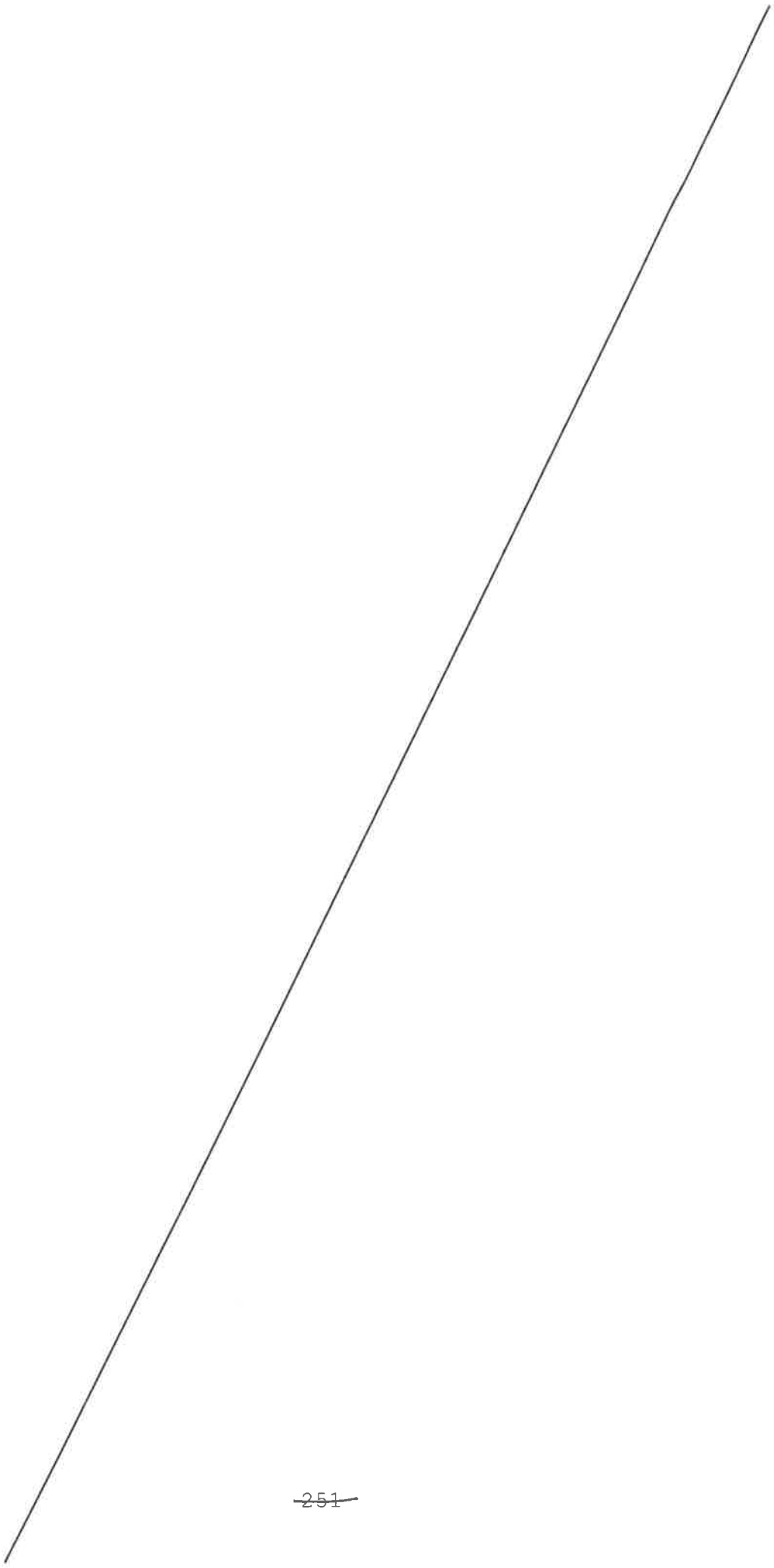
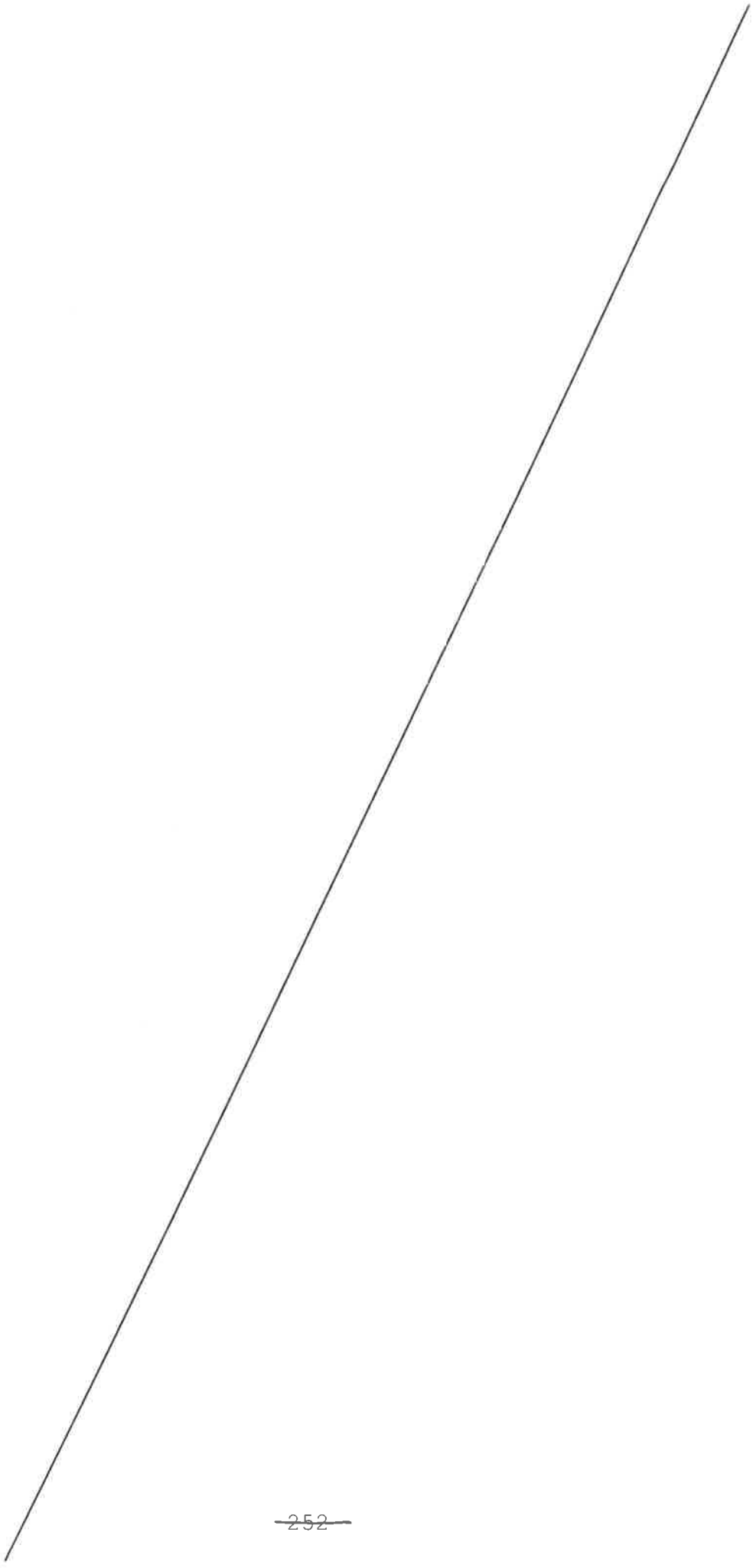
5% distilled water (270 mL) and dried under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (3.3 g) as white crystals (Form A).

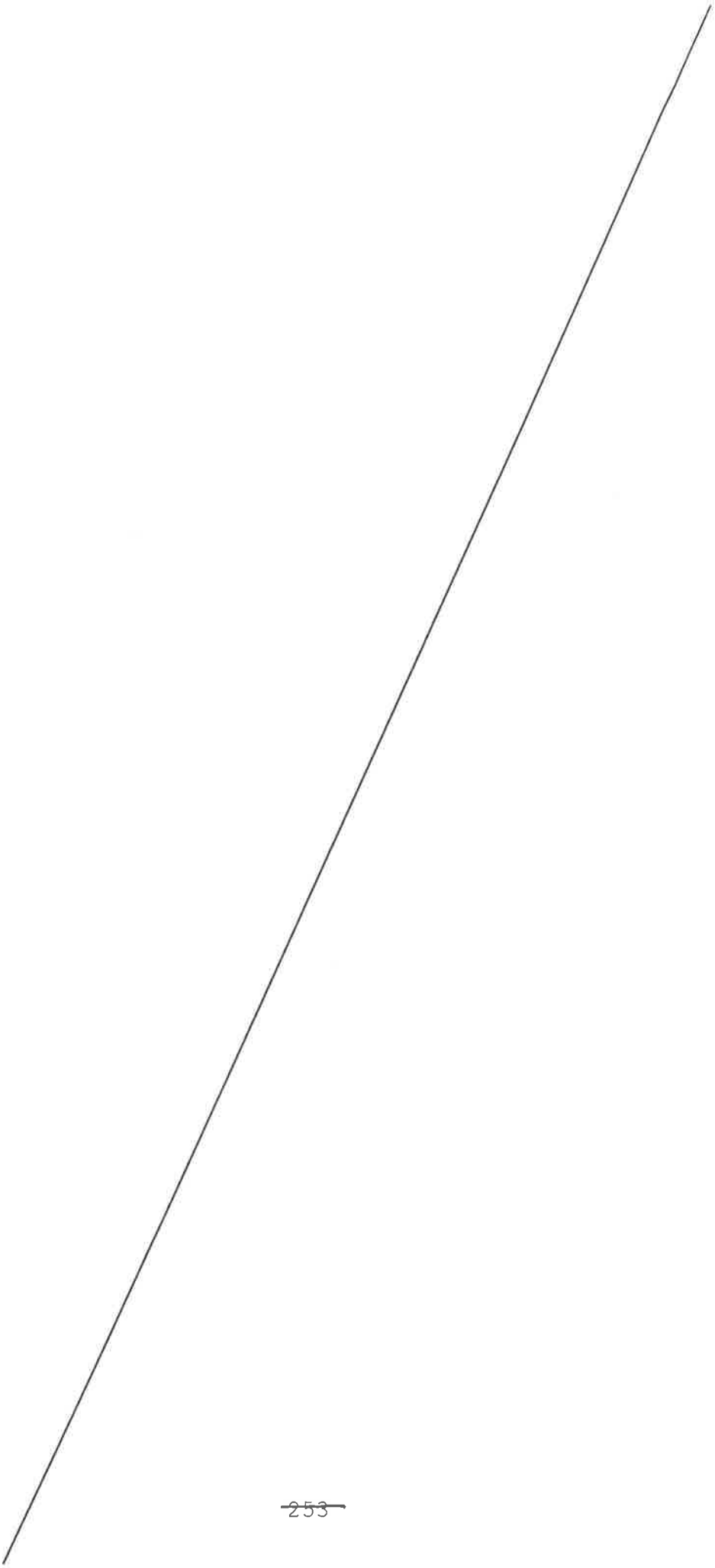
MS (API+): $[M+H]^+$ 401.3

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.32 (3H, t, J = 7.2 Hz), 2.61 (3H, s), 3.77 (3H, s), 4.12 (2H, q, J = 7.2 Hz), 7.00 (1H, d, J = 5.7 Hz), 7.20 (1H, dd, J = 7.9, 4.9 Hz), 7.58-7.66 (2H, m), 7.71-7.78 (2H, m), 7.80 (1H, dd, J = 7.9, 1.1 Hz), 7.87 (1H, d, J = 4.9 Hz), 8.22 (1H, dd, J = 4.9, 1.5 Hz).

Anal. Calcd for $C_{22}H_{20}N_6O_2$: C, 65.99; H, 5.03; N, 20.99. Found: C, 65.76; H, 5.07; N, 20.85.







[0405]

Powder X-ray Diffraction (PXRD) Analysis:

Form A is characterized by PXRD Pattern using CuKα X-ray

5

radiation, having peaks selected from a list consisting of:

9.302 angstrom ; middle

8.1102 angstrom ; middle

5.6255 angstrom ; high

5.487 angstrom ; middle

4.8439 angstrom ; high

4.371 angstrom ; high

3.7479 angstrom ; low

3.6043 angstrom ; high

3.5092 angstrom ; middle

3.2178 angstrom ; high

d-value.

[0406]

Method D

120l) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

Crystals of 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (100 mg, Form A) was dissolved in EtOH (20 mL) at 80°C and the solution was allowed to cool to room temperature. The mixture was stirred at room temperature for 350 h. The solid was collected by filtration to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (50 mg) as crystals (Form G).

Crystals of 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (40.0 g, Form A) was dissolved in DMSO (400 mL) at 95°C and the solution was allowed to cool to 85°C. To the solution was slowly added EtOH (400 mL) at 85°C, and then the mixture was allowed to cool to 80°C. To the solution was added seed crystals (Form G: 50 mg) at 80°C. The mixture was stirred and maintained at 73°C for 20 h. The solid was collected by filtration and washed with EtOH (500 mL) to

give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (19.5 g) as white crystals (Form G).

Method E

120m) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

Crystals of 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (600 mg, Form A) was stirred in EtOH (60 mL) at room temperature for 168 h. The solid was collected by filtration to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (350 mg) as crystals (Form G).
MS (API+): $[M+H]^+$ 401.1.
$^1$H NMR (400 MHz, DMSO-$d_6$) δ 1.25-1.38 (3H, m), 2.61 (3H, s), 3.78 (3H, s), 4.04-4.18 (2H, m), 6.96-7.04 (1H, m), 7.17-7.25 (1H, m), 7.59-7.66 (2H, m), 7.71-7.77 (2H, m), 7.78-7.83 (1H, m), 7.85-7.91 (1H, m), 8.16-8.28 (1H, m).
Anal. Calcd for $C_{22}H_{20}N_6O_2$: C, 65.99; H, 5.03; N, 20.99. Found: C, 65.73; H, 5.12; N, 20.85.

Method F

120n) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

Crystals of 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-

imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (3.0 g) obtained in 120s') was dissolved in DMSO (33 mL) at 90°C. To the solution was slowly added EtOH (30 mL) at 80-90°C. To the solution was added crystals (Form G) obtained in 120m) as seed crystals at 80-90°C. The mixture was stirred at 60-65°C for 6 h and at room temperature for 18 h. The solid was collected by filtration and washed with EtOH (15 mL) to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (1.3 g) as white crystals (Form G).

Method G

120p) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

Crystals of 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (3.0 g) obtained by 120s') was dissolved in DMSO (33 mL) at 90-95°C. To the solution was slowly added AcOEt (30 mL) at 70-90°C. To the solution was added crystals (Form G) obtained in 120n) as seed crystals at 80-90°C. The mixture was stirred at 45-50°C for 25 min and at 70-75°C for 3 h. The mixture was gradually cooled to 0-5°C and stirred for 1 h. The solid was collected by filtration and washed with AcOEt (15 mL) to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.6 g) as white crystals (Form G).

Method H

120q) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

A solution of 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-

b]pyridine (20.4 g, 96.55 mmol) in DMA (117 mL) was added to a solution of 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (26.0 g, 96.55 mmol) and potassium tert-butoxide (11.4 g) in DMA (96 mL) at room temperature. The mixture was stirred at 95-100°C for 1.5 h. Water (221 mL) was added at 80-100°C. The precipitate was collected at room temperature and dried over under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (35.8 g) as crude product. The obtained crude 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (10.0 g) was dissolved in DMSO (150 mL) at 90-100°C. The solution was filtered through filter paper and washed with DMSO (10 mL). The combined filtrate was slowly added to a mixture of crystals (Form G: 100 mg) obtained in 120p) (as seed crystals) in AcOEt (100 mL) at 5-30°C. After stirring at room temperature for 17 h, the mixture was stirred at 70°C for 1 h. The mixture was gradually cooled to 25°C and stirred for 2 h. The mixture was stirred at 0-10°C for 1 h and at room temperature for 1 h. The solids were collected by filtration and dried at 50°C under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (8.0 g) as white crystals (Form G).

[0407]

Method I

120r) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

A solution of 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (40.8 g, 193.09 mmol) in DMA (234 mL) was added to a solution of 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (52.0 g, 193.09 mmol)

and potassium tert-butoxide (22.8 g) in DMA (192 mL) at room temperature. The mixture was stirred at 90-100°C for 1 h. Water (442 mL) was added at 80-100°C. The precipitate was collected at room temperature and dried over under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (72.4 g) as crude product. The crude 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (60.0 g) was dissolved in DMSO (900 mL) at 90-100°C. The solution was filtered through filter paper and washed with DMSO (60 mL). The combined filtrate was slowly added to a mixture of crystals (Form G: 600 mg) obtained in 120q) (as seed crystals) in AcOEt (600 mL) at 0-30°C. The mixture was stirred at 70°C for 0.5 h and cooled to room temperature. After stirring at room temperature for 1 h, the mixture was stirred at 0-10°C for 1 h and at room temperature for 1 h. The solids were collected by filtration and dried at 50°C under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (47.9 g) as white crystals (Form G).

MS (ESI+): $[M+H]^+$ 401.2

$^1H$ NMR (500 MHz, $CDCl_3$) δ 1.42 (3H, t), 2.62 (3H, s), 3.84 (3H, s), 4.15-4.27 (2H, m), 6.81-6.92 (1H, m), 7.10-7.18 (1H, m), 7.52-7.61 (2H, m), 7.73-7.80 (1H, m), 7.82-7.87 (2H, m), 7.91-7.95 (1H, m), 8.20-8.29 (1H, m).

[0408]

Method J

120s) 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (crystals of Form G)

120s')A solution of 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (78.4 g, 371.33 mmol) in DMA (420 mL) was added to a solution of 1-ethyl-3-(4-hydroxyphenyl)-7-

methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (100.0 g, 371.33 mmol) and potassium tert-butoxide (51.5 g) in DMA (370 mL) at room temperature. The mixture was stirred at 90-100°C for 1 h. Water (780 mL) was added at 90-100°C. The precipitate was collected at room temperature and dried under reduced pressure to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (127.7 g) as crystals. The obtained crystals (125.0 g) were dissolved in DMSO (1375 mL) at 90-95°C. To the solution was slowly added EtOH (1250 mL) at 80-95°C, and then the mixture was allowed to cool to room temperature. The solid was collected by filtration and washed with EtOH (625 mL) to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (103.9 g) as crystals.

120s'') The mixture of the obtained crystals (55.0 g) in a solution of DMSO (275 mL) and EtOH (275 mL) was stirred at 70-75°C for 0.5 h and then the mixture was allowed to cool to room temperature. The solid was collected by filtration and washed with EtOH (165 mL) to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (52.2 g) as crystals (Form A). The obtained crystals (5.0 g) were dissolved in DMSO (50 mL) at 95°C. The solution was filtered through filter paper and washed with DMSO (5 mL). To the combined filtrate was added EtOH (50 mL) slowly at 73-95°C. To the solution was added crystals (Form G: 5 mg) obtained in 120p) (as seed crystals) at 73°C. The mixture was allowed to cool to room temperature. After stirring at 70-75°C for 7 h, the mixture was cooled to room temperature. After stirring at 70-75°C for 8 h, the mixture was cooled to room temperature. After stirring at 70-75°C for 2 h, the mixture was stirred at room temperature for 1 h, and at 0-10°C for 1 h. The solids were collected by filtration and dried at 50°C under reduced pressure to give 1-ethyl-7-methyl-3-{4-

[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (4.5 g) as white crystals (Form G).

[0409]

Powder X-ray Diffraction (PXRD) Analysis:

Form G is characterized by PXRD Pattern using CuKα X-ray radiation, having peaks selected from a list consisting of:

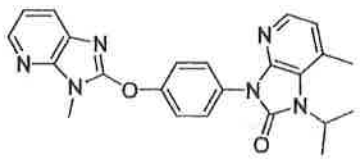
9.2245 angstrom ; middle
7.8796 angstrom ; high
6.763 angstrom ; middle
6.2059 angstrom ; middle
6.1289 angstrom ; middle
5.7268 angstrom ; high
5.1275 angstrom ; middle
4.638 angstrom ; middle
4.267 angstrom ; middle
3.9939 angstrom ; middle
3.9345 angstrom ; middle
3.7921 angstrom ; high
3.7479 angstrom ; high
3.0579 angstrom ; middle

d-value.

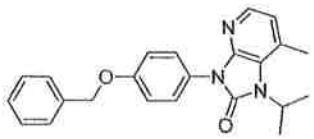
[0410]

Example 121

7-methyl-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



121a) 3-[4-(benzyloxy)phenyl]-7-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



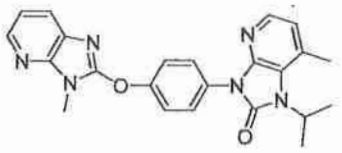
A suspension of 3-[4-(benzyloxy)phenyl]-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (360 mg), 2-iodopropane (0.217 mL) and potassium carbonate (180 mg) in DMF (10 mL) was stirred overnight at room temperature. The reaction mixture was poured into water, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 15% - 20% AcOEt in hexane) to give the title compound (218 mg) as colorless oil.

MS (API+): $[M+H]^+$ 374.3

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.68 (6H, d, J = 6.8 Hz), 2.60 (3H, s), 4.72-4.88 (1H, m), 5.11 (2H, s), 6.78 (1H, d, J = 5.3 Hz), 7.06-7.13 (2H, m), 7.28-7.47 (5H, m), 7.47-7.55 (2H, m), 7.88 (1H, d, J = 5.3 Hz).

[0411]

121b) 7-methyl-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[4-(benzyloxy)phenyl]-7-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (215 mg) and 10% Pd-C (30.6 mg) in EtOH (10 mL) was hydrogenated under balloon pressure at room temperature for 1 h. The catalyst was removed by filtration and the filtrate was concentrated in vacuo to give 3-(4-hydroxyphenyl)-7-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one as a colorless solid. To a solution of this solid in DMF (10 mL) were added sodium hydride (27.8 mg) and 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (164 mg) at 100°C. The mixture was heated at 180°C for 30 min under microwave irradiation. The precipitate was collected by filtration and washed with AcOEt and MeOH to give the title compound (175 mg)

as colorless crystals.

MS (API+): $[M+H]^+$ 415.4

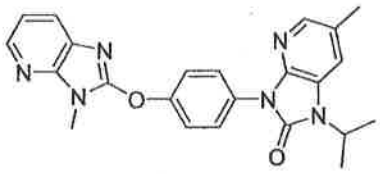
$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.60 (6H, d, J = 6.8 Hz), 2.62 (3H, s), 3.78 (3H, s), 4.83 (1H, quin, J = 6.8 Hz), 6.98 (1H, d, J = 5.3 Hz), 7.20 (1H, dd, J = 7.9, 4.9 Hz), 7.57-7.64 (2H, m), 7.68-7.75 (2H, m), 7.80 (1H, dd, J = 7.9, 1.5 Hz), 7.84 (1H, d, J = 5.3 Hz), 8.22 (1H, dd, J = 4.9, 1.5 Hz).

mp 270 - 271°C.

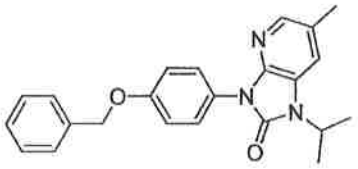
[0412]

Example 122

6-methyl-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



122a) 3-[4-(benzyloxy)phenyl]-6-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

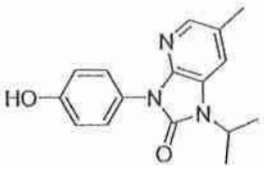


NaH (84 mg) was added to a solution of 3-[4-(benzyloxy)phenyl]-6-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (346 mg) and 2-iodopropane (0.208 mL) in DMF(dry) (4 mL) at room temperature. The mixture was stirred at room temperature under a dry atmosphere ($CaCl_2$ tube) for 1h. The mixture was poured into water, and the mixture was extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, EtOAc/hexane) to give the title compound (283 mg) as a yellow oil.

MS (API+): [M+H]+ 374.2.

[0413]

122b) 3-(4-hydroxyphenyl)-6-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

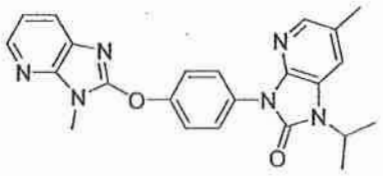


A mixture of 3-[4-(benzyloxy)phenyl]-6-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (283 mg) and 10% palladium on carbon (50% wet) (87 mg) in MeOH (4.2 mL) and EtOAc (4.2 mL) was hydrogenated under balloon pressure at room temperature overnight. The solid was filtrated and washed with MeOH (10 mL) to remove the catalyst. The filtrate was concentrated in vacuo to give the title compound (210 mg) as a gray solid.

$^1$H NMR (300 MHz, $CDCl_3$) δ 1.59 (5H, d, J = 7.2 Hz), 2.40 (3H, s), 4.82 (1H, t, J = 7.0 Hz), 6.60-6.90 (2H, m), 7.25 (2H, s), 7.27-7.32 (2H, m), 7.87 (1H, s).

[0414]

122c) 6-methyl-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a mixture of 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (198 mg) and 3-(4-hydroxyphenyl)-6-methyl-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (177 mg) in DMF (1.5 mL) was added NaH (40.0 mg), and the mixture was stirred at 100°C for 1 h. The mixture was heated at 180°C for 30 min under microwave irradiation. The mixture was poured into water, and the mixture was extracted with EtOAc. The organic layer was separated, washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was

purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (125 mg) as white crystals.

MS (API+): [M+H]+ 415.1.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.52 (6H, d, J = 7.2 Hz), 2.36 (3H, s), 3.77 (3H, s), 4.71 (1H, quin, J = 6.9 Hz), 7.20 (1H, dd, J = 7.9, 4.9 Hz), 7.53-7.71 (3H, m), 7.71-7.86 (4H, m), 8.22 (1H, dd, J = 4.9, 1.5 Hz).

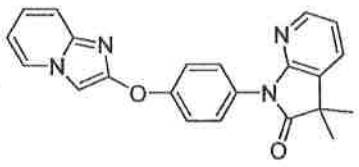
Anal. Calcd for $C_{23}H_{22}N_6O_2$: C, 66.65; H, 5.35; N, 20.28. Found: C, 66.55; H, 5.44; N, 20.23.

mp 252°C

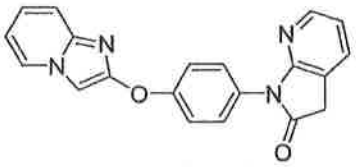
[0415]

Example 123

1-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-3,3-dimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one



123a) 1-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one



Ethyl 2-chloroimidazo[1,2-a]pyridine-3-carboxylate (2.00 g) was added to a solution of p-bromophenol (1.617 g) and NaH (0.427 g) in DMF(dry) (10 mL) at 100°C. The mixture was stirred at 100°C under a dry atmosphere overnight. The reaction mixture was diluted with MeOH, and concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 30% EtOAc in hexane) to give ethyl 2-(4-bromophenoxy)imidazo[1,2-a]pyridine-3-carboxylate (1.5 g) as a colorless solid and 2-(4-bromophenoxy)imidazo[1,2-a]pyridine (530 mg) as a colorless solid. The mixture of 2-(4-bromophenoxy)imidazo[1,2-a]pyridine (410 mg), 1,3-dihydro-2H-

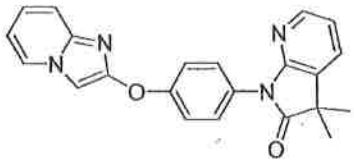
pyrrolo[2.3-b]pyridine-2-one (164 mg), trans-N,N'-dimethylcyclohexane-1,2-diamine (174 mg), copper(I) iodide (116 mg), $K_2CO_3$ (338 mg) and THF(dry) (5 mL) was heated at 180°C for 3 h under microwave irradiation. The solid was removed by filtration, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (72 mg) as an orange solid (mixture with 1,3-dihydro-2H-pyrrolo[2.3-b]pyridine-2-one, ca. 20% purity).

This product was subjected to the next reaction without further purification.

MS (API+): [M+H]+ 343.1.

[0416]

123b) 1-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-3,3-dimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one



A mixture of 1-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one (72 mg, mixture with 1,3-dihydro-2H-pyrrolo[2.3-b]pyridine-2-one, ca. 20% purity), iodomethane (0.110 mL), and sodium hydride (70.8 mg) in DMF (1 mL) was stirred at 0°C to room temperature overnight. The mixture was quenched with water at room temperature and extracted with EtOAc. The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/hexane) and column chromatography (NH silica gel, EtOAc/hexane) to give the title compound (7.40 mg) as a colorless oil.

MS (API+): [M+H]+ 371.3.

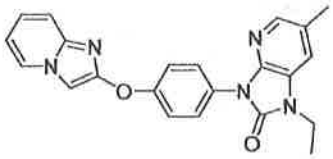
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.46-1.55 (6H, m), 6.81 (1H, t, J = 6.2 Hz), 7.02 (1H, dd, J = 7.6, 5.3 Hz), 7.12 (1H, s), 7.14-7.22 (1H, m), 7.29-7.41 (2H, m), 7.48-7.59 (4H, m), 8.03 (1H,

d, J = 6.8 Hz), 8.17 (1H, dd, J = 5.3, 1.5 Hz).

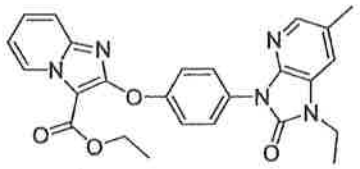
[0417]

Example 124

1-ethyl-3-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-6-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



124a) ethyl 2-[4-(1-ethyl-6-methyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenoxy]imidazo[1,2-a]pyridine-3-carboxylate

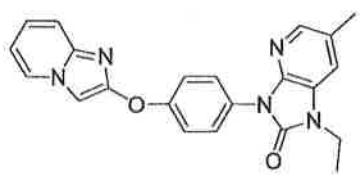


The mixture of ethyl 2-chloroimidazo[1,2-a]pyridine-3-carboxylate (504 mg), 1-ethyl-3-(4-hydroxyphenyl)-6-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (302 mg) and NaH (67.3 mg) in DME (4 mL) was heated at 50°C for 1 h. The mixture was heated at 200°C for 3 h under microwave irradiation. The mixture was poured into sat. $NaHCO_3$, and the mixture was extracted with EtOAc. The organic layer was separated, washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (62.0 mg) as a white solid.

MS (API+): [M+H]+ 458.2.

[0418]

124b) 1-ethyl-3-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-6-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a solution of ethyl 2-[4-(1-ethyl-6-methyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenoxy]imidazo[1,2-a]pyridine-3-carboxylate (62 mg) in EtOH (4 mL) was added sodium hydroxide (1.084 mL). The mixture was stirred at 50°C for 2 h. Hydrochloric acid (2.168 mL) was added to the mixture, and the mixture was stirred at 60°C for 10 h. The mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (42.0 mg) as a colorless oil.

MS (API+): [M+H]+ 386.2.

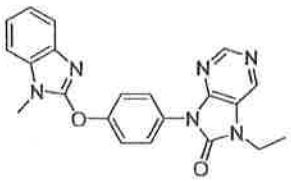
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.41 (3H, t, J = 7.2 Hz), 2.40 (3H, s), 4.00 (2H, q, J = 7.2 Hz), 6.76-6.86 (1H, m), 7.10 (2H, s), 7.13-7.22 (1H, m), 7.30-7.40 (2H, m), 7.51 (1H, d, J = 9.1 Hz), 7.68-7.75 (2H, m), 7.88 (1H, s), 8.02 (1H, d, J = 6.4 Hz).

Anal. Calcd for $C_{22}H_{19}N_5O_2$-0.5 $H_2O$: C, 67.06; H, 5.11; N, 17.77. Found: C, 67.25; H, 5.16; N, 17.71.

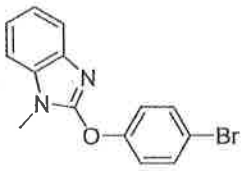
[0419]

Example 125

7-ethyl-9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one



125a) 2-(4-bromophenoxy)-1-methyl-1*H*-benzimidazole



Triethylamine (18 mL) was added to a mixture of 2-chloro-1-methyl-1H-benzimidazole (7.2 g) and *p*-bromophenol (22.5 g) at room temperature. The mixture was stirred at 120°C for 6 h. The mixture was quenched with water at room temperature and extracted with EtOAc. The organic layer was separated, washed with 1 N NaOH aq. and brine, dried over $MgSO_4$ and concentrated

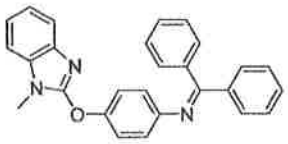
in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 10% - 15% EtOAc in hexane) to give 2-(4-bromophenoxy)-1-methyl-1*H*-benzimidazole (3.2 g) as colorless crystals.

MS (API+): $[M+H]^+$ 304.92.

$^1$H NMR (300 MHz, $CDCl_3$) δ 3.73 (3H, s), 7.13-7.35 (5H, m), 7.50-7.61 (3H, m).

[0420]

125b) *N*-(diphenylmethylidene)-4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline



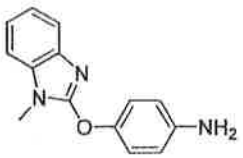
To a suspension of 2-(4-bromophenoxy)-1-methyl-1*H*-benzimidazole (1.0 g), $Pd_2(dba)_3$ (0.076 g), sodium *tert*-butoxide (0.48 g) and xantphos (0.19 g) in dioxane (10 mL) was added benzophenone imine (0.83 mL), and the mixture was stirred at 100°C under Ar atmosphere for 6 h. After stirring at room temperature overnight, the mixture was poured into water, and the mixture was extracted with AcOEt. The organic layer was dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residual crystals were washed with AcOEt to obtain *N*-(diphenylmethylidene)-4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline (0.81 g) as pale yellow crystals.

MS (API+): $[M+H]^+$ 404.2.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 3.67 (3H, s), 6.74-6.82 (2H, m), 7.07-7.26 (6H, m), 7.33-7.59 (8H, m), 7.64-7.71 (2H, m).

[0421]

125c) 4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline



To a suspension of *N*-(diphenylmethylidene)-4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline (810 mg) in THF (10 mL) was added 1 N HCl aq (10 mL) at room temperature, and the mixture

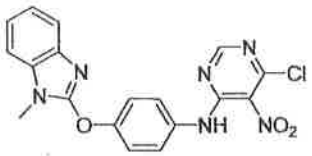
was stirred at room temperature for 1 h. The mixture was neutralized with sat. $NaHCO_3$ aq. and extracted with AcOEt. The organic layer was dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 5% - 100% AcOEt in hexane) to give 4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline (440 mg) as colorless crystals.

MS (API+): $[M+H]^+$ 240.2.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 3.68 (3H, s), 5.06 (2H, s), 6.55-6.64 (2H, m), 6.99-7.18 (4H, m), 7.30-7.43 (2H, m).

[0422]

125d) 6-chloro-*N*-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-5-nitropyrimidin-4-amine



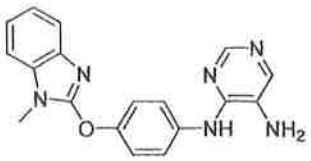
To a solution of 4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]aniline (0.30 g) and TEA (0.26 mL) in THF (15 mL) was added 4,6-dichloro-5-nitropyrimidine (0.24 g) at room temperature, and the mixture was stirred at room temperature for 2 h. The mixture was poured into water, and the mixture was extracted with AcOEt. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (dry charge, silica gel, eluted with 5% - 50% AcOEt in hexane) to give 6-chloro-*N*-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-5-nitropyrimidin-4-amine (0.24 g) as a yellow solid.

MS (API+): $[M+H]^+$ 397.3.

$^1H$ NMR (300 MHz, $CDCl_3$) δ 3.75 (3H, s), 7.17-7.26 (3H, m), 7.43-7.51 (2H, m), 7.54-7.65 (3H, m), 8.48 (1H, s), 9.22 (1H, s).

[0423]

125e) $N^4$-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}pyrimidine-4,5-diamine

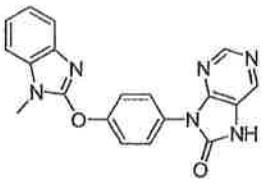


A mixture of 6-chloro-*N*-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-5-nitropyrimidin-4-amine (240 mg) and 10% palladium on carbon (160 mg) in MeOH (10 mL) and THF (10 mL) was hydrogenated under balloon pressure at room temperature overnight. To the mixture was added TEA (0.50 mL). The catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 5% MeOH in AcOEt) to give $N^4$-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}pyrimidine-4,5-diamine (80 mg) as a colorless solid.

MS (API+): $[M+H]^+$ 333.4.

[0424]

125f) 9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one

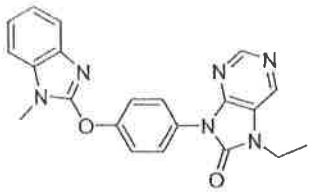


A solution of $N^4$-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}pyrimidine-4,5-diamine (80 mg) and CDI (39 mg) in THF (20 mL) was refluxed for 3 h. CDI (39 mg) was added to the mixture. After refluxing overnight, the mixture was concentrated in vacuo. The residual solid was washed with AcOEt to give 9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one (56 mg) as white crystals.

MS (API+): $[M+H]^+$ 359.3.

[0425]

125g) 7-ethyl-9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one



A mixture of 9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one (56 mg), iodoethane (20 µL) and cesium carbonate (120 mg) in DMF (3 mL) was stirred at 50°C for 4 h. The mixture was poured into water, and the mixture was extracted with AcOEt. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residual crystals were recrystallized from AcOEt to give 7-ethyl-9-{4-[(1-methyl-1*H*-benzimidazol-2-yl)oxy]phenyl}-7,9-dihydro-8*H*-purin-8-one (40 mg) as white crystals.

MS (API+): $[M+H]^+$ 387.4.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.34 (3H, t, J = 7.2 Hz), 3.77 (3H, s), 4.01 (2H, q, J = 7.2 Hz), 7.11-7.24 (2H, m), 7.40-7.51 (2H, m), 7.58-7.66 (2H, m), 7.72-7.79 (2H, m), 8.64 (1H, s), 8.65 (1H, s).

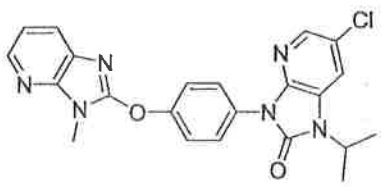
mp 242-243°C

Anal. Calcd for $C_{21}H_{18}N_6O_2$: C, 65.27; H, 4.70; N, 21.75. Found: C, 64.99; H, 4.77; N, 21.70.

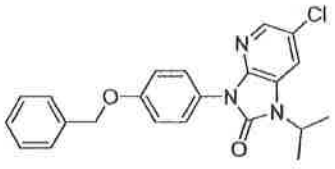
[0426]

Example 126

6-chloro-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



126a) 3-[4-(benzyloxy)phenyl]-6-chloro-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



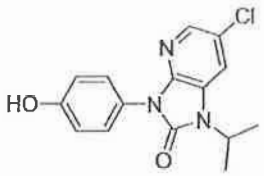
Di-tert-butyl dicarbonate (17.05 mL) was added to a solution of 2,5-dichloropyridin-3-amine (11.4 g) and NaHMDS (81 mL) in THF(dry) (200 mL) at 0°C. The mixture was stirred at 0°C under a dry atmosphere for 1 h. The mixture was neutralized with 1N HCl at 0°C and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 20% EtOAc in hexane) to give tert-butyl 2,5-dichloropyridin-3-ylcarbamate (15.6 g) as colorless oil. The mixture of tert-butyl 2,5-dichloropyridin-3-ylcarbamate (7.5 g), 4-benzyloxyaniline hydrochloride (10.08 g), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (1.319 g), $Pd_2(dba)_3$ (1.044 g) and sodium tert-butoxide (6.57 g) in toluene (160 mL) - 2-propanol (40.0 mL) was stirred at 100°C under Ar overnight. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 100% EtOAc in hexane) to give intermediate. To the intermediate in DMF (100 mL) were added 2-iodopropane (5.69 mL) and NaH (2.280 g), and the mixture was stirred at room temperature under a dry atmosphere ($CaCl_2$ tube) for 1h. The reaction mixture was diluted with MeOH and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 50% EtOAc in hexane) to give 3-[4-(benzyloxy)phenyl]-6-chloro-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (560 mg) as a colorless solid.

MS (API+): [M+H]+ 394.2.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.41-1.57 (6H, m), 4.57-4.78 (1H, m), 5.18 (2H, s), 7.09-7.21 (2H, m), 7.26-7.60 (7H, m), 7.81-8.08 (2H, m).

[0427]

126b) 6-chloro-3-(4-hydroxyphenyl)-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



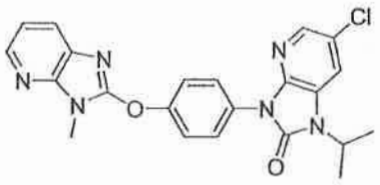
A mixture of 3-[4-(benzyloxy)phenyl]-6-chloro-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (600 mg) and 10% Pd-C (162 mg) in EtOAc (50 mL) was hydrogenated under balloon pressure at room temperature for 1h. The catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 50% EtOAc in hexane) to give 6-chloro-3-(4-hydroxyphenyl)-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (200 mg) as a white solid.

MS (API+): [M+H]+ 304.1.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.38-1.65 (6H, m), 4.54-4.82 (1H, m), 6.84-6.96 (2H, m), 7.30-7.41 (2H, m), 7.89-7.94 (1H, m), 7.93-7.98 (1H, m), 9.74 (1H, s).

[0428]

126c) 6-chloro-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



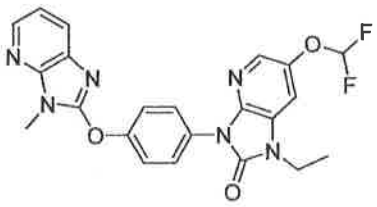
3-Methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (100 mg) was added to a solution of 6-chloro-3-(4-hydroxyphenyl)-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (148 mg) and NaH (20.83 mg) in DMF (3 mL) at room temperature. The mixture was heated at 180°C for 30min under microwave irradiation. The reaction mixture was diluted with MeOH and concentrated in vacuo. The residue was purified

by column chromatography (silica gel, eluted with 0% - 50% EtOAc in hexane) to give 6-chloro-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (120 mg) as white crystals:
MS (API+): [M+H]+ 435.2.
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.38-1.64 (6H, m), 3.77 (3H, s), 4.71 (1H, s), 7.15-7.28 (1H, m), 7.57-7.67 (2H, m), 7.69-7.86 (3H, m), 7.90-8.10 (2H, m), 8.16-8.27 (1H, m).

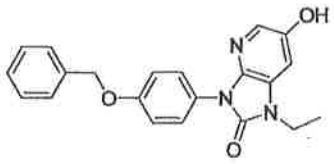
[0429]

Example 127

6-(difluoromethoxy)-1-ethyl-3-{4-[(3-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one



127a) 3-[4-(benzyloxy)phenyl]-1-ethyl-6-hydroxy-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one



A mixture of 3-[4-(benzyloxy)phenyl]-6-chloro-1-ethyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (1.72 g), $Pd_2dba_3$ (0.21 g), 2-di-tert-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropyl-1,1'-biphenyl (0.44 g) and KOH (1.10 g) in dioxane (15 mL) and water (15 mL) was stirred at 100°C under Ar atmosphere for 3 h. After stirring at room temperature overnight, the mixture was acidified with 1 N HCl aq (11 mL) and diluted with water. The mixture was extracted with AcOEt. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 10% - 70% AcOEt in hexane) to give 3-[4-(benzyloxy)phenyl]-1-ethyl-6-hydroxy-1,3-

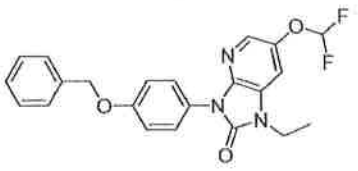
dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (1.31 g) as a pale yellow solid.

MS (API+): $[M+H]^+$ 362.3.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.25 (3H, t, J = 7.2 Hz), 3.90 (2H, q, J = 7.2 Hz), 5.17 (2H, s), 7.08-7.17 (3H, m), 7.30-7.56 (8H, m), 9.58 (1H, brs).

[0430]

127b) 3-[4-(benzyloxy)phenyl]-6-(difluoromethoxy)-1-ethyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one



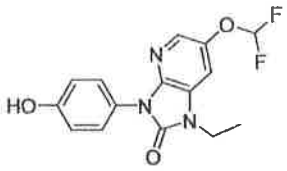
A mixture of 3-[4-(benzyloxy)phenyl]-1-ethyl-6-hydroxy-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (300 mg), sodium chlorodifluoroacetate (253 mg), $K_2CO_3$ (172 mg), DMF (3 mL), and water (0.60 mL) was refluxed overnight. The reaction mixture was poured into water, and the mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 10% - 40% AcOEt in hexane) to give 3-[4-(benzyloxy)phenyl]-6-(difluoromethoxy)-1-ethyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (110 mg) as a pale yellow oil.

MS (API+): $[M+H]^+$ 412.1.

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.39 (3H, t, J = 7.2 Hz), 3.98 (2H, q, J = 7.2 Hz), 5.10 (2H, s), 6.50 (1H, t, J = 73.3 Hz), 7.04-7.17 (3H, m), 7.27-7.49 (5H, m), 7.50-7.61 (2H, m), 7.92 (1H, d, J = 2.3 Hz).

[0431]

127c) 6-(difluoromethoxy)-1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one

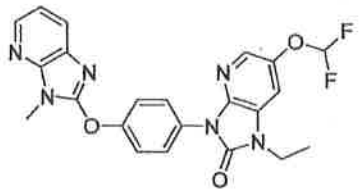


A mixture of 3-[4-(benzyloxy)phenyl]-6-(difluoromethoxy)-1-ethyl-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (110 mg) and 10% palladium on carbon (40 mg) in MeOH (10 mL) was hydrogenated under balloon pressure at room temperature for 2h. The catalyst was removed by filtration and the filtrate was concentrated in vacuo to give 6-(difluoromethoxy)-1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (86 mg) as a pale yellow oil.

MS (API+): $[M+H]^+$ 322.3.

[0432]

127d) 6-(difluoromethoxy)-1-ethyl-3-{4-[(3-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one



To a solution of 3-methyl-2-(methylsulfonyl)-3*H*-imidazo[4,5-*b*]pyridine (62 mg) and 6-(difluoromethoxy)-1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (86 mg) in DMF (3 mL) was added NaH (13 mg) at room temperature, and the mixture was stirred at 180°C under microwave irradiation for 30 min. The mixture was partitioned between water and AcOEt. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated in vacuo. The residue was purified by column chromatography (dry charge, NH silica gel, eluted with 50% - 100% AcOEt in hexane) and recrystallized from AcOEt/hexane to give 6-(difluoromethoxy)-1-ethyl-3-{4-[(3-methyl-3*H*-imidazo[4,5-*b*]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridin-2-one (56 mg) as white crystals.

MS (API+): $[M+H]^+$ 453.4.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.30 (3H, t, J = 7.2 Hz), 3.77 (3H, s), 4.00 (2H, q, J = 7.2 Hz), 7.21 (1H, dd, J = 7.9, 4.9 Hz), 7.24 (1H, t, J = 74.0 Hz), 7.59-7.67 (2H, m), 7.73-7.84 (4H, m), 7.92 (1H, d, J = 2.3 Hz), 8.22 (1H, dd, J = 4.9, 1.5 Hz).

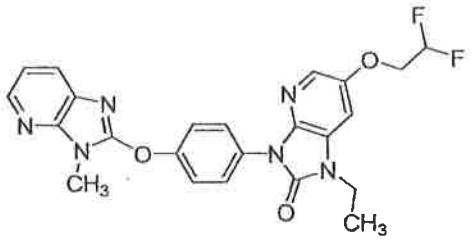
Anal. Calcd for $C_{22}H_{18}N_6O_3F_2$: C, 58.41; H, 4.01; N, 18.58. Found: C, 58.30; H, 4.15; N, 18.43.

Mp: 195-197°C

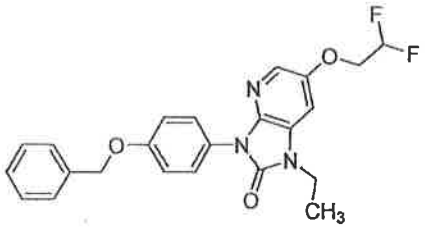
[0433]

Example 128

6-(2,2-difluoroethoxy)-1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



128a) 3-[4-(benzyloxy)phenyl]-6-(2,2-difluoroethoxy)-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



2,2-Difluoroethyl trifluoromethanesulfonate (213 mg) was added to a solution of 3-[4-(benzyloxy)phenyl]-1-ethyl-6-hydroxy-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (300 mg) and potassium carbonate (229 mg) in DMF (5 mL) at room temperature. The mixture was stirred at ambient temperature under a dry atmosphere ($CaCl_2$ tube) for 3 h. The mixture was quenched with water at room temperature and extracted with AcOEt. The organic layer was separated, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with

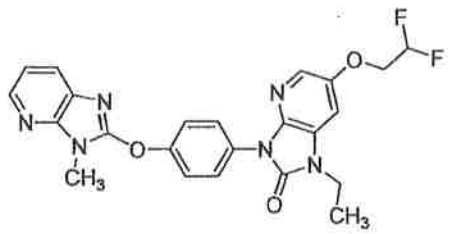
15% - 50% AcOEt in hexane) to give 3-[4-(benzyloxy)phenyl]-6-(2,2-difluoroethoxy)-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (301 mg) as colorless oil.

MS (API+): $[M+H]^+$ 426.4

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.39 (3H, d, J = 7.3 Hz), 3.98 (2H, q, J = 7.3 Hz), 4.24 (2H, td, J = 13.0, 4.0 Hz), 5.11 (2H, s), 6.10 (1H, tt, J = 55.0, 4.0 Hz), 6.96 (1H, d, J = 2.6 Hz), 7.11 (2H, d, J = 8.7 Hz), 7.28-7.48 (5H, m), 7.56 (2H, d, J = 8.7 Hz), 7.73 (1H, d, J = 2.6 Hz).

[0434]

128b) 6-(2,2-difluoroethoxy)-1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[4-(benzyloxy)phenyl]-6-(2,2-difluoroethoxy)-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (300 mg) and 10% Pd-C (37.5 mg) in EtOH (10 mL) was hydrogenated under balloon pressure at room temperature overnight. The catalyst was removed by filtration and the filtrate was concentrated in vacuo to give 6-(2,2-difluoroethoxy)-1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one as a colorless solid. To a solution of this product and 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (153 mg) in DMF (5 mL) was added sodium hydride (34.1 mg) at 100°C, and the mixture was heated at 180°C for 30 min under microwave irradiation. The mixture was quenched with water at room temperature and extracted with AcOEt. The organic layer was separated, washed with sat. $NaHCO_3$ aq. and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 15% - 50% AcOEt in hexane) to give 6-(2,2-

difluoroethoxy)-1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (264 mg) as a colorless solid. The solid was crystallized from AcOEt-hexane.

MS (API+): $[M+H]^+$ 467.3

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.42 (3H, t, J = 7.2 Hz), 3.84 (3H, s), 4.01 (2H, q, J = 7.2 Hz), 4.26 (2H, td, J = 13.0, 4.1 Hz), 6.12 (1H, tt, J = 55.0, 4.0 Hz), 6.98 (1H, d, J = 2.6 Hz), 7.15 (1H, dd, J = 7.9, 4.9 Hz), 7.56 (2H, d, J = 8.7 Hz), 7.72-7.82 (2H, m), 7.88 (2H, d, J = 9.0 Hz), 8.25 (1H, dd, J = 4.9, 1.5 Hz).

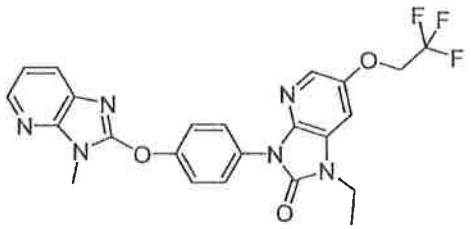
Anal. Calcd for $C_{23}H_{20}N_6O_3F_2 \cdot 0.5H_2O$: C, 58.10; H, 4.45; N,17.68; F, 8.15. Found: C, 58.20; H, 4.39; N, 17.65.

mp 171 - 172°C

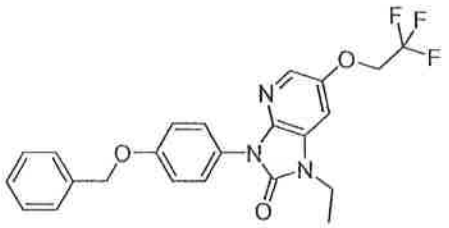
[0435]

Example 129

1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



129a) 3-[4-(benzyloxy)phenyl]-1-ethyl-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



2,2,2-Trifluoroethyl trifluoromethanesulfonate (0.144 mL) was added to a solution of 3-[4-(benzyloxy)phenyl]-1-ethyl-6-hydroxy-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (300 mg) and potassium carbonate (229 mg) in DMF (5 mL) at room

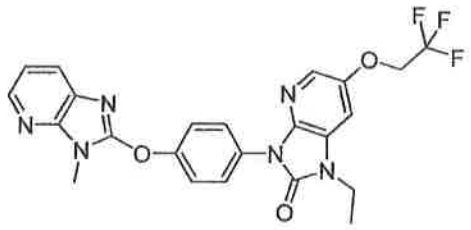
temperature. The mixture was stirred at ambient temperature under a dry atmosphere ($CaCl_2$ tube) for 3 h. The mixture was quenched with water at room temperature and extracted with AcOEt. The organic layer was separated, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 15% - 50% AcOEt in hexane) to give 3-[4-(benzyloxy)phenyl]-1-ethyl-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (308 mg) as colorless oil.

MS (API+): $[M+H]^+$ 444.4

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.40 (3H, d, J = 7.2 Hz), 3.99 (2H, q, J = 7.2 Hz), 4.40 (2H, q, J = 7.9 Hz), 5.11 (2H, s), 6.99 (1H, d, J = 2.3 Hz), 7.11 (2H, d, J = 8.7 Hz), 7.28-7.49 (5H, m), 7.55 (2H, d, J = 9.1 Hz), 7.74 (1H, d, J = 2.6 Hz).

[0436]

129b) 1-Ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[4-(benzyloxy)phenyl]-1-ethyl-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (305 mg) and 10% Pd-C (36.6 mg) in EtOH (10 mL) was hydrogenated under balloon pressure at room temperature overnight. The catalyst was removed by filtration and the filtrate was concentrated in vacuo to give 1-ethyl-3-(4-hydroxyphenyl)-6-(2,2,2-trifluoroethoxy)-1H-imidazo[4,5-b]pyridin-2(3H)-one as colorless solid. To a solution of this product and 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (149 mg) in DMF (5 mL), sodium hydride (33.1 mg) was added at 100°C and the mixture was heated at 180°C for 30 min under microwave irradiation. The mixture was quenched with

water at room temperature and extracted with AcOEt. The organic layer was separated, washed with sat. $NaHCO_3$ aq. and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 15% - 50% AcOEt in hexane) to give 1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-6-(2,2,2-trifluoroethoxy)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (262 mg) as colorless solid. The solid was crystallized from AcOEt-hexane.

MS (API+): $[M+H]^+$ 485.3

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.42 (3H, t, J = 7.3 Hz), 3.85 (3H, s), 4.01 (2H, q, J = 7.3 Hz), 4.43 (2H, q, J = 8.0 Hz), 7.02 (1H, d, J = 2.3 Hz), 7.15 (1H, dd, J = 7.9, 4.9 Hz), 7.56 (2H, d, J = 9.0 Hz), 7.75-7.82 (2H, m), 7.87 (2H, d, J = 9.4 Hz), 8.25 (1H, dd, J = 4.9, 1.5 Hz).

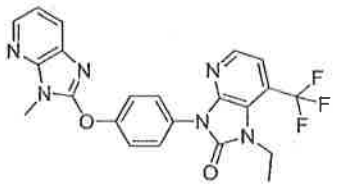
Anal. Calcd for $C_{23}H_{19}N_6O_3F_3$ - $0.5H_2O$: C, 55.98; H, 4.09; N, 17.03. Found: C, 55.88; H, 4.19; N, 16.94.

mp 178 - 179°C

[0437]

Example 130

1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



130a) methyl 2-fluoro-4-(trifluoromethyl)pyridine-3-carboxylate



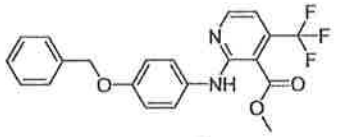
To a mixture of 2-fluoro-4-(trifluoromethyl)pyridine-3-carboxylic acid (1.06 g) and $K_2CO_3$ (0.701 g) in DMF(dry) (10 mL) was added MeI (0.317 mL). The mixture was stirred at room

temperature for 3 h. The mixture was directly purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (1.13 g, containing EtOAc and hexane, ca. 75% purity).

MS (API+): $[M+H]^+$ 224.0

[0438]

130b) methyl 2-{[4-(benzyloxy)phenyl]amino}-4-(trifluoromethyl)pyridine-3-carboxylate

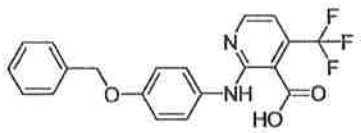


A mixture of 4-(benzyloxy)aniline (1010 mg), DIEA (1.771 mL) and methyl 2-fluoro-4-(trifluoromethyl)pyridine-3-carboxylate (1130 mg) in NMP (10 mL) was stirred at 150°C for 2 h and at 200°C for 1 h under microwave irradiation. The mixture was poured into water, and the mixture was extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound (225 mg).

MS (API+): $[M+H]^+$ 403.3

[0439]

130c) 2-{[4-(benzyloxy)phenyl]amino}-4-(trifluoromethyl)pyridine-3-carboxylic acid

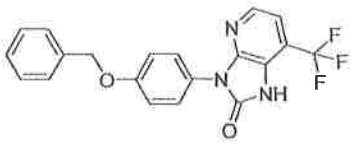


To a mixture of methyl 2-{[4-(benzyloxy)phenyl]amino}-4-(trifluoromethyl)pyridine-3-carboxylate (255 mg) in MeOH (5 mL) was added 1N NaOH (2.54 mL), and the mixture was stirred at 60°C for 3 h. After MeOH was evaporated, to the water phase was added 1N HCl (pH = ca. 2). The precipitate was collected by filtration to give the title compound (221 mg).

MS (API+): $[M+H]^+$ 389.3

[0440]

130d) 3-[4-(benzyloxy)phenyl]-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

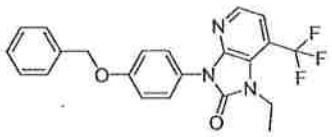


To a solution of 2-{[4-(benzyloxy)phenyl]amino}-4-(trifluoromethyl)pyridine-3-carboxylic acid (221 mg) and $Et_3N$ (0.238 mL) in toluene (15 mL) was added diphenylphosphoryl azide (0.245 mL) at room temperature. The mixture was stirred at 110°C for 4 h. After cooling, the solvent was evaporated, and the precipitate was collected by filtration to give the title compound (197 mg).

MS (API+): $[M+H]^+$ 386.2

[0441]

130e) 3-[4-(benzyloxy)phenyl]-1-ethyl-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

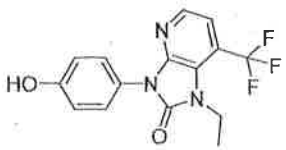


To a mixture of NaH (40.9 mg), 3-[4-(benzyloxy)phenyl]-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (197 mg) in DMF(dry) (3 mL) was added iodoethane (0.082 mL), and the mixture was stirred at room temperature for 3 h. To the mixture was added sat. $NaHCO_3$ aq. and the mixture was extracted with EtOAc. The organic layer was separated, washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo to give the title compound (197 mg).

MS (API+): $[M+H]^+$ 414.1

[0442]

130f) 1-ethyl-3-(4-hydroxyphenyl)-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



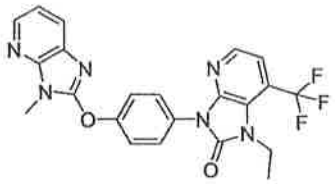
A mixture of 3-[4-(benzyloxy)phenyl]-1-ethyl-7-

(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (197 mg) and 10% palladium on carbon (50% wet, 68 mg) in MeOH (6.5 mL) and EtOAc (6.5 mL) was hydrogenated under balloon pressure at room temperature for 4 h. The solid was filtrated and washed with MeOH (10 mL) to remove the catalyst. The filtrate was concentrated in vacuo to give the title compound (103 mg).

MS (API+): $[M+H]^+$ 324.2

[0443]

130g) 1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a mixture of 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (81 mg) and 1-ethyl-3-(4-hydroxyphenyl)-7-(trifluoromethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (103 mg) in DMF(dry) (1.5 mL) was added NaH (19.12 mg), and the mixture was stirred at 100°C for 1h. The mixture was heated at 180°C for 30 min under microwave irradiation. The mixture was poured into water, and the mixture was extracted with EtOAc. The organic layer was separated, washed with brine, dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, EtOAc/hexane) to give the title compound as white crystals (62.2 mg).

MS (API+): $[M+H]^+$ 455.3.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.30 (3H, t, J = 7.0 Hz), 3.78 (3H, s), 4.00-4.10 (2H, m), 7.21 (1H, dd, J = 7.7, 5.1 Hz), 7.48 (1H, d, J = 5.3 Hz), 7.60-7.69 (2H, m), 7.72-7.78 (2H, m), 7.81 (1H, dd, J = 7.9, 1.5 Hz), 8.17 (1H, d, J = 5.7 Hz), 8.22 (1H, dd, J = 4.9, 1.5 Hz).

Anal. Calcd for $C_{22}H_{17}N_6O_2F_3$: C, 58.15; H, 3.77; N, 18.49. Found:

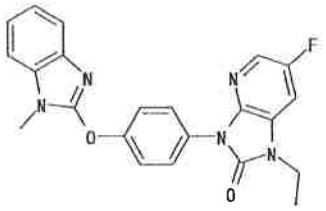
C, 58.05; H, 3.84; N, 18.33.

m.p. 244-246°C

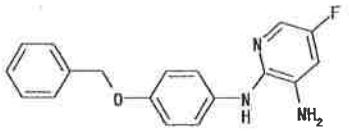
[0444]

Example 132

1-ethyl-6-fluoro-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



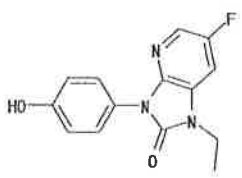
132a) $N^2$-[4-(benzyloxy)phenyl]-5-fluoropyridine-2,3-diamine



A mixture of 4-(benzyloxy)aniline (2.26 g), 2-chloro-5-fluoro-3-nitropyridine (2 g) and $K_2CO_3$ (3.13 g) in DMF (20 mL) was stirred at 120°C for 5h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was suspended in IPE and collected by filtration. The solid obtained above was dissolved in EtOH (20 mL), and Pt/C (2 g) was added. Under $H_2$ atmosphere, the mixture was stirred for 1h, filtered and evaporated. The residue was chromatographed on silica gel eluting with Hexane/AcOEt to give the title compound (0.85 g). $^1H$ NMR (300 MHz, DMSO-$d_6$) δ 5.04 (2H, s), 5.39 (2H, s), 6.69-6.80 (1H, m), 6.86-6.94 (2H, m), 7.29-7.50 (8H, m), 7.54 (1H, s).

[0445]

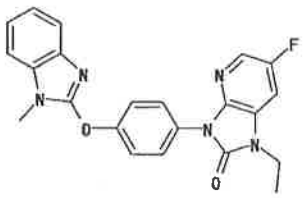
132b) 1-ethyl-6-fluoro-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of $N^2$-[4-(benzyloxy)phenyl]-5-fluoropyridine-2,3-diamine (0.85 g) and 1,1'-carbonylbis(1H-imidazole) (0.45 g) in DME (10 mL) was stirred at 100°C for 4h, and then $Cs_2CO_3$ (0.90 g) and 1,1'-carbonylbis(1H-imidazole) (0.892 g) were added successively. The mixture was stirred at 100°C for 10min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in DMF (10 mL), and then $Cs_2CO_3$ (3.58 g) and iodoethane (1.29 g) were added successively. The mixture was stirred at 100°C for 2h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in EtOH (30 mL), and Pd/C (1.5 g) was added. Under $H_2$ atmosphere, the mixture was stirred at room temperature for 30 min, filtered and evaporated. The residue was chromatographed on silica gel eluting with AcOEt/Hexane to give the title compound (0.52 g). MS (API+): $[M+H]^+$ 274.3.

[0446]

132c) 1-ethyl-6-fluoro-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a stirred solution of 1-ethyl-6-fluoro-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (100 mg) in DMF (4 mL) was added 60% sodium hydride (13.2 mg) at room temperature. The mixture was stirred at room temperature for 30min, and then 2-chloro-1-methyl-1H-benzimidazole (67.1 mg) was added. The mixture was exposed to microwave irradiation at 180°C for 30min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on NH-silica gel eluting with AcOEt/Hexane. Crystallization from AcOEt/Hexane gave the title compound (104 mg).

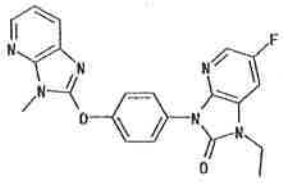
MS (API+): $[M+H]^+$ 404.2.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.30 (3H, t, J = 7.2 Hz), 3.76 (3H, s), 3.98 (2H, q, J = 7.2 Hz), 7.09-7.25 (2H, m), 7.39-7.52 (2H, m), 7.56-7.64 (2H, m), 7.73-7.79 (2H, m), 7.83-7.91 (1H, m), 7.96-8.01 (1H, m).

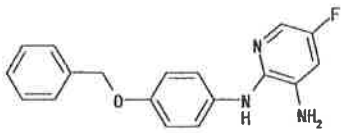
[0447]

Example 133

1-ethyl-6-fluoro-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



133a) $N^2$-[4-(benzyloxy)phenyl]-5-fluoropyridine-2,3-diamine

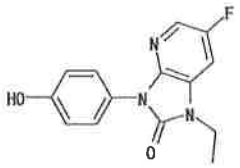


A mixture of 4-(benzyloxy)aniline (2.26 g), 2-chloro-5-fluoro-3-nitropyridine (2 g) and $K_2CO_3$ (3.13 g) in DMF (20 mL) was stirred at 120°C for 5 h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was suspended in IPE and collected by filtration. The obtained solid was dissolved in EtOH (20 mL), and Pt/C (2 g) was added. Under $H_2$ atmosphere, the mixture was stirred for 1 h, filtered and evaporated. The residue was chromatographed on silica gel eluting with Hexane/AcOEt to give the title compound (0.85 g).

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 5.04 (2H, s), 5.39 (2H, s), 6.69-6.80 (1H, m), 6.86-6.94 (2H, m), 7.29-7.50 (8H, m), 7.54 (1H, s).

[0448]

133b) 1-ethyl-6-fluoro-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of $N^2$-[4-(benzyloxy)phenyl]-5-fluoropyridine-2,3-diamine (0.85 g) and 1,1'-carbonylbis(1H-imidazole) (0.45 g) in DME (10 mL) was stirred at 100°C for 4 h, and then $Cs_2CO_3$ (0.90 g) and 1,1'-carbonylbis(1H-imidazole) (0.892 g) were added successively. The mixture was stirred at 100°C for 10 min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in DMF (10 mL), and then $Cs_2CO_3$ (3.58 g) and iodoethane (1.29 g) were added successively. The mixture was stirred at 100°C for 2 h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in EtOH (30 mL), and Pd/C (1.5 g) was added. Under $H_2$ atmosphere, the mixture was stirred at room temperature for 30 min, filtered and evaporated. The residue was chromatographed on silica gel eluting with AcOEt/Hexane to give the title compound (0.52 g). MS (API+): $[M+H]^+$ 274.3.

[0449]

133c) 1-ethyl-6-fluoro-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

To a stirred solution of 1-ethyl-6-fluoro-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (100 mg) in DMF (4 mL) was added 60% sodium hydride (13.2 mg) at room temperature. The mixture was stirred at room temperature for 30min, and then 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (85 mg) was added. The mixture was exposed to microwave irradiation at 180°C for 30min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on NH-silica gel eluting with AcOEt/Hexane.

Crystallization from AcOEt/Hexane gave the title compound (96 mg).

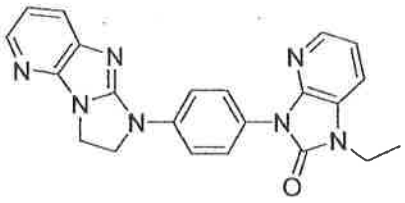
MS (API+): $[M+H]^+$ 405.2.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.31 (3H, t, J = 7.2 Hz), 3.77 (3H, s), 3.98 (2H, q, J = 7.2 Hz), 7.21 (1H, dd, J = 7.9, 4.9 Hz), 7.57-7.66 (2H, m), 7.72-7.91 (4H, m), 7.95-8.05 (1H, m), 8.18-8.24 (1H, m).

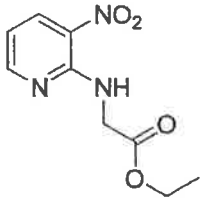
[0450]

Example 134

3-[4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



134a) ethyl N-(3-nitropyridin-2-yl)glycinate



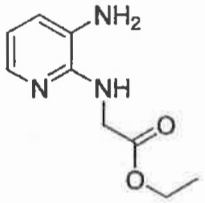
To a solution of 2-chloro-3-nitropyridine (25.3 g) in EtOH (300 mL) were added ethyl 2-aminoacetate hydrochloride (28.7 g) and triethylamine (28.9 mL) at room temperature, and the mixture was refluxed for 1 day. The mixture was concentrated under reduced pressure. The residual crystals were removed by filtration and washed with AcOEt. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 20% - 70% AcOEt in hexane). The residual crystals were removed by filtration and washed with IPE. The filtrate was concentrated under reduced pressure to give the title compound (26.9 g).

$^1H$ NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, t, J = 7.2 Hz), 4.26 (2H, q, J = 7.2 Hz), 4.38 (2H, d, J = 5.3 Hz), 6.72 (1H, dd, J = 8.3,

4.5 Hz), 8.40 (1H, dd, J = 4.5, 1.9 Hz), 8.44 (1H, dd, J = 8.3, 1.9 Hz), 8.50 (1H, brs).

[0451]

134b) ethyl N-(3-aminopyridin-2-yl)glycinate

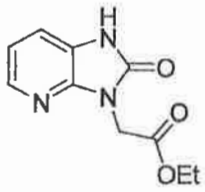


A mixture of ethyl N-(3-nitropyridin-2-yl)glycinate (26 g) and 10% palladium on carbon (50% wet, 7.3 g) in AcOEt (250 mL) was hydrogenated under balloon pressure at room temperature for 8 h. The catalyst was removed by filtration. To the filtrate were added triethylamine (5.0 mL) and 10% palladium on carbon (50% wet, 7.3 g). The mixture was hydrogenated under balloon pressure at room temperature overnight. The mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 10% - 50% AcOEt in hexane) to give the title compound (18 g).

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.17 (3H, t, J = 7.2 Hz), 3.98-4.13 (4H, m), 4.72 (2H, s), 6.07 (1H, t, J = 6.0 Hz), 6.38 (1H, dd, J = 7.3, 5.1 Hz), 6.70 (1H, dd, J = 7.5, 1.5 Hz), 7.31 (1H, dd, J = 4.9, 1.5 Hz).

[0452]

134c) ethyl (2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)acetate



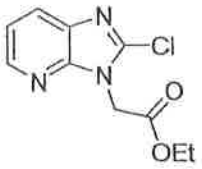
To a solution of ethyl N-(3-aminopyridin-2-yl)glycinate (18 g) in THF (200 mL) was added CDI (15 g) at room temperature, and the mixture was stirred at room temperature overnight. The mixture was concentrated under reduced pressure. The residual crystals were washed with AcOEt to give the title

compound (5.5 g).

$^1$H NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, t, J = 7.2 Hz), 4.26 (2H, q, J = 7.2 Hz), 4.77 (2H, s), 7.02 (1H, dd, J = 7.6, 5.3 Hz), 7.31 (1H, dd, J = 7.6, 1.1 Hz), 8.05 (1H, dd, J = 5.3, 1.1 Hz), 9.70 (1H, brs).

[0453]

134d) ethyl (2-chloro-3H-imidazo[4,5-b]pyridin-3-yl)acetate

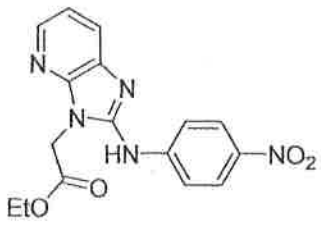



A mixture of ethyl (2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)acetate (14.5 g) and phosphoryl chloride (100 mL) was stirred at 100°C overnight. The mixture was poured into ice, neutrallized with saturated sodium bicarbonate solution and extracted with AcOEt. The organic layer was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The residue was diluted with AcOEt and insoluble crystals were removed by filtration. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 10% - 40% AcOEt in hexane) to give the title compound (5.46 g).

$^1$H NMR (300 MHz, $CDCl_3$) δ 1.29 (3H, t, J = 7.2 Hz), 4.26 (2H, q, J = 7.2 Hz), 5.07 (2H, s), 7.23-7.32 (1H, m), 7.99 (1H, dd, J = 8.1, 1.5 Hz), 8.36 (1H, dd, J = 4.9, 1.5 Hz).

[0454]

134e) ethyl {2-[(4-nitrophenyl)amino]-3H-imidazo[4,5-b]pyridin-3-yl}acetate

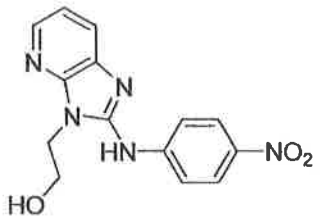



A mixture of ethyl (2-chloro-3H-imidazo[4,5-b]pyridin-3-yl)acetate (2.8 g) and 4-nitroaniline (1.6 g) was stirred at

150°C for 1 h to give the title compound (4.0 g).
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.22 (3H, t, J = 7.2 Hz), 4.18 (2H, q, J = 7.2 Hz), 5.21 (2H, s), 7.20 (1H, dd, J = 7.6, 4.9 Hz), 7.85 (1H, d, J = 7.6 Hz), 8.06-8.20 (3H, m), 8.23-8.34 (2H, m), 9.98 (1H, brs).

[0455]

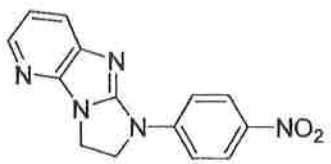
134f) 2-{2-[(4-nitrophenyl)amino]-3H-imidazo[4,5-b]pyridin-3-yl}ethanol



To a suspension of ethyl {2-[(4-nitrophenyl)amino]-3H-imidazo[4,5-b]pyridin-3-yl}acetate (3.6 g) in THF (120 mL) was added lithium borohydride (0.77 g) at room temperature, and the mixture was refluxed for 2 h. The mixture was cooled to room temperature, quenched with water and extracted with AcOEt. The organic layer was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluted with 50% - 100% AcOEt in hexane) to give the title compound (2.2 g).
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 3.80 (2H, t, J = 5.5 Hz), 4.45 (2H, t, J = 5.5 Hz), 7.17 (1H, dd, J = 7.6, 4.9 Hz), 7.82 (1H, dd, J = 7.6, 1.1 Hz), 8.06-8.19 (3H, m), 8.23-8.33 (2H, m).

[0456]

134g) 1-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridine



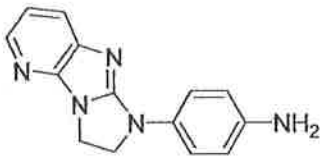
To a solution of 2-{2-[(4-nitrophenyl)amino]-3H-imidazo[4,5-b]pyridin-3-yl}ethanol (2.2 g) and triethylamine (10 mL) in THF (100 mL) was added methanesulfonyl chlorode

(1.1 mL) at 0°C, and the mixture was stirred at 0°C for 2 h. The mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. A mixture of the residue and potassium carbonate (3.1 g) in NMP (30 mL) was stirred at 100°C overnight. After cooling to room temperature, the mixture was diluted with water. The formed crystals were collected by filtration to give the title compound (1.7 g).

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 4.40-4.51 (2H, m), 4.64-4.75 (2H, m), 7.16 (1H, dd, J = 8.0, 4.9 Hz), 7.83 (1H, d, J = 8.0 Hz), 8.03 (2H, d, J = 9.1 Hz), 8.09 (1H, d, J = 4.9 Hz), 8.35 (2H, d, J = 9.1 Hz).

[0457]

134h) 4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)aniline

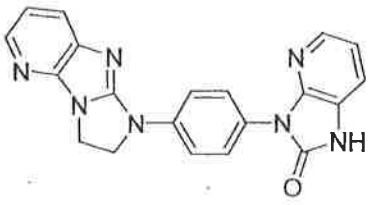


A mixture of 1-(4-nitrophenyl)-2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridine (1.7 g) and 10% palladium on carbon (50% wet, 1.0 g) in MeOH (150 mL) was hydrogenated under balloon pressure at room temperature for 1 day. The catalyst was removed by filtration and the filtrate was concentrated under reduced pressure to give the title compound (1.2 g).

MS (API+): $[M+H]^+$ 252.4.

[0458]

134i) 3-[4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

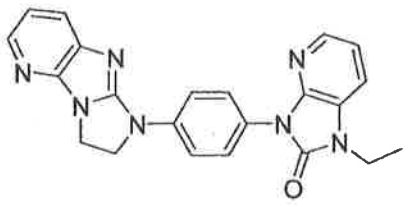


The mixture of 2-chloro-3-nitropyridine (189 mg), 4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)aniline (300 mg) and DIPEA (1.0 mL) in DMSO (5 mL) was stirred at 120°C for 4h. The mixture was diluted with AcOEt and THF, and washed with water. The organic layer was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. A mixture of the residue and 10% palladium on carbon (50% wet, 0.20 g) in MeOH (30 mL) was hydrogenated under balloon pressure at room temperature for 1 day. The catalyst was removed by filtration and the filtrate was concentrated under reduced pressure.

A solution of the residue and CDI (193 mg) in THF (15 mL) was refluxed for overnight. To the mixture was added CDI (193 mg), and the mixture was refluxed for 5 h. After cooling to room temperature, the formed precipitate was collected by filtration to give the title compound (165 mg).
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 4.38-4.49 (2H, m), 4.58-4.70 (2H, m), 7.05-7.14 (2H, m), 7.40 (1H, dd, J = 7.9, 1.5 Hz), 7.67 (2H, d, J = 9.1 Hz), 7.74 (1H, dd, J = 7.7, 1.3 Hz), 7.91-7.99 (3H, m), 8.02 (1H, dd, J = 4.9, 1.5 Hz), 11.36 (1H, s).

[0459]

134j) 3-[4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[4-(2,3-dihydro-1H-imidazo[2',1':2,3]imidazo[4,5-b]pyridin-1-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (165 mg), iodoethane (0.054 mL) and cesium carbonate (291 mg) in DMF (3 mL) was stirred at 50°C for 6 h. The mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered and concentrated under reduced

pressure. The residual crystals were dissolved in THF, and the solution was filtered through NH-silica gel. The filtrate was concentrated under reduced pressure. The residual crystals were recrystallized from EtOH to give the title compound (94 mg).

$^1$H NMR (300 MHz, DMSO-$d_6$) δ 1.30 (3H, t, J = 7.2 Hz), 3.98 (2H, q, J = 7.2 Hz), 4.37-4.49 (2H, m), 4.57-4.71 (2H, m), 7.10 (1H, dd, J = 7.9, 4.9 Hz), 7.17 (1H, dd, J = 7.7, 5.1 Hz), 7.62-7.71 (3H, m), 7.74 (1H, dd, J = 7.7, 1.3 Hz), 7.91-8.06 (4H, m).

MS (ESI+): $[M+H]^+$ 398.1.

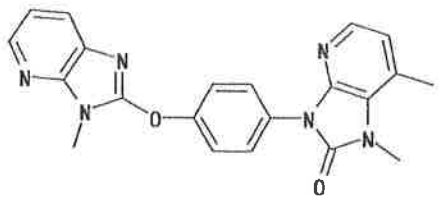
mp 255-256°C

Anal. Calcd for $C_{22}H_{19}N_7O$: C, 66.49; H, 4.82; N, 24.67. Found: C, 66.24; H, 4.85; N, 24.41.

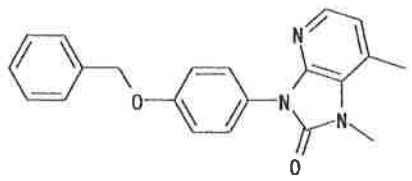
[0460]

Example 135

1,7-dimethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



135a) 3-[4-(benzyloxy)phenyl]-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

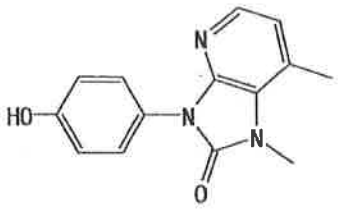


MeI (0.377 mL) was added to a solution of 3-[4-(benzyloxy)phenyl]-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.0 g) and NaH (0.362 g) in DMF (20 mL) at 20°C. The mixture was stirred at 20°C under a dry atmosphere for 1h. The mixture was diluted with sat. $NaHCO_3$ at 20°C and extracted with EtOAc. The organic layer was separated, washed

with water and brine, dried over $MgSO_4$ and concentrated in vacuo to give 3-[4-(benzyloxy)phenyl]-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.0 g). This product was subjected to the next reaction without further purification.

[0461]

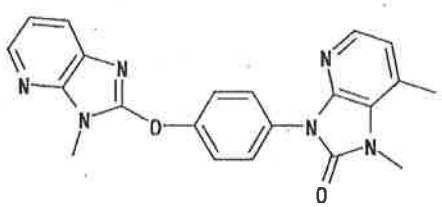
135b) 3-(4-hydroxyphenyl)-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[4-(benzyloxy)phenyl]-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2.0 g) and 10% Pd-C (0.308 g) in DMF (10 mL) - EtOAc (100 mL) was hydrogenated under balloon pressure at 20°C for 1h. The catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 50% - 100% EtOAc in hexane) to give 3-(4-hydroxyphenyl)-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (1.30 g) as a light brown solid. This product was subjected to the next reaction without further purification.

[0462]

135c) 1,7-dimethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



3-Methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (600 mg) was added to a solution of 3-(4-hydroxyphenyl)-1,7-dimethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (725 mg)

and potassium tert-butoxide (351 mg) in DMA (4ml) at 20°C. The mixture was stirred at 150°C under a dry atmosphere for 30 min. The reaction mixture was diluted with MeOH and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 50% EtOAc in hexane) to give 1,7-dimethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (150 mg) as colorless crystals.

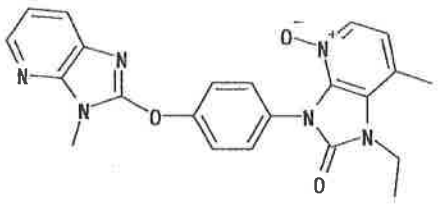
MS (API+): $[M+H]^+$ 387.1.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 2.59-2.69 (3H, s), 3.66 (3H, s), 3.78 (3H, s), 6.91-7.06 (1H, m), 7.13-7.28 (1H, m), 7.56-7.66 (2H, m), 7.70-7.76 (2H, m), 7.77-7.83 (1H, m), 7.83-7.89 (1H, m), 8.15-8.28 (1H, m).

[0463]

Example 136

1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide



Triisopropylsilyl chloride (2.384 mL) was added to a solution of 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (2 g) and NaH (0.594 g) in DMF (20mL) at 20°C. The mixture was stirred at 20°C under a dry atmosphere ($CaCl_2$ tube) for 1 h. The mixture was poured into sat. $NaHCO_3$ at 0°C and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 25% EtOAc in hexane) to give 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (4.0 g) as light brown crystals.

Trifluoroacetic anhydride (3.92 mL) was added to a suspenstion of 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (4 g) and urea hydrogen peroxide (2.74 g) in EtOAc (20 mL) at 0°C. The mixture was stirred at room temperature under a dry atmosphere ($CaCl_2$ tube) overnight. The mixture was neutralized with sat. $NaHCO_3$ at 0°C and extracted with EtOAc. The organic layer was separated, washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 100% EtOAc in hexane) to give 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (250 mg) as colorless crystals.

Tetrabutylammonium fluoride (0.566 mL) was added to a solution of 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (250 mg) in THF (5 mL) at room temperature. The mixture was stirred at room temperature under a dry atmosphere ($CaCl_2$ tube) for 30 min. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 100% EtOAc in hexane) to give 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (170 mg) as a colorless solid. 3-Methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (126 mg) was added to a solution of 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (170 mg) and NaH (23.83 mg) in DMA (1 mL) at room temperature. The mixture was stirred at 150°C under a dry atmosphere ($CaCl_2$ tube) for 30 min. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 50% - 100% EtOAc in hexane) to give 1-ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide as colorless crystals.

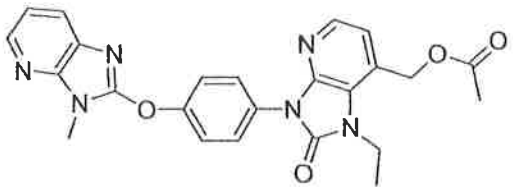
MS (API+): $[M+H]^+$ 417.2.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.23-1.40 (3H, m), 2.58 (3H, s), 3.77 (3H, s), 4.01-4.19 (2H, m), 6.96-7.05 (1H, m), 7.15-7.29 (1H, m), 7.40-7.57 (4H, m), 7.75-7.90 (2H, m), 8.15-8.29 (1H, m).

[0464]

Example 137

(1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)methyl acetate



The mixture of 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (500 mg) in acetic anhydride (10 mL) was stirred at 80°C under a dry atmosphere ($CaCl_2$ tube) for 2 h. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 0% - 30% EtOAc in hexane) to give [1-ethyl-2-oxo-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (300 mg) as colorless oil.

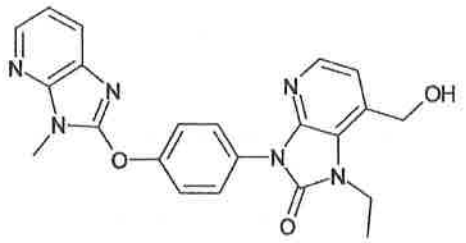
Tetrabutylammonium fluoride (1.241 mL) was added to a solution of [1-ethyl-2-oxo-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (300 mg) in THF(dry) (1 mL) at room temperature. The mixture was stirred at room temperature under a dry atmosphere ($CaCl_2$ tube) for 30 min. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (silica gel, eluted with 20% - 100% EtOAc in hexane) to give [1-ethyl-3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (170 mg) as a white solid.

3-Methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (110 mg) was added to a solution of [1-ethyl-3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (170 mg) and potassium tert-butoxide (69.9 mg) in DMA (1 mL) at room temperature. The mixture was stirred at 100°C under a dry atmosphere ($CaCl_2$ tube) for 30 min. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography (NH silica gel, eluted with 0% - 100% EtOAc in hexane) to give (1-ethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl)methyl acetate (10 mg) as colorless crystals.
MS (API+): $[M+H]^+$ 459.2.
$^1H$ NMR (300 MHz, DMSO-$d_6$) δ1.28-1.41 (3H, m), 2.14 (3H, s), 3.78 (3H, s), 4.00-4.18 (2H, m), 5.40 (2H, s), 7.15-7.26 (2H, m), 7.56-7.87 (5H, m), 7.95-8.04 (1H, m), 8.12-8.28 (1H, m).

[0465]

Example 138

1-ethyl-7-(hydroxymethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one




To a stirred mixture of [1-ethyl-3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (150 mg) and EtOH (3 mL) was added 1 N NaOH (2 mL) at 0°C. The mixture was stirred at 0°C for 30 min, treated with saturated $NH_4Cl$ solution, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in DMA (4 mL) and KOtBu (52 mg) was added at room temperature. The mixture was stirred for 2 min, and then 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (97 mg) was added. The mixture was stirred at 150°C for 30 min, treated

with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on NH-silica gel eluting with AcOEt/MeOH = 20/1. The product was crystallized from AcOEt/Hexane to give 1-ethyl-7-(hydroxymethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (46 mg).

MS (API+): $[M+H]^+$ 417.2.

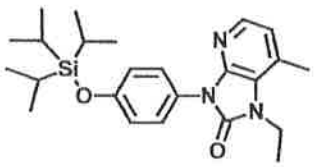
$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.32 (3H, t, J = 7.2 Hz), 3.78 (3H, s), 4.13 (2H, q, J = 7.2 Hz), 4.80 (2H, d, J = 5.5 Hz), 5.67 (1H, t, J = 5.5 Hz), 7.14-7.26 (2H, m), 7.59-7.68 (2H, m), 7.71-7.87 (3H, m), 7.97 (1H, d, J = 5.3 Hz), 8.17-8.28 (1H, m).

[0466]

Alternative route for 1-ethyl-7-(hydroxymethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one is described below.

[0467]

138a) 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a stirred mixture of 1-ethyl-3-(4-hydroxyphenyl)-7-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (10 g) and 1H-imidazole (3.79 g) in DMF (100 mL) was added triisopropylsilyl chloride (9.54 mL) at 0°C. The mixture was stirred at room temperature for 3 days, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hexane = 1/10) to give the title compound (11.5 g).

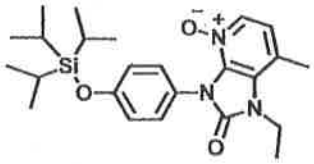
MS (API+): $[M+H]^+$ 426.2.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ1.05-1.19 (18H, m), 1.23-1.37 (6H,

m), 2.59 (3H, s), 4.08 (2H, d, J = 7.2 Hz), 6.89-7.05 (3H, m), 7.46 (2H, d, J = 8.7 Hz), 7.80-7.86 (1H, m).

[0468]

138b) 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide



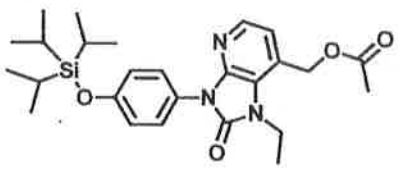
To a stirred mixture of 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (5 g) and urea hydrogen peroxide (2.32 g) in $CH_2Cl_2$ (50 mL) was added trifluoroacetic anhydride (3.32 mL) at 0°C. The mixture was stirred at room temperature for 12 h, and treated with saturated $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with AcOEt. The organic layer was combined, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (NH, AcOEt) to give the title compound (1.0 g).

MS (API+): $[M+H]^+$ 442.3.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ0.99-1.17 (18H, m), 1.22-1.36 (6H, m), 2.56 (3H, s), 4.06 (2H, q, J = 7.2 Hz), 6.82-6.91 (2H, m), 6.92-7.00 (1H, m), 7.14-7.24 (2H, m), 7.73 (1H, d, J = 6.8 Hz).

[0469]

138c) [1-ethyl-2-oxo-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate



A mixture of 1-ethyl-7-methyl-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one 4-oxide (1 g) and $Ac_2O$ (20 mL) was stirred at

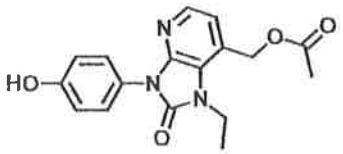
80°C for 2 h, and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/hexane) to give the title compound (0.49 g).

MS (API+): $[M+H]^+$ 484.3.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ1.03-1.15 (18H, m), 1.24-1.39 (6H, m), 2.13 (3H, s), 4.03 (2H, q, J = 7.2 Hz), 5.37 (2H, s), 6.91-7.09 (2H, m), 7.07-7.29 (1H, m), 7.45-7.50 (2H, m), 7.95 (1H, d, J = 5.3 Hz).

[0470]

138d) [1-ethyl-3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate



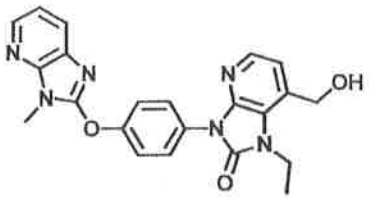
To a stirred solution of [1-ethyl-2-oxo-3-(4-{[tris(1-methylethyl)silyl]oxy}phenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (480 mg) in THF (5 mL) was added a solution of tetrabutylammonium fluoride (778 mg) in THF (2 mL) at 0°C. The mixture was stirred at 0°C for 30 min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/Hexane = 1/1) to give the title compound (276 mg).

MS (API+): $[M+H]^+$ 328.1.

$^1$H NMR (300 MHz, DMSO-$d_6$) δ1.30 (3H, t, J = 7.2 Hz), 2.12 (3H, s), 4.03 (2H, q, J = 7.2 Hz), 5.36 (2H, s), 6.80-6.95 (2H, m), 7.12 (1H, d, J = 5.3 Hz), 7.28-7.41 (2H, m), 7.93 (1H, d, J = 5.3 Hz), 9.71 (1H, s).

[0471]

138e) 1-ethyl-7-(hydroxymethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



To a stirred mixture of [1-ethyl-3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-7-yl]methyl acetate (150 mg) and EtOH (3 mL) was added 1N NaOH (2 mL) at 0°C. The mixture was stirred at 0°C for 30 min, treated with saturated $NH_4Cl$ solution, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in DMA (4 mL) and KOtBu (52 mg) was added at room temperature. The mixture was stirred for 2 min, and then 3-methyl-2-(methylsulfonyl)-3H-imidazo[4,5-b]pyridine (97 mg) was added. The mixture was stirred at 150°C for 30 min, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (NH, AcOEt/MeOH = 20/1) and crystallized from AcOEt/hexane to give the title compound (46 mg).

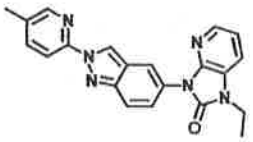
MS (API+): $[M+H]^+$ 417.2.

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 1.32 (3H, t, J = 7.2 Hz), 3.78 (3H, s), 4.13 (2H, q, J = 7.2 Hz), 4.80 (2H, d, J = 5.5 Hz), 5.67 (1H, t, J = 5.5 Hz), 7.14-7.26 (2H, m), 7.59-7.68 (2H, m), 7.71-7.87 (3H, m), 7.97 (1H, d, J = 5.3 Hz), 8.17-8.28 (1H, m).

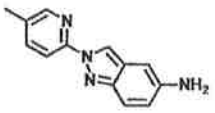
[0472]

Example 139

1-ethyl-3-[2-(5-methylpyridin-2-yl)-2H-indazol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



139a) 1-(5-methylpyridin-2-yl)-2H-indazol-5-amine



To a stirred solution of 5-nitro-1H-indazole (500 mg) in DMF (10 mL) was added 60% sodium hydride (129 mg) at room temperature. The mixture was stirred for 30 min, and 5-bromo-2-chloropyridine (649 mg) was added. The mixture was exposed to microwave irradiation at 230°C for 1 h, treated with sat. ammonium chloride solution, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel eluting with AcOEt/Hexane to give a mixture of 1-(5-bromopyridin-2-yl)-5-nitro-1H-indazole and 2-(5-bromopyridin-2-yl)-5-nitro-2H-indazole.

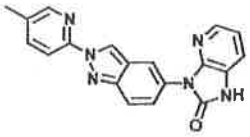
To the mixture of 1-(5-bromopyridin-2-yl)-5-nitro-1H-indazole and 2-(5-bromopyridin-2-yl)-5-nitro-2H-indazole were added methylboronic acid (141 mg), $Pd(Ph_3P)_4$ (91 mg), DME (3 mL) and a solution of $Cs_2CO_3$ (766 mg) in $H_2O$ (1 mL), successively. The mixture was exposed to microwave irradiation 140°C for 1 h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give a mixture of 1-(5-methylpyridin-2-yl)-5-nitro-1H-indazole and 2-(5-methylpyridin-2-yl)-5-nitro-2H-indazole.

The mixture of 1-(5-methylpyridin-2-yl)-5-nitro-1H-indazole and 2-(5-methylpyridin-2-yl)-5-nitro-2H-indazole was dissolved in EtOH (20 mL), and 10% Pd/C (250 mg) was added. Under $H_2$ atmosphere, the mixture was stirred at room temperature for 12 h, filtered and concentrated in vacuo. The residue was chromatographed on silica gel eluting with AcOEt/Hexane to give the title compound (61 mg).

$^1H$ NMR (300 MHz, DMSO-$d_6$) δ 2.36 (3H, s), 5.04 (2H, s), 6.58 (1H, d, J = 1.9 Hz), 6.86 (1H, dd, J = 9.1, 1.9 Hz), 7.44 (1H, d, J = 9.1 Hz), 7.75-7.90 (1H, m), 7.95-8.06 (1H, m), 8.35 (1H, d, J = 2.3 Hz), 8.72 (1H, d, J = 0.8 Hz).

[0473]

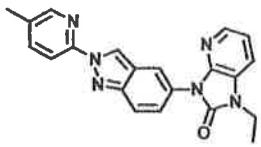
139b) 3-[2-(5-methylpyridin-2-yl)-2H-indazol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



Under argon atmosphere, a mixture of 1-(5-methylpyridin-2-yl)-2H-indazol-5-amine (60 mg), tert-butyl 2-chloropyridin-3-ylcarbamate (67.3 mg), $Pd_2(dba)_3$ (24.5 mg), Xantphos (31.0 mg) and sodium tert-butoxide (28.3 mg) in 2-propanol (2 mL) and toluene (0.5 mL) was stirred at 90°C for 24 h, treated with water and extracted with EtOAc. The organic layer was separated, dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel eluting with AcOEt/Hexane to give the title compound as white crystals (31 mg).
MS (API+): $[M+H]^+$ 343.3.

[0474]

139c) 1-ethyl-3-[2-(5-methylpyridin-2-yl)-2H-indazol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



A mixture of 3-[2-(5-methylpyridin-2-yl)-2H-indazol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one (31 mg) and iodoethane (15.5 mg) in DMF (2 mL) was stirred at 50°C for 3 h, treated with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel eluting with AcOEt/Hexane. The product was crystallized from AcOEt/Hexane to give the title compound as white crystals (5.4 mg).
MS (API+): $[M+H]^+$ 371.0.

[0475]

Example compounds shown in the following Tables 1 - 12 (including compounds shown in the above-mentioned Examples) were obtained by a method known per se, or a method similar to those in the above-mentioned Examples, or a method analogous thereto.

Particularly, the Example compounds described in the

column under "Referred Example No." in Tables 1 - 12 were produced according to the synthetic method described in the Referred Example.

In addition, the compound of each Example in Tables 1 - 12 was synthesized using the compound described in the column under "Raw material".

[0476]

[Table 1]

| Example No. | MS | STRUCTURE | SALT | Name | Reffered Example No. | Raw Material, Conditions |
|---|---|---|---|---|---|---|
| 14 | 345 |  | | 9-[4-(1,3-benzoxazol-2-ylamino)phenyl]-7,9-dihydro-8H-purin-8-one | 1 | 4-chloro-5-nitropyrimidine |
| 15 | 383 |  | | 3-[4-(3,4-dihydropyrimido[1,2-a]benzimidazol-1(2H)-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 2 | 1,3-dibromopropane |
| 16 | 397 |  | | 3-[4-(2,3,4,5-tetrahydro-1H-[1,3]diazepino[1,2-a]benzimidazol-1-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 2 | 1,4-diiodobutane |
| 17 | 358 |  | | 3-[4-(1,3-benzoxazol-2-ylamino)phenyl]-1-methyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12c, 3, 1c, 1a | 12c) tert-butyl 2-chloropyridin-3-ylcarbamate, 4-nitroaniline |
| 18 | 502.1 |  | | 1-ethyl-3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 19 | 386.2 |  | | 1-ethyl-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one hydrochloride |
| 20 | 371.3 |  | | 3-[4-(1H-benzimidazol-2-ylamino)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | - | 3-(4-aminophenyl)-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, phenylenediamine, 1,1'-thiocarbonyldiimidazole, N,N'-dicyclohexylcarbodiimide |

[0477]

[Table 2]

| Example No. | MS | STRUCTURE | SALT | Name | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 21 | 400.1 |  | | 3-[4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl]-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 22 | 386.0 |  | HCl | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one hydrochloride | 3, 1c,7e, 8 | 3) 3-[4-(benzyloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, 2-iodopropane |
| 23 | 426.1 |  | HCl | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one hydrochloride | 22 | 2-Iodo-1,1,1-trifluoroethane |
| 24 | 397.1 |  | | 3-[4-(2,3-dihydro-1H-imidazo[1,2-a]benzimidazol-1-yl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 3-[4-(2,3-dihydro-1H-imidazo[1,2-a]benzimidazol-1-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 25 | 455.3 |  | | ethyl {3-[4-(2,3-dihydro-1H-imidazo[1,2-a]benzimidazol-1-yl)phenyl]-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl}acetate | 3 | ethyl bromoacetate |
| 26 | 413 |  | | 3-[4-(2,3-dihydro-1H-imidazo[1,2-a]benzimidazol-1-yl)phenyl]-1-(2-hydroxyethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | - | ethyl {3-[4-(2,3-dihydro-1H-imidazo[1,2-a]benzimidazol-1-yl)phenyl]-2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl}acetate, LAH |
| 27 | 390.4 |  | | 1-ethyl-3-[4-[(6-fluoro-1,3-benzoxazol-2-yl)amino]phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 17 | 2-chloro-5-fluorobenzoxazol |

[0478]

[Table 3]

| Example No. | MS | STRUCTURE | SALT | Name | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 28 | 404.3 |  | | 1-ethyl-3-{4-[(6-fluoro-1,3-benzoxazol-2-yl)(methyl)amino]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 1-ethyl-3-{4-[(6-fluoro-1,3-benzoxazol-2-yl)amino]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 29 | 422.3 |  | | 3-{4-[(5,6-difluoro-1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7e | 2-chloro-5,6-difluoro-1-methyl-1H-benzimidazole, 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, NaH, DMF, microwave, 200 oC |
| 30 | 444.4 |  | | ethyl 2-[4-(1-ethyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenoxy]imidazo[1,2-a]pyridine-3-carboxylate | 7e | ethyl 2-chloroimidazo[1,2-a]pyridine-3-carboxylate |
| 31 | 372.4 |  | | 1-ethyl-3-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | - | ethyl 2-[4-(1-ethyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenoxy]imidazo[1,2-a]pyridine-3-carboxylate, DMF, 200°C |
| 32 | 404 |  | | 1-ethyl-3-{4-[(6-fluoro-1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 29 | 2-chloro-6-fluoro-1-methyl-1H-benzimidazole (US2003/166637), 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 33 | 404 |  | | 1-ethyl-3-{4-[(5-fluoro-1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 29 | 2-chloro-5-fluoro-1-methyl-1H-benzimidazole, 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 34 | 430.1 |  | | 1-(2-hydroxy-2-methylpropyl)-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 25, 1c, 29 | 25) 3-[4-(benzyloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one<br>29) 2-chloro-1-methyl-1H-benzimidazole, MeMgBr |

[0479]

[Table 4]

| Example No. | MS | STRUCTURE | SALT | Name | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 35 | 402.1 |  | | 1-(2-hydroxyethyl)-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 25, 1c, 29, 26 | 25) 3-[4-(benzyloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one<br>29) 2-chloro-1-methyl-1H-benzimidazole |
| 36 | 384.2 |  | | 1-ethyl-3-[4-(quinoxalin-2-yloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7e | 2-chloroquinoxaline, 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 37 | 428.5 |  | | 3-{4-[(1-butyl-1H-benzimidazol-2-yl)oxy]phenyl}-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7f | 1-ethyl-3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 38 | 414.4 |  | | 3-{4-[(1-acetyl-1H-benzimidazol-2-yl)oxy]phenyl}-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | - | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, acetyl chloride, triethyl amine, THF |
| 39 | 416.5 |  | | 1-ethyl-3-(4-{[1-(2-hydroxyethyl)-1H-benzimidazol-2-yl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 25, 26 | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 40 | 444.4 |  | | 1-ethyl-3-(4-{[1-(2-hydroxy-2-methylpropyl)-1H-benzimidazol-2-yl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 39 | ethyl {2-[4-(1-ethyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenoxy]-1H-benzimidazol-1-yl}acetate, MeMgBr, THF |
| 41 | 386.3 |  | HCl | 3-[4-(1H-benzimidazol-2-yloxy)-3-methylphenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one hydrochloride | 7a, 7b, 7c, 22 | 4-(benzyloxy)-3-methylaniline |

[0480]

[Table 5]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 42 | 400.1 |  | | 1-ethyl-3-{3-methyl-4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 3-[4-(1H-benzimidazol-2-yloxy)-3-methylphenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 43 | 404.3 |  | | 1-ethyl-3-{3-fluoro-4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 3, 1c, 7e | 7a) 4-(benzyloxy)-3-fluoroaniline<br>7e) 1-methyl-2-(methylsulfonyl)-1H-benzimidazole |
| 44 | 371.4 |  | | 1-[4-(2-oxo-3-phenylimidazolidin-1-yl)phenyl]-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one | 5a then 5a | 5a) 1,4-diiodobenzene, 1-phenylimidazolidin-2-one,<br>then 5a) 1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one |
| 45 | 329.4 |  | | 1-[4-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)phenyl]-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one | 44 | 1,4-diiodobenzene, 2,3-dihydro-1H-pyrrolo[2,3-b]pyridine |
| 46 | 373.3 |  | | 1-ethyl-3-[4-([1,2,4]triazolo[1,5-a]pyridin-2-yloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 29 | 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, 2-chloro-[1,2,4]triazolo[1,5-a]pyridine |
| 47 | 390.4 |  | | 1-ethyl-3-{4-[(7-fluoro-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 29, 8 | 1-ethyl-3-(4-hydroxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, 4-fluoro-2-(methylsulfonyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-benzo[d]imidazole |
| 48 | 411.4 |  | | 1-ethyl-3-[1-(1-methyl-1H-benzimidazol-2-yl)-2,3-dihydro-1H-indol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 3-[1-(1H-benzimidazol-2-yl)-2,3-dihydro-1H-indol-5-yl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |

[0481]

[Table 6]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 49 | 386.3 |  | | 3-[4-(1H-benzimidazol-2-yloxy)-2-methylphenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)-2-methylaniline |
| 50 | 412.3 |  | | 3-[4-(1H-benzimidazol-2-yloxy)-2-methylphenyl]-1-(cyclopropylmethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 49 | (bromomethyl)cyclopropane |
| 51 | 400.4 |  | | 1-ethyl-3-[2-methyl-4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 3 | 3-[4-(1H-benzimidazol-2-yloxy)-2-methylphenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 52 | 432.1 |  | | 3-[4-(1-benzyl-2-methyl-1H-benzimidazol-4-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 8 | 3-[4-(1-benzyl-2-methyl-1H-benzimidazol-4-yl)phenyl]-1-[(2-(trimethylsilyl)ethoxy]methyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 53 | 460.1 |  | | 3-[4-(1-benzyl-2-methyl-1H-benzimidazol-4-yl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 3-[4-(1-benzyl-2-methyl-1H-benzimidazol-4-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 54 | 370.1 |  | | 1-ethyl-3-[4-(2-methyl-1H-benzimidazol-4-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 1c | 3-[4-(1-benzyl-2-methyl-1H-benzimidazol-4-yl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 55 | 339.4 |  | | 3-(4-quinolin-8-ylphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 8 | 3-(4-quinolin-8-ylphenyl)-1-[(2-(trimethylsilyl)ethoxy]methyl)-1,3-dihydro-2H-Imidazo[4,5-b]pyridin-2-one |

[0482]

[Table 7]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 56 | 367.3 |  | | 1-ethyl-3-(4-quinolin-8-yiphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 8 | 3-(4-quinolin-8-yiphenyl)-1-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one |
| 57 | 399.2 |  | | 1-{4-[(1-ethyl-1H-benzimidazol-2-yl)oxy]phenyl}-3,3-dimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one | 9 | iodoethane |
| 58 | 374.1 |  | | 4-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)phenyl phenylcarbamate | 9 | PHENYL ISOCYANATE |
| 59 | 388.2 |  | | 4-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)phenyl methyl(phenyl)carbamate | 9 | PHENYL ISOCYANATE |
| 60 | 402.2 |  | 2HCl | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-ethyl-5-methoxy-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 61 | 374.1 |  | 2HCl | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-7-methoxy-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 63 | 402.1 |  | 2HCl | 3-[4-(1H-benzimidazol-2-yloxy)phenyl]-1-ethyl-7-methoxy-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |

[0483]

[Table 8]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 66 | 362 |  | | 1-ethyl-3-[1-(1,3-thiazol-2-yl)-1H-indol-5-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 13f | 2-CHLOROTHIAZOLE |
| 67 | 404.3 |  | | 1-ethyl-3-{2-fluoro-4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)-2-fluoroaniline |
| 68 | 412.3 |  | | 3-[1-(1,3-benzothiazol-2-yl)-1H-indol-5-yl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 13f | 2-Chlorobenzothiazole |
| 73 | 367.3 |  | | 3-{4-[(5-chloropyridin-2-yl)oxy]phenyl}-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 2,5-DICHLOROPYRIDINE |
| 74 | 401.3 |  | | 1-ethyl-3-(4-{[5-(trifluoromethyl)pyridin-2-yl]oxy}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 2-CHLORO-5-TRIFLUOROMETHYLPYRIDINE |
| 76 | 412 |  | | 1-ethyl-3-{4-[(1-methyl-4-phenyl-1H-imidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 4-phenyl-1H-imidazole-2-thiol |

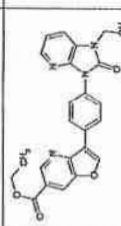
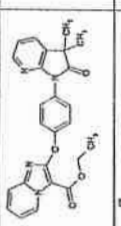
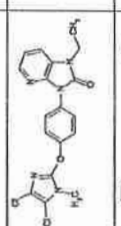
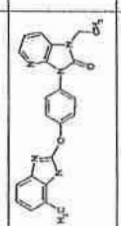
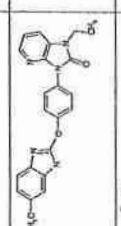
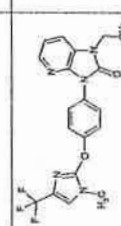
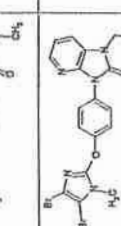
[0484]

[Table 9]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 77 | 486.1 |  | | 3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-benzimidazol-2-yl)carbonyl]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | tert-butyl 4-aminobenzoate |
| 78 | 472.1 |  | | 3-[4-(1-methyl-1H-benzimidazol-4-yl)phenyl]-1-{[2-(trimethylsilyl)ethoxy]methyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 4-bromo-1-methyl-1H-benzimidazole |
| 79 | 514.3 |  | | 1-ethyl-3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-benzimidazol-2-yl)carbonyl]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | tert-butyl 4-aminobenzoate |
| 80 | 384.1 |  | | 3-[4-(1H-benzimidazol-2-ylcarbonyl)phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | tert-butyl 4-aminobenzoate |
| 81 | 370.2 |  | | 1-ethyl-3-[4-(1-methyl-1H-benzimidazol-7-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 7-bromo-1-methyl-1H-benzimidazole |
| 82 | 370.2 |  | | 1-ethyl-3-[4-(1-methyl-1H-benzimidazol-4-yl)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 12d | 4-bromo-1-methyl-1H-benzimidazole |
| 83 | 398.2 |  | | 1-ethyl-3-{4-[(1-methyl-1H-benzimidazol-2-yl)carbonyl]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | tert-butyl 4-aminobenzoate |

[0485]

[Table 10]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 84 | 429.2 |  | | ethyl 3-[4-(1-ethyl-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl)phenyl]furo[3,2-b]pyridine-6-carboxylate | 12d | ethyl 3-bromofuro[3,2-b]pyridine-6-carboxylate |
| 87 | 443.2 |  | | ethyl 2-[4-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)phenoxy]imidazo[1,2-a]pyridine-3-carboxylate | 75 | ethyl 2-chloroimidazo[1,2-a]pyridine-3-carboxylate |
| 88 | 405.1 |  | | 3-[4-[(4,5-dichloro-1-methyl-1H-imidazol-2-yl)oxy]phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 2,4,5-trichloro-1-methyl-1H-imidazole |
| 89 | 386 |  | HCl | 1-ethyl-3-[4-[(7-methyl-1H-benzimidazol-2-yl)oxy]phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 7-methyl-2-(methylsulfonyl)-1H-benzimidazole |
| 90 | 386.2 |  | HCl | 1-ethyl-3-[4-[(6-methyl-1H-benzimidazol-2-yl)oxy]phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 6-methyl-2-(methylsulfonyl)-1H-benzimidazole |
| 91 | 404.2 |  | | 1-ethyl-3-[4-[[1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl]oxy]phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 4-(trifluoromethyl)-1H-imidazole-2-thiol |
| 92 | 494.1 |  | | 3-[4-[(4,5-dibromo-1-methyl-1H-imidazol-2-yl)oxy]phenyl]-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 2,4,5-tribromo-1-methyl-1H-imidazole |

[0486]

[Table 11]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 93 | 336.1 |  | | 1-ethyl-3-{4-[(1-methyl-1H-imidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 75 | 2-bromo-1-methyl-1H-imidazole |
| 94 | 358.1 |  | | 1-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one | 5, 75 | 4-bromophenol |
| 95 | 398.2 |  | | 1'-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}spiro[cyclobutane-1,3'-pyrrolo[2,3-b]pyridin]-2'(1'H)-one | 5, 75 | 4-bromophenol |
| 96 | 386.2 |  | | 3,3-dimethyl-1-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one | 5, 75 | 4-bromophenol |
| 104 | 400.3 |  | | 1-ethyl-5-methyl-3-{4-[(1-methyl-1H-benzimidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 105 | 401.3 |  | | 1-ethyl-5-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 110 | 420 |  | | 3-{4-[(3-bromo-1,2,4-thiadiazol-5-yl)oxy]phenyl}-1-ethyl-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |

[0487]

[Table 12]

| Example No. | MS | MOLSTRUCTURE | SALT | NAME | Reffered Example No. | Raw Material |
|---|---|---|---|---|---|---|
| 111 | 508.2 |  | | 1-ethyl-3-{4-[(1-{[2-(trimethylsilyl)ethoxy]methyl}-1H-thieno[3,4-d]imidazol-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 113 | 378.1 |  | | 1-ethyl-3-[4-(1H-thieno[3,4-d]imidazol-2-yloxy)phenyl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 114 | 503.2 |  | | 1-ethyl-3-{4-[(3-{[2-(trimethylsilyl)ethoxy]methyl}-3H-imidazo[4,5-c]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 116 | 458.1 |  | | ethyl 2-{4-[1-(1-methylethyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-b]pyridin-3-yl]phenoxy}imidazo[1,2-a]pyridine-3-carboxylate | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 117 | 386 |  | | 3-[4-(imidazo[1,2-a]pyridin-2-yloxy)phenyl]-1-(1-methylethyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 7a, 7b, 7c, 22 | 4-(benzyloxy)aniline |
| 131 | 357 |  | | 1-ethyl-3-(1-pyrimidin-2-yl-1H-indol-5-yl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one | 69 | 2-chloropyrimidine |

[0488]

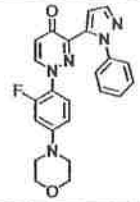
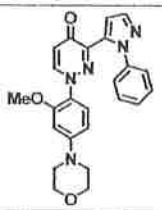
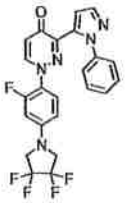
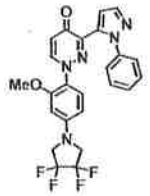
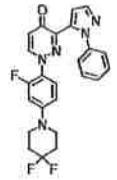
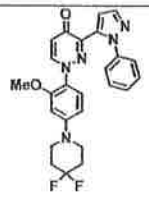
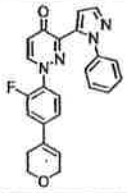
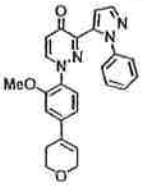
Reference Example

Examples of the compound having a PDE10A inhibitory activity include the compounds described as Reference Examples 1 - 223 in the following Tables 13 - 39. The compounds of Reference Examples 1 - 223 can be produced according to the synthetic methods described in the Examples of the present invention or a method analogous thereto. Furthermore, the compounds of Reference Examples can be produced according to the synthetic methods of the compounds described in WO2008/004117, WO2010/0057121, WO2010/57126, WO2006/072828, WO2008/001182 or WO2010/090737, or a method analogous thereto.

The compounds of Reference Examples 1 - 223 are useful as PDE10A inhibitors or drugs for the prophylaxis or treatment of mental diseases such as schizophrenia and the like, and the administration subject, target disease, administration route, dosage form and the like are the same as those explained for medicaments containing compound (I) or a prodrug thereof.

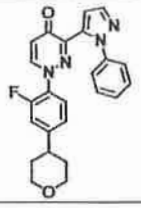
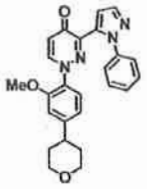
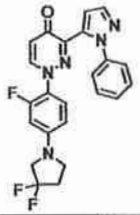
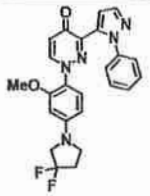
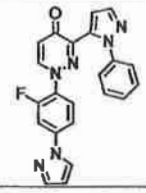
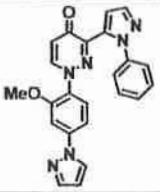
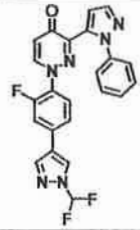
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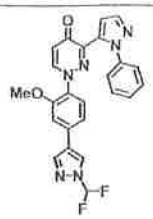
[Table 13]

| Ref. Ex. No. | compound | compound name |
|---|---|---|
| 1 |  | 1-[2-fluoro-4-(morpholin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 2 |  | 1-[2-methoxy-4-(morpholin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 3 |  | 1-[2-fluoro-4-(3,3,4,4-tetrafluoropyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 4 |  | 1-[2-methoxy-4-(3,3,4,4-tetrafluoropyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 5 |  | 1-[4-(4,4-difluoropiperidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 6 |  | 1-[4-(4,4-difluoropiperidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 7 |  | 1-[4-(3,6-dihydro-2H-pyran-4-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 8 |  | 1-[4-(3,6-dihydro-2H-pyran-4-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0490]

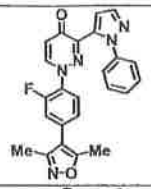
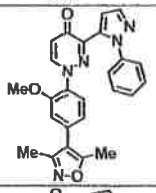
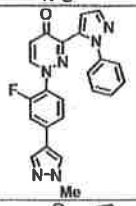
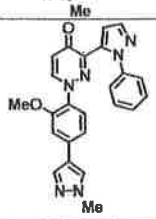
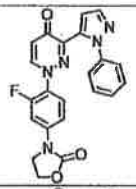
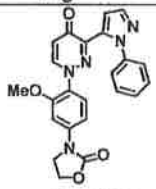
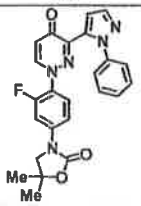
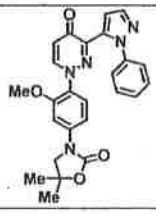
[Table 14]

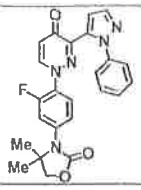
| | | |
|---|---|---|
| 9 |  | 1-[2-fluoro-4-(tetrahydro-2H-pyran-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 10 |  | 1-[2-methoxy-4-(tetrahydro-2H-pyran-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 11 |  | 1-[4-(3,3-difluoropyrrolidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 12 |  | 1-[4-(3,3-difluoropyrrolidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 13 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 14 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 15 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 16 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0491]

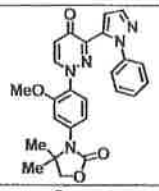
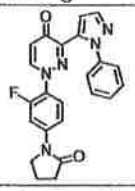
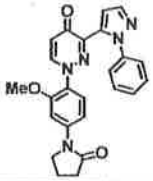
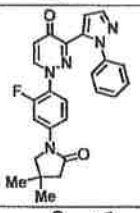
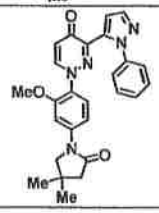
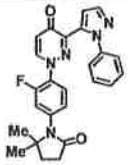
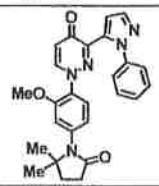
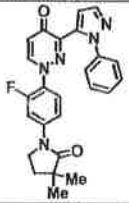
[Table 15]

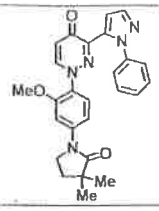
| | | |
|---|---|---|
| 17 |  | 1-[4-(3,5-dimethylisoxazol-4-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 18 |  | 1-[4-(3,5-dimethylisoxazol-4-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 19 |  | 1-[2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 20 |  | 1-[2-methoxy-4-(1-methyl-1H-pyrazol-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 21 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 22 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 23 |  | 1-[4-(5,5-dimethyl-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 24 |  | 1-[4-(5,5-dimethyl-2-oxo-1,3-oxazolidin-3-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 25 |  | 1-[4-(4,4-dimethyl-2-oxo-1,3-oxazolidin-3-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0492]

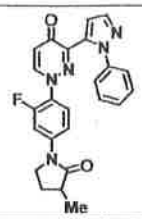
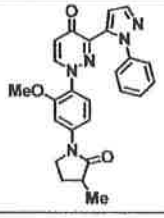
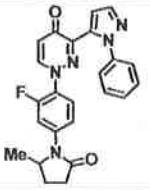
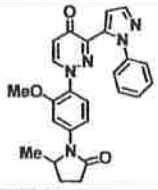
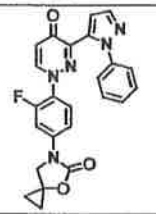
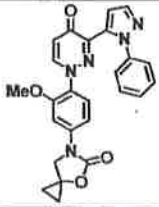
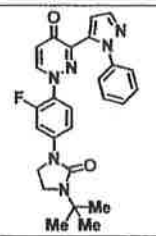
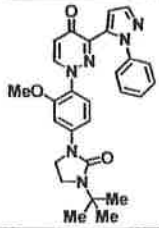
[Table 16]

| | | |
|---|---|---|
| 26 |  | 1-[4-(4,4-dimethyl-2-oxo-1,3-oxazolidin-3-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 27 |  | 1-[2-fluoro-4-(2-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 28 |  | 1-[2-methoxy-4-(2-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 29 |  | 1-[4-(4,4-dimethyl-2-oxopyrrolidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 30 |  | 1-[4-(4,4-dimethyl-2-oxopyrrolidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 31 |  | 1-[4-(2,2-dimethyl-5-oxopyrrolidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 32 |  | 1-[4-(2,2-dimethyl-5-oxopyrrolidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 33 |  | 1-[4-(3,3-dimethyl-2-oxopyrrolidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 34 |  | 1-[4-(3,3-dimethyl-2-oxopyrrolidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

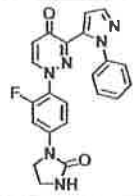
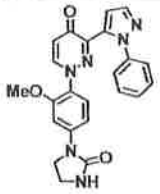
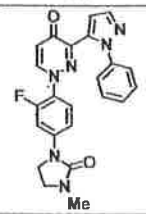
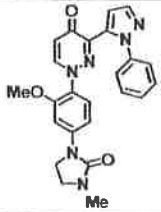
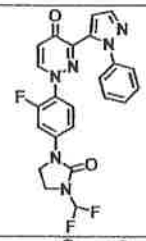
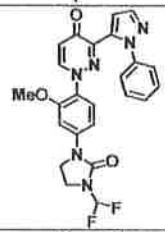
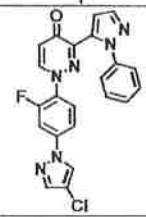
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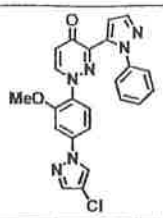
[Table 17]

| | | |
|---|---|---|
| 35 |  | 1-[2-fluoro-4-(3-methyl-2-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 36 |  | 1-[2-methoxy-4-(3-methyl-2-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 37 |  | 1-[2-fluoro-4-(2-methyl-5-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 38 |  | 1-[2-methoxy-4-(2-methyl-5-oxopyrrolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 39 |  | 6-{3-fluoro-4-[4-oxo-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-1(4H)-yl]phenyl}-4-oxa-6-azaspiro[2.4]heptan-5-one |
| 40 |  | 6-{3-methoxy-4-[4-oxo-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-1(4H)-yl]phenyl}-4-oxa-6-azaspiro[2.4]heptan-5-one |
| 41 |  | 1-[4-(3-tert-butyl-2-oxoimidazolidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 42 |  | 1-[4-(3-tert-butyl-2-oxoimidazolidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0494]

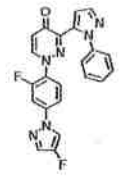
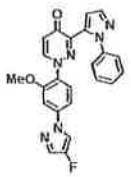
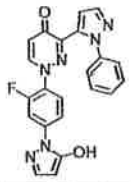
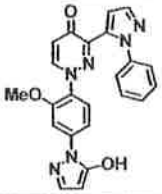
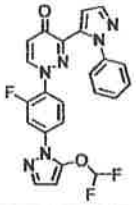
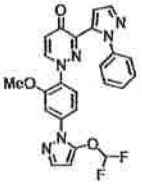
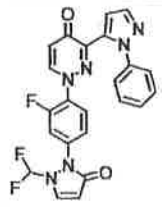
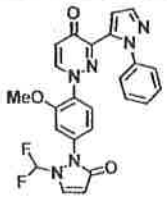
[Table 18]

| | | |
|---|---|---|
| 43 |  | 1-[2-fluoro-4-(2-oxoimidazolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 44 |  | 1-[2-methoxy-4-(2-oxoimidazolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 45 |  | 1-[2-fluoro-4-(3-methyl-2-oxoimidazolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 46 |  | 1-[2-methoxy-4-(3-methyl-2-oxoimidazolidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 47 |  | 1-{4-[3-(difluoromethyl)-2-oxoimidazolidin-1-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 48 |  | 1-{4-[3-(difluoromethyl)-2-oxoimidazolidin-1-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 49 |  | 1-[4-(4-chloro-1H-pyrazol-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 50 |  | 1-[4-(4-chloro-1H-pyrazol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

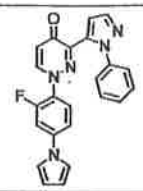
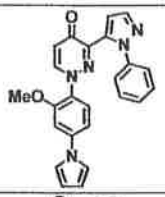
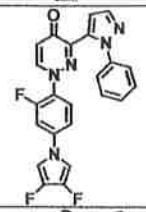
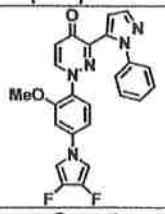
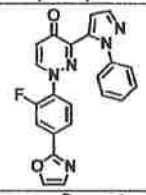
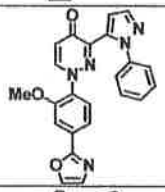
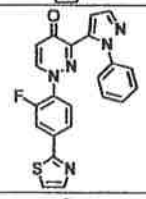
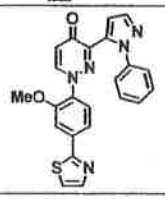
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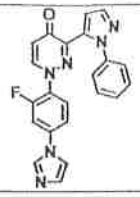
[Table 19]

| | | |
|---|---|---|
| 51 |  | 1-[2-fluoro-4-(4-fluoro-1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 52 |  | 1-[4-(4-fluoro-1H-pyrazol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 53 |  | 1-[2-fluoro-4-(5-hydroxy-1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 54 |  | 1-[4-(5-hydroxy-1H-pyrazol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 55 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 56 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 57 |  | 1-{4-[2-(difluoromethyl)-5-oxo-2,5-dihydro-1H-pyrazol-1-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 58 |  | 1-{4-[2-(difluoromethyl)-5-oxo-2,5-dihydro-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0496]

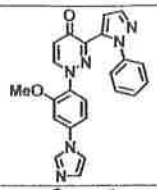
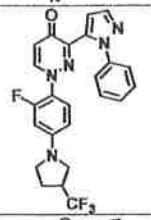
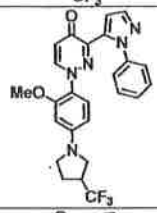
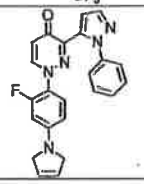
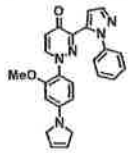
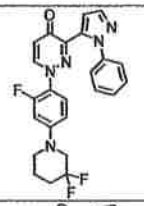
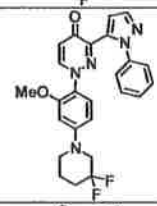
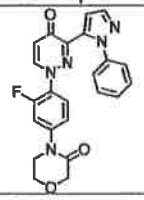
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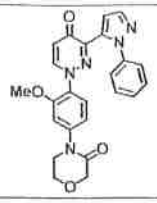
| | | |
|---|---|---|
| 59 |  | 1-[2-fluoro-4-(1H-pyrrol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 60 |  | 1-[2-methoxy-4-(1H-pyrrol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 61 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 62 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 63 |  | 1-[2-fluoro-4-(1,3-oxazol-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 64 |  | 1-[2-methoxy-4-(1,3-oxazol-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 65 |  | 1-[2-fluoro-4-(1,3-thiazol-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 66 |  | 1-[2-methoxy-4-(1,3-thiazol-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 67 |  | 1-[2-fluoro-4-(1H-imidazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0497]

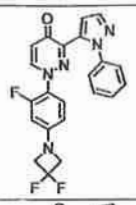
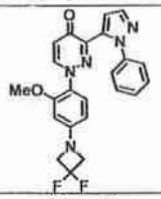
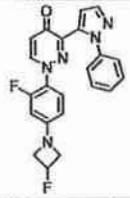
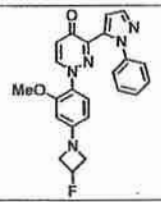
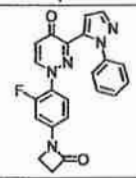
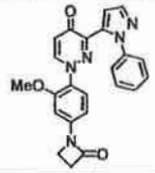
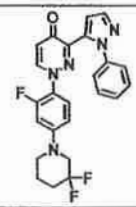
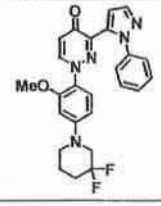
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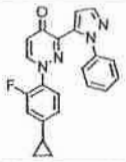
| | | |
|---|---|---|
| 68 |  | 1-[4-(1H-imidazol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 69 |  | 1-{2-fluoro-4-[3-(trifluoromethyl)pyrrolidin-1-yl]phenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 70 |  | 1-{2-methoxy-4-[3-(trifluoromethyl)pyrrolidin-1-yl]phenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 71 |  | 1-[4-(2,5-dihydro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 72 |  | 1-[4-(2,5-dihydro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 73 |  | 1-[4-(3,3-difluoropiperidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 74 |  | 1-[4-(3,3-difluoropiperidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 75 |  | 4-{3-fluoro-4-[4-oxo-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-1(4H)-yl]phenyl}morpholin-3-one |

| | | |
|---|---|---|
| 76 |  | 4-{3-methoxy-4-[4-oxo-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-1(4H)-yl]phenyl}morpholin-3-one |

[0498]

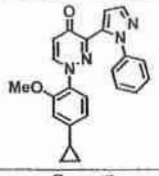
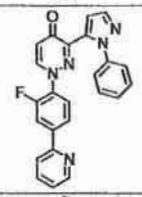
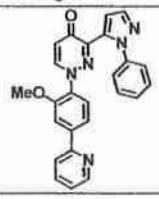
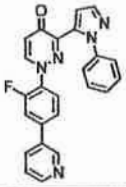
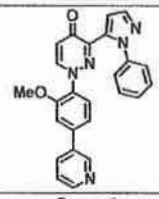
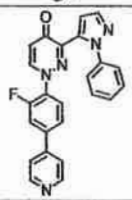
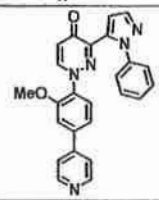
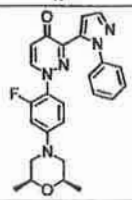
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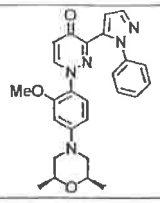
| | | |
|---|---|---|
| 77 |  | 1-[4-(3,3-difluoroazetidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 78 |  | 1-[4-(3,3-difluoroazetidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 79 |  | 1-[2-fluoro-4-(3-fluoroazetidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 80 |  | 1-[4-(3-fluoroazetidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 81 |  | 1-[2-fluoro-4-(2-oxoazetidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 82 |  | 1-[2-methoxy-4-(2-oxoazetidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 83 |  | 1-[4-(3,3-difluoropiperidin-1-yl)-2-fluorophenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 84 |  | 1-[4-(3,3-difluoropiperidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 85 |  | 1-(4-cyclopropyl-2-fluorophenyl)-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0499]

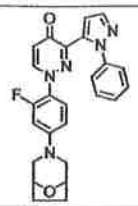
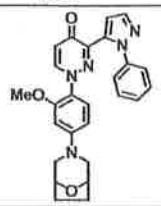
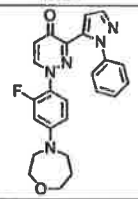
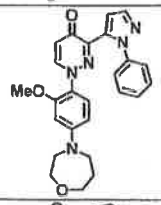
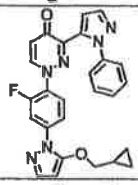
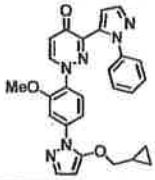
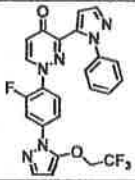
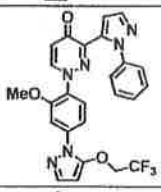
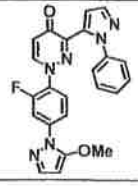
[Table 23]

| | | |
|---|---|---|
| 86 |  | 1-(4-cyclopropyl-2-methoxyphenyl)-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 87 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 88 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 89 |  | 1-[2-fluoro-4-(pyridin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 90 |  | 1-[2-methoxy-4-(pyridin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 91 |  | 1-[2-fluoro-4-(pyridin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 92 |  | 1-[2-methoxy-4-(pyridin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 93 |  | 1-{4-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 94 |  | 1-{4-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

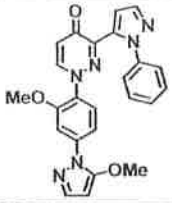
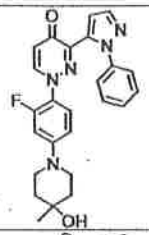
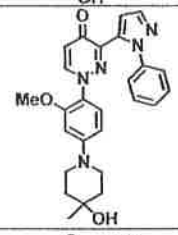
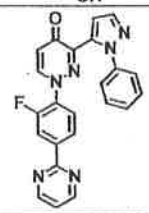
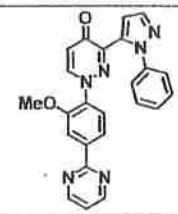
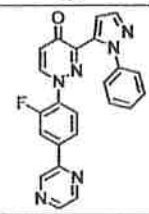
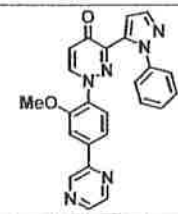
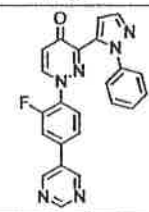
[0500]

[Table 24]

| | | |
|---|---|---|
| 95 |  | 1-[2-fluoro-4-(8-oxa-3-azabicyclo[3.2.1]octa-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 96 |  | 1-[2-methoxy-4-(8-oxa-3-azabicyclo[3.2.1]octa-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 97 |  | 1-[2-fluoro-4-(1,4-oxazepan-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 98 |  | 1-[2-methoxy-4-(1,4-oxazepan-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 99 |  | 1-{4-[5-(cyclopropylmethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 100 |  | 1-{4-[5-(cyclopropylmethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 101 |  | 1-{2-fluoro-4-[5-(2,2,2-trifluoroethoxy)-1H-pyrazol-1-yl]phenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 102 |  | 1-{2-methoxy-4-[5-(2,2,2-trifluoroethoxy)-1H-pyrazol-1-yl]phenyl}-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 103 |  | 1-[2-fluoro-4-(5-methoxy-1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

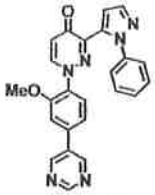
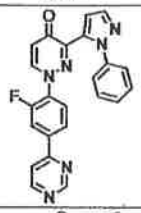
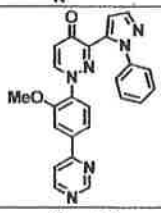
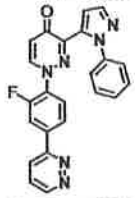
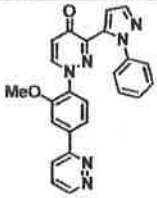
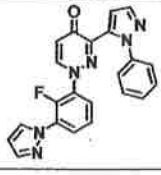
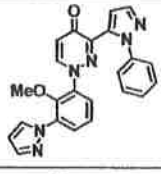
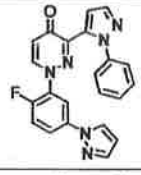
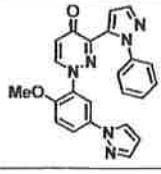
[0501]

[Table 25]

| | | |
|---|---|---|
| 104 |  | 1-[2-methoxy-4-(5-methoxy-1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 105 |  | 1-[2-fluoro-4-(4-hydroxy-4-methylpiperidin-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 106 |  | 1-[4-(4-hydroxy-4-methylpiperidin-1-yl)-2-methoxyphenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 107 |  | 1-[2-fluoro-4-(pyrimidin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 108 |  | 1-[2-methoxy-4-(pyrimidin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 109 |  | 1-[2-fluoro-4-(pyrazin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 110 |  | 1-[2-methoxy-4-(pyrazin-2-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 111 |  | 1-[2-fluoro-4-(pyrimidin-5-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

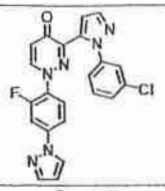
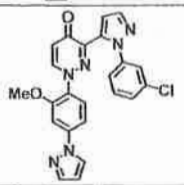
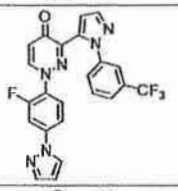
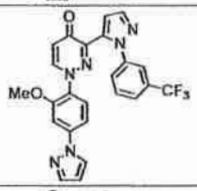
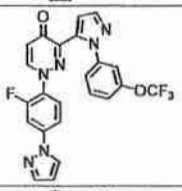
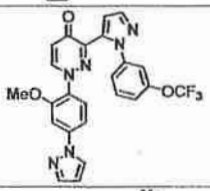
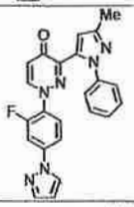
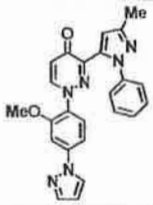
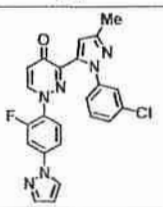
[0502]

[Table 26]

| | | |
|---|---|---|
| 112 |  | 1-[2-methoxy-4-(pyrimidin-5-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 113 |  | 1-[2-fluoro-4-(pyrimidin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 114 |  | 1-[2-methoxy-4-(pyrimidin-4-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 115 |  | 1-[2-fluoro-4-(pyridazin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 116 |  | 1-[2-methoxy-4-(pyridazin-3-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 117 |  | 1-[2-fluoro-3-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 118 |  | 1-[2-methoxy-3-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 119 |  | 1-[2-fluoro-5-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 120 |  | 1-[2-methoxy-5-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

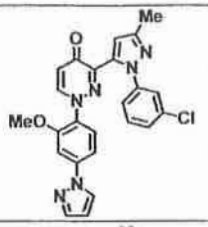
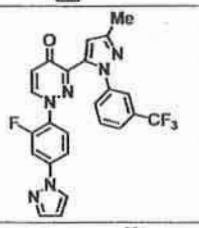
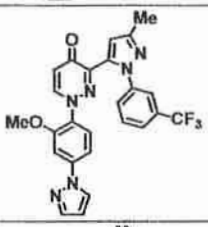
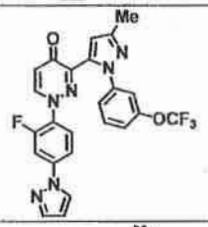
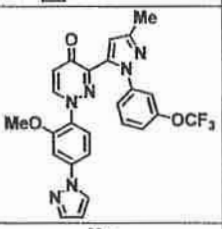
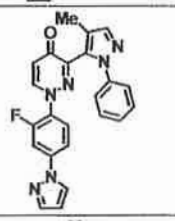
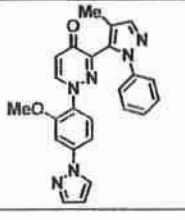
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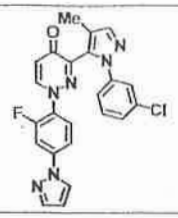
[Table 27]

| | | |
|---|---|---|
| 121 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |
| 122 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |
| 123 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 124 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 125 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 126 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 127 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 128 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 129 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |

[0504]

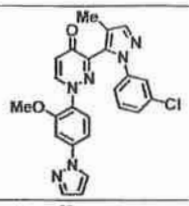
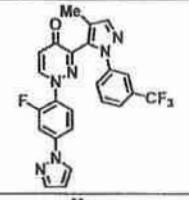
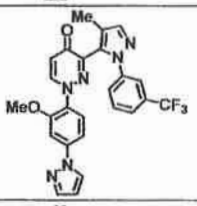
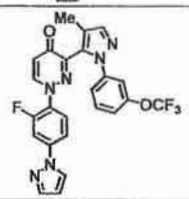
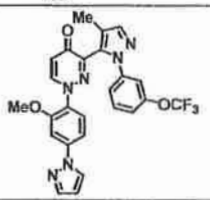
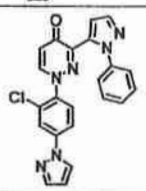
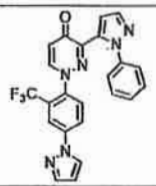
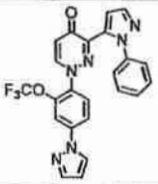
[Table 28]

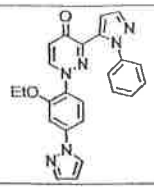
| | | |
|---|---|---|
| 130 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |
| 131 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 132 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 133 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 134 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 135 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-(4-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 136 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-(4-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 137 |  | 3-[1-(3-chlorophenyl)-4-methyl-1H-pyrazol-5-yl]-1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |

[0505]

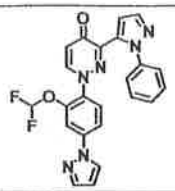
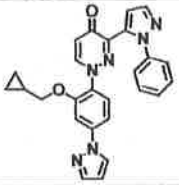
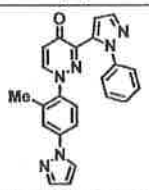
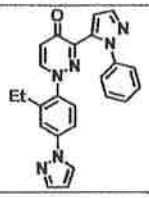
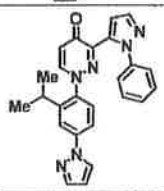
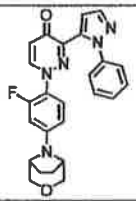
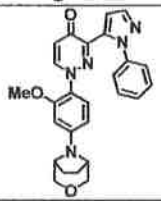
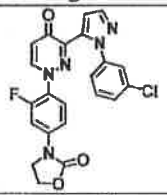
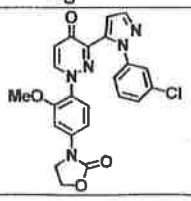
[Table 29]

| | | |
|---|---|---|
| 138 |  | 3-[1-(3-chlorophenyl)-4-methyl-1H-pyrazol-5-yl]-1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]pyridazin-4(1H)-one |
| 139 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{4-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 140 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{4-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 141 |  | 1-[2-fluoro-4-(1H-pyrazol-1-yl)phenyl]-3-{4-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 142 |  | 1-[2-methoxy-4-(1H-pyrazol-1-yl)phenyl]-3-{4-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 143 |  | 1-[2-chloro-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 144 |  | 3-(1-phenyl-1H-pyrazol-5-yl)-1-[4-(1H-pyrazol-1-yl)-2-(trifluoromethyl)phenyl]pyridazin-4(1H)-one |
| 145 |  | 3-(1-phenyl-1H-pyrazol-5-yl)-1-[4-(1H-pyrazol-1-yl)-2-(trifluoromethoxy)phenyl]pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 146 |  | 1-[2-ethoxy-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

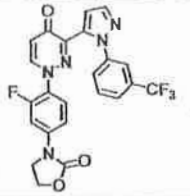
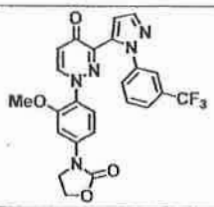
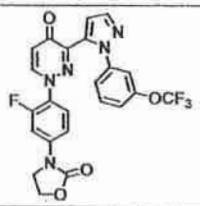
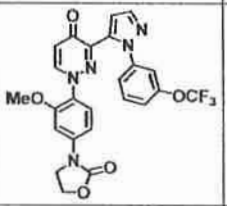
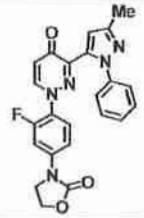
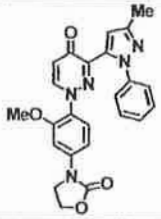
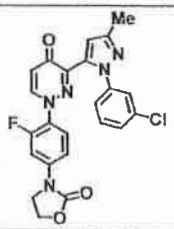
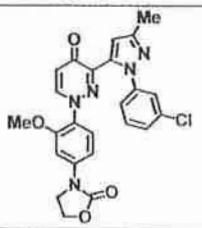
[0506]

[Table 30]

| | | |
|---|---|---|
| 147 |  | 1-[2-(difluoromethoxy)-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 148 |  | 1-[2-(cyclopropylmethoxy)-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 149 |  | 1-[2-methyl-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 150 |  | 1-[2-ethyl-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 151 |  | 1-[2-(1-methylethyl)-4-(1H-pyrazol-1-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 152 |  | 1-[2-fluoro-4-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 153 |  | 1-[2-methoxy-4-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)phenyl]-3-(1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 154 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]pyridazin-4(1H)-one |
| 155 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]pyridazin-4(1H)-one |

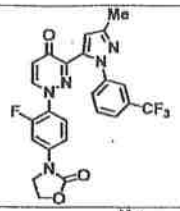
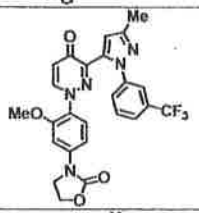
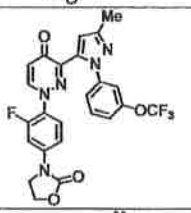
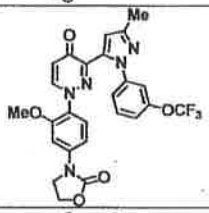
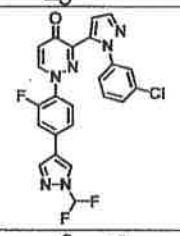
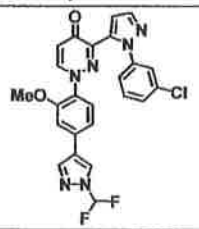
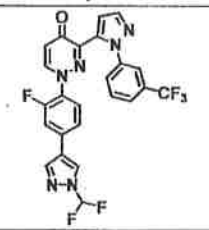
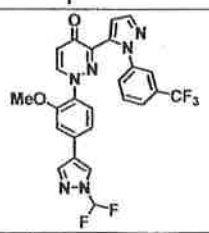
[0507]

[Table 31]

| | | |
|---|---|---|
| 156 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 157 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 158 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 159 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 160 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 161 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 162 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]pyridazin-4(1H)-one |
| 163 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]pyridazin-4(1H)-one |

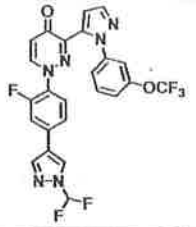
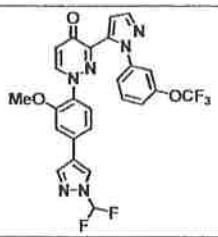
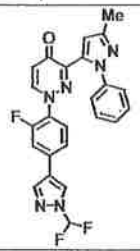
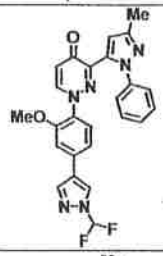
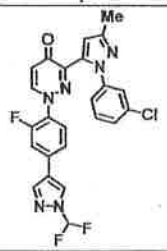
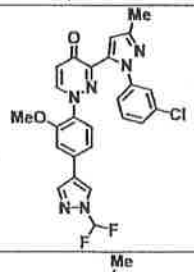
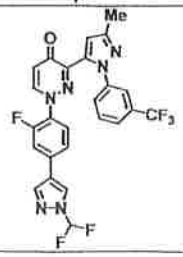
[0508]

[Table 32]

| | | |
|---|---|---|
| 164 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 165 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 166 |  | 1-[2-fluoro-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 167 |  | 1-[2-methoxy-4-(2-oxo-1,3-oxazolidin-3-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 168 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}pyridazin-4(1H)-one |
| 169 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}pyridazin-4(1H)-one |
| 170 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 171 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

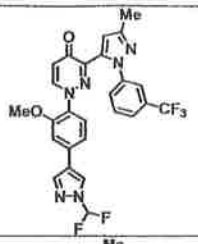
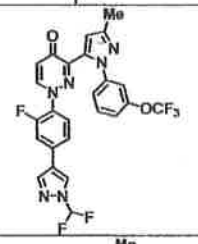
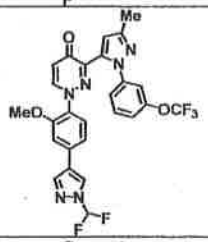
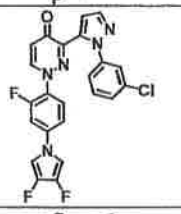
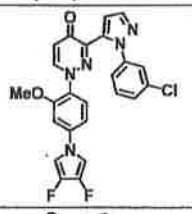
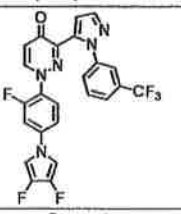
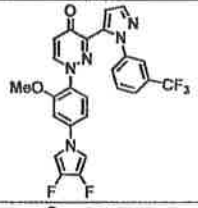
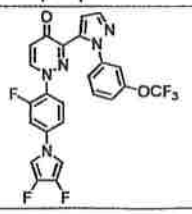
[0509]

[Table 33]

| | | |
|---|---|---|
| 172 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 173 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 174 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 175 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 176 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}pyridazin-4(1H)-one |
| 177 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}pyridazin-4(1H)-one |
| 178 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

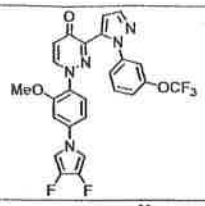
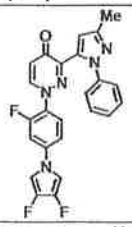
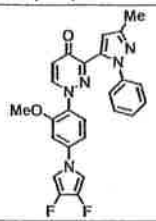
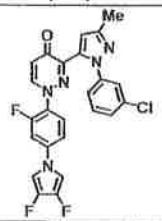
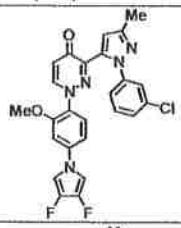
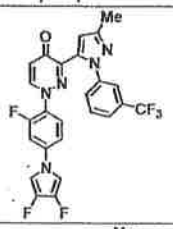
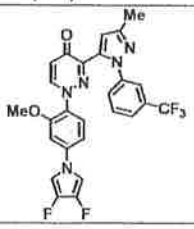
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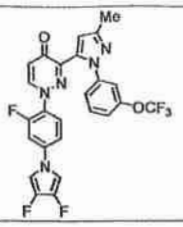
[Table 34]

| | | |
|---|---|---|
| 179 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 180 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-fluorophenyl}-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 181 |  | 1-{4-[1-(difluoromethyl)-1H-pyrazol-4-yl]-2-methoxyphenyl}-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 182 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]pyridazin-4(1H)-one |
| 183 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]pyridazin-4(1H)-one |
| 184 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 185 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 186 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

[0511]

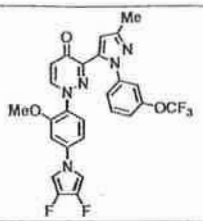
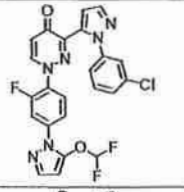
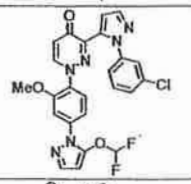
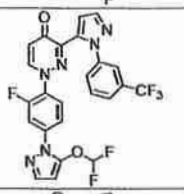
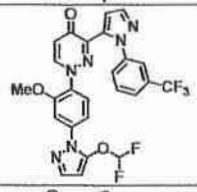
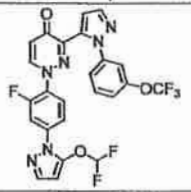
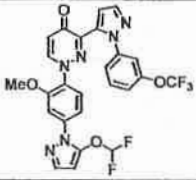
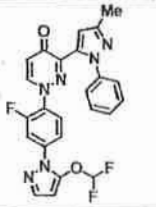
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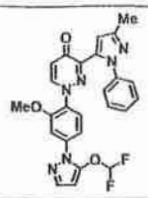
| | | |
|---|---|---|
| 187 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 188 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 189 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 190 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]pyridazin-4(1H)-one |
| 191 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]pyridazin-4(1H)-one |
| 192 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 193 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 194 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-fluorophenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

[0512]

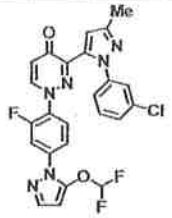
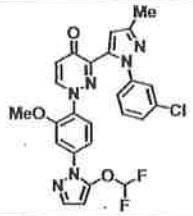
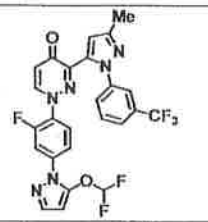
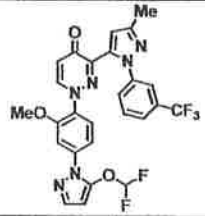
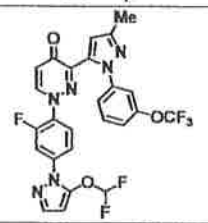
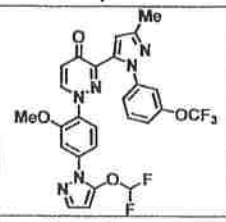
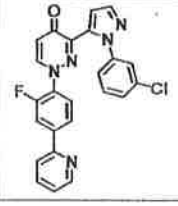
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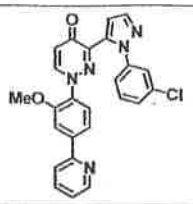
| | | |
|---|---|---|
| 195 |  | 1-[4-(3,4-difluoro-1H-pyrrol-1-yl)-2-methoxyphenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 196 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}pyridazin-4(1H)-one |
| 197 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}pyridazin-4(1H)-one |
| 198 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 199 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 200 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 201 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 202 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 203 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |

[0513]

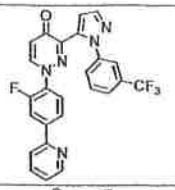
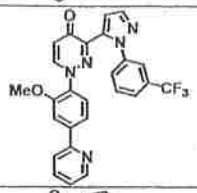
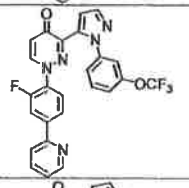
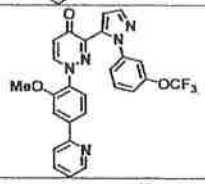
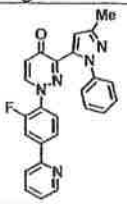
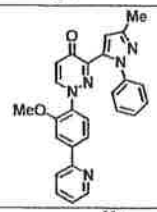
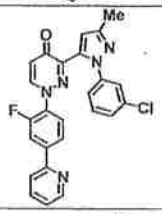
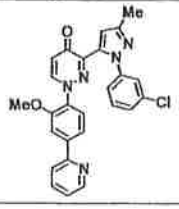
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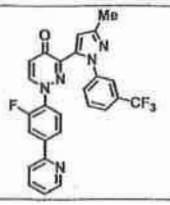
| | | |
|---|---|---|
| 204 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}pyridazin-4(1H)-one |
| 205 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}pyridazin-4(1H)-one |
| 206 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 207 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 208 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-fluorophenyl}-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 209 |  | 1-{4-[5-(difluoromethoxy)-1H-pyrazol-1-yl]-2-methoxyphenyl}-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 210 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-fluoro-4-(pyridin-2-yl)phenyl]pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 211 |  | 3-[1-(3-chlorophenyl)-1H-pyrazol-5-yl]-1-[2-methoxy-4-(pyridin-2-yl)phenyl]pyridazin-4(1H)-one |

[0514]

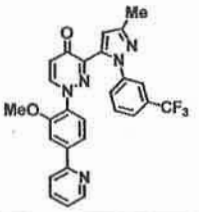
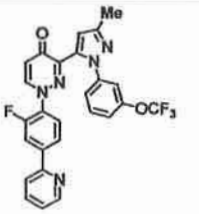
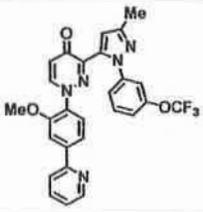
[Table 38]

| | | |
|---|---|---|
| 212 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 213 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-{1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 214 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 215 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-{1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 216 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 217 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-(3-methyl-1-phenyl-1H-pyrazol-5-yl)pyridazin-4(1H)-one |
| 218 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-fluoro-4-(pyridin-2-yl)phenyl]pyridazin-4(1H)-one |
| 219 |  | 3-[1-(3-chlorophenyl)-3-methyl-1H-pyrazol-5-yl]-1-[2-methoxy-4-(pyridin-2-yl)phenyl]pyridazin-4(1H)-one |

| | | |
|---|---|---|
| 220 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

[0515]

[Table 39]

| | | |
|---|---|---|
| 221 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 222 |  | 1-[2-fluoro-4-(pyridin-2-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |
| 223 |  | 1-[2-methoxy-4-(pyridin-2-yl)phenyl]-3-{3-methyl-1-[3-(trifluoromethoxy)phenyl]-1H-pyrazol-5-yl}pyridazin-4(1H)-one |

[0516]

Test Example 1

PDE Enzyme Inhibition

Human PDE10A enzyme was generated from Sf9 or COS-7 cells transfected with the full-length gene. Cloned enzyme was extracted from homogenized cell pellets. The extracted enzyme from sf9 cells was partially purified using His-tag affinity column. The enzyme was stored at -70°C until use. PDE activity was measured using a SPA (Scintillation Proximity Assay) (GE Healthcare). To evaluate the inhibitory activity, 10 µL of serial diluted compounds were incubated with 20 µL of PDE enzyme in assay buffer (50 mM HEPES-NaOH, 8.3 mM $MgCl_2$, 1.7 mM EGTA, 0.1% BSA (pH 7.4)) for 30 min. at room temperature. Final concentration of DMSO in the assay was 1 percent as

compounds were tested in duplicate in 96-well half-area plates (Corning). To start the reaction, 10 μL of substrate [$^3$H] cGMP (25 or 50 nM; enclosed in SPA kits from GE Healthcare or purchased from PerkinElmer, respectively) was added for a final assay volume of 40 μL. After 60 min incubation at room temperature, yttrium SPA beads containing Zinc sulphate were added (20 μL at 6 mg/mL) to terminate the PDE reaction. After being settled for 60 min, assay plates were counted in a scintillation counter (PerkinElmer) to allow calculation of inhibition rate. Inhibition rate was calculated on the basis of 0% control wells with DMSO and 100% control wells without enzyme. The results are shown in Table 40.

[Table 40]

| Ex. No. | Percent inhibition (10 μM) | Percent inhibition (1 μM) | Percent inhibition (0.1 μM) |
|---|---|---|---|
| 1 | 100 | 98 | |
| 2 | 103 | 104 | |
| 3 | | | 99 |
| 8 | | | 98 |
| 9 | 99 | 99 | |
| 12 | 99 | 93 | |
| 13 | 101 | 100 | |
| 24 | | | 98 |
| 27 | | | 102 |
| 31 | 98 | 99 | |
| 39 | 101 | 100 | |
| 40 | 101 | 99 | |
| 48 | 100 | 96 | |
| 64 | 101 | 100 | |
| 65 | 101 | 100 | |
| 71 | 97 | 99 | |
| 72 | 110 | 104 | |
| 75 | 101 | 98 | |
| 85 | 99 | 95 | |
| 86 | 98 | 97 | |
| 97 | 98 | 97 | |
| 98 | 101 | 99 | |
| 99 | 105 | 100 | |
| 100 | 100 | 99 | |
| 101 | 99 | 101 | |
| 102 | 106 | 99 | |
| 103 | 103 | 101 | |

| | | | |
|---|---|---|---|
| 106 | 102 | 103 | |
| 107 | 102 | 103 | |
| 108 | 102 | 100 | |
| 109 | 102 | 99 | |
| 112 | 98 | 99 | |
| 115 | 97 | 100 | |
| 118 | 104 | 102 | |
| 119 | 103 | 99 | |
| 120 | 106 | 109 | |
| 121 | 99 | 103 | |
| 122 | 107 | 109 | |
| 123 | 101 | 96 | |
| 124 | 99 | 99 | |
| 125 | 101 | 99 | |
| 126 | 100 | 98 | |
| 127 | 101 | 101 | |
| 128 | 91 | 94 | |
| 129 | 96 | 89 | |
| 130 | 98 | 95 | |
| 132 | 107 | 104 | |
| 133 | 101 | 104 | |
| 134 | 104 | 101 | |
| 135 | 99 | 94 | |
| 136 | 98 | 81 | |
| 137 | 98 | 88 | |
| 138 | 105 | 93 | |

Test Example 2

(1) Animals

Male ICR mice were supplied by CLEA Japan, Inc (Japan). After arrival to the vivarium, animals were allowed more than 1 week for acclimation. They were housed under a 12 h-12 h light/dark cycle in a temperature- and humidity-controlled laboratory and allowed food and water ad libitum. The care and use of the animals and the experimental protocols used in this research were approved by the Experimental Animal Care and Use Committee of Takeda Pharmaceutical Company, Ltd (Osaka, Japan).

(2) Drug administration

The compounds were suspended in 0.5% (w/v) methylcellulose in distilled water, and the suspension was administered by orally. MK-801 hydrogen maleate ((5R,10S)-(+)-5-Methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine

maleate, Sigma-Aldrich, St Louis, MO) was dissolved in saline, and administered subcutaneously (s.c.). All drugs were dosed in a volume of 20 mL/kg body weight for mice.

(3) Measurement of Striatal Tissue Cyclic Nucleotides

Male ICR mice (28-42 g) were sacrificed by focused microwave irradiation of the brain at 60 min after administration of the compounds. Striatum were isolated and homogenized in 0.5 N HCl followed by centrifugation. Supernatant concentrations of cyclic nucleotides were measured using enzyme immunoassay kits (Cayman Chemical, Ann Arbor, MI). Values were expressed as the percentage of the average of the vehicle-treated samples. All data were represented as means plus the standard errors of the means (n = 8). The variance of data was judged by Bartlett's test. The statistical significance was determined by the Dunnett's t-test (for homogenous data) or the Steel's test (for non-homogenous data) with significance set at #$P < 0.05$.

(4) Inhibition of MK-801-induced hyperlocomotion

The widely used animal models of psychosis have been the measurement of the extent of hyperlocomotion induced by psychostimulants (e.g., amphetamine, cocaine, methamphetamine, MK-801 and phencyclidine) in rodents (Schizophrenia Bulletin 2010, vol. 36: 1066-1072; Psychopharmacology 1999, vol. 145: 237-250). The compounds were tested for its ability to antagonize MK-801-induced hyperlocomotion in mice. Male ICR mice (28-42 g) were habituated to the locomotor chambers with infrared sensors (Brain Science Idea Co., Ltd. Japan) for more than 60 min. Animals were removed from each chamber and treated with either vehicle or test compounds (p.o.) and immediately returned to the chamber. After 60 min, animals were again removed from the chambers and treated with either saline or MK-801 (0.3 mg/kg, s.c.), and then immediately returned to the test chamber. Activity count was recorded every 1 min bins. Total amounts of activity were measured during 120 min after MK-801 treatment. Data were represented

as means plus the standard errors of the means (n = 8-9). Statistical analysis was performed with the Welch's t-test for comparison between control group and MK-801 + vehicle treated group with significance set at ***$P < 0.001$ and the Dunnett's test for comparisons with vehicle-treated group with significance set at #$P < 0.05$.

[0517]

Compounds in Figures (Fig.1 and Fig.2) correspond to the compounds of the following Examples.

Compound A: Example 118

Compound B: Example 119

Compound C: Example 120

Compound D: Example 122

Compound E: Example 133

Compound F: Example 135

Compound G: Example 138

[0518]

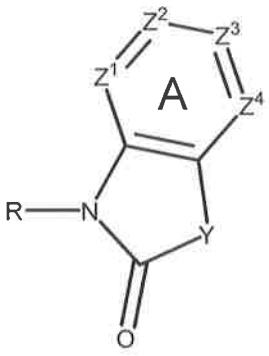
Formulation Example 1

| | |
|---|---|
| (1) Compound of Example 1 | 10.0 g |
| (2) Lactose | 70.0 g |
| (3) Cornstarch | 50.0 g |
| (4) Soluble starch | 7.0 g |
| (5) Magnesium stearate | 3.0 g |

After 10.0 g of the compound of Example 1 and 3.0 g of magnesium stearate are granulated in 70 mL aqueous solution of soluble starch (7.0 g as soluble starch) and then dried, the resulting mixture is mixed with 70.0 g of lactose and 50.0 g of cornstarch (lactose, cornstarch, soluble starch and magnesium stearate are all products in compliance with Japanese Pharmacopoeia 14$^{th}$ Edition). The mixture is compressed to obtain a tablet.

## CLAIMS

1. A compound represented by the formula (I):



(I)

wherein

ring A represents an optionally substituted 6-membered ring, any one or two of from $Z^1$ to $Z^4$ represent -N=, and the others represent -CH=;

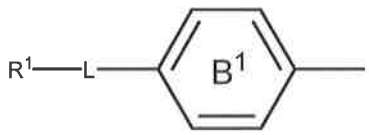
the nitrogen atom of -N= for $Z^1$ to $Z^4$ may be oxidized;

Y represents an oxygen atom, a sulfur atom, an optionally substituted methylene group or $-NR^c-$;

$R^c$ represents a hydrogen atom, or a substituent; and

R represents

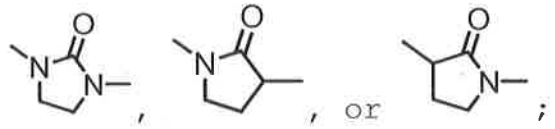
(1) a group represented by the formula:



wherein

$R^1$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

L represents a sulfur atom, an oxygen atom, an optionally substituted methylene group, -CO-, $-NR^a-$, $-CH_2O-$, $-OCH_2-$, $-NR^aCOO-$, $-OCONR^a-$, $-NR^aCONR^b-$, $-NR^aCOCH_2-$, $-CH_2CONR^a-$, $-NR^aCO-$, $-CONR^a-$,

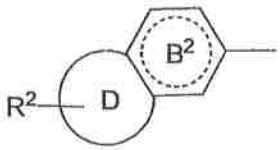


$R^a$ and $R^b$ are the same or different and each represents a hydrogen atom, or an optionally substituted $C_{1-6}$ alkyl group, or L and $R^1$ in combination optionally form an optionally

substituted bi- or tri-cyclic fused heterocyclic group; and

ring $B^1$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; or

(2) a group represented by the formula:




wherein

$R^2$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

ring $B^2$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; and

ring D represents an optionally further substituted 5- or 6-membered ring;

provided that

3,3'-benzene-1,4-diylbis(1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one),

1-cyclohexyl-3-(4-{[4-(methylsulfonyl)piperazin-1-yl]methyl}phenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one,

3-(4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one,

3,3'-benzene-1,4-diylbis(1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one), and

3-[8-(4-methylpiperazin-1-yl)naphthalen-2-yl]-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one

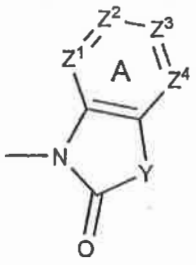
are excluded;

or a salt thereof.

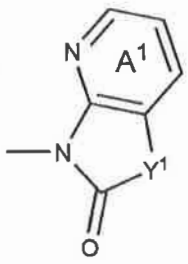
2. The compound according to claim 1, wherein any one of $Z^1$ to $Z^4$ is -N=, and the others are -CH=,

or a salt thereof.

3. The compound according to claim 1, wherein the partial structure of formula (I):



is a group represented by the formula:

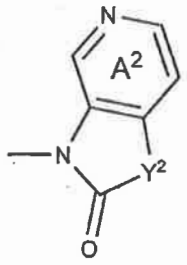


wherein

$Y^1$ represents an optionally substituted methylene group or -$NR^c$-,

$R^c$ represents a hydrogen atom, or a substituent, and

ring $A^1$ represents an optionally substituted pyridine ring, or a group represented by the formula:



wherein

$Y^2$ represents -$NR^d$-,

$R^d$ represents a substituent, and

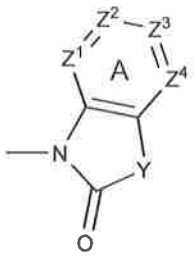
ring $A^2$ represents an optionally substituted pyridine ring, or a salt thereof.

4. The compound according to claim 1, wherein L is an oxygen atom, or -$NR^a$- wherein $R^a$ represents a hydrogen atom or an optionally substituted $C_{1-6}$ alkyl group, or

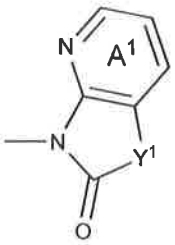
L and $R^1$ in combination optionally form an optionally

substituted bi- or tri-cyclic fused heterocyclic group, or a salt thereof.

5. The compound according to claim 3, wherein the partial structure of formula (I):

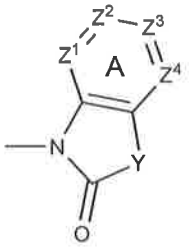



is a group represented by the formula:

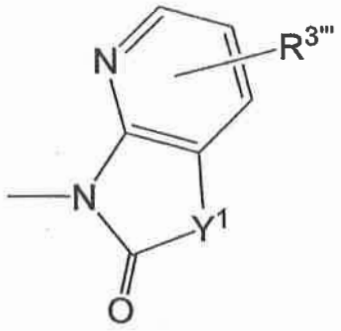



wherein each symbol is as defined in claim 3, or a salt thereof.

6. The compound according to claim 3, wherein the partial structure of formula (I):




is a group represented by the formula:



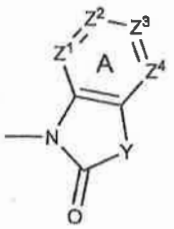
wherein

$R^{3'''}$ represents a hydrogen atom, a halogen atom, an optionally substituted $C_{1-4}$ alkyl group, or an optionally substituted $C_{1-4}$ alkoxy group, and

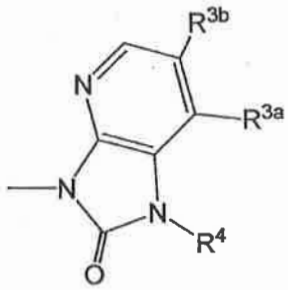
$Y^1$ is as defined in claim 3,

or a salt thereof.

7. The compound according to claim 3, wherein the partial structure of formula (I):



is a group represented by the formula:



wherein

$R^{3a}$ and $R^{3b}$ represent the same or different a hydrogen atom, a halogen atom, cyano, an optionally substituted $C_{1-4}$ alkyl group or an optionally substituted $C_{1-4}$ alkoxy group, and

$R^4$ represents an optionally substituted $C_{1-4}$ alkyl group,

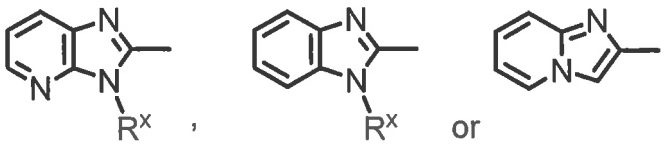
provided that when one of $R^{3a}$ and $R^{3b}$ is a hydrogen atom, the other is not a hydrogen atom

or a salt thereof.

8. The compound according to claim 1, wherein ring $B^1$ is an optionally substituted benzene ring, or a salt thereof.

9. The compound according to claim 1, wherein $R^1$ is a 5- to 10-membered heterocyclic group which may be substituted, or a salt thereof.

10. The compound according to claim 9, wherein the 5- to 10-membered heterocyclic group which may be substituted is a group represented by the formula:



wherein $R^x$ represents a hydrogen atom or an optionally substituted $C_{1-6}$ alkyl group,

or a salt thereof.

11. 1-Ethyl-6-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

12. 1-Ethyl-6-methoxy-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

13. 1-Ethyl-7-methyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

14. 6-Methyl-1-(1-methylethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

15. 1-Ethyl-6-fluoro-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

16. 1,7-Dimethyl-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

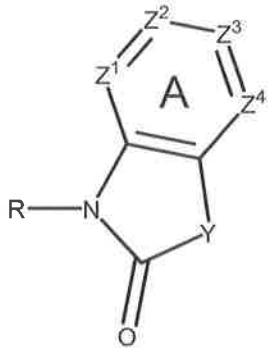
17. 1-Ethyl-7-(hydroxymethyl)-3-{4-[(3-methyl-3H-imidazo[4,5-b]pyridin-2-yl)oxy]phenyl}-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one, or a salt thereof.

18. A medicament comprising the compound according to claim 1, or a salt thereof.

19. The medicament according to claim 18, which is a phosphodiesterase 10A inhibitor.

20. The medicament according to claim 18, which is an agent for preventing or treating schizophrenia, autism, Alzheimer's disease, bipolar disorders, Parkinson's disease, Huntington's disease, obesity, drug addiction or attention deficit/hyperactivity disorder.

21. Use of a compound represented by the formula (I):




(I)

wherein

ring A represents an optionally substituted 6-membered ring,

any one or two of from $Z^1$ to $Z^4$ represent -N=, and the others represent -CH=;

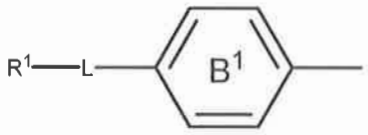
the nitrogen atom of -N= for $Z^1$ to $Z^4$ may be oxidized;

Y represents an oxygen atom, a sulfur atom, an optionally substituted methylene group or $-NR^c-$;

$R^c$ represents a hydrogen atom, or a substituent; and

R represents

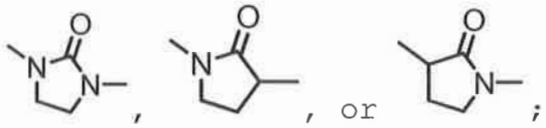
(1) a group represented by the formula:



wherein

$R^1$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

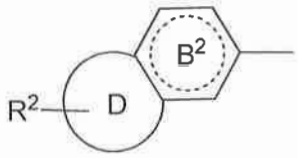
L represents a sulfur atom, an oxygen atom, an optionally substituted methylene group, -CO-, $-NR^a-$, $-CH_2O-$, $-OCH_2-$, $-NR^aCOO-$, $-OCONR^a-$, $-NR^aCONR^b-$, $-NR^aCOCH_2-$, $-CH_2CONR^a-$, $-NR^aCO-$, $-CONR^a-$,



$R^a$ and $R^b$ are the same or different and each represents a hydrogen atom, or an optionally substituted $C_{1-6}$ alkyl group, or L and $R^1$ in combination optionally form an optionally substituted bi- or tri-cyclic fused heterocyclic group; and

ring $B^1$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; or

(2) a group represented by the formula:



wherein

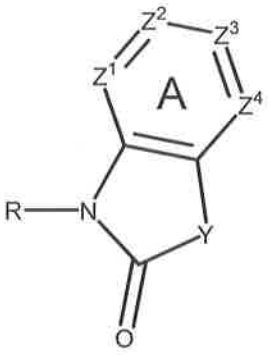
$R^2$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

ring $B^2$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; and

ring D represents an optionally further substituted 5- or 6-membered ring, or a salt thereof for the production of an agent for preventing or treating schizophrenia, autism, Alzheimer's disease, bipolar disorders, Parkinson's disease,

Huntington's disease, obesity, drug addiction or attention deficit/hyperactivity disorder.

22. A compound represented by the formula (I):



(I)

wherein

ring A represents an optionally substituted 6-membered ring, any one or two of from $Z^1$ to $Z^4$ represent -N=, and the others represent -CH=;

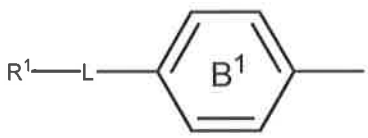
the nitrogen atom of -N= for $Z^1$ to $Z^4$ may be oxidized;

Y represents an oxygen atom, a sulfur atom, an optionally substituted methylene group or $-NR^c-$;

$R^c$ represents a hydrogen atom, or a substituent; and

R represents

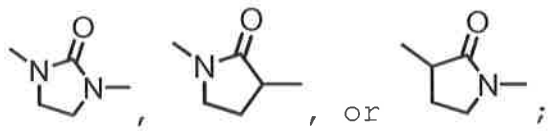
(1) a group represented by the formula:



wherein

$R^1$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

L represents a sulfur atom, an oxygen atom, an optionally substituted methylene group, -CO-, $-NR^a-$, $-CH_2O-$, $-OCH_2-$, $-NR^aCOO-$, $-OCONR^a-$, $-NR^aCONR^b-$, $-NR^aCOCH_2-$, $-CH_2CONR^a-$, $-NR^aCO-$, $-CONR^a-$,

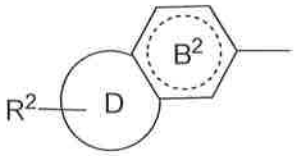


;

$R^a$ and $R^b$ are the same or different and each represents a

hydrogen atom, or an optionally substituted $C_{1-6}$ alkyl group, or L and $R^1$ in combination optionally form an optionally substituted bi- or tri-cyclic fused heterocyclic group; and ring $B^1$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; or

(2) a group represented by the formula:




wherein

$R^2$ represents a phenyl group or 5- to 10-membered heterocyclic group, each of which is optionally substituted;

ring $B^2$ represents a benzene ring, a pyridine ring, a pyrimidine ring, a pyrazine ring or a pyridazine ring, each of which is optionally substituted; and

ring D represents an optionally further substituted 5- or 6-membered ring, or a salt thereof for use in prevention or treatment of schizophrenia, autism, Alzheimer's disease, bipolar disorders, Parkinson's disease, Huntington's disease, obesity, drug addiction or attention deficit/hyperactivity disorder.