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**Benzazepin vegyület**

Az európai szabadalom ellen, megadásának az Európai Szabadalmi Közlönyben való meghirdetésétől számított kilenc hónapon belül, felszólalást lehet benyújtani az Európai Szabadalmi Hivatalnál. (Európai Szabadalmi Egyezmény 99. cikk(1))

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(54) **BENZAZEPINE COMPOUND**

**BENZAZEPINVERBINDUNG**

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**WO-A1-02/074746 WO-A1-02/074746**  
**WO-A1-2005/003096 WO-A1-2005/042490**  
**WO-A1-2005/042491 WO-A1-2005/082859**  
**WO-A2-03/086306 WO-A2-03/086306**  
**WO-A2-2005/118549 WO-A2-2005/118549**

- **FABRIZIO MICHELI ET AL.: 'New fused benzazepine as selective D3 receptor antagonists. Synthesis and biological evaluation. Part one: [h]-fused tricyclic systems' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS vol. 18, 2008, pages 901 - 907, XP022475654**
- **GIANCARLO TRANI ET AL.: 'Tricyclic azepine derivatives as selective brain penetrant 5-HT6 receptor antagonists' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS vol. 18, 2008, pages 5698 - 5700, XP025562139**

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**EP 2 546 255 B1**

## Description

## Technical Field

**[0001]** The present invention relates to a benzazepine compound which is useful as an active ingredient of a pharmaceutical composition, particularly a pharmaceutical composition for treating or preventing 5-HT<sub>2C</sub> receptor-related diseases, particularly incontinence such as stress urinary incontinence, urge urinary incontinence, mixed urinary incontinence, and the like, sexual dysfunction such as erectile dysfunction syndrome and the like, obesity, and the like.

## Background Art

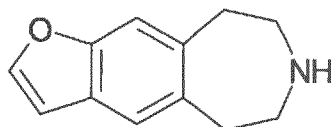
**[0002]** A serotonin 2C (5-HT<sub>2C</sub>) receptor is one of the receptors for serotonin, a transmitter related to various physiological functions in the biological body. Its expression has been recognized mainly in the central nervous system (brain/spinal cord).

**[0003]** An anorectic action is known as a physiological function of the central 5-HT<sub>2C</sub> receptor, and the lowering action of various 5-HT<sub>2C</sub> receptor agonists on food intake has been reported in rats (Non-Patent Documents 1 and 2). Further, it has been confirmed that an anti-obesity action in humans is exhibited due to the anorectic action of the 5-HT<sub>2C</sub> receptor agonist (Non-Patent Document 3).

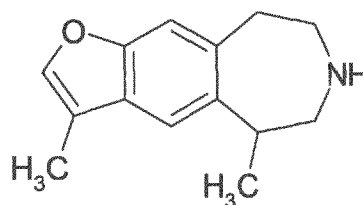
**[0004]** The central 5-HT<sub>2C</sub> receptor is involved in the control of peripheral nerve functions and it has been reported that the rat penile erection is induced by a 5-HT<sub>2C</sub> receptor agonist (Non-Patent Document 4) and that the time taken from insertion to ejaculation in the experiment for mating behavior of monkeys is prolonged (Non-Patent Document 5). Moreover, it has been reported that a 5-HT<sub>2C</sub> receptor agonist increases the urethral resistance when the abdominal pressure is increased in rats (Non-Patent Document 6). In addition, it has been reported that in disease models with neuropathic /inflammatory pain in rats, efficacy is exhibited by intraspinal administration of a 5-HT<sub>2C</sub> receptor agonist (Non-Patent Documents 7 and 8). Various clinical applications are considered for 5-HT<sub>2C</sub> receptor agonists, particularly as anti-obesity drugs, drugs for treating male erectile dysfunction, drugs for treating premature ejaculation, drugs for treating stress urinary incontinence, drugs for treating neuropathic / inflammatory pain, or the like.

**[0005]** As the 5-HT<sub>2C</sub> receptor agonist, a benzazepine derivative has been reported, and as a tricyclic benzazepine derivative, for example, Compound A (Patent Document 1) and Compound B (Patent Document 2) are known.

[Chem. 1]



Compound A

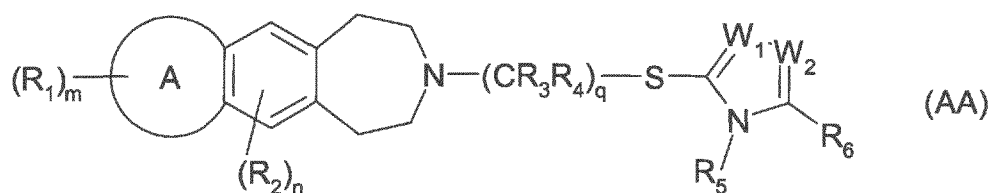


Compound B

**[0006]** As other 5-HT<sub>2C</sub> receptor agonists, bicyclic benzazepine derivatives have been reported (Patent Document 3, Patent Document 4, and Patent Document 5).

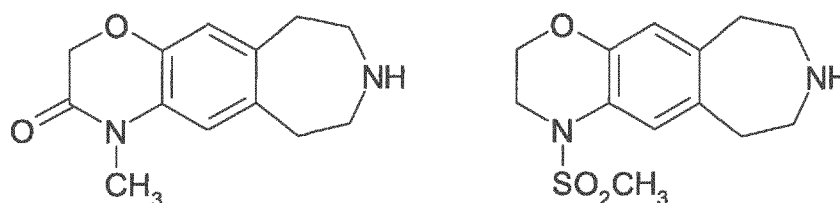
**[0007]** As a 2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline derivative or a 3,4,6,7,9,10-hexahydro[1,4]oxazino[2,3-h][3]benzazepine derivative, which is a tricyclic benzazepine derivative, a compound of the formula (AA) is known to be a Dopamine D3 modulator and be useful for central drug abuse and drug dependence (Patent Document 6).

[Chem. 2]



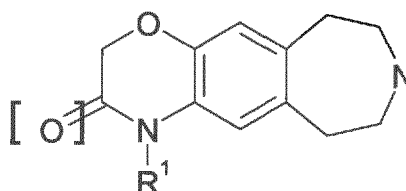
[0008] In addition, in this document, the following compounds are disclosed as a synthetic intermediate for the formula (AA).

[Chem. 3]



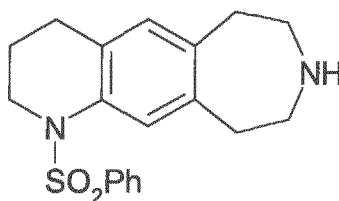
[0009] Furthermore, there is a report on the structure-activity relationship of a specific compound of the formula (AA) (Non-Patent Document 9), and in this report, it is described that the following compound was used in the preparation of the compound of the formula (AA).

[Chem. 4]



[0010] Moreover, there is a report on a 5-HT<sub>6</sub> receptor antagonist (Non-Patent Document 10), and it is disclosed that for the compound below, potency on the 5-HT<sub>6</sub> receptor is lost by changing a ring condensed with benzazepine from a 5-membered ring to a 6-membered ring.

[Chem. 5]



[0011] However, in the documents which disclose such tricyclic benzazepine derivatives, there is no disclosure on the 5-HT<sub>2C</sub> receptor agonist activity of the 2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline derivative or the

3,4,6,7,9,10-hexahydro[1,4]oxazino[2,3-h][3]benzazepine derivative.

[Prior Art Document]

5 [Patent Document]

**[0012]**

10 [Patent Document 1] WO 2002/074746  
 [Patent Document 2] WO 2003/086306  
 [Patent Document 3] WO 2005/042490  
 [Patent Document 4] WO 2005/042491  
 [Patent Document 5] WO 2005/003096  
 15 [Patent Document 6] WO 2005/118549

[Non-Patent Document]

**[0013]**

20 [Non-Patent Document 1] Obesity, 2008, vol. 17, pp. 494-503  
 [Non-Patent Document 2] Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2002, vol. 26, pp. 441-449  
 [Non-Patent Document 3] Journal of Pharmacology and Experimental Therapeutics, 2008, vol. 325, pp. 577-587  
 [Non-Patent Document 4] European Journal of Pharmacology, 2004, vol. 483, pp. 37-43  
 25 [Non-Patent Document 5] Psychopharmacology, 1993, vol. 111, pp. 47-54  
 [Non-Patent Document 6] American Journal of Physiology: Renal Physiology, 2009, vol. 297, pp. 1024-1031  
 [Non-Patent Document 7] Pain, 2004, vol. 108, pp. 163-169 [Non-Patent Document 8] Anesthesia and Analgesia, 2003, vol. 96, pp. 1072-1078  
 [Non-Patent Document 9] Bioorganic & Medicinal Chemistry Letters, 2008, vol. 18, pp. 901-907  
 30 [Non-Patent Document 10] Bioorganic & Medicinal Chemistry Letters, 2008, vol. 18, pp. 5698-5700

[Summary of the Invention]

[Problems to Be Solved by the Invention]

35 **[0014]** A benzazepine compound which is useful as an active ingredient for a pharmaceutical composition, particularly a pharmaceutical composition for treating or preventing 5-HT<sub>2C</sub> receptor-related diseases, particularly incontinence such as stress urinary incontinence, urge urinary incontinence, mixed urinary incontinence, and the like, sexual dysfunction such as erectile dysfunction syndrome and the like, obesity, and the like is provided.

40 [Means for Solving the Problem]

**[0015]** The present inventors have extensively studied compounds having a 5-HT<sub>2C</sub> receptor agonist activity, and as a result, they have found that the benzazepine compounds of the present invention have a 5-HT<sub>2C</sub> receptor agonist activity, thereby completing the present invention.

**[0016]** Specifically, the present invention relates to  
 11-cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinolone,  
 4-(3-methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4] oxazino[2,3-h][3]benzazepine,  
 5-cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine,  
 50 and salts thereof.

**[0017]** Furthermore, the present invention relates to a pharmaceutical composition comprising the compound of the present invention or a salt thereof and a pharmaceutically acceptable excipient.

**[0018]** Furthermore, the present invention relates to a pharmaceutical composition for preventing or treating 5-HT<sub>2C</sub> receptor-related diseases which comprises one of these compounds or a salt thereof.

55 **[0019]** Moreover, the present invention relates to the use of these compounds or salts thereof for the preparation of a pharmaceutical composition for preventing or treating stress urinary incontinence and mixed urinary incontinence. It also relates to these compounds or salts thereof for use in the prevention or treatment of stress urinary incontinence and mixed urinary incontinence.

## [Effects of the Invention]

**[0020]** The compounds of the invention and salts thereof have a 5-HT<sub>2C</sub> receptor agonist activity and can be used as an agent for preventing or treating 5-HT<sub>2C</sub> receptor-related diseases.

**[0021]** Here, examples of the 5-HT<sub>2C</sub> receptor-related diseases include incontinence such as stress urinary incontinence, urge urinary incontinence, mixed urinary incontinence, and the like, sexual dysfunction such as erectile dysfunction syndrome and the like, obesity, and the like.

## [Embodiments for Carrying Out the Invention]

**[0022]** Hereinafter, the present invention will be described in detail.

**[0023]** In the present specification, the "alkyl" includes straight alkyl and branched alkyl. Accordingly, the "C<sub>1-6</sub> alkyl" is a straight or branched alkyl having 1 to 6 carbon atoms, and specific examples thereof include methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, hexyl, and the like, in another embodiment, methyl, ethyl, propyl, isopropyl, in a further embodiment, methyl, ethyl, in a still further embodiment, methyl, and in a still further embodiment, ethyl.

**[0024]** The "alkylene" is a divalent group formed by the removal of any one hydrogen atom of the "alkyl" above. Accordingly, the "C<sub>1-6</sub> alkylene" is straight or branched alkylene having 1 to 6 carbon atoms, and specific examples thereof include methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, methylmethylene, dimethylmethylene, ethylmethylene, methylethylene, dimethylethylene, ethylethylene, and the like, in another embodiment, methylene, ethylene, and in a further embodiment methylene.

**[0025]** The "aryl" is a monocyclic to tricyclic aromatic hydrocarbon ring group having 6 to 14 carbon atoms. Specific examples thereof include phenyl and naphthyl, in another embodiment, phenyl, and in a further embodiment, naphthyl.

**[0026]** The "cycloalkyl" is a saturated hydrocarbon ring group, the cycloalkyl may have a bridge and may be condensed with a benzene ring, and a part of the bonds may be unsaturated. Accordingly, specific examples of the "C<sub>3-8</sub> cycloalkyl" include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctyl, cyclooctadienyl, norbornyl, bicyclo[2.2.2]octyl, indanyl, indenyl, 1,2-dihydronaphthyl, 1,2,3,4-tetrahydronaphthyl, and the like.

**[0027]** The "hetero ring" is a monovalent group of a 3- to 15-membered, in another embodiment, a 5- to 10-membered, monocyclic to tricyclic heterocyclic group containing 1 to 4 hetero atoms selected from oxygen, sulfur, and nitrogen, and includes a saturated ring, an aromatic ring, and a partially hydrogenated ring group thereof. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide. Specific examples thereof include monocyclic aromatic hetero rings such as pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, and the like, bicyclic aromatic hetero rings such as indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, quinoxalyl, quinazolinyl, phthalazinyl, benzothiadiazolyl, and the like, tricyclic aromatic hetero rings such as carbazolyl, dibenzo[b,d]furanyl, dibenzo[b,d]thienyl, and the like, monocyclic non-aromatic hetero rings such as azetidyl, pyrrolidinyl, piperidyl, piperazinyl, azepanyl, diazepanyl, morpholinyl, thiomorpholinyl, tetrahydropyridinyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, dioxolanyl, dioxanyl, tetrahydrothiopyranyl, and the like, bicyclic non-aromatic hetero rings such as indolinyl, tetrahydroquinolyl, tetrahydroisoquinolyl, dihydrobenzimidazolyl, tetrahydrobenzimidazolyl, tetrahydroquinoxalyl, dihydroquinoxalyl, dihydrobenzoxazolyl, dihydrobenzoxazinyl, dihydrobenzofuryl, chromanyl, chromenyl, methylenedioxyphenyl, ethylenedioxyphenyl, and the like, bridged hetero rings such as quinuclidinyl and the like, in another embodiment, a 5- to 10-membered monocyclic to bicyclic hetero ring, in a further embodiment, a 5- to 6-membered monocyclic hetero ring, and in a still further embodiment, a 5- to 6-membered monocyclic aromatic hetero ring.

**[0028]** The "aromatic hetero ring" is a 5- to 10-membered monocyclic to bicyclic aromatic hetero ring among the "hetero rings" above, and specific examples thereof include pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, quinoxalyl, quinazolinyl, phthalazinyl, and the like, and in another embodiment, furyl, thienyl, pyrazolyl, thiazolyl, pyridyl, pyrimidinyl, and pyrazyl.

**[0029]** The "cyclic amino" is a 5- to 7-membered non-aromatic hetero ring having a binding position at a nitrogen atom among the "hetero rings" above, and specific examples thereof include pyrrolidinyl, piperidyl, piperazinyl, azepanyl, diazepanyl, morpholinyl, and thiomorpholinyl.

**[0030]** The "oxygen-containing hetero ring" is a monovalent group of a non-aromatic 5- to 6-membered ring which may be condensed with a benzene ring having one or two oxygen atoms as ring-constituting atoms. Specific examples thereof include tetrahydrofuranyl, tetrahydropyranyl, dioxolanyl, dioxanyl, dihydrobenzofuranyl, dihydrochromenyl, benzodioxolyl, benzodioxinyl, dihydrodioxinyl, dihydrobenzodioxinyl, dihydropyranyl, dioxinyl, chromenyl, and benzodioxinyl.

**[0031]** The "halogen" means -F, -Cl, -Br, or -I, and in another embodiment, -F, -Cl, or -Br.

**[0032]** The "halogeno-C<sub>1-6</sub> alkyl" is C<sub>1-6</sub> alkyl substituted with one or more halogen atoms, and specific examples

thereof include fluoromethyl, difluoromethyl, trifluoromethyl, trifluoroethyl, fluoroethyl, chloroethyl, bromoethyl, fluoro-propyl, dichloropropyl, fluorochloropropyl, and the like, and in another embodiment, difluoromethyl, trifluoromethyl, difluoroethyl, trifluoroethyl, and fluoropropyl.

**[0033]** In the present specification, the expression "which may be substituted" means unsubstituted or substituted with 1 to 5 substituents. Further, if it has a plurality of substituents, the substituents may be the same as or different from each other.

**[0034]** Specific examples of the substituent for the "C<sub>1-6</sub> alkyl which may be substituted", "C<sub>1-6</sub> alkylene which may be substituted", "(C<sub>3-8</sub>) cycloalkyl which may be substituted", "aryl which may be substituted", or "hetero ring which may be substituted" of R<sup>3</sup> and R<sup>4</sup> include amino, nitro, cyano, halogen, C<sub>1-6</sub> alkyl, halogeno-C<sub>1-6</sub> alkyl, -OH, -C<sub>1-6</sub> alkylene-OH, -O-C<sub>1-6</sub> alkyl, -C<sub>1-6</sub> alkylene-O-C<sub>1-6</sub> alkyl, -C<sub>1-6</sub> alkylene-cycloalkyl, -C<sub>1-6</sub> alkylene-aryl, -C<sub>1-6</sub> alkylene-hetero ring, -CO-C<sub>1-6</sub> alkyl, -CO-C<sub>1-6</sub> alkylene-O-C<sub>1-6</sub> alkyl, -CO-cycloalkyl, -CO-aryl, -CO-NR<sup>8</sup>R<sup>9</sup>, -CO-O-C<sub>1-6</sub> alkyl, -CO-O-C<sub>1-6</sub> alkylene-aryl, -SO<sub>2</sub>-C<sub>1-6</sub> alkyl, aryl, a hetero ring, and the like.

**[0035]** Here, R<sup>8</sup> and R<sup>9</sup> are the same or different and each represents -H or C<sub>1-6</sub> alkyl.

**[0036]** The present invention is directed to the following compounds:

11-cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline,  
4-(3-methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine,  
5-cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro [1,4]oxazino[2,3-h][3]benzazepine,

and salts thereof.

**[0037]** The compounds of the present invention may exist in the form of tautomers or geometrical isomers depending on the kind of substituents. In the present specification, the compounds of the present invention shall be described in only one form of isomer, yet the present invention includes other isomer, such as an isolated form of the isomers, or a mixture thereof.

**[0038]** In addition, the compounds of the present invention may have asymmetric carbon atoms or axial asymmetry in some cases, and correspondingly, it may exist in the form of optical isomers. The present invention includes both an isolated form of the optical isomers of the compounds of the present invention or a mixture thereof.

**[0039]** Moreover, the salt of the compound of the present invention is a pharmaceutically acceptable salt and may form an acid addition salt or a salt with a base depending on the kind of substituents. Specific examples thereof include acid addition salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid, and the like, and with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, mandelic acid, tartaric acid, dibenzoyltartaric acid, ditoluoyltartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, aspartic acid, glutamic acid, and the like, and salts with inorganic bases such as sodium, potassium, magnesium, calcium, aluminum, and the like or organic bases such as methylamine, ethylamine, ethanolamine, lysine, ornithine, and the like, salts with various amino acids or amino acid derivatives such as acetylleucine and the like, ammonium salts, etc.

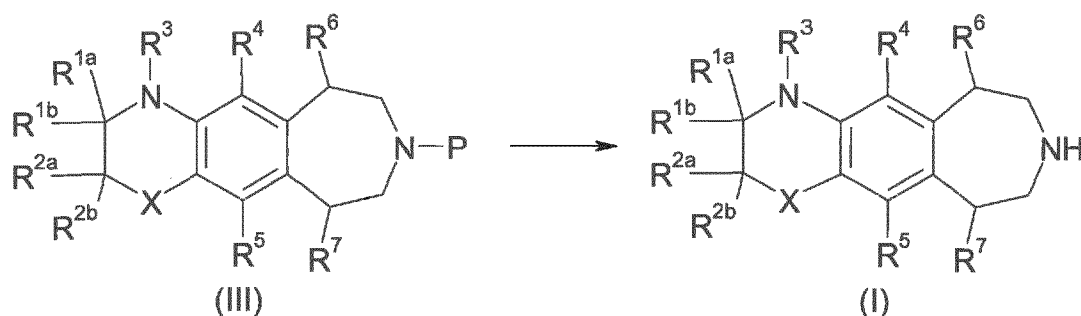
**[0040]** In addition, the present invention also includes various hydrates or solvates, and polymorphic crystal substances of the compounds of the the present invention and a salt thereof. In addition, the present invention also includes compounds labeled with various radioactive or non-radioactive isotopes.

(Preparation Methods)

**[0041]** The compounds of the present invention and salts thereof can be prepared using the characteristics based on the basic structure or the type of substituents thereof and by applying various known synthesis methods. During the preparation, replacing the relevant functional group with a suitable protective group (a group that can be easily converted into the functional group) at the stage from starting material to an intermediate may be effective depending on the type of the functional group in production technology in some cases. The protective group for such a functional group may include, for example, the protective groups described in "Greene's Protective Groups in Organic Synthesis (4<sup>th</sup> Ed., 2006)" written by P. G. M. Wuts and T. W. Greene, and one of these may be selected and used as necessary depending on the reaction conditions. In this kind of method, a desired compound can be obtained by introducing the protective group, by carrying out the reaction and by eliminating the protective group as necessary.

**[0042]** The compounds of the present invention and salts thereof may be prepared in accordance with the methods which are described below for reference purposes. Each of the production processes may also be carried out with reference to the References appended in the present description. Further, the preparation methods of the present invention are not limited to the examples as shown below.

[Chem. 6]



(wherein

R<sup>1a</sup> and R<sup>1b</sup> are the same or different and each represents -H or C<sub>1-6</sub> alkyl, or are combined to form oxo,  
 R<sup>2a</sup> and R<sup>2b</sup> are the same or different and each represents -H or C<sub>1-6</sub> alkyl which may be substituted with -O-C<sub>1-6</sub> alkyl,  
 R<sup>3</sup> represents -H, C<sub>1-6</sub> alkyl which may be substituted, C<sub>3-8</sub> cycloalkyl, aryl which may be substituted, -SO<sub>2</sub>-C<sub>1-6</sub>  
 alkyl, or a hetero ring which may be substituted,  
 R<sup>4</sup> represents -H, halogen, cyano, C<sub>1-6</sub> alkyl which may be substituted, C<sub>2-6</sub> alkenyl, aryl which may be substituted,  
 C<sub>3-8</sub> cycloalkyl which may be substituted, an aromatic hetero ring, or an oxygen-containing hetero ring,  
 R<sup>5</sup> represents -H, halogen, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> cycloalkyl, aryl, or an aromatic hetero ring,  
 R<sup>6</sup> and R<sup>7</sup> are the same or different and each represents -H or C<sub>1-6</sub> alkyl,  
 X represents -C(R<sup>A</sup>)(R<sup>B</sup>)- or -O-, and  
 R<sup>A</sup> and R<sup>B</sup> are the same or different and each represents -H or C<sub>1-6</sub> alkyl.)

**[0043]** The compound of the formula (I) can be obtained by removing P which is a protective group for an amino group. The protective group for P may be any protective group for an amino group which is usually used by a person skilled in the art, and carbonyl such as trifluoroacetyl and the like; oxycarbonyl such as t-butyloxycarbonyl, ethyloxycarbonyl, benzyloxycarbonyl, and the like; or sulfonyl such as methanesulfonyl, p-toluenesulfonyl, trifluoromethanesulfonyl, p-nitrophenylsulfonyl, 2,4-dinitrophenylsulfonyl, and the like is suitably used.

**[0044]** For the deprotection in the present step, the conditions for deprotection usually used by a person skilled in the art can be employed. For example, preparation can be performed by acid treatment, hydrolysis, hydrogenolysis, or the like. For acid treatment, for example, trifluoroacetic acid, hydrochloric acid, sulfuric acid, or the like can be used. In the case of alkali hydrolysis, inorganic bases (for example NaOH, KOH, NaHCO<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub>, and the like) can be used. In the case of acid hydrolysis, hydrochloric acid and the like can be used. For any reaction temperature, the reaction can be performed under the condition from under ice-cooling to under refluxing and under the condition which does not allow the substrate to be decomposed. As the solvent, dioxane, tetrahydrofuran, dichloromethane, chloroform, ethyl acetate, alcohols (MeOH, EtOH, and the like), N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO), water, or a mixed solvent thereof, and the like may be used, but are not limited thereto. In the case of hydrogenolysis, the reaction can usually be performed under a hydrogen atmosphere in the presence of a palladium catalyst. Usually, the reaction can be performed under the condition of from room temperature to under refluxing and under the condition which does not allow the substrate to be decomposed. As the solvent, DMF or alcohols (MeOH, EtOH, and the like) may be used, but are not limited thereto. Further, the conditions for the decarboxamide reaction, the de-carbamate reaction, the de-sulfonamide reaction described in "Greene's Protective Groups in Organic Synthesis (4<sup>th</sup> Ed., 2006)" above can be employed.

**[0045]** Various substituents defined as the groups in the compound of the formula (I), R<sup>1a</sup>, R<sup>1b</sup>, R<sup>2a</sup>, R<sup>2b</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> can be easily converted to other functional groups by using the compound of the formula (I) as a starting material or using the synthetic intermediate of the compound of the formula (I) as a starting material by means of the reaction described in Examples as described later, the reaction apparent to a person skilled in the art, or modified methods thereof. For example, the step that can be usually employed by a person skilled in the art, such as O-alkylation, N-alkylation, reduction, hydrolysis, amidation, and the like can be arbitrarily combined and performed.

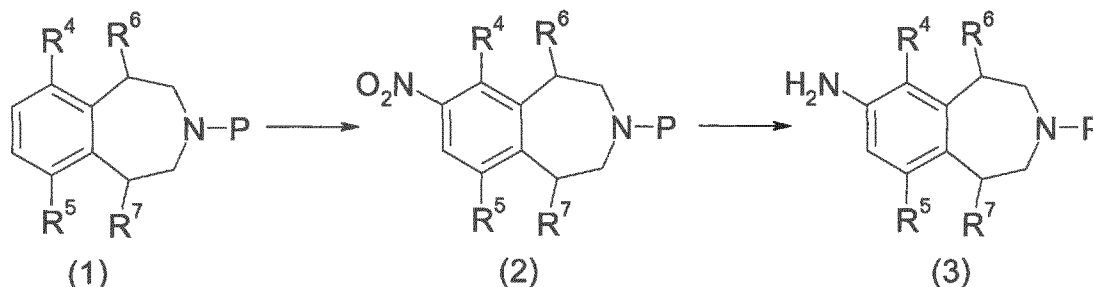
(Preparation of Starting Compound)

**[0046]** The starting compound in the preparation method above can be prepared by, for example, the following method, the method described in Preparation Examples as described later, known methods, or modified methods thereof.

(Starting Material Synthesis 1)

[0047]

[Chem. 7]

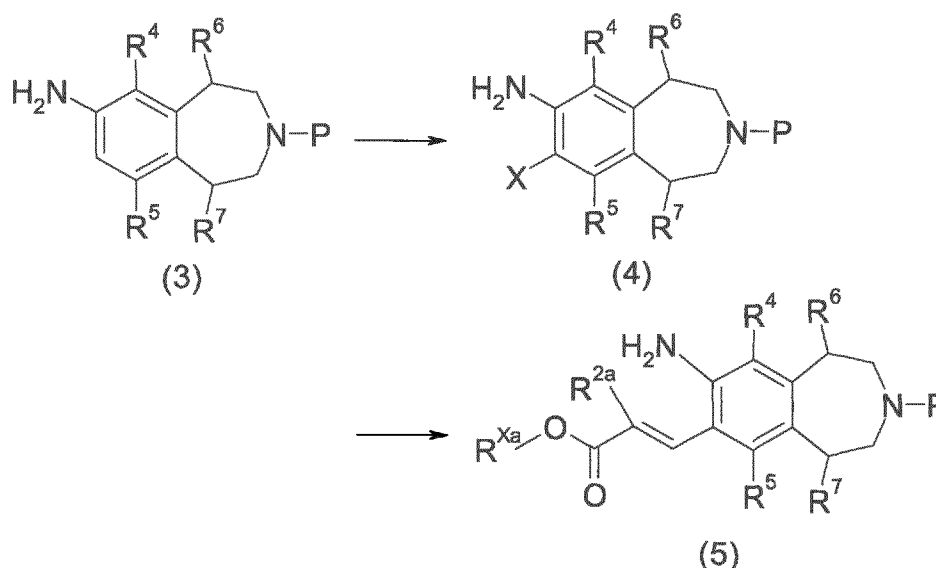


[0048] A compound represented by the general formula (1) which is a starting material for synthesizing a compound of the general formula (2) is commercially available or prepared by a means known to a person skilled in the art. Then, the compound of the general formula (2) can be prepared by nitrating the compound of the general formula (1). For example, a number of known nitration reactions can be used, examples of which include a method using nitric acid, fumed nitric acid, potassium nitrate, or the like in an acid solvent, a method using nitronium tetrafluoroborate, and the like. Then, the compound of the general formula (3) can be prepared by reducing a nitro group of the compound of the general formula (2) to an amino group. For example, a number of known reduction methods can be used, examples of which include a method using metal hydrides such as lithium aluminum hydride and the like, a method using reduced iron or the like, and the like. Further, catalytic hydrogenation using noble metal catalysts such as Raney nickel, palladium, ruthenium, rhodium, platinum, and the like can also be used.

(Starting Material Synthesis 2)

[0049]

[Chem. 8]

(wherein  $R^{Xa}$  is  $C_{1-6}$  alkyl).

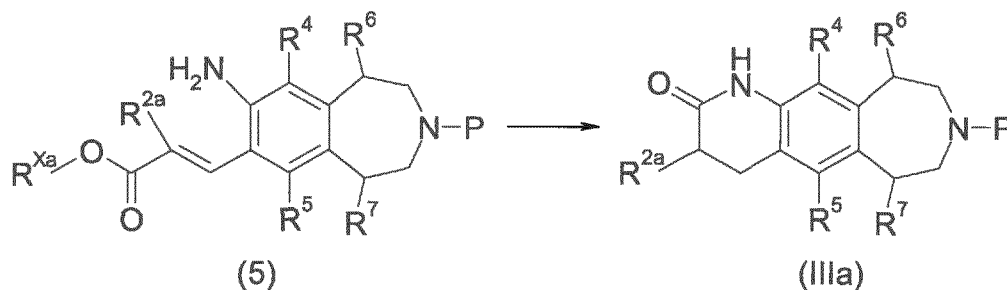
[0050] A compound of the general formula (4) can be prepared by halogenating the compound of the general formula (3). For example, a number of known halogenation reactions can be used, examples of which include a method using N-bromosuccinimide or N-chlorosuccinimide, and the like. Then, the compound of the general formula (5) can be prepared

from the compound of the general formula (4) by a coupling reaction using a transition metal catalyst. Examples of the coupling reaction include a Heck reaction. The reaction conditions for the Heck reaction vary depending on the starting materials, solvents, and transition metal catalysts used, and techniques known to a person skilled in the art can be used. Examples of the preferred solvent include acetonitrile, tetrahydrofuran, 1,4-dioxane or DMF, and the like, but are not limited thereto. The transition metal catalyst is preferably a palladium complex, and more preferably known palladium complexes such as palladium(II) acetate, dichlorobis(triphenylphosphine)palladium(II), tetrakis(triphenylphosphine)palladium(0), and the like. Further, for the present reaction, a phosphorous ligand (preferably, triphenylphosphine, tri-*o*-tolylphosphine, tri-*tert*-butylphosphine, 2-(di-*tert*-butylphosphino)biphenyl, or the like) may be added in order to obtain excellent results. Also, the present reaction can yield preferable results in the presence of a base, and the base used herein is not particularly limited as long as it is used for the coupling reaction of the present reaction, but it is preferably triethylamine, *N,N*-diisopropylethylamine, or the like.

(Starting Material Synthesis 3)

[0051]

[Chem. 9]



[0052] The compound of the general formula (IIIa) can be obtained by allowing an intramolecular amide condensation cyclization reaction to proceed by carrying out a hydrogenation reaction of the double bond of the  $\alpha,\beta$ -unsaturated esters of the compound of the general formula (5). In this reaction, the compound of the general formula (5) is stirred in the presence of a metal catalyst, usually for 1 hour to 5 days, in a solvent inert to the reaction, under a hydrogen atmosphere. This reaction is usually carried out in the range from cooling to heating, preferably at room temperature. Examples of the solvent used herein are not particularly limited, but include alcohols such as methanol, ethanol, 2-propanol, and the like, ethers such as diethylether, tetrahydrofuran, dioxane, dimethoxyethane, and the like, water, ethyl acetate, DMF, DMSO and a mixture thereof. As the metal catalyst, palladium catalysts such as palladium on carbon, palladium black, palladium hydroxide, and the like, platinum catalysts such as a platinum plate, platinum oxide, and the like, nickel catalysts such as reduced nickel, Raney nickel, and the like, rhodium catalysts such as tetrakis(triphenylphosphine)chlororhodium, and the like, iron catalysts such as reduced iron and the like, etc. are preferably used. Instead of hydrogen gas, formic acid or ammonium formate in an equivalent amount or in an excess amount to the compound of the general formula (5) can be used as a hydrogen source.

[0053] Furthermore, for the compound in which  $R^{2b}$  is other than -H, an  $R^{2b}$  group other than -H can be introduced to a desired position by using an electrophilic substitution reaction to the  $\alpha$ -position of carbonyl by the use of a base or by a method which can be usually employed by a person skilled in the art for the compound (IIIa).

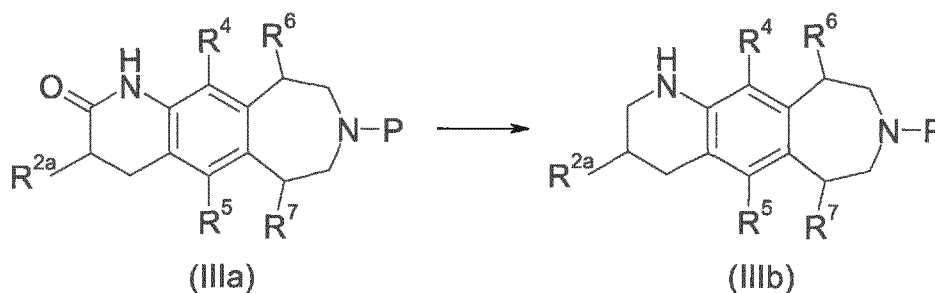
[References]

[0054] "Reductions in Organic Chemistry, 2nd Ed. (ACS Monograph: 188)" written by M. Hudlicky, ACS, 1996

(Starting Material Synthesis 4)

[0055]

[Chem. 10]

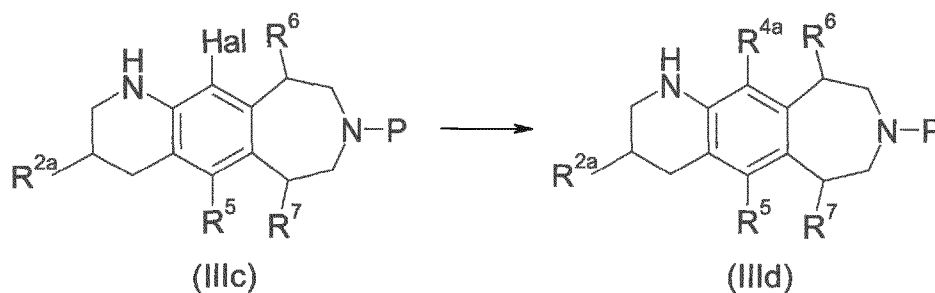


**[0056]** A compound of the general formula (IIIb) can be obtained by carrying out reduction of a carbonyl group of the compound of the general formula (IIIa). This reaction is usually carried out in the presence of a reducing agent in a solvent. Examples of the solvent used herein are not particularly limited, but include ethers such as diethylether, tetrahydrofuran, dioxane, dimethoxyethane, and the like, and aromatic hydrocarbons such as benzene, toluene, xylene, and the like. Examples of the reducing agent include aluminum hydride compounds such as lithium aluminum hydride, sodium bis(2-methoxyethoxy)aluminum hydride, and the like, and borohydride compounds such as sodium borohydride, diborane, a borane-tetrahydrofuran complex, and the like.

(Starting Material Synthesis 5)

**[0057]**

[Chem. 11]



(wherein  $R^{4a}$  represents  $C_{1-6}$  alkyl, halogeno- $C_{1-6}$  alkyl, cycloalkyl which may be substituted, or aryl which may be substituted, and Hal represents halogen).

**[0058]** A compound of the general formula (IIId) can be obtained by a coupling reaction of a compound of the general formula (IIIc). For example, the Suzuki coupling described in the following references, the Heck reaction described for the Starting Material Synthesis 2 above, or the like can be employed.

[References]

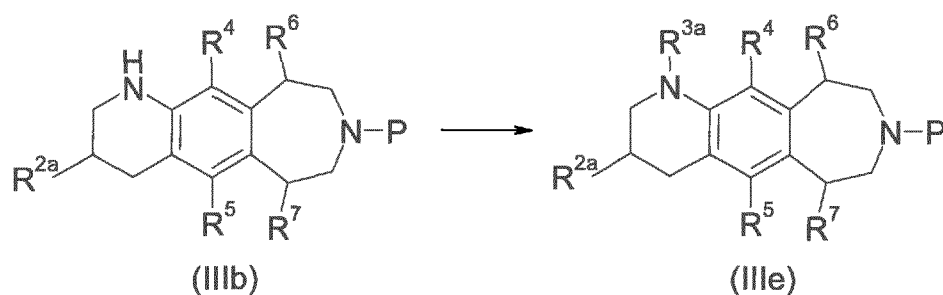
**[0059]** Chemical Reviews, vol. 95, No. 7, p. 2457 (1995), Journal of American Chemical Society, vol. 127, p. 4685 (2005), Synlett, No. 13, p. 2327 (2004), Tetrahedron letters, No. 41, p. 4363 (2000), or Tetrahedron letters, No. 43, p. 2695 (2002)

**[0060]** The compound of the general formula (IIId) can also be obtained by the method described in Examples as described later.

(Starting Material Synthesis 6)

**[0061]**

[Chem. 12]



(wherein R<sup>3a</sup> represents a group other than -H among the groups defined as R<sup>3</sup>).

**[0062]** A compound of the general formula (IIIe) can be obtained by alkylation, acylation, or the like of the compound of the general formula (IIIb). For the specific reaction conditions, the conditions described in the following references can be employed.

[References]

**[0063]**

"Organic Functional Group Preparations" written by S. R. Sandler and W. Karo, 2nd Ed., vol. 1, Academic Press Inc., 1991

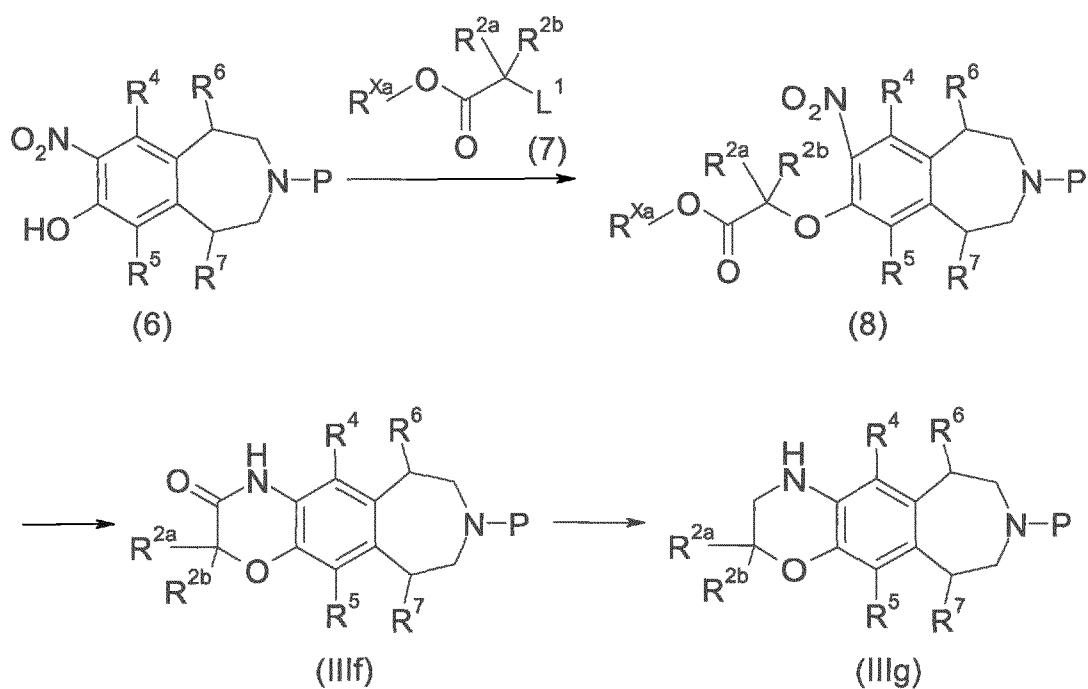
"Courses in Experimental Chemistry (5th Ed.)", edited by The Chemical Society of Japan, vol. 14 (2005) (Maruzen)

**[0064]** The compound of the general formula (IIIe) can also be obtained by the method described in the Examples as described later and the method described for the Starting Material Synthesis 4 above.

(Starting Material Synthesis 7)

**[0065]**

[Chem. 13]



**[0066]** A compound of the general formula (8) can be obtained by the reaction of a compound of the general formula (6) with a compound of the general formula (7). In this regard, examples of the leaving group of  $L^1$  include halogen, methanesulfonyloxy, p-toluenesulfonyloxy groups, and the like.

**[0067]** In this reaction, the compound of the general formula (6) and the compound of the general formula (7) are used in equivalent amounts, or with either one of them in an excess amount, and a mixture thereof is stirred under a temperature condition from cooling to heating and refluxing, preferably at 0°C to 80°C, usually for 0.1 hours to 5 days, in a solvent inert to the reaction in the presence of a base. Examples of the solvent used herein are not particularly limited, but include aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethylether, tetrahydrofuran, dioxane, dimethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, DMF, DMSO, ethyl acetate, acetonitrile, and a mixture thereof. Examples of the base include organic bases such as triethylamine, N,N-diisopropylethylamine, 1,8-diazabicyclo[5.4.0]-7-undecene, n-butyllithium, and the like, and inorganic bases such as sodium carbonate, potassium carbonate, sodium hydride, potassium tert-butoxide, and the like. It may be advantageous to carry out a reaction in the presence of a phase transfer catalyst such as tetra-n-butylammonium chloride and the like in some cases.

**[0068]** A compound of the general formula (III<sub>f</sub>) can be obtained by the method described in the Starting Material Synthesis 3 above and a compound of the general formula (III<sub>g</sub>) can be obtained by the method described in the Starting Material Synthesis 4 above.

[References]

**[0069]**

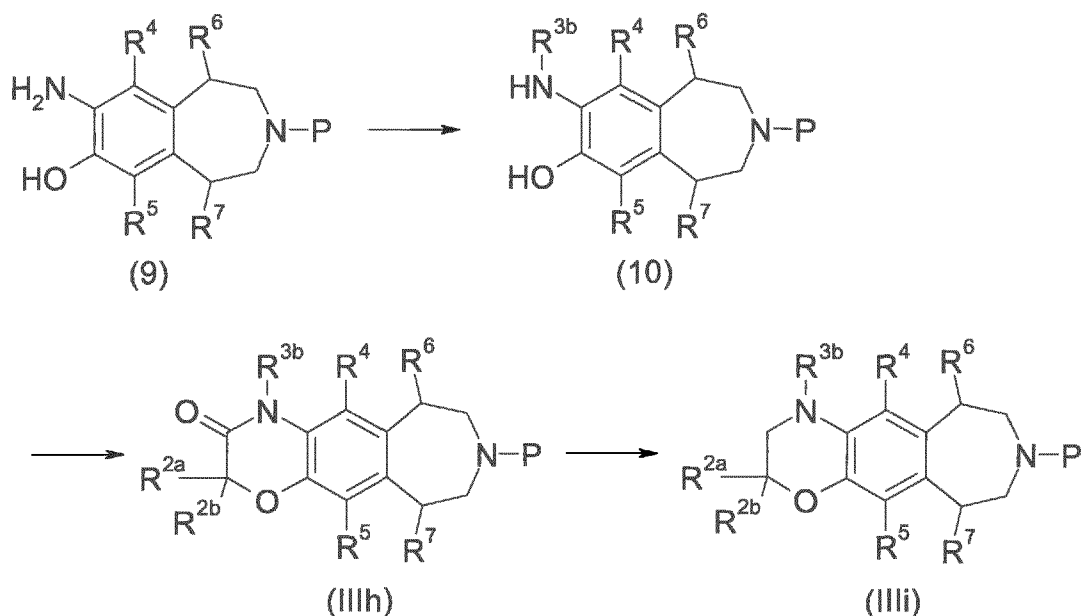
"Organic Functional Group Preparations" written by S. R. Sandler and W. Karo, 2nd Ed., vol. 1, Academic Press Inc., 1991

"Courses in Experimental Chemistry (5th Ed.)", edited by The Chemical Society of Japan, vol. 14 (2005) (Maruzen)

(Starting Material Synthesis 8)

**[0070]**

[Chem. 14]



(wherein  $R^{3b}$  represents  $C_{1-6}$  alkyl which maybe substituted,  $C_{3-8}$  cycloalkyl, aryl which may be substituted, or a hetero ring which may be substituted, among the groups defined as  $R^3$ . Further, among the  $C_{1-6}$  alkyl which may be substituted, one having oxo substituted on a carbon atom directly bonded to a nitrogen atom connected with  $R^{3b}$  is excluded).

**[0071]** The compound of the general formula (10) can be obtained by using the compound of the general formula (9)

and a suitable aldehyde or ketone compound in equivalent amounts, and stirring a mixture thereof under a temperature condition from -45°C to heating and refluxing, preferably at 0°C to room temperature, usually for 0.1 hours to 5 days, in a solvent inert to the reaction in the presence of a reducing agent. Examples of the solvent used herein are not particularly limited, but include alcohols such as methanol, ethanol, and the like, ethers such as diethylether, tetrahydrofuran, dioxane, dimethoxyethane, and the like, and a mixture thereof. Examples of the reducing agent include sodium cyanoborohydride, sodium triacetoxyborohydride, sodium borohydride, and the like. It is preferable in some cases to carry out the reaction in the presence of a dehydrating agent such as molecular sieves, and the like or an acid such as acetic acid, hydrochloric acid, a titanium(IV) isopropoxide complex, and the like. Further, the reaction can be carried out in a solvent such as methanol, ethanol, ethyl acetate, and the like, in the presence or absence of an acid such as acetic acid, hydrochloric acid, and the like, using a reduction catalyst (for example, palladium on carbon, Raney nickel, and the like), instead of treatment with the reducing agent. In this case, it is preferable to carry out the reaction under a hydrogen atmosphere from normal pressure to 50 atmospheres under a temperature condition ranging from cooling to heating.

**[0072]** A compound of the general formula (IIIh) can be obtained by using the compound of the general formula (10) and a suitable halogenocarboxylic ester and reacting them in the presence of a base.

**[0073]** The compound of the general formula (IIIi) can be obtained by using the method described in the Starting Material Synthesis 4 above and carrying out reduction of a carbonyl group of the compound of the general formula (IIIh).

[References]

**[0074]**

"Comprehensive Organic Functional Group Transformations II" written by A. R. Katritzky and R. J. K. Taylor, vol. 2, Elsevier Pergamon, 2005

"Courses in Experimental Chemistry (5th Ed.)", edited by The Chemical Society of Japan, vol. 14 (2005) (Maruzen)

**[0075]** The compounds of the formula (I) can be isolated and purified as their free compounds, salts, hydrates, solvates, or polymorphic crystal substances thereof. The salts of the compound of the formula (I) can be prepared by carrying out the treatment of a conventional salt forming reaction.

**[0076]** Isolation and purification are carried out by employing ordinary scientific operations such as extraction, fractional crystallization, various types of fractional chromatography, and the like.

**[0077]** Various isomers can be prepared by selecting an appropriate starting compound or separated by using the difference in the physicochemical properties between the isomers. For example, the optical isomers can be obtained by means of a general method for designing optical resolution of racemic products (for example, fractional crystallization for inducing diastereomer salts with optically active bases or acids, chromatography using a chiral column or the like, and others), and further, the isomers can also be prepared from an appropriate optically active starting material.

**[0078]** The pharmacological activity of the compounds of the present invention was confirmed by the tests shown below.

Test Example 1 Evaluation of 5-HT<sub>2C</sub> Receptor Agonist Activity

**[0079]** The agonist activity of the compounds of the present invention on the 5-HT<sub>2C</sub> receptor was confirmed by the method shown below.

**[0080]** The human 5-HT<sub>2C</sub> receptor agonist activity was evaluated by measuring the increase of the ligand-dependent intracellular calcium concentration. CHO cells which stably expressing a human 5-HT<sub>2C</sub> receptor were used. The receptor-expressing cells were prepared by transfecting the genes of the human 5-HT<sub>2C</sub> receptor (Accession numbers: AF498983 (5-HT<sub>2C</sub>)) into CHO cells (dihydrofolic acid-deficient strain, DS Pharma Biomedical Co., Ltd.) using a pEF-BOS vector (Nucleic Acids Research, vol. 18, No. 17). After transcription, the 5-HT<sub>2C</sub> is known to be subjected to RNA editing to cause differences in three kinds of amino acids, resulting in fourteen receptor isoforms. Among them, cells stably expressing an INI type of 5-HT<sub>2C</sub> receptor which had not been subjected to editing were used. Cells used for evaluation were cultured in a 10% fetal bovine serum (FBS)-containing medium (trade name:  $\alpha$ -MEM, Invitrogen) at 37°C and 5% carbon dioxide. On the day before the evaluation, the cells were suspended in a serum-free medium (trade name: CD-CHO, Invitrogen) containing 8 mM L-glutamine (trade name: L-glutamine 200 mM, Invitrogen, added to the medium at a final concentration of 8 mM) and dispensed into a 96-well poly-D-lysine-coated plate (trade name: Biocoat PDL96W Black/Clear, Japan Becton, Dickinson and Company)) at  $4 \times 10^4$  cells/well and cultured at 37°C and 5% carbon dioxide overnight. A solution including a washing solution (mixture of Hank's Balanced Salt Solution (HBSS)-sodium hydroxide (NaOH), 20 mM 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid (HEPES)-sodium hydroxide (NaOH), 2.5 mM probenecid, and 0.1% bovine serum albumin (BSA)), and a 4  $\mu$ M fluorescent reagent (trade name: Fluo4-AM, Dojindo Co., Ltd.) was used as a loading buffer and the medium of the 96-well plate which had been cultured overnight was replaced with a loading buffer. After leaving to stand (with light-shielding) at room temperature for 3 hours, the cells were

washed with a plate washer (trade name: ELx405, BioTek Instruments, Inc.) in which a washing solution had been set up. The plates of the washed cells were set up in a system for measuring a calcium (Ca) concentration in a cell (trade name: FLIPR, Molecular Devices, Inc.). In this device, a test compound that had been dissolved in dimethyl sulfoxide and diluted in the washing solution at a predetermined concentration was added and set up to measure a change in the Ca concentrations in a cell. The difference between a maximum value and a minimum value in the change of the intracellular Ca concentration was determined and kept as measurement data.

**[0081]** Taking the maximum reaction of the 5-HT (agonist action with addition of 5-HT 10  $\mu$ M) as 100% and the reaction of a solvent alone as 0%, efficacy (Emax (%)) of the present invention compound to the maximum reaction of the 5-HT was obtained and potency (EC50 (nM)) was calculated with a logistic regression method, as the agonist activity.

**[0082]** The results of several compounds are shown in Table 1. In the Table, Ex represents Example Compound No. below.

[Table 1]

| Ex | 5-HT <sub>2C</sub> agonist activity |          |
|----|-------------------------------------|----------|
|    | EC50 (nM)                           | Emax (%) |
| 1  | 7.1                                 | 108      |
| 2  | 0.84                                | 114      |
| 3  | 0.53                                | 96       |

#### Test Example 2 Measurement of External Urethral Sphincter Electromyography

**[0083]** The activating action of the compounds of the present invention on the urethral sphincter electromyography was confirmed with the method shown below.

**[0084]** Hartley female guinea pigs with a body weight of 250 to 350 g were anesthetized with urethane (Sigma). The guinea pigs were fixed in a supine position and catheters (PE-50; Clay Adams) for administration of test compounds were inserted into the jugular vein. Further, a catheters (PE-160; Clay Adams), for an infusion of physiological saline into bladder and measurement of the intravesical pressure, were inserted through an incision into the dome of the bladder. Further, in order to measure the external urethral sphincter electromyography, two electrodes were inserted into both the left and right sides of the urethral opening to the urethral sphincter. The electrodes for measuring base voltages were placed under the skin of the hind part. The bladder catheter was branched over a three-way stopcock, and one was connected with a 50 mL syringe (Terumo) fixed to an infusion pump (Terumo). The other was connected to a pressure transducer (DX-100; Nihon Kohden Corporation) to transfer the signal of the transducer through an amplifier (AP-630G; Nihon Kohden Corporation) and a data acquisition system (PowerLab; AD Instruments) to a computer and record on a hard disk. The electrodes for electromyography measurement were connected to a control unit (JB-101J; Nihon Kohden Corporation) to transfer the signal through an amplifier (AP-651J; Nihon Kohden Corporation) and a data acquisition system (PowerLab; AD Instruments) to a computer and record on a hard disk. Further, the data were analyzed on the computer using a software (Chart; AD Instruments). Physiological saline was continuously injected into the bladder using an infusion pump at a rate of 18 mL/hour and it was confirmed that a micturition reflexes were stably induced. The electromyography activity was analyzed by taking the lowest potential amplitude as a standard during the stabilization period and using the firing frequency over the standard amplitude as an indicator. At intervals between the respective urinations (urine filling phase), the activity of the urethral sphincter electromyography was analyzed and its average value was calculated. After the stabilization period, the solvent and the test compound were administered at an increased dose at an interval of 40 minutes through the catheter placed into the jugular vein. The urethral sphincter electromyography activity after the administration of the solvent was taken as 100% and the urethral sphincter electromyography activity after the administration of the test compound was denoted as a percentage (%) of the electromyography activity after the administration of the solvent.

**[0085]** As a result, the compounds of Examples 1 to 3 as shown later showed an external urethral sphincter electromyography activity of 200% or more with intravenous administration at 3 mg/kg.

**[0086]** As a result of each test above, it was confirmed that the compounds of the present invention have a 5-HT<sub>2C</sub> receptor agonist activity, and can be used for treatment or prevention of 5-HT<sub>2C</sub> receptor-related diseases, particularly incontinence such as stress urinary incontinence, urge urinary incontinence, mixed urinary incontinence, and the like, sexual dysfunction such as erectile dysfunction syndrome and the like, obesity, and the like as a pharmaceutical.

**[0087]** According to the results obtained by the tests above, it is considered that the compounds have a 5-HT<sub>2C</sub> receptor agonist activity and thus have substantially the same or a higher activity value than Lorcaserin under development as an anti-obesity drug (The Journal of Pharmacology and Experimental Therapeutics vol. 325, No. 2 p. 577-587 (2008)).

**[0088]** A pharmaceutical composition containing one or two or more kinds of the compound of the present invention or a salt thereof as an active ingredient can be prepared using excipients that are usually used in the art, that is, excipients for pharmaceutical preparation, carriers for pharmaceutical preparation, and the like according to the methods usually used.

**[0089]** Administration can be accomplished either by oral administration via tablets, pills, capsules, granules, powders, solutions, and the like, or parenteral administration injections, such as intraarticular, intravenous, or intramuscular injections, and the like, suppositories, ophthalmic solutions, eye ointments, transdermal liquid preparations, ointments, transdermal patches, transmucosal liquid preparations, transmucosal patches, inhalations, and the like.

**[0090]** The solid composition for oral administration is used in the form of tablets, powders, granules, or the like. In such a solid composition, one or more active ingredient(s) are mixed with at least one inactive excipient. According to a usual method, the composition may contain inactive additives, such as lubricants, disintegrating agents, stabilizing agents, and solubilization assisting agents. If necessary, tablets or pills may be coated with sugar or a film of a gastric or enteric coating substance.

**[0091]** The liquid composition for oral administration contains pharmaceutically acceptable emulsions, solutions, suspensions, syrups, elixirs, or the like, and also contains generally used inert diluents, for example, purified water or ethanol. In addition to the inert diluent, the liquid composition may also contain auxiliary agents, such as a solubilization assisting agent, a moistening agent, and a suspending agent, as well as sweeteners, flavors, aromatics, and antiseptics.

**[0092]** The injections for parenteral administration contain sterile aqueous or non-aqueous solutions, suspensions, or emulsions. Examples of the aqueous solvent include distilled water for injection use and physiological saline. Examples of the non-aqueous solvent include alcohols such as ethanol. Such a composition may further contain a tonicity agent, an antiseptic, a moistening agent, an emulsifying agent, a dispersing agent, a stabilizing agent, and a solubilization assisting agent. These are sterilized by filtration through a bacteria retaining filter, blending of a germicide, or irradiation. Furthermore, they may also be prepared in the form of sterile solid compositions and dissolved or suspended in sterile water or a sterile solvent for injecting prior to their use.

**[0093]** Examples of the formulation for external use include ointments, plasters, creams, jellies, patches, sprays, lotions, eye-drops, eye ointments, and the like. The drug contains generally used ointment bases, lotion bases, aqueous or non-aqueous liquid preparations, suspensions, emulsions, or the like.

**[0094]** Transmucosal agents such as inhalers, transnasal agents, and the like are used in the form of solids, liquids, or semisolids and can be prepared according to conventional known methods. For example, known excipients, and further, pH adjusters, antiseptics, surfactants, lubricants, stabilizing agents, thickeners, or the like may also be added where appropriate. For administration, suitable devices for inhalation or insufflation can be used. For example, using known devices and sprayers such as a metered dose inhaler, the compound can be administered independently or in the form of prescribed mixture powders. Furthermore, the compound combined with pharmaceutically acceptable carriers can also be administered in the form of solutions or suspensions. Dry powder inhalers and the like may be devices for single or multiple administrations, and dry powders or capsules containing powders can also be used. Still further, the devices may be in the form of a pressure aerosol spray or the like that use suitable ejection agents, for example, chlorofluoroalkane, hydrofluoroalkane, or a suitable gas such as carbon dioxide and the like.

**[0095]** Usually, in the case of oral administration, the daily dose is suitably from 0.001 to 100 mg/kg per body weight, preferably from 0.1 to 30 mg/kg, and more preferably from 0.1 to 10 mg/kg, and this is administered in one portion or dividing it into 2 to 4 portions. In the case of intravenous administration, the daily dose is suitably from about 0.0001 to 10 mg/kg per body weight, and this is administered once a day or two or more times a day. In addition, a transmucosal agent is administered at a dose from about 0.001 to 100 mg/kg per body weight, and this is administered once a day or two or more times a day. The dose is appropriately decided in response to an individual case by taking the symptoms, the age, the gender, and the like into consideration.

**[0096]** Although varying depending on administration routes, dosage forms, administration sites, or the types of excipients and additives, the pharmaceutical composition of the present invention contains 0.01 to 100% by weight, and in a certain embodiment, 0.01 to 50% by weight of one or more kinds of the compound of the present invention or a salt thereof, which is an active ingredient.

**[0097]** The compound of the present invention or a salt thereof can be used in combination with various agents for treating or preventing the diseases, in which it is considered effective, as described above. The combined preparation may be administered simultaneously or separately and continuously, or at a desired time interval. The preparations to be co-administered may be prepared individually, or may be a pharmaceutical composition including various agents and the compound of the present invention or a salt thereof.

[Examples]

**[0098]** Hereinbelow, the preparation methods for the compounds of the present invention and salts thereof and the starting compounds thereof will be described in more detail. Furthermore, the production processes for the starting

compounds will be described in Preparation Examples. The preparation methods for the compounds of the present invention and salts thereof are not limited to the preparation methods of the specific Examples as below, and these compounds can be prepared by any combination of the preparation methods or the methods that are apparent to a person skilled in the art.

**[0099]** Furthermore, the following abbreviations may be used in some cases in the Preparation Examples, Examples, and Tables below.

**[0100]** PEx: Preparation Example No., Ex: Example No., PSyn: Preparation Example No. prepared by the same method, Syn: Example No. prepared by the same method, No: Compound No., Str: Structural formula, Dat: Physico-chemical Data, EI: m/z values in mass spectroscopy (ionization EI, representing (M)<sup>+</sup> unless otherwise specified), ESI+: m/z values in mass spectroscopy (ionization ESI, representing (M+H)<sup>+</sup> unless otherwise specified), FAB+: m/z values in mass spectroscopy (ionization FAB, representing (M+H)<sup>+</sup> unless otherwise specified), FAB-: m/z values in mass spectroscopy (ionization FAB, representing (M-H)<sup>-</sup> unless otherwise specified), APCI+: m/z values in mass spectroscopy (ionization APCI, representing (M+H)<sup>+</sup> unless otherwise specified), NMR:  $\delta$  (ppm) in <sup>1</sup>H NMR in DMSO-d<sub>6</sub>, s: singlet (spectrum), d: doublet (spectrum), t: triplet (spectrum), mp: melting point (°C).

**[0101]** Me: methyl, Et: ethyl, iPr: isopropyl, iBu: isobutyl, cPr: cyclopropyl, Boc: t-butoxycarbonyl, MeOH: methanol, EtOH: ethanol, EtOAc: ethyl acetate, HEX: n-hexane, DMF: N,N-dimethylformamide, THF: tetrahydrofuran.

**[0102]** A case where the structural formula of fumaric acid is described together in the structural formula indicates that the Example compound is isolated as fumarate.

**[0103]** Furthermore, in the Example Compounds in which the structural formula of fumaric acid is described together in the structural formula, "M" described under the Example No. indicates that the Example Compound is isolated as monofumarate.

**[0104]** Furthermore, for the sake of convenience, a concentration mol/l is expressed as M. For example, a 1 M aqueous sodium hydroxide solution means a 1 mol/l aqueous sodium hydroxide solution.

#### Preparation Example 5

**[0105]** A solution of 11.86 g of ethyl 6-chloro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 30 ml of chloroform was ice-cooled, and while maintaining the inner temperature at 10°C or lower, 60 ml of concentrated sulfuric acid was added thereto. Then, 3.2 ml of concentrated nitric acid was added dropwise thereto, followed by stirring for 30 minutes. The reaction mixture was poured into ice, followed by extraction with chloroform, the organic layer was dried over anhydrous sodium sulfate and then filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 6.442 g of ethyl 6-chloro-7-nitro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a reddish orange viscous substance and 5.201 g of ethyl 6-chloro-9-nitro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a pale yellow solid.

#### Preparation Example 7

**[0106]** To a solution of 5.74 g of ethyl 7-amino-6-chloro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 100 ml of dichloromethane was added portionwise 3.9 g of N-bromosuccinimide under ice-cooling, followed by stirring for 40 minutes. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 5.769 g of ethyl 7-amino-8-bromo-6-chloro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a brown solid.

#### Preparation Example 8

**[0107]** To a solution of 4.37 g of ethyl 7-amino-8-bromo-6-chloro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 40 ml of DMF were added 2.1 ml of ethyl acrylate, 230 mg of tris-o-tolylphosphine, 85 mg of palladium(II) acetate, and 3.6 ml of triethylamine, followed by stirring at 120°C for 3 hours. The reaction mixture was diluted with EtOAc, washed with water and saturated brine, dried over anhydrous sodium sulfate, and then filtered, and the filtrate was concentrated under reduced pressure. The resulting yellow solid was stirred and washed in diisopropylether to obtain 3.125 g of ethyl 7-amino-6-chloro-8-[(1E)-3-ethoxy-3-oxoprop-1-en-1-yl]-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a pale yellow solid.

#### Preparation Example 9

**[0108]** To a solution of 2.12 g of ethyl 7-amino-6-chloro-8-[(1E)-3-ethoxy-3-oxoprop-1-en-1-yl]-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 20 ml of chloroform and 20 ml of MeOH was added 65 mg of platinum(IV) oxide, followed by stirring for 20 hours at 1 atm under a hydrogen atmosphere. The reaction mixture was filtered through celite and the

filtrate was concentrated under reduced pressure to obtain 2.256 g of ethyl 11-chloro-2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate as a milky white solid.

#### Preparation Example 11

**[0109]** To a solution of 1.772 g of t-butyl 11-chloro-2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 10 ml of THF was added 10.1 ml of a 1 M solution of a borane-THF complex in THF under ice-cooling, followed by elevating to room temperature and stirring for 3 hours. To the reaction mixture was added dropwise 10 ml of EtOH, and subsequently 10 ml of a 1 M aqueous sodium hydroxide solution was added dropwise thereto, followed by stirring. The mixed solution was diluted with water, followed by extraction with EtOAc. The organic layer was dried over anhydrous sodium sulfate and then filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 2.0707 g of t-butyl 11-chloro-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate as a colorless viscous substance.

#### Preparation Example 14

**[0110]** To a solution of 1.75 g of 2,3,4,5-tetrahydro-1H-3-benzazepine in 20 ml of dichloromethane was added 2.884 ml of pyridine. The reaction mixture was ice-cooled, and 1.705 ml of ethyl chloroformate which had been dissolved in 5 ml of dichloromethane was added dropwise thereto, followed by stirring overnight. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 2.15 g of ethyl 1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a pale yellow oily substance.

#### Preparation Example 15

**[0111]** 287 mg of ethyl 2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate was dissolved in 5 ml of DMF, and 65 mg of 60% sodium hydride was added thereto in an ice-bath, followed by stirring for 1 hour. 0.3 ml of methyl iodide was added thereto, followed by stirring at room temperature for 3 hours. Then, a saturated aqueous sodium hydrogen carbonate solution was added thereto, followed by extraction with chloroform. The solvent was concentrated under reduced pressure and the residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 94 mg of ethyl 1-methyl-2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate as a colorless solid.

#### Preparation Example 71

**[0112]** To 5 g of ethyl 2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate were added 40 ml of ethylene glycol and 28 ml of a 4 M aqueous sodium hydroxide solution, followed by stirring at 150°C. After stirring overnight, the reaction mixture was ice-cooled, then acidified by the addition of concentrated hydrochloric acid, and stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and then the residue was alkalified by the addition of a 1 M aqueous sodium hydroxide solution, followed by extraction with chloroform. The solvent was concentrated under reduced pressure and then the resulting dark brown residue was dissolved in dichloromethane, followed by addition of 4 g of di-t-butyl dicarbonate and 3.5 ml of triethylamine. The reaction mixture was stirred at room temperature overnight and concentrated under reduced pressure, and the residue was purified by silica gel chromatography (elution solvent: chloroform-MeOH) to obtain 3.39 g of t-butyl 2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

#### Preparation Example 17

**[0113]** To a solution of 250 mg of t-butyl 1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 2.5 ml of dichloroethane were added 0.175 ml of isobutyryl chloride and 0.4 ml of triethylamine, followed by elevating the temperature to 60°C and stirring for 30 minutes. The reaction mixture was diluted with EtOAc and washed with 1 M hydrochloric acid, water, a 1 M aqueous sodium hydroxide solution, and saturated brine, and the solvent was concentrated. To the resulting residue was added 2 ml of THF and 3.5 ml of a 1 M solution of a borane-THF complex in THF was added thereto in an ice-bath, followed by stirring at room temperature overnight. The reaction mixture was ice-cooled, and EtOH was added thereto, followed by stirring at room temperature for 30 minutes. The reaction mixture was concentrated and the resulting residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 213 mg of t-butyl 1-isobutyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

## Preparation Example 18

**[0114]** To a solution of 460 mg of t-butyl 11-bromo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 9 ml of dioxane were added 1.6 ml of a 2 M aqueous potassium carbonate solution under an argon atmosphere, and subsequently 449 mg of trimethylboroxine and 70 mg of tetrakis(triphenyl)phosphine palladium, followed by stirring at 90°C for 13 hours. The reaction mixture was allowed to cool, filtered, and then concentrated under reduced pressure, the resulting residue was diluted with EtOAc, and the organic layer was washed with water and saturated brine. The solvent was evaporated under reduced pressure and the resulting residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 380 mg of t-butyl 11-methyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

## Preparation Example 19

**[0115]** To a solution of 670 mg of t-butyl 11-isopropenyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 10 ml of MeOH was added 200 mg of palladium on carbon, followed by stirring at room temperature for 3.5 hours at normal pressure under a hydrogen atmosphere. Further, after stirring overnight at 4.5 atm under a hydrogen atmosphere, the reaction mixture was filtered through celite, and the solvent was evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 512 mg of t-butyl 11-isopropyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

## Preparation Example 20

**[0116]** To a solution of 140 mg of t-butyl 11-ethyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 1.86 ml of acetonitrile was added 0.12 ml of glycidylmethylether, followed by substitution with argon. In an ice-bath, 9 mg of ytterbium(III) trifluoromethanesulfonate was added thereto, followed by stirring at room temperature for 2 hours, then elevating the temperature to 50°C, and stirring overnight. To the reaction mixture were added EtOAc and aqueous sodium bicarbonate, and the organic layer was washed with water and saturated brine. The solvent was evaporated under reduced pressure and the resulting residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 147 mg of t-butyl 11-ethyl-1-(2-hydroxy-3-methoxypropyl)-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

## Preparation Example 22

**[0117]** To a solution of 828 mg of t-butyl 7-hydroxy-6-methyl-8-nitro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 25 ml of DMF were added 0.268 ml of methyl bromoacetate and 390 mg of potassium carbonate, followed by stirring at 55°C for 13 hours. The reaction mixture was allowed to cool, and water added, followed by extraction with EtOAc twice. The combined organic layer was washed with saturated brine, the organic layer was dried over anhydrous sodium sulfate and then filtered, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 1.076 g of t-butyl 7-(2-methoxy-2-oxoethoxy)-6-methyl-8-nitro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate as a yellowish white solid.

## Preparation Example 23

**[0118]** To a mixture of 967 mg of t-butyl 7-(2-methoxy-2-oxoethoxy)-6-methyl-8-nitro-1,2,4,5-tetrahydro-3H-3-benzazepine-3-carboxylate in 25 ml of EtOH was added 97 mg of 10% palladium on carbon under an argon atmosphere, followed by stirring for 2 hours at normal pressure under a hydrogen atmosphere. To the reaction mixture was added 200 ml of THF, then the catalyst was removed using celite, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel chromatography (elution solvent: HEX-EtOAc) to obtain 629 mg of t-butyl 11-methyl-3-oxo-3,4,6,7,9,10-hexahydro[1,4]oxazino[2,3-h][3]benzazepine-8(2H)-carboxylate as a white solid.

## Preparation Example 411

**[0119]** To a solution of t-butyl 1-(3-methoxypropyl)-2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate in 4.2 ml of acetonitrile were added 107 mg of N-bromosuccinimide and 3.7 mg of ammonium nitrate, followed by stirring at room temperature for 3.5 hours. The reaction mixture was concentrated to about 1/4, and ethyl acetate, an aqueous sodium thiosulfate solution, and aqueous sodium bicarbonate was added thereto. The organic layer was washed with saturated brine and then dried over anhydrous magnesium sulfate. The solvent was evaporated to obtain 198 mg of t-butyl 11-bromo-1-(3-methoxypropyl)-2-oxo-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate.

boxylate.

**[0120]** In the same manner as in the methods of Preparation Examples above, the compounds of Preparation Examples as shown in the Tables below were prepared. For the compounds of the Preparation Examples, the structures are shown in Tables 2 to 6 and the preparation methods and the physicochemical data are shown in Table 7.

#### Example A

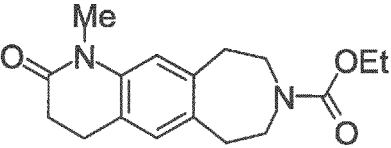
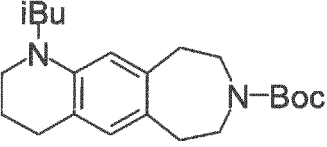
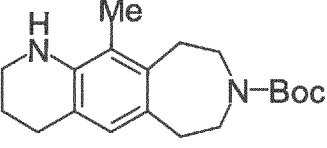
**[0121]** To 47 mg of 11-chloro-1-isobutyl-1,2,3,4,6,7,9,10-octahydro-8H-azepino[4,5-g]quinoline-8-carboxylate was added 1 ml of a 4 M hydrogen chloride solution in EtOAc, followed by stirring at room temperature for 3 hours. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography (elution solvent: chloroform-MeOH). 26 mg of the resulting pale yellow viscous substance was dissolved in EtOH, followed by addition of 10.3 mg of fumaric acid and stirring. The precipitated solid was collected by filtration to obtain 23.2 mg of 11-chloro-1-isobutyl-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline monofumarate as a white solid.

**[0122]** In the same manner as in the methods of Examples above, the compounds of Examples shown in the Tables below were prepared. The structures of the compounds of the Examples are shown in Table 8 and the preparation methods and the physicochemical data are shown in Table 9.

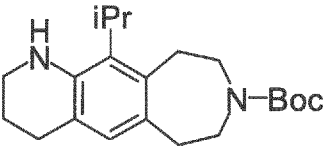
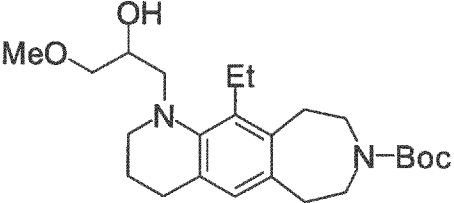
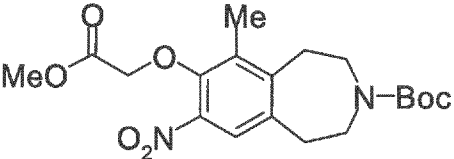
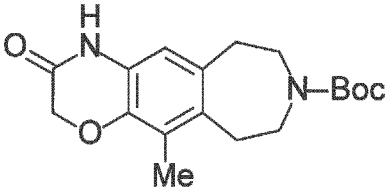
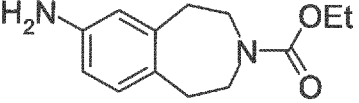
[Table 2]

| PEX | Str |
|-----|-----|
| 5   |     |
| 7   |     |
| 8   |     |
| 9   |     |
| 11  |     |
| 14  |     |

(continued)

| PEx | Str                                                                                |
|-----|------------------------------------------------------------------------------------|
| 15  |  |
| 17  |  |
| 18  |  |

[Table 3]

| PEx | Str                                                                                  |
|-----|--------------------------------------------------------------------------------------|
| 19  |   |
| 20  |  |
| 22  |  |
| 23  |  |
| 45  |  |

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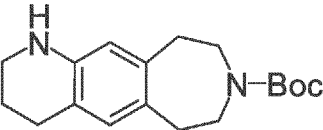
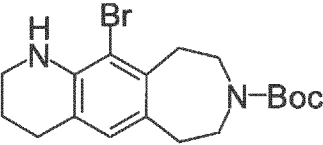
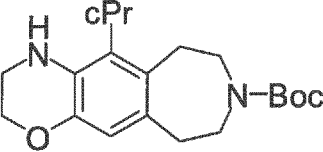
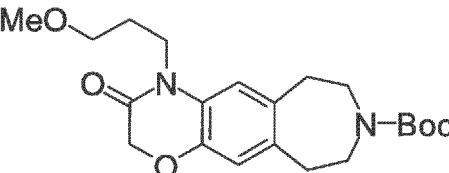
(continued)

| PEX | Str |
|-----|-----|
| 46  |     |
| 47  |     |
| 48  |     |
| 49  |     |

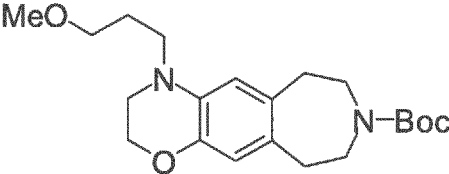
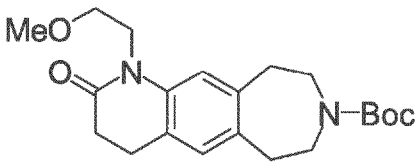
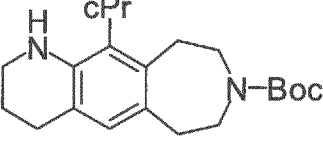
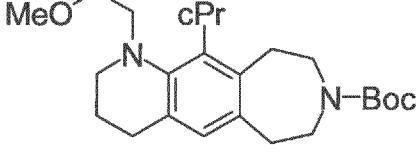
[Table 4]

| PEX | Str |
|-----|-----|
| 50  |     |
| 54  |     |
| 58  |     |
| 67  |     |
| 71  |     |

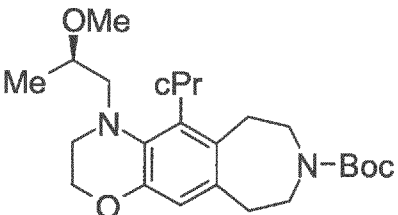
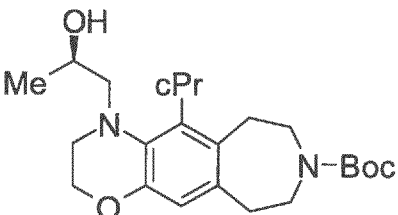
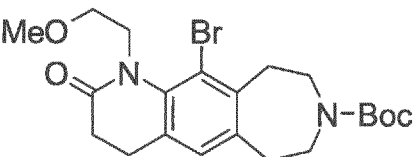
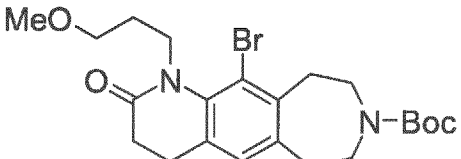
(continued)

| PEx | Str                                                                                |
|-----|------------------------------------------------------------------------------------|
| 72  |  |
| 73  |  |
| 78  |  |
| 98  |  |

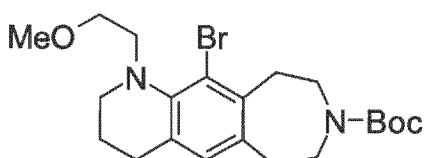
[Table 5]

| PEx | Str                                                                                  |
|-----|--------------------------------------------------------------------------------------|
| 99  |  |
| 123 |  |
| 124 |  |
| 126 |  |

(continued)

| PEx | Str                                                                                 |
|-----|-------------------------------------------------------------------------------------|
| 299 |   |
| 304 |   |
| 410 |   |
| 411 |  |

[Table 6]

| PEx | Str                                                                                  |
|-----|--------------------------------------------------------------------------------------|
| 433 |  |

[Table 7]

| PEx | Psyn | Dat            |
|-----|------|----------------|
| 5   | 5    | FAB+:299,301   |
| 7   | 7    | El:346,348,350 |
| 8   | 8    | ESI+:367,369   |
| 9   | 9    | El:322,324     |
| 11  | 11   | ESI+:337,339   |
| 14  | 14   | APCI+:220      |
| 15  | 15   | ESI+:303       |

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(continued)

5

10

15

20

25

30

35

40

45

| PEx | Psyn | Dat                            |
|-----|------|--------------------------------|
| 17  | 17   | ESI+;359                       |
| 18  | 18   | ESI+;317                       |
| 19  | 19   | ESI+;345                       |
| 20  | 20   | ESI+;419                       |
| 22  | 22   | ESI+;417                       |
| 23  | 23   | FAB-;331                       |
| 45  | 19   | ESI+;235                       |
| 46  | 7    | El;312                         |
| 47  | 8    | ESI+;333                       |
| 48  | 5    | El;264                         |
| 49  | 9    | El;288                         |
| 50  | 22   | ESI+;403([M+Na] <sup>+</sup> ) |
| 54  | 11   | ESI+;305                       |
| 58  | 23   | FAB-;317                       |
| 67  | 7    | ESI+;383,385                   |
| 71  | 71   | ESI+;317                       |
| 72  | 11   | ESI+;203                       |
| 73  | 7    | ESI+;381,383                   |
| 78  | 18   | ESI+;345                       |
| 98  | 15   | ESI+;391                       |
| 99  | 11   | ESI+;377                       |
| 123 | 15   | ESI+;375                       |
| 124 | 18   | ESI+;343                       |
| 126 | 17   | ESI+;401                       |
| 299 | 15   | ESI+;417                       |
| 304 | 20   | ESI+;403                       |
| 410 | 411  | ESI+;453; 455                  |
| 411 | 411  | ESI+;467; 469                  |
| 433 | 11   | ESI+;439, 441                  |

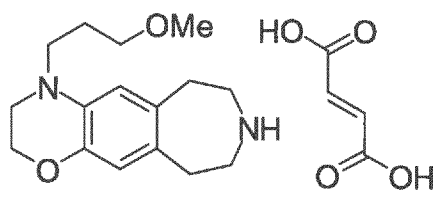
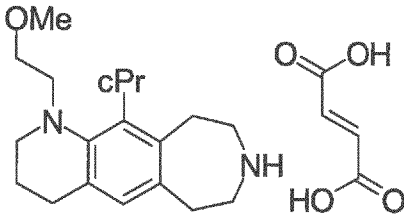
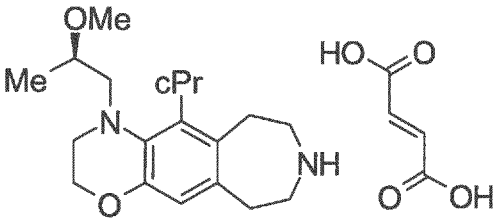
[Table 8]

50

55

| Ex  | Str |
|-----|-----|
| A M |     |

(continued)

| Ex  | Str                                                                                |
|-----|------------------------------------------------------------------------------------|
| 1 M |  |
| 2 M |  |
| 3 M |  |

[Table 9]

| Ex | Syn | Dat                                                                                                                                                                               |
|----|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| A  | A   | ESI+:293,295<br>NMR:0.96(6H,d,J=6.5Hz),1.69-1.75(2H,m),1.98-2.07(1H,m),2.67-2.70(4H,m),2.90-2.95(2H,m),2.97-3.04(6H,m),3.10-3.65(5H,m),6.46(2H,s),6.81(1H,s) mp:159-163           |
| 1  | A   | ESI+:277<br>NMR:1.68-1.80(2H,m),2.77-2.92(4H,m),2.96-3.09(4H,m),3.17-3.30(7H,m),3.36(2H,t,J=6.1Hz),4.05-4.15(2H,m),6.44(2H,s),6.49(1H,s),6.51(1H,s) mp:141-145                    |
| 2  | A   | ESI+:301<br>NMR:0.30-0.42(2H,m),0.93-1.04(2H,m),1.57-1.74(3H,m),2.61(2H,t,J=6.4Hz),2.83-2.94(2H,m),2.98-3.32(13H,m),3.56(2H,t,J=6.2Hz),6.43(2H,s),6.65(1H,s)                      |
| 3  | A   | ESI+:317<br>NMR:0.30-0.42(1H,m),0.46-0.59(1H,m),0.95-1.09(5H,m),1.55-1.67(1H,m),2.80-3.30(14H,m),3.33-3.43(1H,m),3.62-3.75(1H,m),3.95-4.09(2H,m),6.42(2H,s),6.50(1H,s) mp:133-136 |

[Industrial Applicability]

**[0123]** The compounds of the present invention or salts thereof have a 5-HT<sub>2C</sub> receptor agonist activity and can be used as an agent for preventing or treating 5-HT<sub>2C</sub> receptor-related diseases.

**[0124]** Here, examples of the 5-HT<sub>2C</sub> receptor-related diseases include incontinence such as stress urinary incontinence, urge urinary incontinence, mixed urinary incontinence, and the like, sexual dysfunction such as erectile dysfunction syndrome and the like, obesity, and the like.

## Claims

1. A compound, which is  
11-cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline,  
4-(3-methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine, or  
5-cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine,  
or a salt thereof.
2. A compound as described in claim 1, which is  
11-cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]quinoline or a salt thereof.
3. A compound as described in claim 1, which is  
4-(3-methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine or a salt thereof.
4. A compound as described in claim 1, which is  
5-cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepine or a salt thereof.
5. A pharmaceutical composition comprising a compound or a salt thereof as described in claim 1 and a pharmaceutically acceptable excipient.
6. A pharmaceutical composition for use in a method for preventing or treating 5-HT<sub>2C</sub> receptor-related diseases selected from the group consisting of stress urinary incontinence and mixed urinary incontinence, comprising a compound or a salt thereof as described in claim 1.
7. Use of a compound or a salt thereof as described in claim 1 for preparation of a pharmaceutical composition for preventing or treating stress urinary incontinence and mixed urinary incontinence.
8. A compound or a salt thereof as described in claim 1 for use in the prevention or treatment of stress urinary incontinence and mixed urinary incontinence.

## Patentansprüche

1. Eine Verbindung, bei der es sich um 11-Cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]chinolin, 4-(3-Methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepin, oder 5-Cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepin, oder ein Salz davon handelt.
2. Verbindung wie beschrieben in Anspruch 1, bei der es sich um 11-Cyclopropyl-1-(2-methoxyethyl)-2,3,4,6,7,8,9,10-octahydro-1H-azepino[4,5-g]chinolin oder ein Salz davon handelt.
3. Verbindung wie beschrieben in Anspruch 1, bei der es sich um 4-(3-Methoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepin oder ein Salz davon handelt.
4. Verbindung wie beschrieben in Anspruch 1, bei der es sich um 5-Cyclopropyl-4-[(2R)-2-methoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazepin oder ein Salz davon handelt.
5. Pharmazeutische Zusammensetzung, die eine Verbindung oder ein Salz davon wie beschrieben in Anspruch 1 und

einen pharmazeutisch akzeptablen Exzipienten enthält.

6. Pharmazeutische Zusammensetzung zur Verwendung in einer Verfahrensweise zur Verhinderung oder Behandlung von 5-HT<sub>2C</sub>-Rezeptor-bezogenen Erkrankungen ausgewählt aus der Gruppe bestehend aus Stressharninkontinenz und Mischharninkontinenz, die eine Verbindung oder ein Salz derselben wie beschrieben in Anspruch 1 enthält.
7. Verwendung einer Verbindung oder eines Salzes davon wie beschrieben in Anspruch 1 zur Herstellung einer pharmazeutischen Zusammensetzung zur Verhinderung oder Behandlung von Stressharninkontinenz und Mischharninkontinenz.
8. Eine Verbindung oder ein Salz davon wie beschrieben in Anspruch 1 zur Verwendung bei der Verhinderung oder Behandlung von Stressharninkontinenz und Mischharninkontinenz.

## Revendications

1. Composé, qui est  
la 11-cyclopropyl-1-(2-méthoxyéthyl)-2,3,4,6,7,8,9,10-octahydro-1H-azépino[4,5-g]quinoléine,  
la 4-(3-méthoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazépine, ou  
la 5-cyclopropyl-4-[(2R)-2-méthoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazépine,  
ou un sel de celles-ci.
2. Composé tel que décrit dans la revendication 1, qui est la 11-cyclopropyl-1-(2-méthoxyéthyl)-2,3,4,6,7,8,9,10-octahydro-1H-azépino[4,5-g]quinoléine ou un sel de celle-ci.
3. Composé tel que décrit dans la revendication 1, qui est la 4-(3-méthoxypropyl)-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazépine ou un sel de celle-ci.
4. Composé tel que décrit dans la revendication 1, qui est la 5-cyclopropyl-4-[(2R)-2-méthoxypropyl]-2,3,4,6,7,8,9,10-octahydro[1,4]oxazino[2,3-h][3]benzazépine ou un sel de celle-ci.
5. Composition pharmaceutique comprenant un composé ou un sel de celui-ci tel que décrit dans la revendication 1 et un excipient pharmaceutiquement acceptable.
6. Composition pharmaceutique pour une utilisation dans un procédé pour prévenir ou traiter des maladies liées au récepteur 5-HT<sub>2C</sub> choisies dans le groupe constitué de l'incontinence urinaire d'effort et l'incontinence urinaire mixte, comprenant un composé ou un sel de celui-ci tel que décrit dans la revendication 1.
7. Utilisation d'un composé ou d'un sel de celui-ci tel que décrit dans la revendication 1 pour la préparation d'une composition pharmaceutique pour prévenir ou traiter l'incontinence urinaire d'effort et l'incontinence urinaire mixte.
8. Composé ou un sel de celui-ci tel que décrit dans la revendication 1 pour une utilisation dans la prévention ou le traitement de l'incontinence urinaire d'effort et de l'incontinence urinaire mixte.

## REFERENCES CITED IN THE DESCRIPTION

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## Szabadalmi igénypontok

1. Vegyület, amely  
11-ciklopropil-1-(2-metoxietil)-2,3,4,6,7,8,9,10-oktahidro-1H-azepino[4,5-g]kinolin,  
4-(3-metoxipropil)-2,3,4,6,7,8,9,10-oktahidro[1,4]oxazino[2,3-h][3]benzazepin, vagy  
5-ciklopropil-4-[(2R)-2-metoxipropil]-2,3,4,6,7,8,9,10-oktahidro[1,4]oxazino[2,3-h][3]benzazepin,  
vagy annak sója.
2. Az 1. igényponi szerinti vegyület, amely  
11-ciklopropil-1-(2-metoxietil)-2,3,4,6,7,8,9,10-oktahidro-1H-azepino[4,5-g]kinolin vagy annak  
sója.
3. Az 1. igénypont szerinti vegyület, amely  
4-(3-metoxipropil)-2,3,4,6,7,8,9,10-oktahidro[1,4]oxazino[2,3-h][3]benzazepin vagy annak sója.
4. Az 1. igényponi szerinti vegyület, amely  
5-ciklopropil-4-[(2R)-2-metoxipropil]-2,3,4,6,7,8,9,10-oktahidro[1,4]oxazino[2,3-h][3]benzazepin  
vagy annak sója.
5. Gyógyszerészeti kompozíció, amely tartalmaz 1. igénypont szerinti vegyületet vagy annak sóját,  
és gyógyszerészetileg elfogadható excipienst.
6. Gyógyszerészeti kompozíció felhasználásra eljárásban 5-HT<sub>2C</sub> receptorral kapcsolatos betegségek  
megelőzésére vagy kezelésére, amelyek ki van vannak választva stressz vizeletinkontinenciából és kevert  
vizeletinkontinenciából álló csoportból, amely tartalmaz 1. igénypont szerinti vegyületet vagy annak sóját.
7. Az 1. igénypont szerinti vegyület vagy annak sója felhasználásra gyógyszerészeti kompozíció  
készítésére, amely stressz vizeletinkontinencia és kevert vizeletinkontinencia megelőzésére vagy kezelésére  
szolgál.
8. Az 1. igénypont szerinti vegyület vagy annak sója felhasználásra stressz vizeletinkontinencia és  
kevert vizeletinkontinencia megelőzésére vagy kezelésére.

