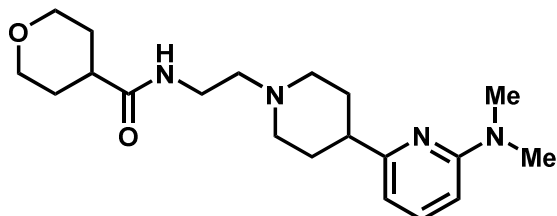


N-(2-{4-[6-(Dimethylamino)pyridin-2-yl]piperidin-1-yl}ethyl)-tetrahydro-2H-pyran-4-carboxamide



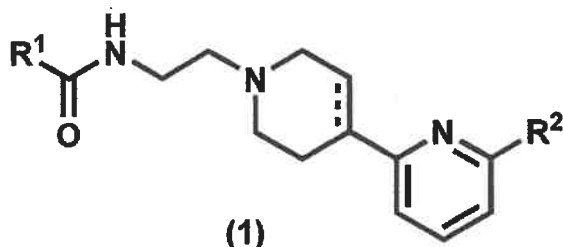
To a solution of the compound of Example 36 (50.0 mg) in
 5 dichloroethane (1.5 mL) was added paraformaldehyde (18.0
 mg), and the reaction mixture was stirred at room
 temperature for 1 hour. Sodium cyanoborohydride (23.9 mg)
 was added thereto, and the reaction mixture was stirred at
 room temperature for 24 hours. To the reaction mixture was
 10 added dichloromethane (30 mL). The mixture was washed with
 aqueous saturated sodium bicarbonate (10 mL × 2), dried
 over anhydrous sodium sulfate, filtrated, and then
 concentrated. The residue was purified by preparative
 thin-layer column chromatography (dichloromethane/3 mol/L
 15 ammonia/methanol) to give the title compound (36.0 mg).

¹H-NMR (300 MHz, CDCl₃) δ: 1.75-2.02 (8H, m), 2.15 (2H, t,
 J = 11.5 Hz), 2.32-2.46 (1H, m), 2.48-2.64 (3H, m), 3.00
 (2H, d, J = 11.3 Hz), 3.10 (6H, s), 3.33-3.53 (4H, m), 4.04
 (2H, td, J = 11.4, 3.4 Hz), 6.28 (1H, s), 6.37 (1H, d, J =
 20 8.6 Hz), 6.44 (1H, d, J = 7.3 Hz), 7.40 (1H, dd, J = 8.4,
 7.3 Hz).

[0111]

CLAIMS

1. A compound of formula (1):



or a pharmaceutically acceptable salt thereof, wherein

5 R¹ is optionally-substituted C₁₋₆ alkyl, optionally-substituted C₃₋₁₀ cycloalkyl, or optionally-substituted 5- to 10-membered saturated or partially-unsaturated heterocyclyl group;

 R² is halogen atom, cyano, C₁₋₆ alkyl which may be
10 optionally substituted with 1 to 3 the same or different halogen atoms, C₁₋₆ alkoxy which may be optionally substituted with 1 to 3 the same or different halogen atoms, or amino which may be optionally substituted with 1 or 2 the same or different C₁₋₆ alkyl groups; and

15 the bond accompanied with broken line is single bond or double bond.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

20 R¹ is

 (1) C₁₋₆ alkyl which may be optionally substituted with 1 to 3 the same or different substituents selected from the

group consisting of halogen atom, hydroxy, C₃₋₇ cycloalkyl, and C₁₋₆ alkoxy,

(2) C₃₋₁₀ cycloalkyl which may be optionally substituted with 1 to 4 the same or different substituents selected from the group consisting of halogen atom, hydroxy, cyano, C₁₋₆ alkyl which may be optionally substituted with 1 to 3 the same or different halogen atom or C₁₋₆ alkoxy, C₁₋₆ alkoxy which may be optionally substituted with 1 to 3 the same or different halogen atom or C₁₋₆ alkoxy, and amino which may be optionally substituted with 1 or 2 the same or different C₁₋₆ alkyl, or

(3) 5- to 10-membered saturated or partially-unsaturated heterocyclyl group which may be optionally substituted with 1 to 4 the same or different substituents selected from the group consisting of halogen atom, hydroxy, cyano, C₁₋₆ alkyl which may be optionally substituted with 1 to 3 the same or different halogen atom or C₁₋₆ alkoxy, C₁₋₆ alkoxy which may be optionally substituted with 1 to 3 the same or different halogen atom or C₁₋₆ alkoxy, and amino which may be optionally substituted with 1 or 2 the same or different C₁₋₆ alkyl.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein

25 R¹ is

(1) C₃₋₇ cycloalkyl which may be optionally substituted with 1 to 4 the same or different substituents selected from the group consisting of halogen atom, and C₁₋₆ alkyl which may be optionally substituted with 1 to 3 the same or
5 different halogen atom or C₁₋₆ alkoxy, or

(2) 5- or 6-membered saturated or partially-unsaturated heterocyclyl group which may be optionally substituted with 1 to 4 the same or different substituents selected from the group consisting of halogen atom, and C₁₋₆ alkyl which may be
10 optionally substituted with 1 to 3 the same or different halogen atom or C₁₋₆ alkoxy.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R¹ is C₃₋₇
15 cycloalkyl which may be optionally substituted with 1 to 4 fluorine atoms, or 5- or 6-membered saturated or partially-unsaturated heterocyclyl group which may be optionally substituted with 1 to 4 fluorine atoms.

20 5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R¹ is cyclohexyl which may be optionally substituted with 1 to 4 fluorine atoms, tetrahydropyranyl, tetrahydrofuryl, dihydropyranyl, or dihydrofuryl.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R¹ is difluorocyclohexyl, or tetrahydropyranyl.

5 7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R² is halogen atom, or C₁₋₆ alkyl which may be optionally substituted with 1 to 3 the same or different halogen atoms.

10 8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R² is C₁₋₄ alkyl which may be optionally substituted with 1 to 3 fluorine atoms.

15 9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein the bond accompanied with broken line is single bond.

10. The compound of claim 1 selected from the following compounds, or a pharmaceutically acceptable salt thereof,

4,4-difluoro-N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)cyclohexane-carboxamide,

N-{2-[4-(6-methylpyridin-2-yl)piperidin-1-yl]ethyl}-tetrahydro-2H-pyran-4-carboxamide,

25 2,2-dimethyl-N-(2-{4-[6-(trifluoromethyl)pyridin-2-

yl]piperidin-1-yl}ethyl)propanamide, and

N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)-tetrahydro-2H-pyran-4-carboxamide.

- 5 11. The compound of claim 1 selected from the following compounds, or a pharmaceutically acceptable salt thereof,

4,4-difluoro-N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)cyclohexane-carboxamide,

- 10 N-{2-[4-(6-methylpyridin-2-yl)piperidin-1-yl]ethyl}-tetrahydro-2H-pyran-4-carboxamide, and

N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)-tetrahydro-2H-pyran-4-carboxamide.

12. The compound of claim 1 of the following compound, or
15 a pharmaceutically acceptable salt thereof,

4,4-difluoro-N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)cyclohexane-carboxamide.

13. The compound of claim 1 of the following compound, or
20 a pharmaceutically acceptable salt thereof,

N-{2-[4-(6-methylpyridin-2-yl)piperidin-1-yl]ethyl}-tetrahydro-2H-pyran-4-carboxamide.

14. The compound of claim 1 of the following compound, or
25 a pharmaceutically acceptable salt thereof,

2,2-dimethyl-N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)propanamide.

15. The compound of claim 1 of the following compound, or
5 a pharmaceutically acceptable salt thereof,

N-(2-{4-[6-(trifluoromethyl)pyridin-2-yl]piperidin-1-yl}ethyl)-tetrahydro-2H-pyran-4-carboxamide.

16. A medicament comprising the compound of any one of
10 claims 1 to 15 or a pharmaceutically acceptable salt thereof as an active ingredient.

17. A medicament for treating generalized anxiety disorder, major depression, obsessive-compulsive disorder,
15 Parkinson's disease, Rett syndrome, attention-deficit hyperactivity disorder, autism spectrum disorder, or dementia, comprising the compound of any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof as an active ingredient.

20

18. Use of the compound of any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating generalized anxiety disorder, major depression, obsessive-compulsive
25 disorder, Parkinson's disease, Rett syndrome, attention-deficit hyperactivity disorder, autism spectrum disorder, or dementia.

19. The compound of any one of claims 1 to 15 or a
30 pharmaceutically acceptable salt thereof, for use in the treatment of generalized anxiety disorder, major depression, obsessive-compulsive disorder, Parkinson's disease, Rett syndrome, attention-deficit hyperactivity disorder, autism

spectrum disorder, or dementia.

20. A medicament comprising the compound of any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof, and at least one other medicament selected from
5 drugs classified as an antianxiety drug or an antidepressant drug.

21. A medicament for treating generalized anxiety disorder, major depression, obsessive-compulsive disorder, Parkinson's disease, Rett syndrome, attention-deficit hyperactivity disorder, autism spectrum disorder, or dementia, comprising the compound of any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof, which is
15 used in combination with at least one other medicament selected from drugs classified as an antianxiety drug or an antidepressant drug.

22. The medicament of claim 20 or 21, wherein the
20 antianxiety drug is a selective serotonin reuptake inhibitor.

23. The medicament of claim 22, wherein the selective serotonin reuptake inhibitor is at least one drug selected
25 from the group consisting of sertraline, escitalopram, fluvoxamine, fluoxetine, paroxetine, clomipramine, and pharmaceutically acceptable salts thereof.

24. The medicament of any one of claims 20 to 23, wherein
30 the antidepressant drug is a serotonin reuptake inhibitor.

25. The medicament of claim 24, wherein the serotonin reuptake inhibitor is at least one drug selected from the

group consisting of milnacipran, duloxetine, venlafaxine, amoxapine, clomipramine, nortriptyline, imipramine, vortioxetine, and pharmaceutically acceptable salts thereof.