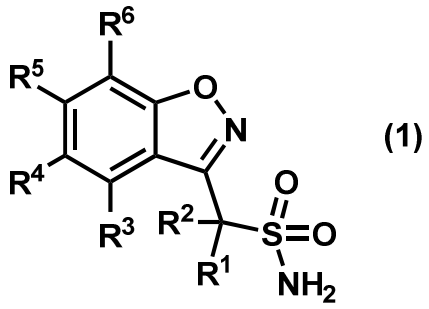
CLAIMS

1. A compound of formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is hydrogen, halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy),

R^2 is halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or

R^1 and R^2 are taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl which may be substituted with 1 – 3 substituents selected independently

from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy, and

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, cyano, nitro, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{1-6} alkoxy (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy).

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

R^1 is hydrogen, fluorine, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), and

R^2 is fluorine, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{3-6} cycloalkyl, and

C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or

R^1 and R^2 are taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy.

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

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, cyano, nitro, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{1-6} alkoxy (which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy).

4. The compound of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof, wherein

R^1 is hydrogen, fluorine, or C_{1-6} alkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy, and

R^2 is fluorine, or C_{1-6} alkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy, or

R^1 and R^2 are taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy.

5. The compound of any one of claims 1 to 4 or a pharmaceutically acceptable salt thereof, wherein

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, or C_{1-3} alkoxy which may be substituted with 1 – 3 fluorine.

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

R^1 is hydrogen, fluorine, or C_{1-6} alkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy,

R^2 is fluorine, or C_{1-6} alkyl which may be substituted

with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy, or

R^1 and R^2 are taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl which may be substituted with 1 – 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy, and

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, or C_{1-3} alkoxy which may be substituted with 1 – 3 fluorine.

7. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following compounds:

1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide,

2-(1,2-benzoxazol-3-yl)propane-2-sulfonamide,

1-(1,2-benzoxazol-3-yl)-1-fluoromethane-sulfonamide,

1-(1,2-benzoxazol-3-yl)-1,1-difluoromethane-sulfonamide ,

1-(1,2-benzoxazol-3-yl)cyclopropane-1-sulfonamide,

1-(1,2-benzoxazol-3-yl)propane-1-sulfonamide,

1-(1,2-benzoxazol-3-yl)butane-1-sulfonamide,

1-(1,2-benzoxazol-3-yl)-1-fluoroethane-1-sulfonamide,

1-(1,2-benzoxazol-3-yl)-2-methylpropane-1-sulfonamide,

1-(5-methoxy-1,2-benzoxazol-3-yl)ethane-1-sulfonamide,

1-(5-fluoro-1,2-benzoxazol-3-yl)ethane-1-sulfonamide,

1-(5-chloro-1,2-benzoxazol-3-yl)ethane-1-sulfonamide,
(1R)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide, or
(1S)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

8. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following compounds:
1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide,
2-(1,2-benzoxazol-3-yl)propane-2-sulfonamide,
1-(1,2-benzoxazol-3-yl)-1-fluoromethane-sulfonamide,
1-(1,2-benzoxazol-3-yl)-1,1-difluoromethane-sulfonamide,
1-(1,2-benzoxazol-3-yl)cyclopropane-1-sulfonamide,
1-(1,2-benzoxazol-3-yl)-1-fluoroethane-1-sulfonamide,
(1R)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide, or
(1S)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

9. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the following compounds:
1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide,
2-(1,2-benzoxazol-3-yl)propane-2-sulfonamide,
1-(1,2-benzoxazol-3-yl)cyclopropane-1-sulfonamide,
(1R)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide, or
(1S)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

10. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is 1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

11. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is (1R)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

12. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is (1S)-1-(1,2-benzoxazol-3-yl)ethane-1-sulfonamide.

13. A pharmaceutical composition comprising the compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof.

14. Use of the compound of any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating and/or preventing nervous system diseases or psychiatric diseases which are initiated by abnormality of T-type calcium channel.

15. The use of claim 14, wherein the nervous system diseases or psychiatric diseases which are initiated by abnormality of T-type calcium channel are various diseases or disorders, including epilepsy; seizure disorder; motor

dysfunction (e.g. muscle spasm-related disorder including convulsion; tremor; essential tremor; Huntington's disease; myoclonus; tic; restless legs syndrome; and dystonia); movement disorder including akinesia and stiff-man syndrome, and parkinsonism (which includes Parkinson's disease (including a symptom such as tremor, muscle stiffness/muscle rigidity, akinesia/bradykinesia, impairment of postural reflex, smell disorder, REM sleep disorder, constipation, sleep disorder, memory impairment, depression, anxiety, headache, and backache), episodic and drug-induced parkinsonism, postencephalitic parkinsonism, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration, dementia with Lewy body, cerebellar ataxia, parkinsonism-ALS dementia complex, and basal ganglia calcification); levodopa-induced dyskinesia in Parkinson's disease; drug-induced dyskinesia; nociceptive pain (including traumatic pain, migraine, headache, chronic pain (e.g. low back pain, rheumatoid arthralgia, fibromyalgia, osteoarthritis, and the like), inflammatory pain); neuropathic pain (including zoster-associated pain, trigeminal neuralgia, complex regional pain syndrome, peripheral neuropathy (e.g. diabetic neuropathy, leprosy, and the like), chemotherapy-induced peripheral neuropathy, phantom pain, central pain (e.g. spinal post-injury pain, post-stroke pain, and the like), pain associated with Guillain-Barre syndrome, pain

associated with multiple sclerosis, pain associated with Parkinson's disease, and hyperalgesia or allodynia associated with neuropathic pain); fatigue (e.g. Parkinson fatigue, multiple sclerosis fatigue, fatigue caused by sleep disorder or circadian rhythm disorder, chronic fatigue syndrome including drug-induced parkinsonism, and the like); migraine; schizophrenia; autism; Gilles de la Tourette syndrome; bipolar disorder; depressive disorder; anxiety (including generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder); sleep disorder (including insomnia, hypersomnia, narcolepsy, and REM sleep disorder); sleep disorder in depressive disorder; cardiac arrhythmia; hypertension; cancer; diabetes; infertility; and sexual dysfunction.

16. The use of claim 14, wherein the nervous system diseases or psychiatric diseases which are initiated by abnormality of T-type calcium channel are Parkinson's disease (including a symptom such as tremor, muscle stiffness/muscle rigidity, akinesia/bradykinesia, impairment of postural reflex, smell disorder, REM sleep disorder, constipation, sleep disorder, memory impairment, depression, anxiety, headache, and backache), levodopa-induced dyskinesia in Parkinson's disease, essential tremor, anxiety (including generalized anxiety disorder), or neuropathic pain (including zoster-associated pain,

trigeminal neuralgia, complex regional pain syndrome, peripheral neuropathy (e.g. diabetic neuropathy, leprosy, and the like), chemotherapy-induced peripheral neuropathy, phantom pain, central pain (e.g. spinal post-injury pain, post-stroke pain, and the like), pain associated with Guillain-Barre syndrome, pain associated with multiple sclerosis, pain associated with Parkinson's disease, and hyperalgesia or allodynia associated with neuropathic pain).

17. The use of claim 14, wherein the nervous system diseases or psychiatric diseases which are initiated by abnormality of T-type calcium channel are Parkinson's disease (including tremor, muscle stiffness/muscle rigidity, akinesia/bradykinesia, and impairment of postural reflex), essential tremor, or chemotherapy-induced peripheral neuropathy.

18. The compound of any one of claims 1 to 12 or a pharmaceutically acceptable salt thereof for use in treating and/or preventing nervous system diseases or psychiatric diseases which are initiated by abnormality of T-type calcium channel.

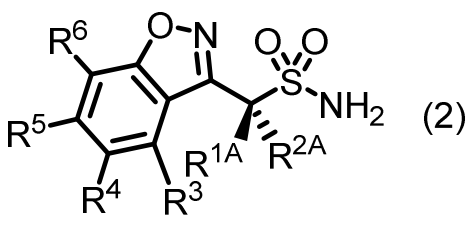
19. A medicament for treating a disease associated with abnormality of T-type calcium channel, comprising the compound of any one of claims 1 to 12, or a

pharmaceutically acceptable salt thereof, which is used in combination with at least one drug selected from the drug-group classified as drugs for treating Parkinson's disease, drugs for treating essential tremor, or drugs for treating neuropathic pain.

20. A medicament comprising the compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof with at least one drug selected from the drug-group classified as drugs for treating Parkinson's disease, drugs for treating essential tremor, or drugs for treating neuropathic pain.

21. A medicament for treating nervous system disease or psychiatric disease, comprising the compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, which is used in combination with at least one drug selected from the drug-group classified as drugs for treating Parkinson's disease, drugs for treating essential tremor, or drugs for treating neuropathic pain.

22. A process for preparing a compound of formula (2):



(2)

or a pharmaceutically acceptable salt thereof, wherein

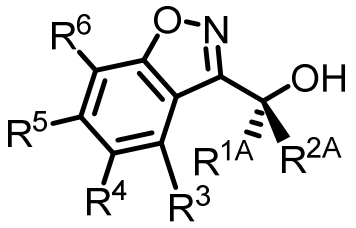
R^{1A} is hydrogen, halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy),

R^{2A} is halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), provided that R^{1A} and R^{2A} are different, and

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, cyano, nitro, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{1-6} alkoxy (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy),

which comprises Steps 1 to 3 below,

(Step 1) reacting a compound of formula (3):



(3)

or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, and R^6 are as defined above, and

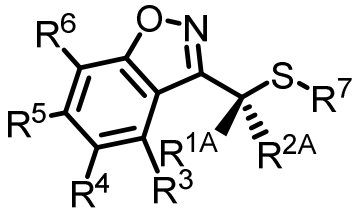
a compound of formula (4a) or (4b):

R^7—SH (4a) R^7–S–S–R^7 (4b)

or a salt thereof, wherein R^7 is a leaving group selected from 2-(methoxycarbonyl)ethyl, mesitylenecarbonyloxymethyl, 2-benzothiazolyl (the benzene ring of which may be substituted with 1 - 3 substituents selected independently from the group consisting of halogen, C_{1-6} alkyl (which may be substituted with 1 - 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{1-6} alkoxy (which may be substituted with 1 - 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), hydroxy, cyano, nitro, amino (which may be substituted with 1 - 2 C_{1-3} alkyl), carboxylic acid, carbamoyl (the amino moiety of which may be substituted with 1 - 2 C_{1-3} alkyl), and C_{1-6} alkoxycarbonyl), 2-pyridyl, 2-pyrimidinyl, or 2-(trimethylsilyl)ethyl, which

can release a sulfinic acid salt in the reaction

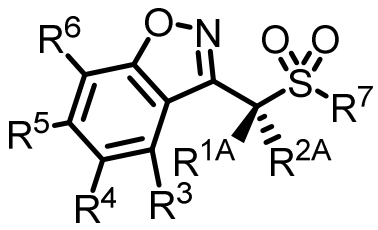
to prepare a compound of formula (5):



(5)

or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, R^6, and R^7 are as defined above,

(Step 2) oxidizing the compound of formula (5) or a salt thereof to prepare a compound of formula (6):



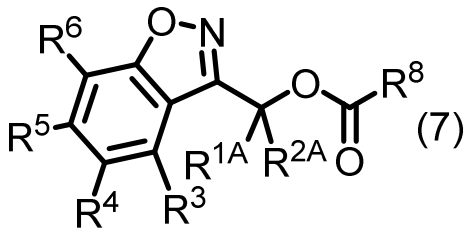
(6)

or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, R^6, and R^7 are as defined above, and

(Step 3) removing R^7 from the compound of formula (6) or a salt thereof and sulfonamidating the site to prepare the compound of formula (2) or a pharmaceutically acceptable salt thereof.

23. The process of claim 22, which further comprises the following step;

(Step 4a) optically-selectively hydrolyzing a compound of formula (7):



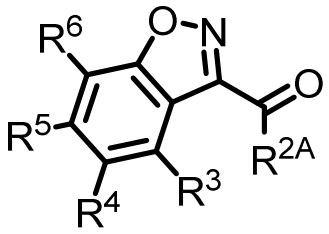
(7)

or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, and R^6 are as defined in Item 27, and R^8 is C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{1-6} alkoxy, or C_{1-6} alkylcarbonyloxymethoxy,

with a hydrolase selected from lipase, esterase, amidase, or protease to prepare the compound of formula (3).

24. The process of claim 22, wherein R^{1A} is hydrogen, which further comprises the following step;

(Step 4b) optically-selectively reducing a compound of formula (8):



(8)

or a salt thereof, wherein R^{2A}, R^3, R^4, R^5, and R^6 are as defined in claim 21,

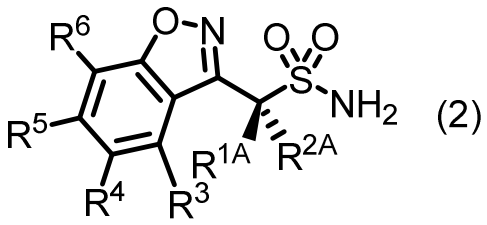
with reductase and a coenzyme selected from NADH or NADPH to prepare the compound of formula (3).

25. The process of any one of claims 22 to 24, wherein R^7 is 2-benzothiazolyl.

26. The process of claim 23 or 25, wherein R^8 is methyl, and the hydrolase is lipase.

27. The process of claim 24 or 25, wherein R^{2A} is methyl, and the reductase is carbonyl reductase or alcohol dehydrogenase.

28. A process for preparing a compound of formula (2):



(2)

or a pharmaceutically acceptable salt thereof, wherein

R^{1A} is hydrogen, halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy),

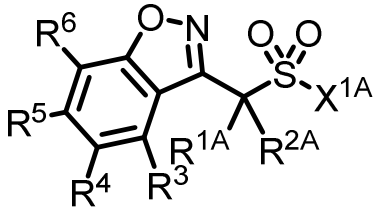
R^{2A} is halogen, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and

C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), provided that R^{1A} and R^{2A} are different, and

R^3, R^4, R^5, and R^6 are the same or different and are hydrogen, halogen, cyano, nitro, C_{1-6} alkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), C_{3-6} cycloalkyl (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{1-6} alkoxy (which may be substituted with 1 – 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy),

which comprises Steps 1 to 2 below,

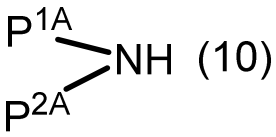
(Step 1) reacting a compound of formula (9):



(9)

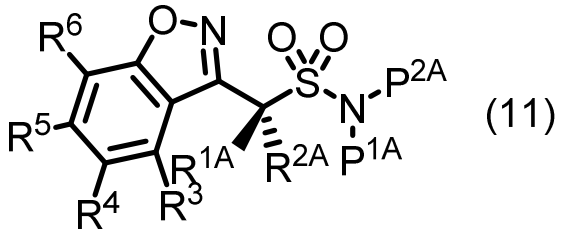
or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, and R^6 are as defined above, and X^{1A} is halogen, and

an optically-active compound of formula (10):



or a salt thereof, wherein P^{1A} is 2-indanol-1-yl, 2-phenylethan-1-ol-2-yl, or 3-methylbutan-1-ol-2-yl, P^{2A} is hydrogen or benzyl (the benzene ring of which may be substituted with 1 – 5 substituents selected independently from the group consisting of halogen, C_{1-6} alkyl, and C_{1-6} alkoxy, and

dividing the prepared diastereomers to prepare a compound of formula (11):



(11)

or a salt thereof, wherein R^{1A}, R^{2A}, R^3, R^4, R^5, R^6, P^{1A}, and P^{2A} are as defined above, and

(Step 2) deprotecting the compound of formula (11) or a salt thereof to prepare the compound of formula (2) or a pharmaceutically acceptable salt thereof.

29. The process of claim 28, wherein R^{1A} is hydrogen, and R^{2A} is methyl.

30. The process of claim 28 or 29, wherein P^{1A} is 2-

indanol-1-yl, and P^{2A} is hydrogen.

31. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form I which is characterized by a powder x-ray diffraction pattern having diffraction angle (2θ°) peaks of 5.7° ± 0.2 and 17.3° ± 0.2°.

32. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form I which is characterized by a powder x-ray diffraction pattern having four or more diffraction angle (2θ°) peaks selected from 5.7° ± 0.2, 14.1 ± 0.2°, 17.3° ± 0.2°, 19.1° ± 0.2°, 19.3 ± 0.2°, 21.6° ± 0.2°, 22.5 ± 0.2°, 23.1° ± 0.2°, 23.3° ± 0.2°, and 26.5° ± 0.2°.

33. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form II which is characterized by a powder x-ray diffraction pattern having diffraction angle (2θ°) peaks of 8.7° ± 0.2° and 17.6° ± 0.2°.

34. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form II which is characterized by a powder x-ray diffraction pattern having four or more diffraction angle (2θ°) peaks selected from 8.7° ± 0.2°, 13.5° ± 0.2°, 15.5° ± 0.2°, 17.6° ± 0.2°, 20.3° ± 0.2°, 21.6° ± 0.2°, 22.6° ± 0.2°, 26.2° ± 0.2°, 26.8° ± 0.2°, and

35.2° ± 0.2°.

35. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form III which is characterized by a powder x-ray diffraction pattern having diffraction angle (2θ°) peaks of 11.1° ± 0.2° and 20.3° ± 0.2°.

36. (1R)-1-(1,2-Benzoxazol-3-yl)ethane-1-sulfonamide in crystalline form of form III which is characterized by a powder x-ray diffraction pattern having four or more diffraction angle (2θ°) peaks selected from 11.1° ± 0.2°, 13.8° ± 0.2°, 17.0° ± 0.2°, 20.3° ± 0.2°, 21.4° ± 0.2°, 22.1° ± 0.2°, 22.4° ± 0.2°, 24.8° ± 0.2°, 26.3° ± 0.2°, and 27.9° ± 0.2°.