)-3-hydroxycyclopentyl]methyl}amino)-3-nitrophenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

EXAMPLE 164

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(1-cyclopropylpiperidin-4-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

The title compound was prepared by substituting EXAMPLE 163B for (S)-tert-butyl pyrrolidin-3-ylcarbamate in EXAMPLE 142A. ^{1}H NMR (500MHz, dimethylsulfoxide-d_6) δ 11.96 (br s, 1H), 11.62 (br s, 1H), 8.50 (m, 2H), 7.98 (d, 1H), 7.72 (m, 1H), 7.52 (d, 1H), 7.45 (m, 2H), 7.34 (d, 2H), 7.04 (m, 2H), 6.94 (m, 1H), 6.64 (dd, 1H), 6.34 (m, 1H), 6.22 (d, 1H), 3.28 (m, 3H), 3.04 (m, 5H), 2.72 (s, 2H), 2.64 (m, 1H), 2.64 (m, 1H), 2.36 (m, 1H), 2.16 (m, 7H), 1.95 (s, 2H), 1.68 (m, 3H), 1.38 (t, 2H), 1.18 (m, 3H), 0.94 (s, 6H), 0.35 (m, 3H).

EXAMPLE 165

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({[4-(2-fluoroethyl)morpholin-2-yl]methyl}amino)-3-nitrophenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

EXAMPLE 165A

4-((4-(2-fluoroethyl)morpholin-2-yl)methylamino)-3-nitrobenzenesulfonamide

The title compound was prepared by substituting 2-fluoro-ethyl bromide for methyl iodide in EXAMPLE 134B.

EXAMPLE 165B

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({[4-(2-fluoroethyl)morpholin-2-yl]methyl}amino)-3-nitrophenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

The title compound was prepared by substituting EXAMPLE 165A for EXAMPLE 130C in EXAMPLE 130D. ^{1}H NMR (500MHz, pyridine-d_5) δ 13.00 (s, 1H), 9.26 (d, 1H), 8.87 (t, 1H), 8.43 (d, 1H), 8.32 (dd, 1H), 8.11 (d, 1H), 7.66 (m, 2H), 7.44 (d, 2H), 7.07 (d, 2H), 6.92 (d, 1H), 6.75 (dd, 1H), 6.54 (d, 1H), 6.48 (dd, 1H), 3.93 (m, 1H), 4.63, 4.51(dt, 2H), 3.95-3.85 (m, 2H), 3.68 (dt, 1H), 3.43-3.37 (m, 2H), 3.07 (m, 4H), 2.92 (d, 1H), 2.77 (s, 2H), 2.65 (m, 2H), 2.59 (m, 1H), 2.26 (m, 2H), 2.17-2.08 (m, 5H), 1.97 (s, 2H), 1.39 (t, 2H), 0.93 (s, 6H).

ethoxycyclopropoxy)trimethylsilane (0.64 mL), and sodium cyanoborohydride (0.148 g). The reaction was heated under reflux overnight. After cooling, the reaction mixture was loaded onto a silica gel column. After drying, the column was eluted with 100:2:0.2 ethyl acetate/methanol/NH_4OH to give the title compound.

EXAMPLE 173C

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(1-cyclopropyl-4-fluoropiperidin-4-yl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

The title compound was prepared by substituting EXAMPLE 173B for EXAMPLE 11B in EXAMPLE 11D. ^{1}H NMR (500MHz, dimethylsulfoxide-d_6) δ 11.65 (s, 1H), 8.33 (s, 1H), 8.01 (m, 2H), 7.53 (d, 1H), 7.48-7.49 (m, 2H), 7.34-7.38 (m, 3H), 7.04 (d, 2H), 6.66 (dd, 1H), 6.38 (dd, 1H), 6.21 (d, 1H), 4.32 (d, 2H), 3.70-3.77 (m, 2H), 3.07 (s, 4H), 2.92 (s, 2H), 2.80 (s, 2H), 2.58 (s, 2H), 2.25 (s, 4H), 2.13-2.16 (m 2H), 1.38 (t, 2H), 0.92 (s, 6H), 0.40-0.49 (m, 4H).

EXAMPLE 174

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-methoxybenzyl)amino]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

A suspension of EXAMPLE 53A (120 mg), (4-methoxyphenyl)methanamine (31 mg) and Hunig'sBase (0.159 mL) in dimethylsulfoxide (2 mL) was heated for 2 hours at 150 °C in a Biotage Initiator microwave reactor. The reaction mixture was diluted with methanol (2 mL) and purified by reverse phase HPLC (C8, 30% - 100% CH_3CN/water/0.1% trifluoroacetic acid). ^{1}H NMR (500 MHz, pyridine-d_5) δ 13.07 (s, 1H), 9.32 (d, 1H), 9.17 (t, 1H), 8.43 (d, 1H), 8.28 (dd, 1H), 8.08 (d, 1H), 7.64 - 7.68 (m, 2H), 7.44 (d, 2H), 7.38 (d, 2H), 7.07 (d, 2H), 6.97 - 7.02 (m, 2H), 6.90 (d, 1H), 6.74 (dd, 1H), 6.52 (d, 1H), 6.49 (dd, 1H), 4.55 (d, 2H), 3.68 (s, 3H), 3.03 - 3.09 (m, 4H), 2.77 (s, 2H), 2.26 (t, 2H), 2.10 - 2.17 (m, 4H), 1.97 (s, 2H), 1.39 (t, 2H), 0.93 (s, 6H).

The title compound was prepared by substituting (R)-tert-butyl pyrrolidin-3-ylcarbamate for tert-butyl piperazine-1-carboxylate and 3-oxetanone for 4'-chlorobiphenyl-2-carboxaldehyde in EXAMPLE 1A.

EXAMPLE 224B

(R)-1-(oxetan-3-yl)pyrrolidin-3-amine

The title compound was prepared by substituting EXAMPLE 224A for (S)-1-tert-butyl 2-methyl 4,4-difluoropyrrolidine-1,2-dicarboxylate in EXAMPLE 168A.

EXAMPLE 224C

(R)-3-nitro-4-(1-(oxetan-3-yl)pyrrolidin-3-ylamino)benzenesulfonamide

The title compound was prepared by substituting 4-fluoro-3-nitrobenzenesulfonamide for 4-chloro-3-nitrobenzenesulfonamide and EXAMPLE 224B for 4-methylpiperazin-1-amine dihydrochloride in EXAMPLE 6A.

EXAMPLE 224D

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-nitro-4-{[(3R)-1-(oxetan-3-yl)pyrrolidin-3-yl]amino}phenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

The title compound was prepared by substituting EXAMPLE 224C for EXAMPLE 11B in EXAMPLE 11D. ^{1}H NMR (400 MHz, pyridine-d_5) δ 13.03 (s, 1H), 9.26 (d, 1H), 8.57 (d, 1H), 8.42 (d, 1H), 8.36 (dd, 1H), 8.09 (d, 1H), 7.66 (m, 1H), 7.64 (d, 1H), 7.44 (m, 2H), 7.07 (m, 2H), 6.86 (d, 1H), 6.75 (dd, 1H), 6.54 (d, 1H), 6.48 (dd, 1H), 4.67 (m, 4H), 3.58 (m, 1H), 3.07 (m, 4H), 2.77 (m, 2H), 2.68 (m, 2H), 2.61 (m, 1H), 2.28 (m, 4H), 2.14 (m, 4H), 1.97 (m, 2H), 1.67 (m, 1H), 1.39 (t, 2H), 0.93 (s, 6H).

EXAMPLE 225

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(3R)-1-(1,3-difluoropropan-2-yl)pyrrolidin-3-yl]amino}-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide

(bromomethyl)piperidine-1-carboxylate (11.1 g) in dimethylsulfoxide (30 mL) was added, and the reaction was stirred at 50°C for 24 hours. The reaction was cooled, poured into water (300 mL), extracted three times with ether, and the combined extracts were washed three times with water, and brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was chromatographed on silica gel using 5-20% ethyl acetate in hexanes to provide the title compound.

EXAMPLE 296B

tert-butyl 4-((2-(4-chlorophenyl)-2-hydroxy-4,4-dimethylcyclohexyl)methyl)piperidine-1-carboxylate

(4-Chlorophenyl)magnesium bromide (14.1 mL, 1M in ether) was added to EXAMPLE 296A (3.25 g) in tetrahydrofuran (40 mL) at -78°C, and the reaction was stirred for 20 minutes, and then allowed to warm to room temperature overnight. The reaction was quenched with pH 7 buffer (20 mL), extracted with 2x ether, and the combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was chromatographed on silica gel using 1-20% ethyl acetate in hexanes to provide the title compound.

EXAMPLE 296C

trans-4-((2-(4-chlorophenyl)-4,4-dimethylcyclohexyl)methyl)piperidine

The title compound was prepared by substituting EXAMPLE 296B for EXAMPLE 1A in EXAMPLE 1B.

EXAMPLE 296D

Trans-methyl 2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohexyl)methyl)piperidin-1-yl)benzoate

The title compound was prepared by substituting EXAMPLE 296C for EXAMPLE 263G in EXAMPLE 263H.

EXAMPLE 296E

Trans-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)-4-(4-((2-(4-chlorophenyl)-4,4-dimethylcyclohexyl)methyl)piperidin-1-yl)benzoic acid

The title compound was prepared by substituting EXAMPLE 296D for EXAMPLE 3I in EXAMPLE 3J.