{5-[3-hydroxy-2-(hydroxymethyl)propoxy]pyrimidin-2-yl}piperidin-4-yl)-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-2-(1-{5-[3-hydroxy-2-(hydroxymethyl)-2-methylpropoxy]pyrimidin-2-yl}piperidin-4-yl)-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-[1-(5-{[methyl(methylsulphonyl)amino]methyl}pyrimidin-2-yl)piperidin-4-yl]-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-[1-(5-{[methyl(propan-2-ylsulfonyl)amino]methyl}pyrimidin-2-yl)piperidin-4-yl]-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-[1-(5-methylthiopyrimidin-2-yl)piperidin-4-yl]-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(methylsulphonyl)pyrimidin-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-2-{1-[5-(3-Carboxyphenyl)pyrimidin-2-yl]piperidin-4-yl}-4-(4,4-difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-2-(1-{5-[(2-hydroxyethyl)(methyl)amino]pyrimidin-2-yl}piperidin-4-yl)-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol, and

(5S)-4-(4,4-Difluorocyclohexyl)-3-{(S)-fluoro[4-(trifluoromethyl)phenyl]methyl}-2-(1-{5-[(3S)-3-hydroxypyrrolidin-1-yl]pyrimidine-2-yl}piperidin-4-yl)-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol.

(16A) A pharmaceutical composition comprising the compound according to any one

wherein R^1 is a 5- or 6-membered nitrogen-containing saturated heterocyclyl group, a substituted 5- or 6-membered nitrogen-containing saturated heterocyclyl group in which the substituent(s) represent 1 to 4 groups independently selected from the substituent group α2 or a substituted 5- or 6-membered nitrogen-containing saturated heterocyclyloxy group in which the substituent(s) represent 1 to 4 groups independently selected from the substituent group α2, and

the substituent group α2 represents the group consisting of a C_1-C_4 alkyl group and a hydroxy group.

(11) The compound according to (1) or a pharmacologically acceptable salt thereof, wherein

R^1 is a substituted pyrrolidinyl group, a substituted piperidyl group, a substituted piperazyl group, a substituted thiomorpholinyl group, a substituted pyrrolidinyloxy group or a substituted piperidyloxy group in which the substituent(s) of the pyrrolidinyl group, piperidyl group, piperazyl group, thiomorpholinyl group, pyrrolidinyloxy group and piperidyloxy group represent 1 to 2 groups independently selected from the substituent group α3, and

the substituent group α3 represents the group consisting of a methyl group and a hydroxy group.

(12) The compound according to (1) or a pharmacologically acceptable salt thereof, which is selected from the group consisting of,

(-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(4-methylpiperazin-1-yl)pyrimidin-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroquinolin-5-ol,

(-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-{1-[5-(2-hydroxyethoxy)pyrimidin-2-yl]piperidin-4-yl}-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

(-)-2-{1-[5-(4-Carboxybutoxy)pyrimidine-2-yl]piperidin-4-yl}-4-(4,4-difluorocyclohex

yl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinoli n-5-ol,

(-)-2-{1-[5-(4-Carboxybutyl)pyrimidine-2-yl]piperidin-4-yl}-4-(4,4-difluorocyclohexyl) -3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(methylcarbamoyl)pyrimidin-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroquinolin-5-ol,

(-)-4-(4,4-Difluorocyclohexyl)-2-{1-[5-(dimethylcarbamoyl)pyrimidin-2-yl]piperidin-4-yl}-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinoli n-5-ol,

4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(morpholin-4-yl-carbonyl)pyrimidin-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroqui nolin-5-ol,

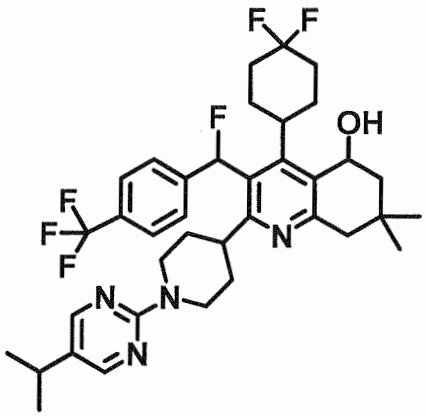
(-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-{1-(5-{[(2-hydroxyethyl)(methyl)amino]methyl}pyrimidin-2-yl)piperidin-4-yl}-7,7-dimethyl-5,6 ,7,8-tetrahydroquinolin-5-ol,

(-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-[1-(5-{[(2S)-2-hydroxypropyl]oxy}pyrimidin-2-yl)piperidin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydr oquinolin-5-ol,

4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-(1-{5-[(1-methylpiperidin-4-yl)oxy]pyrimidin-2-yl}piperidin-4-yl)-5,6,7,8-tetrahydro quinolin-5-ol,

(-)-4-(4,4-Difluorocyclohexyl)-2-[1-(5-{[(2S)-2,3-dihydroxypropyl]oxy}pyrimidin-2-yl)piperidin-4-yl]-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetra hydroquinolin-5-ol,

(-)-4-(4,4-Difluorocyclohexyl)-2-[1-(5-{[(2R)-2,3-dihydroxypropyl]oxy}pyrimidin-2-yl



Reactions similar to those of the first step of Example 2 and Example 38 were performed except for using 2-chloro-5-(propan-2-yl) pyrimidine instead of 5-bromo-2-chloropyrimidine, and from 96 mg (0.14 mmol) of (-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-5-[(4-methoxybenzyl)oxy]-7,7-dimethyl-2-(piperidin-4-yl)-5,6,7,8-tetrahydroquinoline, which was prepared by a method similar to that of Reference Example 10, 47 mg of the title compound was obtained as a white solid (yield: 50%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 8.14 (2H, s), 7.64 (2H, d, J = 8 Hz), 7.37 (2H, d, J = 8 Hz), 7.21 (1H, d, J = 45 Hz), 5.12 (1H, q, J = 6 Hz), 4.80-4.69 (1H, m), 4.52-4.41 (1H, m), 3.68-3.56 (1H, m), 2.84-2.58 (4H, m), 2.34-2.05 (6H, m), 1.97-1.48 (10H, m), 1.20 (6H, d, J = 7 Hz), 1.15 (3H, s), 1.00 (3H, s), 0.67-0.58 (1H, m).

(Example 13)

4-(4,4-Difluorocyclohexyl)-2-[1-(5-ethoxypyrimidine-2-yl)piperidin-4-yl]-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol

xymethyl)pyrimidin-2-yl]piperidin-4-yl]-5-[(4-methoxybenzyl)oxy]-7,7-dimethyl-5,6,7,8-tetrahydroquinoline obtained above, 0.5 ml of 1,4-dioxane, 0.5 ml of water and 0.5 ml of 4 N hydrogen chloride-1,4-dioxane solution were added, and the reaction solution was stirred at 50°C for 6 hours. After completion of the reaction, the reaction solution was poured into saturated sodium hydrogencarbonate aqueous solution and extracted with ethyl acetate. The organic layer was washed with saturated sodium chloride aqueous solution and dried with anhydrous magnesium sulfate, and then the solvent was distilled off under reduced pressure. The obtained residue was subjected to silica gel column chromatography [n-hexane/ethyl acetate = 100/0-50/50 (V/V)] and the fraction including the desired compound was concentrated under reduced pressure to provide 41 mg of the title compound as a white solid (yield: 54%).

Specific optical rotation: $[\alpha]_D^{24} = -81°$ (C = 0.15, chloroform).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 8.23 (2H, s), 7.64 (2H, d, J = 8 Hz), 7.37 (2H, d, J = 8 Hz), 7.21 (1H, d, J = 46 Hz), 5.16-5.06 (1H, m), 4.84-4.74 (1H, m), 4.56-4.44 (1H, m), 4.46 (2H, s), 3.71-3.54 (1H, m), 2.88-2.69 (3H, m), 2.63 (1H, d, J = 17 Hz), 2.37-1.50 (16H, m), 1.14 (3H, s), 1.00 (3H, s), 0.70-0.57 (1H, m).

Mass spectrum (FAB, m/z): 663 $[(M+1)^+]$.

(Example 21)

(-)-4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(2-methylpropoxy)pyrimidine-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroquinoline-5-ol

provide 41 mg of the title compound as a white solid (yield: 68%).

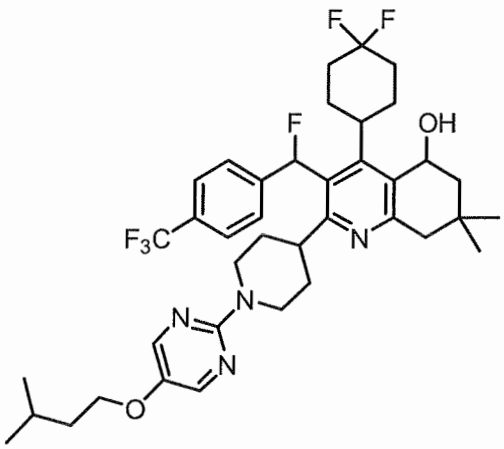
Specific optical rotation: $[\alpha]_D^{27} = -65°$ (C = 0.15, methanol).

^{1}H-NMR spectrum (300 MHz, CD_2Cl_2) δ: 8.01 (2H, s), 7.65 (2H, d, J = 8 Hz), 7.38 (2H, d, J = 8 Hz), 7.22 (1H, d, J = 47 Hz), 5.13 (1H, dt, J = 6, 6 Hz), 4.71-4.59 (1H, m), 4.41-4.30 (1H, m), 3.70-3.57 (1H, m), 3.67 (2H, d, J = 7 Hz), 2.88-2.55 (4H, m), 2.37-1.57 (16H, m), 1.13 (3H, s), 1.00 (3H, s), 0.99 (6H, d, J = 7 Hz), 0.66-0.55 (1H, m).

Mass spectrum (EI, m/z): 704 [M^+].

(Example 22)

(-)-4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-2-{1-[5-(3-methylbutoxy)pyrimidine-2-yl]piperidin-4-yl}-5,6,7,8-tetrahydroquinoline-5-ol



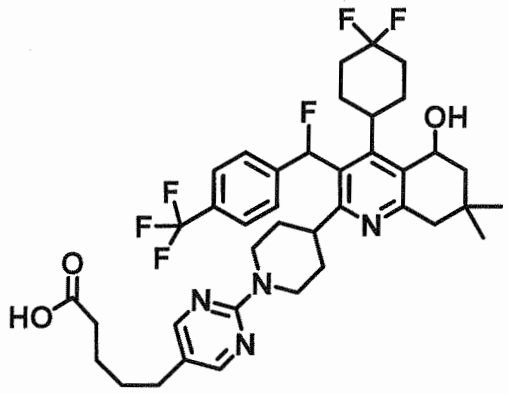
Reactions similar to those of Example 21 were performed except for using 62 μl (0.47 mmol) of 1-iodo-3-methylbutane instead of 1-iodo-2-methylpropane, and from 55 mg (0.085 mmol) of (-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-[1-(5-hydroxypyrimidin-2-yl)piperidin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol,

(3H, s), 0.99 (3H, s), 0.88 (6H, d, J = 7 Hz), 0.68-0.57 (1H, m).

Mass spectrum (EI, m/z): 688 [M^+].

(Example 25)

(-)-2-{1-[5-(4-carboxybutyl)pyrimidine-2-yl]piperidin-4-yl}-4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimethyl-5,6,7,8-tetrahydroquinoline-5-ol



Reactions similar to those of the first step of Example 2, Example 38 and Example (23-2) were performed, and from 100 mg (0.148 mmol) of (-)-4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-5-[(4-methoxybenzyl)oxy]-7,7-dimethyl-2-(piperidin-4-yl)-5,6,7,8-tetrahydroquinoline, which was prepared by a method similar to that of Reference Example 10, 79 mg of the title compound was obtained as a white solid (yield: 73%). Methyl 5-(2-chloropyrimidin-5-yl) pentanoate, which was prepared by a method similar to that of Reference Example 20, was used instead of 5-bromo-2-chloropyrimidine in the step corresponding to the first step of Example 2.

Specific optical rotation: $[\alpha]_D^{25}$ = -68° (C = 0.14, chloroform).

^{1}H-NMR spectrum (500 MHz, $CDCl_3$) δ ppm: 8.09 (2H, s), 7.63 (2H, d, J = 8 Hz), 7.36 (2H, d, J = 8 Hz), 7.21 (1H, d, J = 47 Hz), 5.15-5.08 (1H, m), 4.78-4.68 (1H,

Reactions similar to those of Example 24 were performed except for using 42 mg (0.053 mmol) of 4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-5-[(4-methoxy benzyl)oxy]-2-{1-[5-(methoxymethyl)pyrimidin-2-yl]piperidin-4-yl}-7,7-dimethyl-5,6, 7,8-tetrahydroquinoline, which was prepared by a method similar to that of Reference Example 22 instead of 4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-{1-[5-(1-hyd roxy-2-methylpropyl)pyrimidin-2-yl]piperidin-4-yl}-5-[(4-methoxybenzyl)oxy]-7,7-di methyl-5,6,7,8-tetrahydroquinoline to provide 34 mg of the title compound as a foam (yield: 96%).

Specific optical rotation: $[\alpha]_D^{24} = -82°$ (C = 0.090, methanol).

^{1}H-NMR spectrum (300 MHz, CD_2Cl_2) δ: 8.19 (2H, s), 7.66 (2H, d, J = 8 Hz), 7.39 (2H, d, J = 8 Hz), 7.23 (1H, d, J = 47 Hz), 5.13 (1H, dt, J = 6, 6 Hz), 4.86-4.74 (1H, m), 4.56-4.45 (1H, m), 4.20 (2H, s), 3.72-3.56 (1H, m), 3.30 (3H, s), 2.90-2.55 (4H, m), 2.37-1.48 (15H, m), 1.13 (3H, s), 0.99 (3H, s), 0.68-0.58 (1H, m).

Mass spectrum (EI, m/z): 676 [M^+].

(Example 28)

(-)-4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-7,7-dimeth yl-2-(1-{5-[(propan-2-yloxy)methyl]pyrimidine-2-yl}piperidin-4-yl)-5,6,7,8-tetrahydro quinoline-5-ol

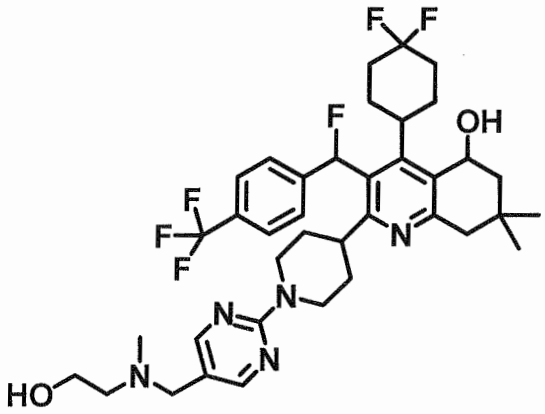
din-4-yl}-5,6,7,8-tetrahydroquinoline obtained above to provide the title compound 35 mg of as a white solid (yield: 72%).

^{1}H-NMR spectrum (400 MHz, $CDCl_3$) δ ppm: 8.87 (2H, s), 7.65 (2H, d, J = 8 Hz), 7.38 (2H, d, J = 8 Hz), 7.22 (1H, d, J = 47 Hz), 5.16-5.08 (1H, m), 4.99-4.90 (1H, m), 4.73-4.63 (1H, m), 3.69-3.57 (1H, m), 2.90-2.58 (4H, m), 2.43 (3H, s), 2.36-2.06 (6H, m), 1.98-1.58 (9H, m), 1.14 (3H, s), 1.00 (3H, s), 0.73-0.64 (1H, m).

Mass spectrum (FAB, m/z): 715 [$(M+1)^+$].

(Example 36)

(-)-4-(4,4-difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-{1-(5-{[(2-hydroxyethyl)(methyl)amino]methyl}pyrimidine-2-yl)piperidin-4-yl}-7,7-dimethyl-5,6,7,8-tetrahydroquinoline-5-ol



(36-1)

4-(4,4-Difluorocyclohexyl)-3-{fluoro[4-(trifluoromethyl)phenyl]methyl}-2-[1-(5-formylpyrimidin-2-yl)piperidin-4-yl]-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-5-ol

Column: CHIRALPAK (trade name) AD-H (0.46 cm ID × 25 cm, manufactured by Daicel Chemical Industries, Ltd.)

Eluent: n-hexane/2-propanol/isopropylamine = 80/20/0.1 (V/V/V)

Flow rate: 1.0 ml/min

Column temperature: 40°C

Detection wavelength: 271 nm

Retention time: 5.5 minutes

[Enantiomer of title compound]

Specific optical rotation: $[\alpha]_D^{24} = 100°$ (C = 0.25, methanol).

^{1}H-NMR spectrum (300 MHz, CD_2Cl_2) δ ppm: 7.61 (2H, d, J = 8 Hz), 7.35 (2H, d, J = 8 Hz), 7.26 (2H, d, J = 9 Hz), 7.14 (1H, d, J = 47 Hz), 6.86 (2H, d, J = 9 Hz), 4.85 (1H, t, J = 5 Hz), 4.80 (1H, d, J = 11 Hz), 4.39 (1H, d, J = 11 Hz), 3.77 (3H, s), 3.25-3.08 (1H, m), 3.04-2.92 (1H, m), 2.91-2.80 (1H, m), 2.76-2.53 (3H, m), 2.45 (1H, td, J = 12, 3 Hz), 2.28-2.10 (3H, m), 2.00-1.39 (11H, m), 1.20 (3H, s), 1.07 (3H, s), 0.61-0.50 (1H, m).

Mass spectrum (CI, m/z): 675 [$(M+1)^+$].

Analysis conditions of the high performance liquid chromatography:

Column: CHIRALPAK (trade name) AD-H (0.46 cm ID × 25 cm, manufactured by Daicel Chemical Industries, Ltd.)

Eluent: n-hexane/2-propanol/isopropylamine = 80/20/0.1 (V/V/V)

Flow rate: 1.0 ml/min

Column temperature: 40°C

Detection wavelength: 271 nm

Retention time: 4.0 minutes

(Reference Example 11)

(-)-2-[1-(5-Bromopyrimidine-2-yl)piperidin-4-yl]-4-(4,4-difluorocyclohexyl)-3-{fluoro[