[Compound 51];

(*E*)-3-(2-Fluorophenyl)-*N*-[3-(2*H*-pyrazol-3-yl)phenyl]-2-propenamide [Compound 52];

(*E*)-3-(2-Fluorophenyl)-*N*-[4-(isoxazol-5-yl)phenyl]-2-propenamide [Compound 53];

(*E*)-3-(2-Fluorophenyl)-*N*-[3-(isoxazol-5-yl)phenyl]-2-propenamide [Compound 54];

(*E*)-3-(2-Fluorophenyl)-*N*-(1*H*-indazol-6-yl)-2-propenamide [Compound 55];

(*E*)-3-(2-Fluorophenyl)-*N*-(1*H*-indazol-5-yl)-2-propenamide [Compound 56];

(*E*)-*N*-(3-Morpholinopropyl)-3-(2-trifluoromethylphenyl)-2-propenamide hydrochloride [Compound 57];

(*E*)-2-Cyano-3-(4-fluorophenyl)-*N*-(3-morpholinopropyl)-2-propenamide [Compound 58];

(*E*)-3-(2-Fluorphenyl)-*N*-[3-(1-piperidyl)propyl]-2-propenamide hydrochloride [Compound 59];

(*E*)-3-(4-Fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide [Compound 60];

[**0019**] (*E*)-3-(2-Fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide hydrochloride [Compound 61];

(*E*)-*N*-[3-(1,1-Dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide hydrochloride [Compound 62];

(*E*)-*N*-[3-(1,1-Dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide hydrochloride [Compound 63];

sodium hydrogencarbonate solution, and a saturated sodium chloride solution, and an organic layer was then dried over anhydrous sodium sulfate. The residue obtained by distilling off the solvents under a reduced pressure was purified with silica gel column chromatography (chlorofor : methanol = 50:1), to give the captioned compound (5.9 g, 37%) as a solid. Mp 95-96°C. ^{1}H-NMR (DMSO-d_6) δ: 1.70-1.80 (m, 2H), 2.38-2.48 (m, 2H), 2.50-2.64 (m, 6H), 2.77-3.33 (m, 2H), 3.64 (t, J=6.8 Hz, 2H), 7.83-7.88 (m, 4H).

[0126] Example 100

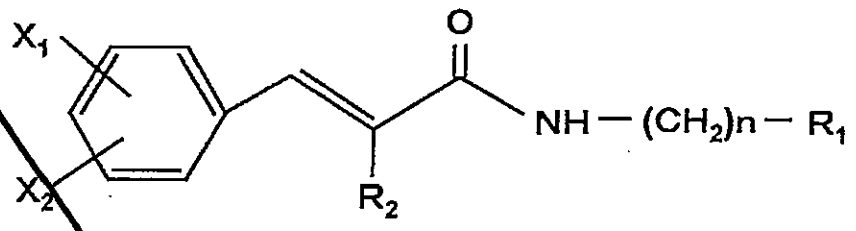
Production of 3-(Oxo-1,4-thiazinan-4-yl)propan-1-amine.

Hydrazine monohydrate (1.9 mL, 38 mmol) was added to an ethanol (180 mL) solution of the compound obtained in Example 99 (5.8 g, 19 mmol) at room temperature, and the mixture was heated under refluxing for 5 hours. The reaction mixture was cooled to room temperature, and the precipitated solid was filtered away. Thereafter, methylene chloride (50 mL) was added to the residue obtained by distilling off the solvent of the filtrate under a reduced pressure, and insoluble substances were filtered away. Methylene chloride (30 mL) was added to the residue obtained by distilling off the solvents of the filtrate under a reduced pressure, and insoluble substances were again filtered away. The solvents of the filtrate were distilled off under a reduced pressure, to give the captioned compound (3.3 g, 98%) as an oily product. ^{1}H-NMR (DMSO-d_6) δ: 1.53-1.55 (m, 2H), 2.37-2.50 (m, 2H), 2.57-2.61 (m, 4H), 2.68-2.72 (m, 2H), 2.78-2.85 (m, 4H).

[0127] Example 101

CLAIMS

[Claim 1] A compound or a pharmaceutically acceptable salt thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos;

- an amino which may be substituted with one or two alkyls having 1 to 4 carbon atoms; or

- any one of substituents selected from guanidino, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms, with proviso that in a case of n=0, R_1 stands for a substituent other than a phenyl substituted with morpholino; in a case of n=1, R_1 stands for a substituent other than a pyridyl; in a case where R_1 is a morpholino and R_2 is a hydrogen, when either one of X_1 and X_2 is a hydrogen, the other stands for a substituent other than a fluorine.

[Claim 2] The compound or a pharmaceutically acceptable salt thereof according to claim 1, wherein R_2 is a hydrogen.

[Claim 3] The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein either one of X_1 and X_2 is a hydrogen, and the other is a fluorine.

[Claim 4] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl.

[Claim 5] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms.

[Claim 6] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl, or morpholino.

[Claim 7] The compound or a pharmaceutically acceptable salt thereof according to claim 3, which is a phenyl substituted with thiomorpholino which may be substituted with oxo.

[Claim 8] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl.

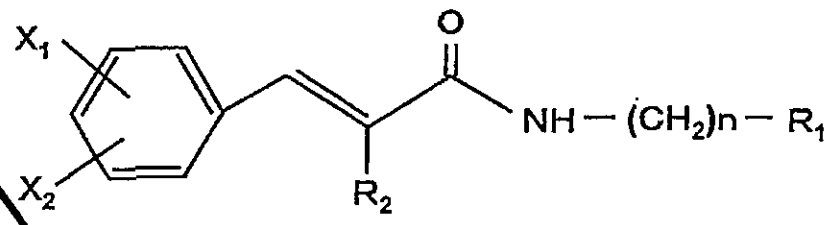
[Claim 9] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is a thiomorpholino which may be substituted with one or two oxos.

[Claim 10] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is an amino which may be substituted with one or two alkyls having 1 to 4 carbon atoms.

[Claim 11] The compound or a pharmaceutically acceptable salt thereof according to claim 3, wherein R_1 is any one of substituents selected from guanidino, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino.

[Claim 12] The compound or a pharmaceutically acceptable salt thereof according to claim 11, wherein R_1 is any one of substituents selected from pyrazolyl, triazolyl, piperidino, and morpholino.

[Claim 13] A pharmaceutical agent comprising, as an active ingredient, at least one member of a compound and a pharmaceutically acceptable salt thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos;
- an amino which may be substituted with one or two alkyls having 1 to 4 carbon atoms; or
- any one of substituents selected from carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl,

piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 14] The pharmaceutical agent according to claim 13, which is an analgesic.

[Claim 15] The pharmaceutical agent according to claim 14, wherein the analgesic is a therapeutic agent for chronic pains.

[Claim 16] The pharmaceutical agent according to claim 15, wherein the therapeutic agent for chronic pains is a therapeutic agent for lumbago, arthralgia, or neuropathic pains.

[Claim 17] The pharmaceutical agent according to claim 14, wherein the analgesic is a therapeutic agent for neuropathic pains.

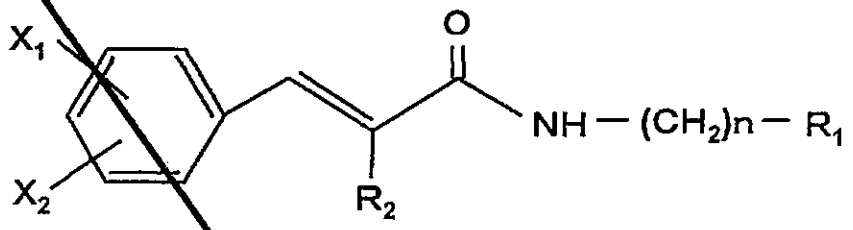
[Claim 18] The pharmaceutical agent according to any one of claims 13 to 17, which is an oral preparation.

[Claim 19] The pharmaceutical agent according to any one of claims 13 to 17, which is an injectable preparation.

Amended Claims

[Received by International Bureau on 25 April 2014 (25.04.2014)]

[Claim 1] (Amended) A compound or a pharmaceutically acceptable salt thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;

- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from guanidino, indazolyl, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms, with proviso that in a case of n=0, R_1 stands for a substituent other than a phenyl substituted with morpholino.

[Claim 2] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 1, wherein R_2 is a hydrogen, and wherein either one of X_1 and X_2 is a hydrogen, and the other is a fluorine.

[Claim 3] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl.

[Claim 4] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms.

[Claim 5] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is a phenyl substituted with amino, isoxazolyl, or morpholino.

[Claim 6] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, which is a phenyl substituted with thiomorpholino which may be substituted with oxo.

[Claim 7] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl.

[Claim 8] (Amended) The compound or a pharmaceutically acceptable salt

thereof according to claim 2, wherein R_1 is a thiomorpholino which may be substituted with one or two oxos.

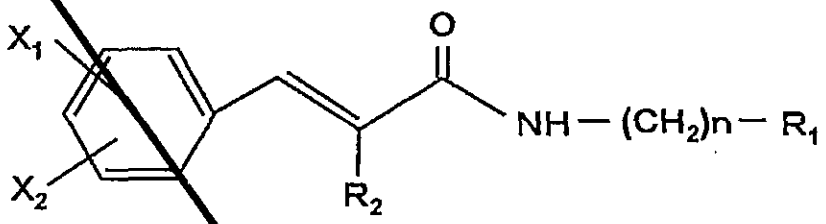
[Claim 9] (Amended) The compound or a pharmaceutically acceptable salt thereof according to claim 2, wherein R_1 is any one of substituents selected from guanidino, indazolyl, and cyclohexylamino.

[Claim 10] (Added) The compound or a pharmaceutically acceptable salt thereof according to claim 1, which is selected from the group consisting of (*E*)-*N*-[2-(4-cyclohexylpiperazin-1-yl)ethyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(4-cyclohexylpiperazin-1-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(4-methylpiperazin-1-yl)propyl]-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(isoxazol-5-yl)phenyl]-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

[Claim 11] (Added) The compound or a pharmaceutically acceptable salt thereof according to claim 1, which is selected from the group consisting of (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-

propenamide.

[Claim 12] (Amended) A pharmaceutical agent, comprising, as an active ingredient, at least one member of a compound and a pharmaceutically acceptable salt thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;

- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 13] (Amended) The pharmaceutical agent according to claim 12, which is an analgesic.

[Claim 14] (Amended) The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for chronic pains.

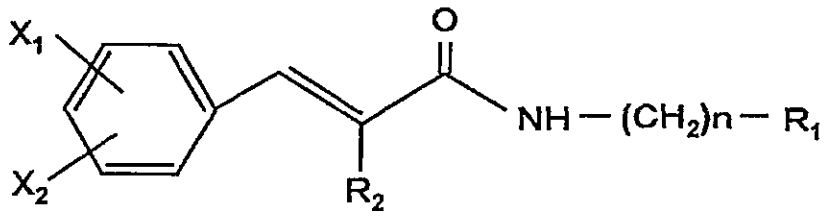
[Claim 15] (Amended) The pharmaceutical agent according to claim 14, wherein the therapeutic agent for chronic pains is a therapeutic agent for lumbago, arthralgia, or neuropathic pains.

[Claim 16] (Amended) The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for neuropathic pains.

[Claim 17] (Amended) The pharmaceutical agent according to any one of claims 12 to 16, which is an oral preparation.

[Claim 18] (Amended) The pharmaceutical agent according to any one of claims 12 to 16, which is an injectable preparation.

[Claim 19] (Added) Use of a compound or a pharmaceutically acceptable salt thereof as a pharmaceutical agent, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 20] (Added) The use according to claim 19, wherein the pharmaceutical agent is an analgesic.

[Compound 51];

(*E*)-3-(2-Fluorophenyl)-*N*-[3-(2*H*-pyrazol-3-yl)phenyl]-2-propenamide [Compound 52];

(*E*)-3-(2-Fluorophenyl)-*N*-[4-(isoxazol-5-yl)phenyl]-2-propenamide [Compound 53];

(*E*)-3-(2-Fluorophenyl)-*N*-[3-(isoxazol-5-yl)phenyl]-2-propenamide [Compound 54];

(*E*)-3-(2-Fluorophenyl)-*N*-(1*H*-indazol-6-yl)-2-propenamide [Compound 55];

(*E*)-3-(2-Fluorophenyl)-*N*-(1*H*-indazol-5-yl)-2-propenamide [Compound 56];

(*E*)-*N*-(3-Morpholinopropyl)-3-(2-trifluoromethylphenyl)-2-propenamide hydrochloride [Compound 57];

(*E*)-2-Cyano-3-(4-fluorophenyl)-*N*-(3-morpholinopropyl)-2-propenamide [Compound 58];

(*E*)-3-(2-Fluorophenyl)-*N*-[3-(1-piperidyl)propyl]-2-propenamide hydrochloride [Compound 59];

(*E*)-3-(4-Fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide [Compound 60];

[0019] (*E*)-3-(2-Fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide hydrochloride [Compound 61];

(*E*)-*N*-[3-(1,1-Dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide hydrochloride [Compound 62];

(*E*)-*N*-[3-(1,1-Dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide hydrochloride [Compound 63];

sodium hydrogencarbonate solution, and a saturated sodium chloride solution, and an organic layer was then dried over anhydrous sodium sulfate. The residue obtained by distilling off the solvents under a reduced pressure was purified with silica gel column chromatography (chloroform : methanol = 50:1), to give the captioned compound (5.9 g, 37%) as a solid. Mp 95-96°C. ^{1}H-NMR (DMSO-d_6) δ: 1.70-1.80 (m, 2H), 2.38-2.48 (m, 2H), 2.50-2.64 (m, 6H), 2.77-3.33 (m, 2H), 3.64 (t, J=6.8 Hz, 2H), 7.83-7.88 (m, 4H).

[0126] Example 100

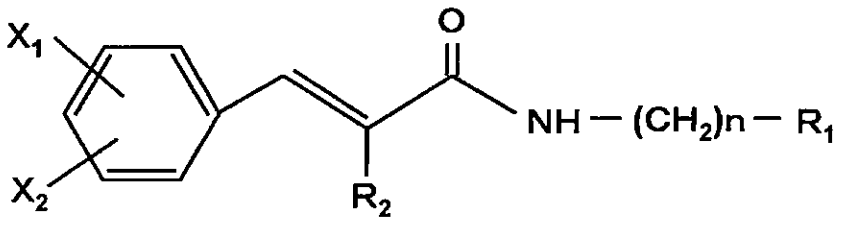
Production of 3-(Oxo-1,4-thiazinan-4-yl)propan-1-amine.

Hydrazine monohydrate (1.9 mL, 38 mmol) was added to an ethanol (180 mL) solution of the compound obtained in Example 99 (5.8 g, 19 mmol) at room temperature, and the mixture was heated under refluxing for 5 hours. The reaction mixture was cooled to room temperature, and the precipitated solid was filtered away. Thereafter, methylene chloride (50 mL) was added to the residue obtained by distilling off the solvent of the filtrate under a reduced pressure, and insoluble substances were filtered away. Methylene chloride (30 mL) was added to the residue obtained by distilling off the solvents of the filtrate under a reduced pressure, and insoluble substances were again filtered away. The solvents of the filtrate were distilled off under a reduced pressure, to give the captioned compound (3.3 g, 98%) as an oily product. ^{1}H-NMR (DMSO-d_6) δ: 1.53-1.55 (m, 2H), 2.37-2.50 (m, 2H), 2.57-2.61 (m, 4H), 2.68-2.72 (m, 2H), 2.78-2.85 (m, 4H).

[0127] Example 101

Claims

[Claim 1] A compound or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from guanidino, indazolyl, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms, with proviso that in a case of n=0, R_1 stands for a substituent other than a phenyl substituted with morpholino.

[Claim 2] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, wherein R_2 is a hydrogen, and wherein either one of X_1 and X_2 is a hydrogen, and the other is a fluorine.

[Claim 3] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl.

[Claim 4] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms.

[Claim 5] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a phenyl substituted with amino, isoxazolyl, or morpholino.

[Claim 6] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a phenyl substituted with thiomorpholino which may be substituted with oxo.

[Claim 7] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl.

[Claim 8] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a thiomorpholino which may be

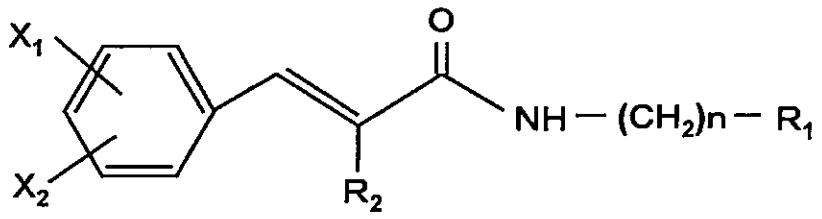
substituted with one or two oxos.

[Claim 9] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is any one of substituents selected from guanidino, indazolyl, and cyclohexylamino.

[Claim 10] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, which is selected from the group consisting of (*E*)-*N*-[2-(4-cyclohexylpiperazin-1-yl)ethyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(4-cyclohexylpiperazin-1-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(4-methylpiperazin-1-yl)propyl]-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(isoxazol-5-yl)phenyl]-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

[Claim 11] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, which is selected from the group consisting of (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

[Claim 12] A pharmaceutical agent, comprising, as an active ingredient, at least one member of a compound, and salt and hydrate thereof that are pharmaceutically acceptable, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 13] The pharmaceutical agent according to claim 12, which is an analgesic.

[Claim 14] The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for chronic pains.

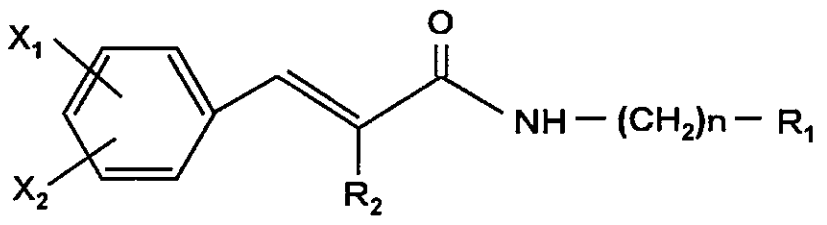
[Claim 15] The pharmaceutical agent according to claim 14, wherein the therapeutic agent for chronic pains is a therapeutic agent for lumbago, arthralgia, or neuropathic pains.

[Claim 16] The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for neuropathic pains.

[Claim 17] The pharmaceutical agent according to any one of claims 12 to 16, which is an oral preparation.

[Claim 18] The pharmaceutical agent according to any one of claims 12 to 16, which is an injectable preparation.

[Claim 19] Use of a compound or a pharmaceutically acceptable salt or hydrate thereof as a pharmaceutical agent, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 20] The use according to claim 19, wherein the pharmaceutical agent is an analgesic.