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(54) Title: SULFAMATE DERIVATIVE COMPOUND FOR USE IN PREVENTING OR TREATING EPILEPSY

(57) Abstract: The present invention relates to a pharmaceutical composition for treating or preventing epilepsy containing a sulfamate derivative compound and/or pharmaceutically acceptable salt thereof as an active ingredient. Furthermore, the present invention relates to a method for treatment or prevention epilepsy comprising administering a sulfamate derivative compound in a pharmaceutically effective amount to a subject in need of treatment or prevention of epilepsy.



WO 2015/088271 A1

【DISCRIPTION】**【Invention Title】**

SULFAMATE DERIVATIVE COMPOUND FOR USE IN PREVENTING OR TREATING EPILEPSY

5 【Technical Field】

The present invention relates to a pharmaceutical composition for treating or preventing epilepsy containing a sulfamate derivative compound and/or pharmaceutically acceptable salt thereof as an active ingredient. Furthermore, the present invention relates to a method for treatment or prevention epilepsy comprising administering a sulfamate derivative compound in a pharmaceutically effective amount to a subject in need of treatment or prevention of epilepsy.

10 【Background Art】

CNS disorders nowadays concern large sections of the population. In particular on account of the increase in elderly people, the numbers of patients are increasing continuously.

Epilepsy is the most common neurological disorder, affecting about 1% of the population worldwide. Epilepsy describes a condition in which a person has recurrent seizures due to a chronic, underlying process. Epilepsy refers to a clinical phenomenon rather than a single disease entity, since there are many forms and causes of epilepsy. Using a definition of epilepsy as two or more unprovoked seizures, the incidence of epilepsy is estimated at 5 to 10 people per 1000. An essential step in the diagnosis and treatment of a patient with a seizure is to determine the type of seizure that has occurred. The main characteristic that distinguishes the different categories of seizure is whether the seizure activity is partial or generalized or unclassified.

For the general population there are approximately 20-70 new cases per 100,000 diagnosed each year with a 3-5% lifetime probability of developing the disease. The older established antiepileptic drugs (AEDs) phenytoin, carbamazepine, clonazepam, ethosuximide, valproic acid and barbiturates are widely prescribed but suffer from a range of side effects. Furthermore, there is a significant group of patients (20-30%) that are resistant to the currently available therapeutic agents. Since 1989 several new drugs have been launched, including felbamate, gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate, vigabatrin, zonisamide and levetiracetam. While many of new AEDs show improved efficacies and side-effect profiles, about 30% of patients with epilepsy remain untreated. There is clearly a need for improved medication.

40 【Disclosure】**【Technical Problem】**

The older established antiepileptic drugs (AEDs) phenytoin, carbamazepine, clonazepam, ethosuximide, valproic acid and barbiturates are widely prescribed but suffer from a range of side effects. Furthermore, there is a significant group of patients (20-30%) that are resistant to the currently available therapeutic agents. Since 1989 several new drugs have been launched, including felbamate, gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate, vigabatrin, zonisamide and levetiracetam. While many of new AEDs show improved efficacies and side-effect profiles, about 30% of patients with epilepsy remain untreated. There is clearly a need for improved medication.

【Technical Solution】

The present invention relates to a pharmaceutical composition for treating or preventing epilepsy containing a sulfamate derivative compound and/or pharmaceutically acceptable salt thereof as an active ingredient.

【Advantageous Effects】

The present inventors have discovered that the sulfamate derivatives represented by the above formula 1 provide highly enhanced anti-epileptic activity with significantly decreased side effects.

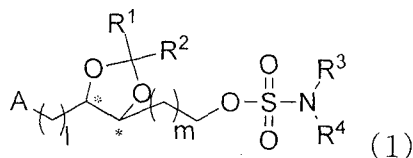
【Best Mode】

The present inventor has done intensive studies to develop a novel anti-epileptic drug with excellent activity and low toxicity which may be an effective treatment for epilepsy. As a result, the present inventors have discovered that the sulfamate derivatives represented by the above formula 1 provide highly enhanced anti-epileptic activity with significantly decreased side effects.

Accordingly, it is an object of this invention to provide a novel sulfamate derivative or pharmaceutically acceptable salt thereof.

【Mode for Invention】

In one aspect of this invention, there is provided a compound represented by the following formula 1 or pharmaceutically acceptable salt thereof:



wherein R^1 and R^2 are each independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl and C_6 - C_{10} aryl, R^1 and R^2 together with the carbon atom to which they attach form a C_3 - C_{12} cycloalkyl group, or R^1 and R^2 are bond and they together with the oxygen atom to which they attach form a carbonyl group; A is an aryl moiety or a

heterocyclic moiety optionally substituted by one or more substituents selected from the group consisting of hydrogen, hydroxyl, C₁-C₅ alkoxy, C₁-C₅ alkyl, C₂-C₅ alkenyl, C₆-C₁₀ aryl, C₁-C₅ alkoxy carbonyl, carboxyl, C₂-C₅ acyl, C₁-C₅ alkylthio, cyano, nitro, amine, C₁-C₅ alkylamine and halogen; R³ and R⁴ are each independently hydrogen or C₁-C₃ alkyl; and l and m are each independently an integer of 0~4.

According to a concrete embodiment, R¹ and R² are each independently selected from the group consisting of hydrogen, C₁-C₃ alkyl and phenyl or R¹ and R² together with the carbon atom to which they attach form a C₃-C₆ cycloalkyl group.

In a preferred embodiment according to the invention, an aryl moiety represents a C₆-C₁₀ aryl group.

In a preferred embodiment according to the invention, a heterocyclic moiety represents a C₃-C₁₀ heterocyclic group.

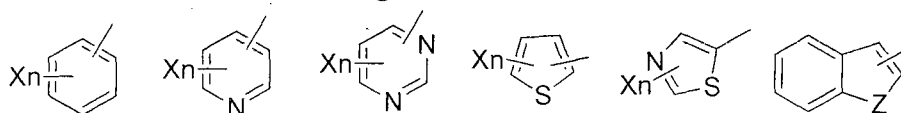
In a preferred embodiment according to the invention, A is a phenyl optionally substituted by one or more substituents selected from the group consisting of hydrogen, halogen, C₁-C₅ alkyl, nitro, amine and C₁-C₅ alkylamine or C₃-C₁₀ heterocyclic group optionally substituted by one or more substituents selected from the group consisting of hydrogen, halogen, C₁-C₅ alkyl, and C₆-C₁₀ aryl.

According to a concrete embodiment, R³ and R⁴ are each independently hydrogen or methyl.

In a preferred embodiment according to the invention, l and m are each independently an integer of 0~2.

In a more preferred embodiment according to the invention, l and m are each independently an integer of 0~1.

Particular examples of the substituents represented by A in Chemical Formula 1 include the following:



wherein X is each independently selected from the group consisting of hydrogen, halogen, nitro, amine, and C₁-C₅ alkyl; n is an integer of 0~5; and Z is selected from S, O or NH.

In a preferred embodiment according to the invention, n is an integer of 0~2.

In a more preferred embodiment according to the invention, n is an integer of 0~1.

The term "alkyl" as used herein, refers to a linear or branched chain of a saturated hydrocarbon group, e.g., methyl, ethyl, propyl, butyl, isobutyl, tert-butyl and pentyl. "C₁-C₅ alkyl group" as used herein,

refers to an alkyl group with a carbon number of 1-5.

The term "alkenyl", as used herein, unless otherwise indicated, includes alkyl moieties having at least one carbon-carbon double bond wherein alkyl is as defined above.

5 The term "alkoxy", as used herein, unless otherwise indicated, includes O-alkyl groups wherein alkyl is as defined above.

The term "alkylthio", as used herein, unless otherwise indicated, includes S-alkyl groups wherein alkyl is as defined above.

10 The term "alkoxycarbonyl", as used herein, unless otherwise indicated, includes -C(O)O-alkyl groups wherein alkyl is as defined above.

The term "acyl", as used herein, unless otherwise indicated, includes -C(O)-alkyl groups wherein alkyl is as defined above.

15 The term "aryl" or "aryl group" as used herein, refers to totally or partially unsaturated monocyclic or polycyclic carbon rings having aromaticity. The aryl group of the present invention is preferably monoaryl or biaryl, such as phenyl or naphthyl. The aryl radical may be optionally substituted by one or more substituents such as hydroxy, mercapto, halo, alkyl, phenyl, alkoxy, haloalkyl, nitro, cyano, dialkylamino, aminoalkyl, acyl and alkoxycarbonyl, as defined herein.

20 The term "cycloalkyl" or "cycloalkyl group" as used herein, refers to a monocyclic or polycyclic saturated ring comprising carbon and hydrogen atoms.

25 The term "heterocyclic" or "heterocyclic group", as used herein, unless otherwise indicated, means aromatic and non-aromatic heterocyclic groups (including saturated heterocyclic groups) containing one or more heteroatoms each selected from O, S and N, wherein each ring of a heterocyclic group has from 4 to 10 atoms. Non-aromatic heterocyclic groups may include rings having only 4 atoms, but aromatic heterocyclic rings must have at least 5 atoms. Heterocyclic groups of this invention unless
30 otherwise indicated may contain one ring or more than one ring, i.e. they may be monocyclic or polycyclic, for example bicyclic (which may comprise non-aromatic and/or aromatic rings).

According to more concrete embodiment, the compound is selected from the group consisting of:

35 (1) (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;

(2) (5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;

(3) (5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

40 (4) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

- (5) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (6) (5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (7) (5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 5 (8) (5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (9) (5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (10) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 10 (11) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (12) (5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (13) (5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 15 (14) (5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (15) (5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (16) (3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl) methyl sulfamate;
- 20 (17) (3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (18) (5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (19) (5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 25 (20) (5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (21) (5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 30 (22) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (23) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (24) (5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 35 (25) (5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (26) (5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 40 (27) (5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- (28) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (29) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 5 (30) (5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (31) (5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (32) (5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 10 (33) (5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (34) (3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (35) (3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 15 (36) (5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (37) (5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (38) (5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 20 (39) (5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (40) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (41) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 25 (42) (5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (43) (5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
- (44) (5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 30 (45) (5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (46) (5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (47) (3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 35 (48) (3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (49) (5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (50) (5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methyl sulfamate;
- 40 (51) (5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (52) (5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- (53) (3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
(54) (3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(55) 2-(5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(56) 2-(5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
5 (57) 2-(3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
(58) 2-(3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
(59) (5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(60) (5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(61) (3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
10 (62) (3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(63) 2-(5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(64) 2-(5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(65) 2-(3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
(66) 2-(3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
15 (67) 2-(5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
(68) 2-(5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
(69) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
20 sulfamate;
(70) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
sulfamate;
(71) (5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
25 (72) (5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(73) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;
(74) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
30 sulfamate;
(75) 2-(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
(76) 2-(5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
35 (77) 2-(3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
sulfamate;
(78) 2-(3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
sulfamate;
(79) (5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
40 yl)methyl sulfamate;
(80) (5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-

yl)methylsulfamate;

(81) (2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-

yl)methylsulfamate;

(82) (2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-

5 yl)methylsulfamate;

(83) (2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-

yl)methylsulfamate;

(84) (2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-

yl)methylsulfamate;

10 (85) (5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-dioxolan-4-

yl)methylsulfamate;

(86) (5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolan-4-

yl)methylsulfamate;

(87) (2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolan-4-

15 yl)methylsulfamate; and

(88) (2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolan-4-

yl)methylsulfamate.

20 According to a concrete embodiment, the compound is in the form of a racemate, an enantiomer, a diastereomer, a mixture of enantiomers or a mixture of diastereomers.

As seen in the Examples, the present inventors have synthesized the compounds of various stereochemistries, and investigated their anti-epileptic activity by multilateral experiments.

25 The term "enantiomer" as used herein, refers to one of two stereoisomers that are mirror images of each other which are non-superimposable due to the existence of one or more chiral carbons. According to a concrete embodiment, the enantiomer of the present invention is one in which chiral carbons of C4 and C5 are diverse in stereo-configuration.

30 The term "diastereomer" as used herein, refers to stereoisomers that are not enantiomers, which occurs when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent chiral centers and thus are not mirror images of each other.

35 The term "racemate" as used herein, refers to one that has equal amounts of two enantiomers of different stereo-configuration, and lack in optical activity.

It would be obvious to the skilled artisan from the Examples below that the compounds of this invention are not limited to those with specific stereochemistry.

40 According to a concrete embodiment, the pharmaceutically acceptable salt is produced by reacting the compound with an inorganic acid, an

organic acid, an amino acid, sulfonic acid, an alkali metal or ammonium ion.

The pharmaceutically acceptable salts of the present invention are those which can be manufactured by using a method known in the art, for example, but not limited to, salts with inorganic acids such as hydrochloric acid, bromic acid, sulfuric acid, sodium hydrogen sulfate, phosphate, nitrate and carbonate; and salts with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, succinic acid, benzoic acid, citric acid, maleic acid, malonic acid, tartaric acid, gluconic acid, lactic acid, gestisic acid, fumaric acid, lactobionic acid, salicylic acid, trifluoroacetic acid and acetylsalicylic acid (aspirin); or salts with amino acids such as glycine, alanine, valine, isoleucine, serine, cysteine, cystine, aspartic acid, glutamine, lysine, arginine, tyrosine, and proline; salts with sulfonic acid such as methane sulfonate, ethane sulfonate, benzene sulfonate and toluene sulfonate; metal salts by reaction with an alkali metal such as sodium, lithium and potassium; or salts with ammonium ion.

In another aspect of this invention, there is provided a method for the management of epilepsy comprising administering a pharmaceutically effective amount of the compound of the present invention or pharmaceutically acceptable salt thereof to a subject in need thereof.

The term "pharmaceutically effective amount" as used herein, refers to an amount enough to show and accomplish efficacies and activities for preventing, alleviating, or treating a disease associated with epilepsy.

The pharmaceutical composition of this invention includes a pharmaceutically acceptable carrier besides the active ingredient compound. The pharmaceutically acceptable carrier contained in the pharmaceutical composition of the present invention, which is commonly used in pharmaceutical formulation, but is not limited to, includes lactose, dextrose, sucrose, sorbitol, mannitol, starch, rubber arable, potassium phosphate, arginate, gelatin, potassium silicate, microcrystalline cellulose, polyvinylpyrrolidone, cellulose, water, syrups, methylcellulose, methylhydroxy benzoate, propylhydroxy benzoate, talc, magnesium stearate, and mineral oils. The pharmaceutical composition according to the present invention may further include a lubricant, a humectant, a sweetener, a flavoring agent, an emulsifier, a suspending agent, and a preservative. Details of suitable pharmaceutically acceptable carriers and formulations can be found in Remington's Pharmaceutical Sciences (19th ed., 1995).

The pharmaceutical composition according to the present invention may be administered orally or parenterally, and concretely, administered parenterally. For parenteral administration, it may be administered

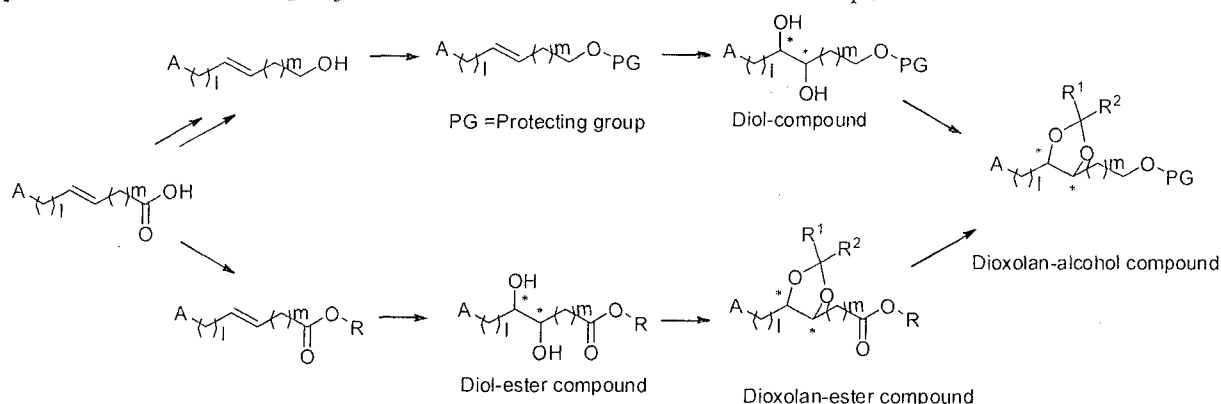
intravenously, subcutaneously, intramuscularly, intraperitoneally, transdermally or intra-articularly. More concretely, it is administered intramuscularly or intraperitoneally.

A suitable dosage amount of the pharmaceutical composition of the present invention may vary depending on pharmaceutical formulation methods, administration methods, the patient's age, body weight, sex, pathogenic state, diet, administration time, administration route, an excretion rate and sensitivity for a used pharmaceutical composition. Preferably, pharmaceutical composition of the present invention may be administered with a daily dosage of 0.001-10000 mg/kg (body weight).

According to the conventional techniques known to those skilled in the art, the pharmaceutical composition according to the present invention may be formulated with a pharmaceutically acceptable carrier and/or vehicle as described above, finally providing several forms including a unit dose form and a multi-dose form. Non-limiting examples of the formulations include, but are not limited to, a solution, a suspension or an emulsion in oil or aqueous medium, an elixir, a powder, a granule, a tablet and a capsule, and may further comprise a dispersion agent or a stabilizer.

The sulfamate derivatives compound of the present invention may be prepared by the following reaction scheme.

[Reaction scheme 1] Synthesis of dioxolan-alcohol compound



A dioxolan-alcohol compound used in the synthesis of a sulfamate compound is synthesized by dihydroxylation, condensation and a deprotection reaction.

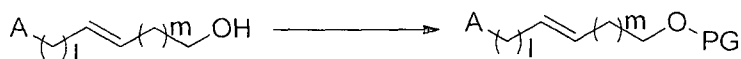
[Reaction scheme 2] Synthesis of alcohol compound



Alcohol compound of formula 3 is synthesized by a reduction reaction using a reducing agent, including but not limited to, LiAlH_4 (Lithium

aluminum hydride), NaBH_4 (Sodium borohydride), $\text{Zn}(\text{BH}_4)_2$ (Zincborohydride), NaH (Sodium hydride), KH (Potassium hydride), AlH_3 (Aluminum hydride), and NaOMe (Sodiummethoxyde) in the basic condition from the Carboxylic acid compound of formula 2

[Reaction scheme 3] Synthesis of protected alcohol compound



PG = Protecting group

Formula 3

Formula 4

OH of Alcohol compound of formula 3 is protected by a protecting group, including but not limited to, TMS(Trimethyl silyl), TES(Triethyl silyl), TIPS(Triisopropyl silyl), TBDMS(tert-butyldimethyl silyl), TBDPS(tert-butyldiphenyl silyl), Piv(Pivaloyl), MOM(Methoxymethyl), Acetyl, Benzoyl, and Tityl(Triphenylmethyl) in the basic condition for using in the next reaction.

[Reaction scheme 4] Synthesis of diol compound



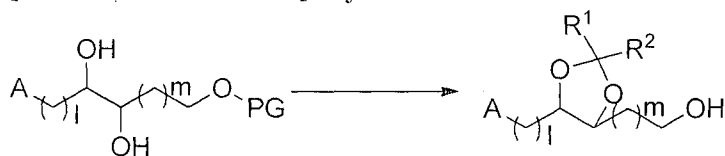
PG = Protecting group

Formula 4

Formula 5

The asymmetric dihydroxylation catalyst may be one or more selected from the group consisting of a chiral ligand (e.g., $(\text{DHQD})_2\text{PHAL}$, $(\text{DHQ})_2\text{PHAL}$, etc.), an osmium catalyst (e.g., OsO_4 , $\text{K}_2\text{OsO}_2(\text{OH})_4$, etc.), K_2CO_3 , $\text{K}_3\text{Fe}(\text{CN})_6$, N-methylmorpholine oxide (NMO), methane sulfone amide ($\text{CH}_3\text{SO}_2\text{NH}_2$), and the like. For example, the asymmetric dihydroxylation catalyst may be AD-mix- α ($\text{K}_2\text{OsO}_2(\text{OH})_4(\text{cat})$, K_2CO_3 , $\text{K}_3\text{Fe}(\text{CN})_6$, $(\text{DHQ})_2\text{PHAL}(\text{cat})$) and methane sulfone amide ($\text{CH}_3\text{SO}_2\text{NH}_2$), or OsO_4 and N-methylmorpholine oxide (NMO), it is not limited thereto and may be appropriately selected depending on the intended purpose.

[Reaction scheme 5] Synthesis of dioxolan-alcohol compound



Formula 5

Formula 6

Diol compound of formula 5 is reacted with a ketone compound(such as acetone, 3-pentanone, cyclopentanone, or cyclohexanone), alkoxy compound(such as dimethoxymethane, dimethoxypropan, diethoxyethane, or methoxy propene, 3-methoxypente-2-ene, 1-methoxycyclopent-1-ene, 1-methoxycyclohex-1-ene), or aldehyde compound(such as benzaldehyde, cyclopentanecarboxaldehyde, or cyclohexaacarboxaldehyde) in the acidic

condition, for example, a solution dissolved with an acid such as p-TsOH(p-toluenesulfonic acid), H₂SO₄(Sulfuric acid), HNO₃(Nitric acid), followed by removing a protecting group to afford the Dioxolan-alcohol compound of formula 6. But while we have described several examples of the ketone compound, the alkoxy compound, the aldehyde compound and the acid for the above reaction, it is not limited thereto and may be appropriately selected depending on the intended purpose.

[Reaction scheme 6] Synthesis of ester compound



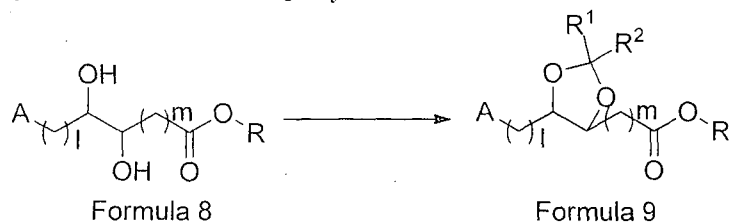
An ester compound of formula 7 having R selected from the group consisting of linear or branched C₁-C₁₀ alkyl, or cyclic C₃-C₁₀ alkyl, allyl and benzyl is synthesized by an esterification reaction in the acidic condition from the carboxylic acid compound of formula 2.

[Reaction scheme 7] Synthesis of ester-diol compound



The asymmetric dihydroxylation catalyst may be one or more selected from the group consisting of a chiral ligand (e.g., (DHQD)₂PHAL, (DHQ)₂PHAL, etc.), an osmium catalyst (e.g., OsO₄, K₂OsO₂(OH)₄, etc.), K₂CO₃, K₃Fe(CN)₆, N-methylmorpholine oxide (NMO), methane sulfone amide (CH₃SO₂NH₂), and the like. For example, the asymmetric dihydroxylation catalyst may be AD-mix-α (K₂OsO₂(OH)₄(cat), K₂CO₃, K₃Fe(CN)₆, (DHQ)₂PHAL(cat)) and methane sulfone amide (CH₃SO₂NH₂), or OsO₄ and N-methylmorpholine oxide (NMO), it is not limited thereto and may be appropriately selected depending on the intended purpose.

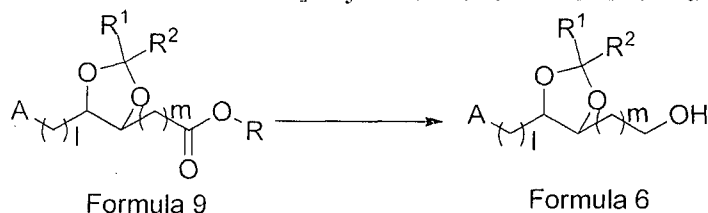
[Reaction scheme8] Synthesis of dioxolan-ester compound



Diol compound of formula 8 is reacted with a ketone compound (such as

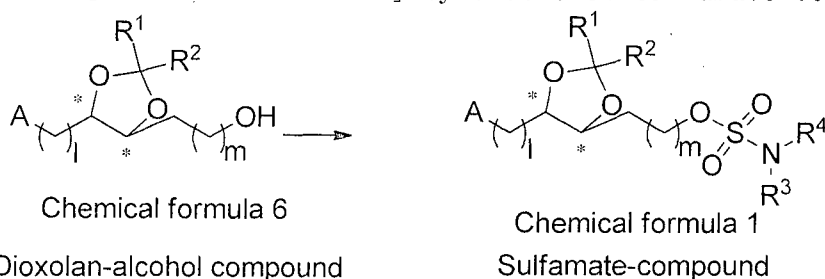
acetone, 3-pentanone, cyclopentanone, or cyclohexanone), an alkoxy compound (such as dimethoxymethane, dimethoxypropan, diethoxyethane, or methoxy propene, 3-methoxypente-2-ene, 1-methoxycyclopent-1-ene, 1-methoxycyclohex-1-ene), or an aldehyde compound (such as benzaldehyde, cyclopentanecarboxaldehyde, or cyclohexaenecarboxaldehyde) in the acidic condition, for example, a solution dissolved with an acid such as p-TsOH (p-toluenesulfonic acid), H_2SO_4 (Sulfuric acid), HNO_3 (Nitric acid) to afford the Dioxolan-alcohol compound of formula 9. But while we have described several examples of the ketone compound, the alkoxy compound, the aldehyde compound and the acid for the above reaction, it is not limited thereto and may be appropriately selected depending on the intended purpose.

[Reaction scheme 9] Synthesis of dioxolan-alcohol compound



Dioxolan-alcohol compound of formula 6 is synthesized by a reduction reaction using a reducing agent, including but not limited to, LiAlH_4 (Lithium aluminum hydride), NaBH_4 (Sodium borohydride), $\text{Zn}(\text{BH}_4)_2$ (Zincborohydride), NaH (Sodium hydride), KH (Potassium hydride), AlH_3 (Aluminum hydride), and NaOMe (Sodium methoxyde) in the basic condition from the dioxolan-ester compound of formula 9.

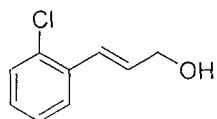
[Reaction scheme 10] Synthesis of Sulfamate compound



Dioxolan-alcohol compound of formula 6 is reacted with sulfamide or sulfamoyl chloride in the basic condition using a base, including but not limited to, pyridine, piperidine, and piperazine to produce the sulfamate compound of formula 1.

EXAMPLES

Preparation example 1: (E)-3-(2-chlorophenyl)prop-2-en-1-ol

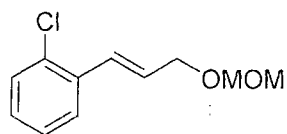


To a 100ml round-bottomed flask, 2-Chlorocinnamic acid (5g, 7.3mmol) and THF (20ml) were added and the reaction mixture was cooled to 0°C. Triethylamine (4.2ml, 30.1mmol) and Ethyl chloroformate (2.88ml, 30.1mmol) were added. The reaction mixture was precipitated as a white solid during stirring. After 2hr, the reaction mixture was filtered with THF (white solid + yellow solution).

The yellow solution was added dropwise to Sodium borohydride (2.68g, 142.3mmol) in H₂O at 0°C and stirred for 2hrs, quenched with 1N HCl solution. The reaction mixture was extracted by EtOAc and washed with H₂O. The combined organic extracts were dried over anhydrous magnesium sulfate (MgSO₄), filtered and concentrated under vacuum. The crude compound was purified by a silica gel column to produce the title compound (2.96g, 60~70%).

¹H NMR (400MHz, CDCl₃) δ 1.67(s, 1H), 4.39(t, J=4.0, 2H), 6.37(dt J=5.6, 16.0, 1H), 7.03(d, J=16.0, 1H), 7.18~7.38(m, 4H),

Preparation example 2: (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene



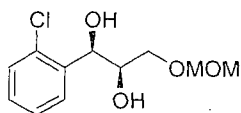
To a 250ml round-bottomed flask, (E)-3-(2-chlorophenyl)prop-2-en-1-ol (2.96g, 17.5mmol, Preparation example 1) and Dichloromethane (17.5ml) were added and the reaction mixture was cooled to 0°C. Diisopropylethylamine (6.1ml, 35.1mmol) was added and stirred at 0°C. Methyl chloromethyl ether (2.77ml, 35.1mmol) was added dropwise and stirred for overnight. The reaction mixture was quenched with 1N NaOH solution, extracted by dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate (MgSO₄), filtered and concentrated under vacuum. The crude compound was purified by a silica gel column to produce the title

compound (3.43g, 85~95%).

^1H NMR (400MHz, CDCl_3) δ 3.44(s, 3H), 4.30(dd, $J=8.0, 1.6$, 1H), 4.73(s, 2H), 6.30(1H, dt, $J=6.0, 16$), 7.04(d, $J=16.0$, 1H), 7.20~7.57(m, 4H)

5

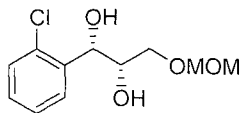
Preparation example 3: (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol



A 250ml round-bottomed flask, equipped with a magnetic stirrer, was filled with 80 ml of tert-butyl alcohol, 80ml of water, and $\text{K}_3\text{Fe}(\text{CN})_6$ (15.93g, 48.3mmol), K_2CO_3 (6.7g, 48.3mmol), $(\text{DHQD})_2\text{-PHAL}$ (0.12g, 0.16mmol), $\text{K}_2\text{OsO}_2(\text{OH})_4$ (11.8mg, 0.03mmol), and Methanesulfonamide (1.53g, 16.1mmol). Stirring at 0°C . (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (3.43g, 16.1mmol, Preparation example 2) was added at once, and the mixture was stirred vigorously at 0°C overnight. While the mixture was stirred at 0°C , solid sodium sulfite (Na_2SO_3 , 24.4g, 193.5mmol) was added and the mixture was allowed to warm to room temperature. Ethyl acetate was added to the reaction mixture, and after the separation of the layers, the aqueous phase was further extracted with the organic solvent. The combined organic layers were washed with 2 N KOH. The combined organic extracts were dried over anhydrous magnesium sulfate (MgSO_4), filtered and concentrated under vacuum. The crude compound was purified by a silica gel column to produce the title compound (3.31g, 75~90%).

^1H NMR (400MHz, CDCl_3) δ 3.09(d, $J=5.6$, 1H), 3.27(d, $J=4.4$, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, $J=4.4$, 1H), 7.23~7.61(m, 1H)

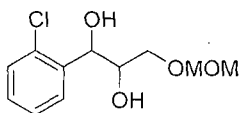
Preparation example 4: (1S,2S)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol



The substantially same method as described in Preparation Example 3 was conducted, except that (DHQ)₂-PHAL was used instead of (DHQD)₂-PHAL, to obtain the title compound. 3.1g (75~90%).

- 5 ¹H NMR (400MHz, CDCl₃) δ 3.09(d, J=5.6, 1H), 3.27(d, J=4.4, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, J=4.4, 1H), 7.23~7.61(m, 4H)

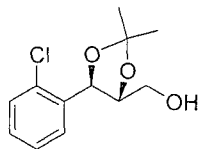
Preparation example 5: 1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol



- 10 (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-en-1-yl)benzene(9.1g, Preparation Example 2) was dissolved in 45mL of a mixture of acetone/t-BuOH/H₂O(5:1:1 V/V). At room temperature, N-methylmorpholine-N-oxide (7.51g) and OsO₄ (0.54g) were added thereto and stirred for 2-3 hours. When the reaction was completed, the obtained product was washed with water and methylenechloride (MC). Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgSO₄), filtrated, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (7.42g, 70~90%).

- 20 ¹H NMR (400MHz, CDCl₃) δ 3.09(d, J=5.6, 1H), 3.27(d, J=4.4, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, J=4.4, 1H), 7.23~7.61(m, 4H)

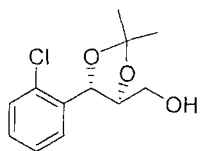
- 25 Preparation example 6: ((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



To (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (3.31g, 13.4mmol, Preparation example 3), Dichloromethane was added and cooled to 0°C. 2,2-Dimethoxypropane (3.3ml, 26.8mmol) and p-toluenesulfonic acid (2g, 10.7mmol) was added and stirred at room temperature for 5hrs. The reaction mixture was quenched with H₂O, extracted with DCM, and washed with H₂O. The organic layer was dried over anhydrous magnesium sulfate (MgSO₄), filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (1.05g, 30~40%).

¹H NMR (400MHz, CDCl₃) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, J=8.4, 1H), 7.25~7.66(m, 4H)

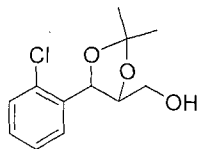
Preparation example 7: ((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 6 was conducted, except that (1S,2S)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 4) was used instead of (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 3), to obtain the title compound (1.1g, 30~40%).

¹H NMR (400MHz, CDCl₃) δ 1.57(s, 3H), 1.64(s, 3H), 1.98(m, 1H), 3.76~3.83(m, 1H), 3.88~3.90(m, 2H), 5.41(d, J=8.4, 1H), 7.25~7.66(m, 4H)

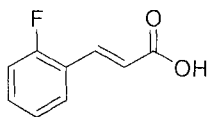
Preparation example 8: (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 6 was conducted, except that 1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 5) was used instead of (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 3), to obtain the title compound (2.1g, 30~40%).

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

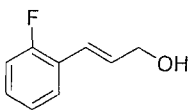
10 Preparation example 9: (E)-3-(2-fluorophenyl)-acrylic acid



Piperidine (247mg, 2.90mmol) was added to a stirred solution of malonic acid (3.1g, 29.00mmol) and 2-fluoroaldehyde (3g, 24.17mmol) in pyridine at room temperature under N_2 condition. The solution was cooled to room temperature, then quenched with HCl solution. The residue was treated with EA and H_2O . The organic layer was separated and the aqueous layer was extracted further with EA. The combined extracts were washed with brine. The organic layer was dried over Na_2SO_4 , filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (3.66g, 70~90%).

^1H NMR (400MHz, CDCl_3) δ 6.60(d, $J=16.0$, 1H), 7.24~7.50(m, 3H), 7.66(d, $J=16.0$, 1H), 7.84(t, $J=8.0$, 1H)

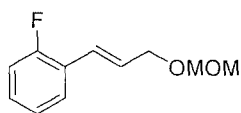
Preparation example 10: (E)-3-(2-fluorophenyl)-prop-2-en-1-ol



The substantially same method as described in Preparation Example 1 was conducted, except that (E)-3-(2-fluorophenyl)-acrylic acid (Preparation example 9) was used instead of 2-Chlorocinnamic acid, to obtain the title compound (1.6g, 30~40%).

5 ^1H NMR (400MHz, CDCl_3) δ 1.67 (s, 1H), 4.39 (t, $J=4.0$, 2H), 6.34~6.41 (m, 1H), 7.00~7.38 (m, 4H)

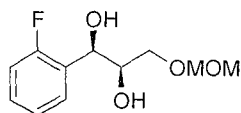
Preparation example 11: (E)-1-Fluoro-2-(3-(methoxymethoxy)prop-1-enyl)benzene



The substantially same method as described in Preparation Example 2 was conducted, except that (E)-3-(2-fluorophenyl)-prop-2-en-1-ol (Preparation example 10) was used instead of (E)-3-(2-chlorophenyl)-prop-2-en-1-ol (Preparation example 1), to obtain the title compound (2.23g, 85~95%).

15 ^1H NMR (400MHz, CDCl_3) δ 3.44(s, 3H), 4.30 (dd, $J=1.6$, 8.0, 1H), 4.73(s, 2H), 6.27~6.37(m, 1H), 7.02~7.57(m, 4H)

Preparation example 12: (1R,2R)-1-(2-fluorophenyl)-3-(methoxymethoxy)propane-1,2-diol

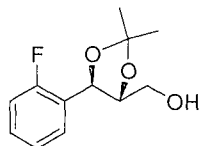


The substantially same method as described in Preparation Example 3 was conducted, except that (E)-1-Fluoro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 11) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy) prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (2.13g, 75~90%).

25 ^1H NMR (400MHz, CDCl_3) δ 3.09(d, $J=5.6$, 1H), 3.27(d, $J=4.4$, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, $J=4.4$, 1H),

7.23~7.61(m, 4H)

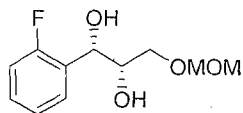
Preparation example 13: ((4R,5R)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 6 was conducted, except that (1R, 2R)-1-(2-fluorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 12) was used instead of (1R, 2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 3), to obtain the title compound (1.73g, 30~40%).

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

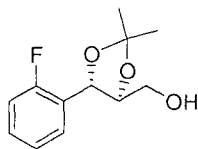
Preparation example 14: (1S,2S)-1-(2-fluorophenyl)-3-(methoxymethoxy)propane-1,2-diol



The substantially same method as described in Preparation Example 4 was conducted, except that (E)-1-Fluoro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 11) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (2.13g, 75~90%).

^1H NMR (400MHz, CDCl_3) δ 3.09(d, $J=5.6$, 1H), 3.27(d, $J=4.4$, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, $J=4.4$, 1H), 7.23~7.61(m, 4H)

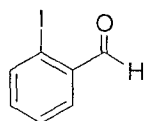
Preparation example 15: ((4S,5S)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 6 was conducted, except that (1S, 2S)-1-(2-fluorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 14) was used instead of (1R, 2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 3), to obtain the title compound (1.73g, 30~40%).

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

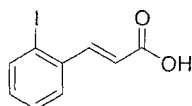
Preparation example 16: 2-Iodobenzenealdehyde



In a flask, 2-iodobenzyl alcohol (4g, 17.09mmol) was dissolved in dichloromethane (MC, 85ml), and then, manganese oxide (MnO_2 , 14.86g, 170.92mmol) was added thereto. The obtained reaction product was stirred under reflux. When the reaction was completed, the obtained reaction product was cooled to room temperature, and then, filtered and concentrated using celite, to obtain the title compound (3.6g, yield 75~90%).

^1H NMR (400MHz, CDCl_3) δ 7.30~7.99(m, 4H), 10.10(s, 1H)

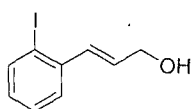
Preparation example 17: (E)-3-(2-iodophenyl)-acrylic acid



The substantially same method as described in Preparation Example 9 was conducted, except that 2-Iodobenzenealdehyde (Preparation example 16) was used instead of 2-Fluoroaldehyde, to obtain the title compound (2.06g, 70~90%)

- 5 ^1H NMR (400MHz, CDCl_3) δ 6.60(d, $J=16.0$, 1H), 7.24~7.50(m, 3H), 7.66(d, $J=16.0$, 1H), 7.84(t, $J=8.0$, 1H)

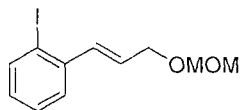
Preparation example 18: (E)-3-(2-iodophenyl)-prop-2-en-1-ol



- 10 The substantially same method as described in Preparation Example 1 was conducted, except that (E)-3-(2-iodophenyl)-acrylic acid (Preparation example 17) was used instead of 2-Chlorocinnamic acid, to obtain the title compound (1.08g, 30~40%).

- 15 ^1H NMR (400MHz, CDCl_3) δ 1.67 (s, 1H), 4.39 (t, $J=4.0$, 2H), 6.34~6.41 (m, 1H), 7.00~7.38 (m, 4H)

Preparation example 19: (E)-1-Iodo-2-(3-(methoxymethoxy)prop-1-enyl)benzene



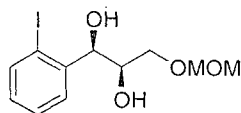
- 20 The substantially same method as described in Preparation Example 2 was conducted, except that (E)-3-(2-iodophenyl)-prop-2-en-1-ol (Preparation example 18) was used instead of (E)-3-(2-chlorophenyl)-prop-2-en-1-ol (Preparation example 1), to obtain the title compound (1.37g, 85~95%).

^1H NMR (400MHz, CDCl_3) δ 3.44(s, 3H), 4.30(dd, $J=8.0$, 1.6, 1H), 4.73(s, 2H), 6.27~6.34(m, 1H), 7.02~7.57(m, 4H)

25

Preparation example 20: (1R, 2R)-1-(2-iodophenyl)-3-(methoxymethoxy)propane-

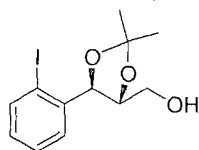
1,2-diol



The substantially same method as described in Preparation Example 3 was conducted, except that (E)-1-iodo-2-(3-(methoxymethoxy)prop-1-en-1-yl)benzene(Preparation example 19) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-en-1-yl)benzene(Preparation example 2), to obtain the title compound (1.32g, 75~90%).

^1H NMR (400MHz, CDCl_3) δ 3.09(d, $J=5.6$, 1H), 3.27(d, $J=4.4$, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, $J=4.4$, 1H), 7.23~7.61(m, 4H)

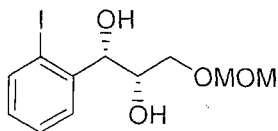
Preparation example 21: ((4R, 5R)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 6 was conducted, except that (1R, 2R)-1-(2-iodophenyl)-3-(methoxymethoxy)propane-1,2-diol(Preparation example 20) was used instead of (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol(Preparation example 3), to obtain the title compound (1.33g, 30~40%).

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

Preparation example 22: (1S,2S)-1-(2-iodophenyl)-3-(methoxymethoxy)propane-1,2-diol

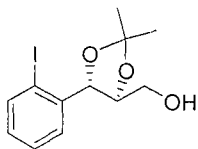


The substantially same method as described in Preparation Example 4 was conducted, except that (E)-1-Iodo-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 19) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (1.32g, 75~90%).

^1H NMR (400MHz, CDCl_3) δ 3.09(d, $J=5.6$, 1H), 3.27(d, $J=4.4$, 1H), 3.41(s, 3H), 3.69~3.77(m, 2H), 3.96~3.99(m, 1H), 4.69(s, 2H), 5.19(t, $J=4.4$, 1H), 7.23~7.61(m, 4H)

10

Preparation example 23: ((4S,5S)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol

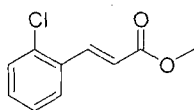


The substantially same method as described in Preparation Example 6 was conducted, except that (1S,2S)-1-(2-iodophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 22) was used instead of (1R,2R)-1-(2-chlorophenyl)-3-(methoxymethoxy)propane-1,2-diol (Preparation example 3), to obtain the title compound (1.33g, 30~40%).

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.63(s, 3H), 1.95~1.98(m, 1H), 3.88~3.89(m, 1H), 3.90~3.96(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

20

Preparation example 24: (E)-Methyl-3-(2-chlorophenyl)acrylate



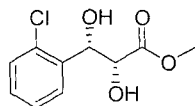
To a 250ml round-bottomed flask, 2-Chlorocinnamic acid (25g, 136.9mmol) and

MeOH (56ml) were added. POCl_3 (1.27ml, 13.6mmol) was added dropwise. The reaction mixture was stirred under reflux for 3~4h. The reaction mixture was cooled to room temperature, quenched with 1N NaOH solution. The mixture was extracted by EtOAc and washed with H_2O . The aqueous layer was further
5 extracted with EtOAc. The combined organic layer was dried over anhydrous magnesium sulfate (MgSO_4), filtered and concentrated under vacuum (26.98g, 85~97%)

^1H NMR (400MHz, CDCl_3) δ 3.84 (s, 3H), 6.45 (d, $J=16.0$, 1H), 7.28~7.65 (m, 4H), 8.12 (d, $J=16.0$, 1H)

10

Preparation example 25: (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate

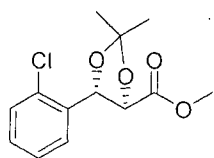


A 1000ml round-bottomed flask, equipped with a magnetic stirrer, was
15 filled with 362 ml of tert-butyl alcohol, 362ml of water, $\text{K}_3\text{Fe}(\text{CN})_6$ (135.53g, 411.63mmol), K_2CO_3 (56.89g, 411.63mmol), $(\text{DHQ})_2\text{PHAL}$ (1.06g, 1.37mmol), $\text{K}_2\text{OsO}_2(\text{OH})_4$ (0.1g, 0.27mmol), and Methanesulfonamide (13.05g, 137.21mmol) and stirred at 0°C . (E)-Methyl-3-(2-chlorophenyl)acrylate (26.98g, Preparation example 24) was added at once, and the mixture was
20 stirred vigorously at 0°C overnight. While the mixture was stirred at 0°C , solid sodium sulfite (Na_2SO_3 , 24.4g, 193.5mmol), EtOAc and water was added and the mixture was allowed to warm to room temperature and stirred. After the separation of the layer, the aqueous layer was added to EtOAc, and the aqueous layer was separated. The combined organic layers were washed with
25 0.3M $\text{H}_2\text{SO}_4/\text{Na}_2\text{SO}_4$ solution (H_2SO_4 76ml, H_2O 2L, Na_2SO_4 360g) twice. After separation of the organic layer, the organic layer was washed with H_2O . After separating of the layer, the organic layer were dried over anhydrous MgSO_4 , filtered and concentrated under vacuum. The crude compound was purified by a silica gel column to produce the title compound (24.42g,
30 70~90%)

^1H NMR (400MHz, CDCl_3) δ 7.62~7.26 (4H, m), 5.51(1H, dd, $J=7.2$, 2.4),

4.50(1H, dd, $J=5.6, 2.4$), 3.86(3H, s), 3.13(1H, d, $J=6.0$), 2.79(1H, d, $J=7.2$)

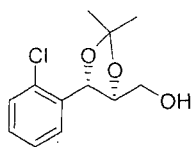
Preparation example 26: (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



Dichloromethane(DMC) was added to (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(24.4g, Preparation example 25) and cooled to 0°C. 2,2-Dimethoxypropane (26ml, 211.77mmol) and p-toluenesulfonic acid (2g, 10.58mmol) was added and stirred at room temperature. The reaction mixture was quenched with H₂O, extracted with DCM, washed with H₂O, dried over anhydrous magnesium sulfate, filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (23.6g, 70~95%).

¹H NMR (400MHz, CDCl₃) δ 1.63(s, 3H), 1.65(s, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.62(d, $J=7.6$, 1H), 7.28~7.64(m, 4H)

Preparation example 27: ((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



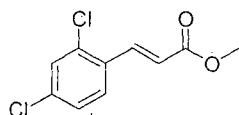
A solution of To a solution LAH(LiAlH₄ 3.31g, 87.25mmol) in THF was added dropwise to a solution of (4R,5S)-methyl 5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (23.6g, Preparation 26) in THF at 0°C, and the mixture stirred at room temp. The reaction mixture was quenched with H₂O at 0°C, cellite filtered with EtOAc, washed with EtOAc, dried over anhydrous magnesium sulfate(MgSO₄), filtered and concentrated. The crude compound was

purified by a silica gel column to produce the title compound (21.13g 70~95%)

^1H NMR (400MHz, CDCl_3) δ 1.57(s, 3H), 1.64(s, 3H), 1.98(m, 1H), 3.76~3.83(m, 1H), 3.88~3.90(m, 2H), 5.41(d, $J=8.4$, 1H), 7.25~7.66(m, 4H)

5

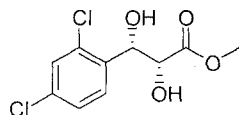
Preparation example 28: (E)-Methyl-3-(2,4-dichlorophenyl)acrylate



The substantially same method as described in Preparation Example 24 was conducted, except that 2,4-dichlorocinnamic acid was used instead of 2-chlorocinnamic acid, to obtain the title compound(9.7g, 70~90%)

^1H NMR (400MHz, CDCl_3): δ 3.84(s, 3H), 6.44(d, $J=16$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.55(d, $J=8.4$, 1H), 8.04(d, $J=16$, 1H).

Preparation example 29: (2R,3S)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate

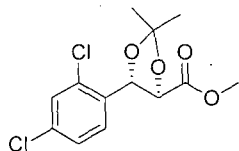


The substantially same method as described in Preparation Example 25 was conducted, except that (E)-Methyl-3-(2,4-dichlorophenyl)acrylate (Preparation example 28) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate (Preparation example 24), to obtain the title compound (3.8g, 60~80%)

^1H NMR (400MHz, CDCl_3): δ 3.11(s, 1H), 3.88(s, 3H), 4.42(d, $J=2.4$, 1H), 5.43(d, $J=2.0$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.55(d, $J=8.4$, 1H).

25

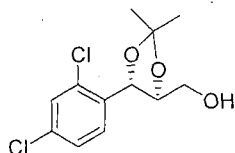
Preparation example 30: (4R,5S)-methyl-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 26 was conducted, except that (2R,3S)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 29) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound (3.5g, 60~80%)

^1H NMR (400MHz, CDCl_3): δ 1.59(s, 3H), 1.63(d, $J=8.8$, 3H), 3.78(s, 3H), 4.25(d, $J=7.6$, 1H), 5.56(d, $J=8.0$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.56(d, $J=8.4$, 1H).

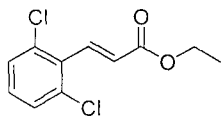
Preparation example 31: ((4S,5S)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-methyl-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 30) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (3.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.56(s, 3H), 1.62(d, $J=4.8$, 6H), 1.97(dd, $J=7.6$, $J=7.2$, 1H), 3.75~3.80(m, 1H), 3.82~3.86(m, 1H), 3.89~3.94(m, 1H), 5.36(d, $J=8.4$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.56(d, $J=8.4$, 1H).

Preparation example 32: (E)-Ethyl-3-(2,6-dichlorophenyl)acrylate

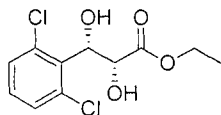


To a stirred solution of 2,6-dichlorobenzaldehyde (5.0g, 28.56mmol) in THF was added triethyl phosphono acetate (6.4g, 28.56mmol) at 0°C. The reaction mixture was added *t*-BuOK (3.2g, 28.56mmol) at room temperature.

- 5 The mixture was stirred for 10h then the resulting mixture was quenched with 1N HCl, diluted with ether, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by SiO₂ gel column chromatography (4.3g 40~60%)

10 ¹H NMR (400MHz, CDCl₃): δ 1.36(t, *J*=3.6, 3H), 4.31(q, *J*=3.7, 2H), 6.61(d, *J*=16, 1H), 7.21(t, *J*=4.2, 1H), 7.38(d, *J*=5.2, 1H), 7.81(d, *J*= 16, 1H).

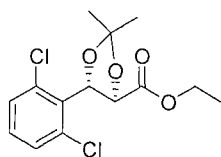
Preparation example 33: (2R,3S)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate



- 15 The substantially same method as described in Preparation Example 25 was conducted, except that (E)-ethyl-3-(2,6-dichlorophenyl)acrylate (Preparation example 32) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate (Preparation example 24), to obtain the title compound (3.9g, 60~80%)

20 ¹H NMR (400MHz, CDCl₃): δ 1.21(t, *J*=7.2, 3H), 3.22(s, 1H), 3.69(s, 1H), 4.20~4.28(m, 1H), 4.70(d, *J*=5.2, 1H), 5.62(d, *J*=5.6, 1H), 7.19~7.36(m, 3H).

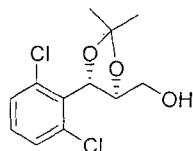
Preparation example 34: (4R,5S)-ethyl-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 26 was conducted, except that (2R,3S)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 29) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(4.1g, 60~90%)

^1H NMR (400MHz, CDCl_3): δ 1.26(t, $J=7.2$, 3H), 1.58(s, 3H), 1.70(s, 3H), 3.77(s, 3H), 4.24(q, $J=7.2$, 1H), 4.95(q, $J=4.4$, 1H), 5.95(q, $J=3.0$, 1H), 7.20~7.39(m, 3H).

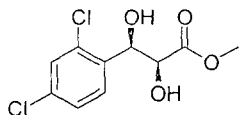
Preparation example 35: ((4S,5S)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-ethyl-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 33) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(3.5g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.55(s, 3H), 1.68(s, 3H), 3.66(q, $J=5.5$, 1H), 3.85(q, $J=5.1$, 1H), 4.56~4.61(m, 1H), 5.78(d, $J=9.2$, 1H), 7.19~7.37(m, 3H).

Preparation example 36: (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate

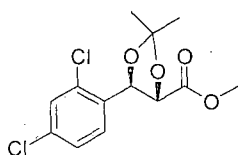


The substantially same method as described in Preparation Example 3 was conducted, except that (E)-Methyl-3-(2,4-dichlorophenyl)acrylate(Preparation example 28) was used instead of (E)-1-

chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene(Preparation example 2), to obtain the title compound (2.4g, 75~90%).

¹H NMR (400MHz, CDCl₃): δ 3.11(s, 1H), 3.88(s, 3H), 4.42(d, J=2.4, 1H), 5.43(d, J=2.0, 1H), 7.28~7.33(m, 1H), 7.41(d, J=2.0, 1H), 7.55(d, J= 8.4, 1H).

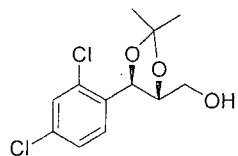
Preparation example 37: (4S, 5R)-methyl-5-(2,4-dichlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 26 was conducted, except that (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 36) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(3.2g, 60~80%)

¹H NMR (400MHz, CDCl₃): δ 1.59(s, 3H), 1.63(d, J=8.8, 3H), 3.78(s, 3H), 4.25(d, J=7.6, 1H), 5.56(d, J=8.0, 1H), 7.28~7.33(m, 1H), 7.41(d, J=2.0, 1H), 7.56(d, J= 8.4, 1H).

Preparation example 38: ((4R,5R)-5-(2,4-dichlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-yl)methanol



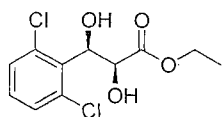
The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2,4-dichlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate(Preparation example 37) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate

(Preparation example 26), to obtain the title compound(3.5g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.56(s, 3H), 1.62(d, $J=4.8$, 6H), 1.97(dd, $J=7.6$, $J=7.2$, 1H), 3.75~3.80(m, 1H), 3.82~3.86(m, 1H), 3.89~3.94(m, 1H), 5.36(d, $J=8.4$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.56(d, $J=8.4$, 1H).

5

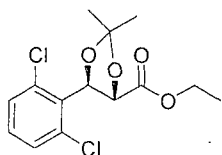
Preparation example 39: (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 3 was conducted, except that (E)-ethyl-3-(2,6-dichlorophenyl)acrylate(Preparation example 32) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene(Preparation example 2), to obtain the title compound (2.8g, 75~90%).

^1H NMR (400MHz, CDCl_3): δ 3.11(s, 1H), 3.88(s, 3H), 4.42(d, $J=2.4$, 1H), 5.43(d, $J=2.0$, 1H), 7.28~7.33(m, 1H), 7.41(d, $J=2.0$, 1H), 7.55(d, $J=8.4$, 1H). ^1H NMR (400MHz, CDCl_3): δ 1.21(t, $J=7.2$, 3H), 3.22(s, 1H), 3.69(s, 1H), 4.20~4.28(m, 1H), 4.70(d, $J=5.2$, 1H), 5.62(d, $J=5.6$, 1H), 7.19~7.36(m, 3H).

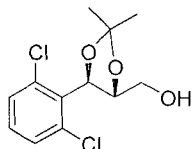
Preparation example 40: (4S,5R)-ethyl-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 26 was conducted, except that (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 39) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(4.1g, 60~90%)

^1H NMR (400MHz, CDCl_3): δ 1.26 (t, $J=7.2$, 3H), 1.58(s, 3H), 1.70(s, 3H), 3.77(s, 3H), 4.24(q, $J=7.2$, 1H), 4.95(q, $J=4.4$, 1H), 5.95(q, $J=3.0$, 1H), 7.20~7.39(m, 3H).

- 5 Preparation example 41: ((4R,5R)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol

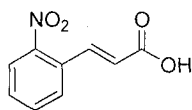


The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 40) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26). to obtain the title compound(5.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.55(s, 3H), 1.68(s, 3H), 3.66(q, $J=5.5$, 1H), 3.85(q, $J=5.1$, 1H), 4.56~4.61(m, 1H), 5.78(d, $J=9.2$, 1H), 7.19~7.37(m, 3H).

15

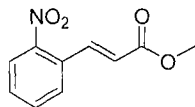
Preparation example 42: (E)-3-(2-nitrophenyl)-acrylic acid



The substantially same method as described in Preparation Example 9 was conducted, except that 2-nitrobenzenealdehyde was used instead of 2-Fluoroaldehyde, to obtain the title compound (2.06g, 70~90%)

^1H NMR (400MHz, DMSO) δ 6.52(d, $J=15.6$, 1H), 7.65(t, $J=8.1$, 1H), 7.75(t, $J=7.4$, 1H), 7.83(d, $J=15.8$, 1H), 7.92(dd, $J=7.6$, 1.1, 1H), 8.05(dd, $J=8.1$, 1.2, 1H)

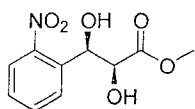
- 25 Preparation example 43: (E)-Methyl-3-(2-nitrophenyl)acrylate



The substantially same method as described in Preparation Example 24 was conducted, except that (E)-3-(2-nitrophenyl)-acrylic acid (Preparation example 42) was used instead of 2-chlorocinnamic acid, to obtain the title compound (15.8g, 70~90%)

^1H NMR (400MHz, CDCl_3) δ 3.80 (s, 3H), 6.34 (d, $J=15.9$ Hz, 1H), 7.49-7.68 (m, 4H), 8.01 (d, $J=7.9$ Hz, 1H), 8.08 (d, $J=15.9$, 1H).

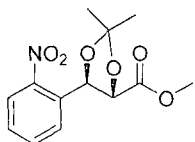
Preparation example 44: (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 3 was conducted, except that (E)-Methyl-3-(2-nitrophenyl)acrylate (Preparation example 43) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (12.5g, 75~90%).

^1H NMR (400MHz, CDCl_3): δ = 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H), 7.53~7.90(m, 4H).

Preparation example 45: (4S, 5R)-methyl-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate

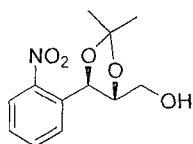


The substantially same method as described in Preparation Example 26 was

conducted, except that (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 44) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(11g, 60~80%)

5 ^1H NMR (400MHz, CDCl_3): δ 1.38(s, 3H), 1.40(s, 3H), 3.75(s, 3H), 4.49(d, $J=7.4$, 1H), 5.25(d, $J=7.4$, 1H), 7.48~7.77(m, 3H), 8.08(m, 1H)

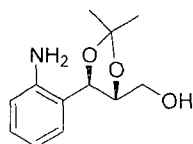
Preparation example 46: ((4R,5R)-5-(2-nitrophenyl)-2,2-dimehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2-nitrophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 45) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(13.1g, 70~95%)

15 ^1H NMR (400MHz, CDCl_3): δ 1.38(s, 3H), 1.40(s, 3H), 3.89(d, $J=4.1$, 2H), 4.26(dt, $J=7.0$, 4.1, 1H), 5.26(d, $J=7.0$, 1H), 7.55~7.86(m, 3H), 8.08(m, 1H).

Preparation example 47: ((4R,5R)-5-(2-aminophenyl)-2,2-dimehtyl-1.3-dioxolane-4-yl)methanol



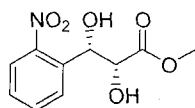
To a stirred solution of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimehtyl-1.3-dioxolane-4-yl)methanol(Preparation example 46, 14g) in EtOAc was added $\text{Pd}(\text{OH})_2$ (20wt%, 2.8g) under hydrogen gas(balloon). The mixture was stirred for 6h then the resulting mixture was filtered through celite and concentrated under reduced pressure. The crude product was purified by SiO_2

gel column chromatography to give title compound (7.5g 65-85%)

^1H NMR (400MHz, CDCl_3): δ 1.39 (s, 3H), 1.40 (s, 3H), 3.88 (d, $J=4.27$, 2H), 3.99 (dt, $J=7.02$, $J=4.30$, 1H), 4.74 (d, $J=7.02$, 1H), 6.65-6.72 (m, 2H), 6.98 (m, 1H), 7.25 (m, 1H).

5

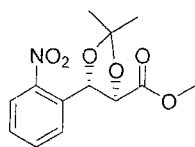
Preparation example 48: (2R,3S)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate



10 The substantially same method as described in Preparation Example 25 was conducted, except that (E)-methyl-3-(2-nitrophenyl)acrylate(Preparation example 43) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate(Preparation example 24), to obtain the title compound(21.7g, 60~80%)

15 ^1H NMR (400MHz, CDCl_3): δ 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H), 7.53~7.90(m, 4H)

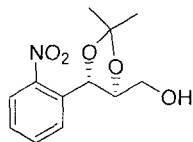
Preparation example 49: (4R,5S)-methyl-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



20 The substantially same method as described in Preparation Example 26 was conducted, except that (2R,3S)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 48) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(21g, 60~90%)

25 ^1H NMR (400MHz, CDCl_3): δ 1.38(s, 3H), 1.40(s, 3H), 3.75(s, 3H), 4.49(d, $J=7.4$, 1H), 5.25(d, $J=7.4$, 1H), 7.48~7.77(m, 3H), 8.08(m, 1H)

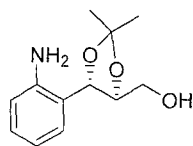
Preparation example 50: ((4S,5S)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



5 The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-methyl-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 48) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (14g, 70~95%)

10 ^1H NMR (400MHz, CDCl_3): δ 1.38(s, 3H), 1.40(s, 3H), 3.89(d, $J=4.1$, 2H), 4.26(dt, $J=7.0$, 4.1, 1H), 5.26(d, $J=7.0$, 1H), 7.55~7.86(m, 3H), 8.08(m, 1H).

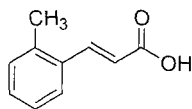
Preparation example 51: ((4S,5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



15 The substantially same method as described in Preparation Example 47 was conducted, except that (4S,5S)-methyl-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 50) was used instead of (4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (11g, 70~95%)

20 ^1H NMR (400MHz, CDCl_3): δ 1.38(s, 3H), 1.40(s, 3H), 3.89(d, $J=4.1$, 2H), 4.26(dt, $J=7.0$, 4.1, 1H), 5.26(d, $J=7.0$, 1H), 7.55~7.86(m, 3H), 8.08(m, 1H).

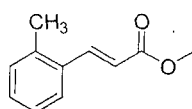
25 Preparation example 52: (E)-3-*o*-tolylacrylic acid



The substantially same method as described in Preparation Example 9 was conducted, except that 2-methylbenzenealdehyde was used instead of 2-Fluoroaldehyde, to obtain the title compound (1.5g, 70~90%)

- 5 ^1H NMR (400MHz, CDCl_3): δ 2.48(s, 3H), 6.16(d, $J=15.1$, 1H), 7.00~7.10(m, 1H), 7.21~7.26(m, 3H), 8.04(d, $J=15.1$, 1H), 11.0(s, 1H).

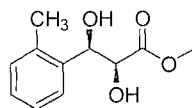
Preparation example 53: (E)-Methyl-3-*o*-tolylacrylate



- 10 The substantially same method as described in Preparation Example 24 was conducted, except that (E)-3-*o*-tolylacrylic acid (Preparation example 52) was used instead of 2-chlorocinnamic acid, to obtain the title compound (1.5g, 70~90%)

- 15 ^1H NMR (400MHz, CDCl_3): δ 2.48(s, 3H), 3.77(s, 3H), 6.14(d, $J=15.1$, 1H), 7.00~7.10(m, 1H), 7.21~7.26(m, 3H), 8.07(d, $J=15.1$, 1H).

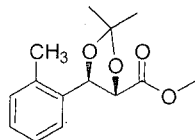
Preparation example 54: (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate



- 20 The substantially same method as described in Preparation Example 3 was conducted, except that (E)-Methyl-3-*o*-tolylacrylate (Preparation example 53) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (1.3g, 75~90%).

- 25 ^1H NMR (400MHz, CDCl_3): δ 2.34(s, 3H), 2.80(s, 1H), 3.65(s, 1H), 3.68(s, 3H), 4.52(d, $J=7.0$, 1H), 5.22(d, $J=7.0$, 1H), 7.19~7.39(m, 4H).

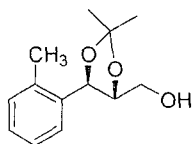
Preparation example 55: (4S, 5R)-methyl-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



5 The substantially same method as described in Preparation Example 26 was conducted, except that (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate (Preparation example 54) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(1.7g, 60~80%)

10 ^1H NMR (400MHz, CDCl_3): δ 1.27(s, 6H), 2.34(s, 3H), 3.68(s, 3H), 5.11(d, $J=7.0$, 1H), 5.81(d, $J=7.0$, 1H), 7.19~7.26(m, 3H), 7.37~7.39(m, 1H).

Preparation example 56: ((4R,5R)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol

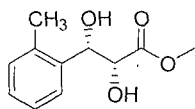


15 The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 55) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(1.3g, 70~95%)

20 ^1H NMR (400MHz, CDCl_3): δ 1.27(s, 6H), 2.34(s, 3H), 3.52~3.60(m, 2H), 3.65(s, 1H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.19~7.26(m, 3H), 7.37~7.39(m, 1H).

25 Preparation example 57: (2R,3S)-methyl-3-(2-methylphenyl)-2,3-

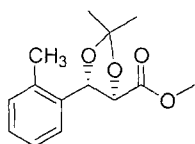
dihydroxypropanoate



The substantially same method as described in Preparation Example 25 was conducted, except that (E)-methyl-3-o-tolylacrylate(Preparation example 53) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate(Preparation example 24), to obtain the title compound(1.7g, 60-80%)

^1H NMR (400MHz, CDCl_3): δ 2.34(s, 3H), 2.80(s, 1H), 3.65(s, 1H), 3.68(s, 3H), 4.52(d, $J=7.0$, 1H), 5.22(d, $J=7.0$, 1H), 7.19~7.39(m, 4H).

Preparation example 58: (4R,5S)-methyl-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate

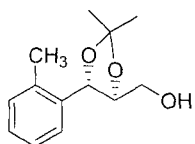


The substantially same method as described in Preparation Example 26 was conducted, except that (2R,3S)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate (Preparation example 57) was used instead of (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound(1.9g, 60~90%)

^1H NMR (400MHz, CDCl_3): δ 1.27(s, 6H), 2.34(s, 3H), 3.68(s, 3H), 5.11(d, $J=7.0$, 1H), 5.81(d, $J=7.0$, 1H), 7.19~7.26(m, 3H), 7.37~7.39(m, 1H).

20

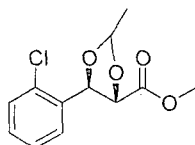
Preparation example 59: ((4S,5S)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-methyl-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 58) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (1.5g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.27(s, 6H), 2.34(s, 3H), 3.52~3.60(m, 2H), 3.65(s, 1H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.19~7.26(m, 3H), 7.37~7.39(m, 1H).

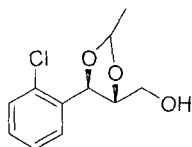
Preparation example 60: ((4S,5R)-methyl-5-(2-chlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



Dichloromethane (MC) was added to (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 433) at room temperature. 1,1-Diethoxyethane (8ml) and p-toluenesulfonic acid (0.27g) was added and stirred at room temperature. The reaction mixture was quenched with H_2O , extracted with MC, washed with H_2O , dried over anhydrous magnesium sulfate (MgSO_4), filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (3.6g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.28~7.64(m, 4H)

Preparation example 61: ((4R,5R)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol

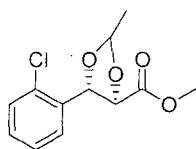


The substantially same method as described in Preparation Example 27 was

conducted, except that (4S,5R)-methyl-5-(2-chlorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 60) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(3.1g, 70~95%)

5 ^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.19~7.26(m, 3H), 7.37~7.39(m, 1H).

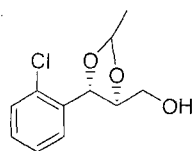
Preparation example 62: ((4R,5S)-methyl-5-(2-chlorophenyl)-2-mehtyl-1.3-
10 dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 60 was conducted, except that (2R,3S)-methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 25) was used instead of (2S,3R)-
15 methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 54), to obtain the title compound(2.1g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.28~7.64(m, 4H)

20 Preparation example 63: ((4S,5S)-5-(2-chlorophenyl)-2-mehtyl-1.3-dioxolane-4-yl)methanol

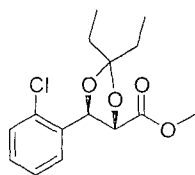


The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-methyl-5-(2-chlorophenyl)-2-mehtyl-1.3-
25 dioxolane-4-carboxylate(Preparation example 62) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-

carboxylate(Preparation example 26), to obtain the title compound(3.1g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.19~7.26(m, 3H),
5 7.37~7.39(m, 1H).

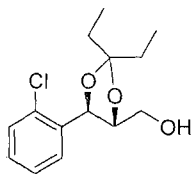
Preparation example 64: (4S, 5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-carboxylate



10 3-pentanone was added to (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433) at room temperature. Sulfuric acid (H_2SO_4) was added and stirred at room temperature. The reaction mixture was quenched with H_2O , extracted with EA, washed with H_2O , dried over anhydrous sodium sulfate (Na_2SO_4), filtered and concentrated. The
15 crude compound was purified by a silica gel column to produce the title compound (1.6g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.22~7.60(m, 4H)

20 Preparation example 65: ((4R,5R)-5-(2-chlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-yl)methanol

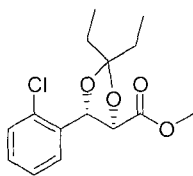


The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1,3-

dioxolane-4-carboxylate(Preparation example 64) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(2.0g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 0.96(m, 6H), 1.59(m, 4H), 3.66(d, J=8.0, 2H),
5 5.09 (d, J=7.6, 1H), 5.88(d, J=7.6, 1H), 7.26~7.62(m, 4H).

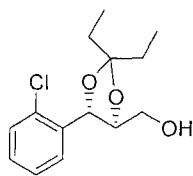
Preparation example 66: (4R, 5S)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



10 The substantially same method as described in Preparation Example 64 was conducted, except that (2R,3S)-methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 25) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 54), to obtain the title compound(1.4g, 70~95%).

15 ¹H NMR (400MHz, CDCl₃) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, J=7.6, 1H), 5.81(d, J=7.6, 1H), 7.22~7.60(m, 4H)

Preparation example 67: ((4S,5S)-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



20

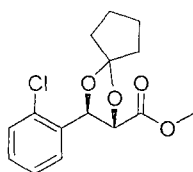
The substantially same method as described in Preparation Example 65 was conducted, except that (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 66) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-

carboxylate(Preparation example 64), to obtain the title compound(2.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.66(d, $J=8.0$, 2H), 5.09 (d, $J=7.6$, 1H), 5.88(d, $J=7.6$, 1H), 7.26~7.62(m, 4H).

5

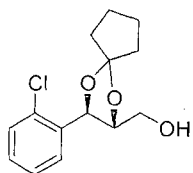
Preparation example 68: (2S, 3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation Example 64 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.2g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.39~7.61(m, 4H)

Preparation example 69: ((2R,3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol

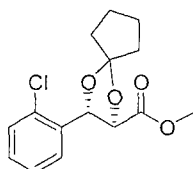


The substantially same method as described in Preparation Example 65 was conducted, except that (2S, 3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 68) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound (1.7g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m,

2H), 3.82~3.86(m, 1H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.34~7.58(m, 4H)

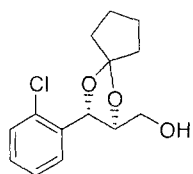
Preparation example 70: (2R, 3S)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation Example 68 was conducted, except that (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 25) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound(1.5g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.39~7.61(m, 4H)

Preparation example 71: ((2R,3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol

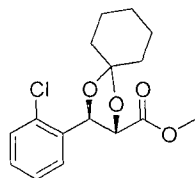


The substantially same method as described in Preparation Example 69 was conducted, except that (2R, 3S)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 70) was used instead of (2S, 3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 68), to obtain the title compound(1.8g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.34~7.58(m,

4H)

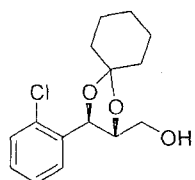
Preparation example 72: (2S, 3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation Example 64 was conducted, except that cyclohexanone was used instead of 3-pentanone, to obtain the title compound (1.2g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.35~7.63(m, 4H)

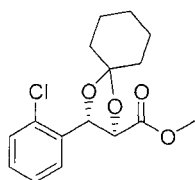
Preparation example 73: ((2R,3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation Example 65 was conducted, except that (2S, 3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 72) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound(1.8g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.48~7.87(m, 4H)

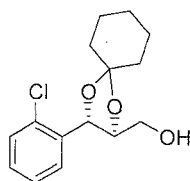
Preparation example 74: (2R, 3S)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation Example 72 was conducted, except that (2R,3S)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 25) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound (2.1 g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, J=8.0, 1H), 5.85(d, J=8.0, 1H), 7.35~7.63(m, 4H)

Preparation example 75: ((2S,3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

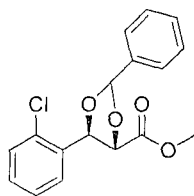


The substantially same method as described in Preparation Example 65 was conducted, except that (2R, 3S)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 74) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound(1.6g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, J=8.0, 1H), 5.43(d, J=7.6, 1H), 7.48~7.87(m, 4H)

Preparation example 76: (4S, 5R)-methyl-5-(2-chlorophenyl)-2-phenyl-1,3-

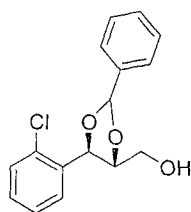
dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 64 was conducted, except that benzaldehyde was used instead of 3-pentanone, to obtain the title compound (1.1g, 50~70%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.35~7.63(m, 4H)

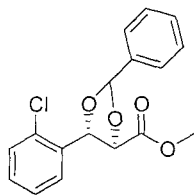
Preparation example 77: ((4R,5R)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 65 was conducted, except that (2S, 3R)-methyl-3-(2-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 76) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound(0.7g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.48~7.87(m, 4H)

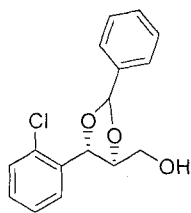
Preparation example 78: (4R, 5S)-methyl-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 66 was conducted, except that benzaldehyde was used instead of 3-pentanone, to obtain the title compound (1.9g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.35~7.63(m, 4H)

Preparation example 79: ((4S,5S)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



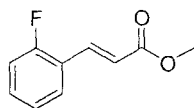
10

The substantially same method as described in Preparation Example 65 was conducted, except that (2R, 3S)-methyl-3-(2-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 78) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 64), to obtain the title compound (1.3g, 70~95%)

15

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.48~7.87(m, 4H)

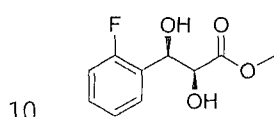
20 Preparation example 80: (E)-Methyl-3-(2-fluorophenyl)acrylate



The substantially same method as described in Preparation Example 24 was conducted, except that (E)-3-(2-fluorophenyl)-acrylic acid (Preparation example 9) was used instead of 2-chlorocinnamic acid, to obtain the title compound. (6.98g, 70~90%)

- 5 ^1H NMR (400MHz, CDCl_3) δ 3.84 (s, 3H), 6.45 (d, $J=16.0$, 1H), 7.24~7.62 (m, 4H), 8.12 (d, $J=16.0$, 1H)

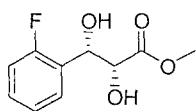
Preparation example 81: (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate



- The substantially same method as described in Preparation Example 3 was conducted, except that (E)-Methyl-3-(2-fluorophenyl)acrylate (Preparation example 80) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl) benzene (Preparation example 2), to obtain the title compound (7.5g, 75~90%).

^1H NMR (400MHz, CDCl_3): δ = 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H), 7.32~7.70(m, 4H).

- Preparation example 82: (2R,3S)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate

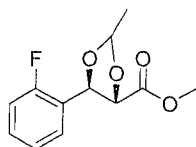


- The substantially same method as described in Preparation Example 25 was conducted, except that (E)-methyl-3-(2-fluorophenyl)acrylate (Preparation example 80) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate (Preparation example 24), to obtain the title compound (7.2g, 60~80%)

^1H NMR (400MHz, CDCl_3): δ = 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H),

7.32~7.70(m, 4H).

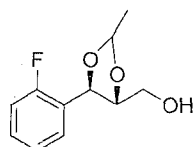
Preparation example 83: ((4S,5R)-methyl-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 60 was conducted, except that (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate(Preparation example 81) was used instead of ((2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound(3.1g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.29~7.67(m, 4H)

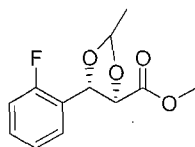
Preparation example 84: ((4R,5R)-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 83) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(3.3g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.19~7.39(m, 4H).

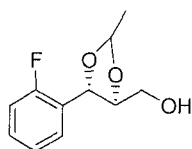
Preparation example 85: ((4R,5S)-methyl-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 60 was conducted, except that (2R,3S)-methyl-3-(2-fluorophenyl)-2.3-dihydroxypropanote(Preparation example 82) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 433), to obtain the title compound (2.9g, 70~95%).

¹H NMR (400MHz, CDCl₃) δ 1.36(d, J=6.4, 3H), 3.78(s, 3H), 4.30(d, J=7.6, 1H), 5.07(m, 1H), 5.62(d, J=7.6, 1H), 7.29~7.69(m, 4H)

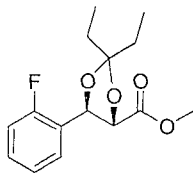
Preparation example 86: ((4S,5S)-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4R,5S)-methyl-5-(2-fluorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 85) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(3.8g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 1.37(d, J=6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J=7.0, J=7.0, 1H), 5.06(m, 1H), 5.17(d, J=7.0, 1H), 7.19~7.4.2(m, 4H).

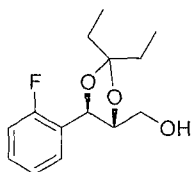
Preparation example 87: (4S, 5R)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 64 was conducted, except that (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 81) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 433), to obtain the title compound (2.1g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.20~7.61(m, 4H)

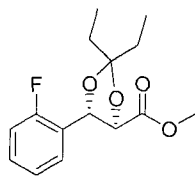
Preparation example 88: ((4R,5R)-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 27 was conducted, except that (4S,5R)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 87) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (2.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.66(d, $J=8.0$, 2H), 5.09 (d, $J=7.6$, 1H), 5.88(d, $J=7.6$, 1H), 7.23~7.60(m, 4H).

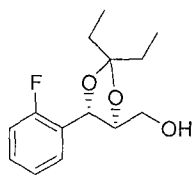
Preparation example 89: (4R, 5S)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 87 was conducted, except that (2R,3S)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 82) was used instead of (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 81), to obtain the title compound (2.3g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.20~7.61(m, 4H)

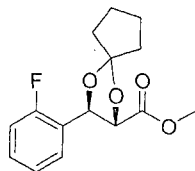
Preparation example 90: ((4S,5S)-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation Example 88 was conducted, except that (4R,5S)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 89) was used instead of (4S,5R)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 87), to obtain the title compound (2.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.66(d, $J=8.0$, 2H), 5.09 (d, $J=7.6$, 1H), 5.88(d, $J=7.6$, 1H), 7.23~7.62(m, 4H).

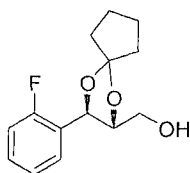
Preparation example 91: (2S, 3R)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation Example 87 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.1g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, *J*=7.2, 1H), 5.39(d, *J*=7.2, 1H), 7.33~7.62(m, 4H)

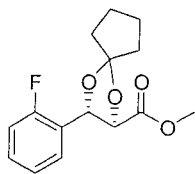
Preparation example 92: ((2R,3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation Example 65 was conducted, except that (2S, 3R)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 91) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound(1.9g, 70~95%).

¹H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, *J*=5.2, 1H), 5.12(d, *J*=7.6, 1H), 7.32~7.57(m, 4H)

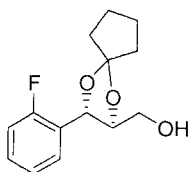
Preparation example 93: (2R, 3S)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation Example 91 was conducted, except that (2R,3S)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 82) was used instead of (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 81), to obtain the title compound (1.5g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.39~7.61(m, 4H)

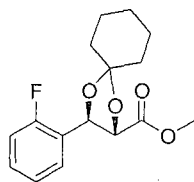
10 Preparation example 94: ((2R,3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation Example 88 was conducted, except that (2R,3S)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 93) was used instead of (4S,5R)-methyl-5-(2-fluorophenyl)-2,2-diehtyl-1,3-dioxolane-4-carboxylate (Preparation example 87), to obtain the title compound (1.2g, 70~95%)

20 ^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.38~7.63(m, 4H)

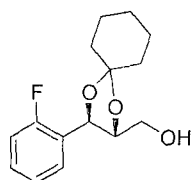
Preparation example 95: (2S, 3R)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation Example 91 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.7g, 70~95%).

5 ^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.37~7.63(m, 4H)

Preparation example 96: ((2R,3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



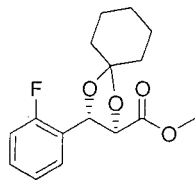
10

The substantially same method as described in Preparation Example 73 was conducted, except that (2S, 3R)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 95) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 72), to obtain the title compound (1.4g, 70~95%)

15

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.42~7.89(m, 4H)

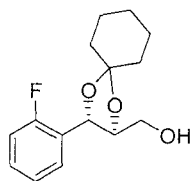
20 Preparation example 97: (2R, 3S)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation Example 95 was conducted, except that (2R,3S)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 82) was used instead of (2S,3R)-methyl-3-(2-fluorophenyl)-2,3-dihydroxypropanoate (Preparation example 81), to obtain the title compound (1.8 g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.32~7.64(m, 4H)

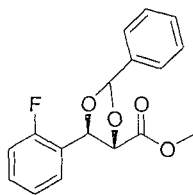
10 Preparation example 98: ((2S,3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation Example 96 was conducted, except that (2R, 3S)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 97) was used instead of (2S, 3R)-methyl-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 95), to obtain the title compound (1.5g, 70~95%)

20 ^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.33~7.67(m, 4H)

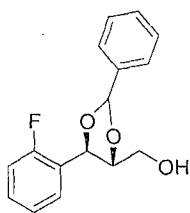
Preparation example 99: (4S, 5R)-methyl-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 87 was conducted, except that benzaldehyde was used instead of 3-pentanone, to obtain the title compound (1.6g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.33~7.64(m, 4H)

Preparation example 100: ((4R,5R)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

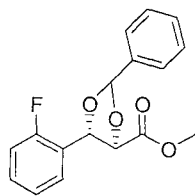


10

The substantially same method as described in Preparation example 65 was conducted, except that (2S, 3R)-methyl-3-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 99) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-
 15 carboxylate(Preparation example 64), to obtain the title compound(1.3g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.43~7.85(m, 4H)

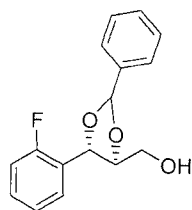
- 20 Preparation example 101: (4R, 5S)-methyl-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 89 was conducted, except that benzaldehyde was used instead of 3-pentanone, to obtain the title compound (1.7g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.33~7.64(m, 4H)

Preparation example 102: ((4S,5S)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

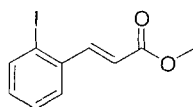


10

The substantially same method as described in Preparation example 65 was conducted, except that (2R, 3S)-methyl-3-(2-fluorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 101) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-
 15 carboxylate(Preparation example 64), to obtain the title compound (1.1g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.43~7.85(m, 4H)

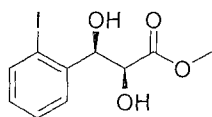
20 Preparation example 103: (E)-Methyl-3-(2-iodophenyl)acrylate



The substantially same method as described in Preparation example 24 was conducted, except that (E)-3(2-iodophenyl)-acrylic acid (Preparation example 17) was used instead of 2-chlorocinnamic acid, to obtain the title compound. (3.2g, 70~90%)

- 5 ^1H NMR (400MHz, CDCl_3) δ 3.84 (s, 3H), 6.45 (d, $J=16.0$, 1H), 7.01~7.35 (m, 4H), 8.09 (d, $J=16.0$, 1H)

Preparation example 104: (2S,3R)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate



10

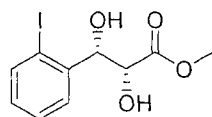
The substantially same method as described in Preparation Example 3 was conducted, except that (E)-Methyl-3-(2-iodophenyl)acrylate (Preparation example 103) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (3.2g, 75~90%).

15

^1H NMR (400MHz, CDCl_3): δ = 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H), 7.30~7.71(m, 4H).

Preparation example 105: (2R,3S)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate

20

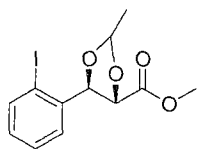


The substantially same method as described in Preparation example 25 was conducted, except that (E)-methyl-3-(2-iodophenyl)acrylate (Preparation example 103) was used instead of (E)-Methyl-3-(2-chlorophenyl)acrylate (Preparation example 24), to obtain the title compound (3.1g, 60~80%).

25

^1H NMR (400MHz, CDCl_3): δ = 4.31(s, 3H), 5.44(m, 4H), 5.89(s, 1H), 7.31~7.72(m, 4H).

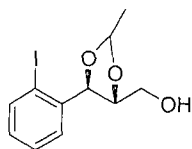
Preparation example 106: ((4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 60 was conducted, except that (2S,3R)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate(Preparation example 104) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound (2.7g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, J =6.4, 3H), 3.78(s, 3H), 4.30(d, J =7.6, 1H), 5.07(m, 1H), 5.62(d, J =7.6, 1H), 7.29~7.70 (m, 4H)

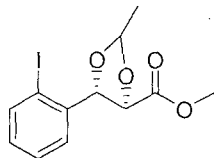
Preparation example 107: ((4R,5R)-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 27 was conducted, except that (4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 106) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate(Preparation example 26), to obtain the title compound (2.3g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, J =6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J =7.0, J =7.0, 1H), 5.06(m, 1H), 5.17(d, J =7.0, 1H), 7.17~7.41(m, 4H).

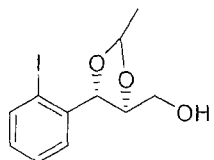
Preparation example 108: ((4R,5S)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate



5 The substantially same method as described in Preparation example 60 was conducted, except that (2R,3S)-methyl-3-(2-iodophenyl)-2.3-dihydroxypropanote(Preparation example 104) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2.3-dihydroxypropanote(Preparation example 433), to obtain the title compound (2.4g, 70~95%).

10 ^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.29~7.70 (m, 4H)

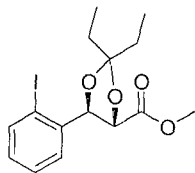
Preparation example 109: ((4S,5S)-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-yl)methanol



15 The substantially same method as described in Preparation example 107 was conducted, except that (4R,5S)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 108) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound (1.9g, 70~95%)

20 ^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.17~7.41(m, 4H)

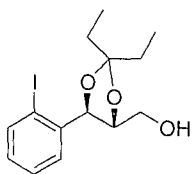
Preparation example 110: (4S, 5R)-methyl-5-(2-iodophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 64 was
5 conducted, except that (2R,3S)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate(Preparation example 104) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound (2.6g, 60~85%).

¹H NMR (400MHz, CDCl₃) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d,
10 J=7.6, 1H), 5.81(d, J=7.6, 1H), 7.23~7.65(m, 4H)

Preparation example 111: ((4R,5R)-5-(2-iodophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol

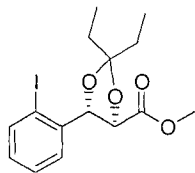


15 The substantially same method as described in Preparation example 107 was conducted, except that (4S,5R)-methyl-5-(2-iodophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 110) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound(2.1g,
20 70~95%)

¹H NMR (400MHz, CDCl₃): δ 1.37(d, J=6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J=7.0, J=7.0, 1H), 5.06(m, 1H), 5.17(d, J=7.0, 1H), 7.17~7.41(m, 4H)

Preparation example 112: (4R, 5S)-methyl-5-(2-iodophenyl)-2,2-diehtyl-1.3-

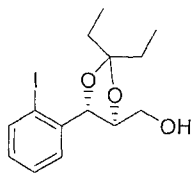
dioxolane-4-carboxylate



The substantially same method as described in Preparation example 110 was conducted, except that (2R,3S)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate (Preparation example 105) was used instead of (2S,3R)-methyl-3-(2-iodophenyl)-2,3-dihydroxypropanoate (Preparation example 104), to obtain the title compound (2.3g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.20~7.61(m, 4H)

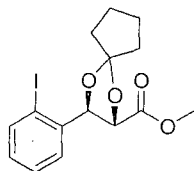
Preparation example 113: ((4S,5S)-5-(2-iodophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 107 was conducted, except that (4R,5S)-methyl-5-(2-iodophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 112) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound(1.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.17~7.41(m, 4H)

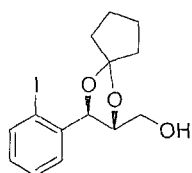
Preparation example 114: (2S, 3R)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 110 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.7g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, *J*=7.2, 1H), 5.39(d, *J*=7.2, 1H), 7.19~7.44(m, 4H)

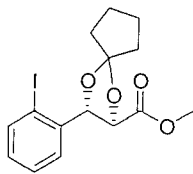
Preparation example 115: ((2R,2R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 107 was conducted, except that (2S,3R)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 114) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound (2.1g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, *J*=5.2, 1H), 5.12(d, *J*=7.6, 1H), 7.20~7.45(m, 4H)

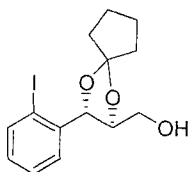
Preparation example 116: (2R, 3S)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 112 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.9g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, *J*=7.2, 1H), 5.39(d, *J*=7.2, 1H), 7.19~7.44(m, 4H)

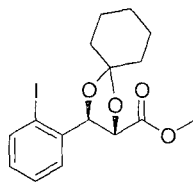
Preparation example 117: ((2S,2S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 107 was conducted, except that (2R,3S)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 116) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound(1.5g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, *J*=5.2, 1H), 5.12(d, *J*=7.6, 1H), 7.20~7.45(m, 4H)

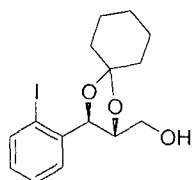
Preparation example 118: (2S, 3R)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 114 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.9g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, *J*=8.0, 1H), 5.85(d, *J*=8.0, 1H), 7.17~7.43(m, 4H)

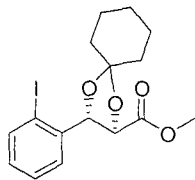
Preparation example 119: ((2R,3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation example 107 was conducted, except that (2S,3R)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 118) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 106), to obtain the title compound (1.3g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, *J*=8.0, 1H), 5.43(d, *J*=7.6, 1H), 7.19~7.49(m, 4H)

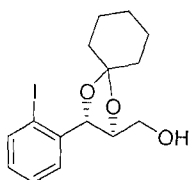
Preparation example 120: (2R, 3S)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 116 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (2.3g, 70~95%).

- 5 ^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.17~7.43(m, 4H)

Preparation example 121: ((2S,3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



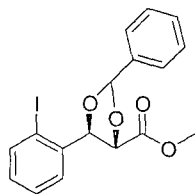
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- The substantially same method as described in Preparation example 107 was conducted, except that (2R,3S)-methyl-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate(Preparation example 120) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 106), to obtain the title compound(1.7g, 70~95%)

15

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.19~7.49(m, 4H)

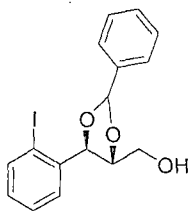
- 20 Preparation example 122: (4S, 5R)-methyl-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 118 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound(1.9g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 3.67(s, 3H), 5.11(d, $J=8.0$, 1H), 5.81(d, $J=8.0$, 1H), 6.18(s, 1H), 6.96~7.57(m, 9H)

Preparation example 123: ((4R,5R)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

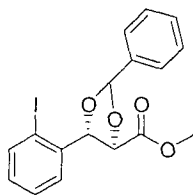


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The substantially same method as described in Preparation example 107 was conducted, except that (4S, 5R)-methyl-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 122) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-mehtyl-1.3-dioxolane-4-
 15 carboxylate(Preparation example 106), to obtain the title compound(1.4g, 70~95%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 6.94~7.59(m, 9H)

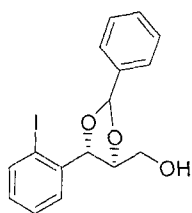
- 20 Preparation example 124: (4R, 5S)-methyl-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 120 was conducted, except benzaldehyde that was used instead of cyclohexanone, to obtain the title compound (2.1g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 3.67(s, 3H), 5.11(d, $J=8.0$, 1H), 5.81(d, $J=8.0$, 1H), 6.18(s, 1H), 6.96~7.57(m, 9H)

Preparation example 125: ((4S,5S)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

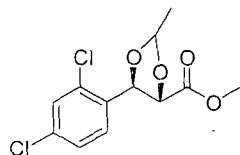


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The substantially same method as described in Preparation example 107 was conducted, except that (4R, 5S)-methyl-5-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 124) was used instead of (4S,5R)-methyl-5-(2-iodophenyl)-2-methyl-1,3-dioxolane-4-
 15 carboxylate(Preparation example 106), to obtain the title compound(1.3g, 70~95%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 6.94~7.59(m, 9H)

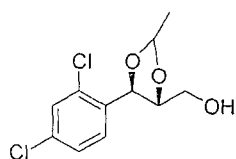
- 20 Preparation example 126: ((4S,5R)-methyl-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 60 was conducted, except that (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate(Preparation example 36) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound(0.9g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.07~7.21(m, 3H)

- 10 Preparation example 127: ((4R,5R)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol

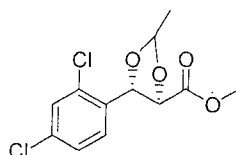


The substantially same method as described in Preparation example 27 was conducted, except that ((4S,5R)-methyl-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 126) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(0.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.08~7.39(m, 3H).

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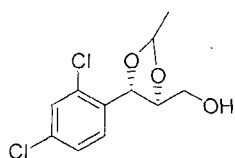
- Preparation example 128: ((4R,5S)-methyl-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 126 was conducted, except that (2R,3S)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 29) was used instead of (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 5 36), to obtain the title compound (1.9g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.07~7.21(m, 3H).

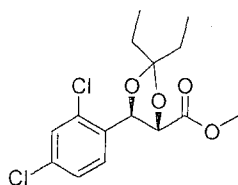
Preparation example 129: ((4S,5S)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol
10 dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 27 was conducted, except that (4R,5S)-methyl-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 128) was used instead of 15 (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (1.5g, 70~95%).

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.08~7.39(m, 3H).

Preparation example 130: (4S, 5R)-methyl-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate
20 1,3-dioxolane-4-carboxylate



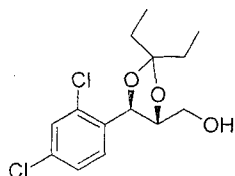
The substantially same method as described in Preparation example 64 was conducted, except that (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 36) was used instead of (2S,3R)-
25 dihydroxypropanoate (Preparation example 36) was used instead of (2S,3R)-

methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound (2.2g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.12~7.37(m, 3H)

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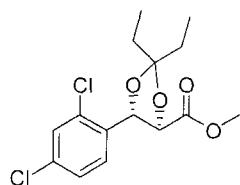
Preparation example 131: ((4R,5R)-5-(2,4-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



10 The substantially same method as described in Preparation example 27 was conducted, except that (4S,5R)-methyl-5-(2,4-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 130)was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimehtyl-1.3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound(1.4g, 70~95%)

15 ^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.08~7.39(m, 3H).

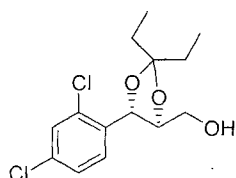
Preparation example 132: (4R, 5S)-methyl-5-(2,4-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



20 The substantially same method as described in Preparation example 130 was conducted, except that (2R,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 29) was used instead of (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 36), to obtain the title compound (2.1g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.12~7.37(m, 3H)

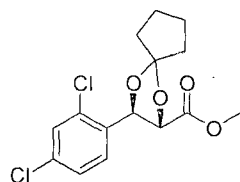
Preparation example 133: ((4S,5S)-5-(2,4-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 131 was conducted, except that (4R,5S)-methyl-5-(2,4-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 132) was used instead of ((4S,5R)-methyl-5-(2,4-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 130), to obtain the title compound (1.2g, 70~95%).

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.08~7.39(m, 3H).

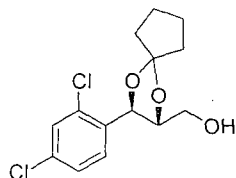
Preparation example 134: (2S, 3R)-methyl-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 131 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.5g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.03~7.36(m, 3H)

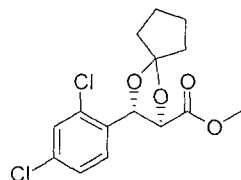
Preparation example 135: ((2R,3R)-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 65 was conducted, except that (2S,3R)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 134) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 64), to obtain the title compound (1.8g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, J=5.2, 1H), 5.12(d, J=7.6, 1H), 7.02~7.37(m, 3H)

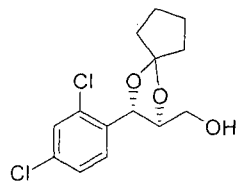
Preparation example 136: (2R, 3S)-methyl-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 132 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.2g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 1H), 1.91~2.00(m, 3H), 3.68(s, 3H), 4.40(d, J=7.2, 1H), 5.39(d, J=7.2, 1H), 7.03~7.36(m, 3H)

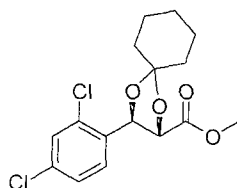
Preparation example 137: ((2S,3S)-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 135 was conducted, except that (2R,3S)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 136) was used instead of (2S, 3R)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 134), to obtain the title compound (1.2g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 1H), 3.52~3.65(m, 2H), 3.82~3.86(m, 1H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.02~7.37(m, 3H)

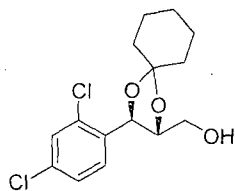
Preparation example 138: (2S, 3R)-methyl-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 134 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.8g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.07~7.41(m, 3H)

Preparation example 139: ((2R,3R)-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

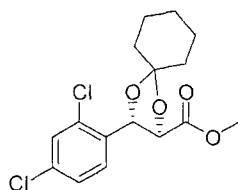


The substantially same method as described in Preparation example 73 was conducted, except that (2S,3R)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 138) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 72), to obtain the title compound (1.3g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.04~7.40(m, 3H)

10

Preparation example 140: (2R, 3S)-methyl-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate

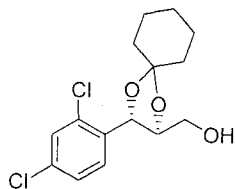


The substantially same method as described in Preparation example 136 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.6g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.07~7.41(m, 3H)

Preparation example 141: ((2S,3S)-3-(2,4-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

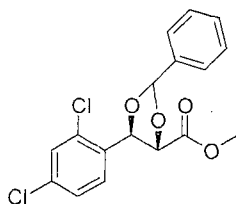
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The substantially same method as described in Preparation example 139 was conducted, except that (2R,3S)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 140) was used instead of (2S, 3R)-methyl-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 138), to obtain the title compound (1.2g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.04~7.40(m, 3H)

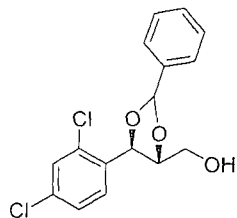
Preparation example 142: (4S, 5R)-methyl-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 138 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (1.9g, 50~70%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.03~7.41(m, 3H)

Preparation example 143: ((4R,5R)-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

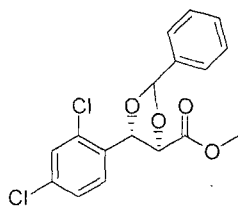


The substantially same method as described in Preparation example 65 was conducted, except that (4S,5R)-methyl-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 142) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 64), to obtain the title compound(1.5g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, J =8.0, 1H), 5.43(d, J =7.6, 1H), 7.04~7.42(m, 3H)

10

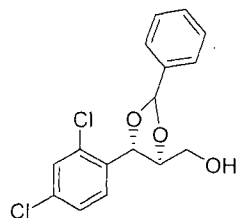
Preparation example 144: (4R, 5S)-methyl-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 140 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (1.6g, 50~70%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, J =8.0, 1H), 5.85(d, J =8.0, 1H), 7.03~7.41(m, 3H)

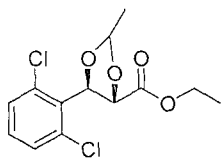
Preparation example 145: ((4S,5S)-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 143 was conducted, except that (4R, 5S)-methyl-5-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 144) was used instead of (2S, 3R)-methyl-3-(2,4-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 142), to obtain the title compound (1.2g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.04~7.42(m, 3H)

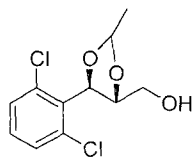
Preparation example 146: ((4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 60 was conducted, except that (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 39) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 433), to obtain the title compound (1.7g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.15(m, 2H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.17~7.36(m, 3H)

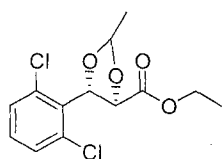
Preparation example 147: ((4R,5R)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 27 was conducted, except that ((4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 146) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (1.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.18~7.39(m, 3H).

- 10 Preparation example 148: ((4R,5S)-ethyl-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate

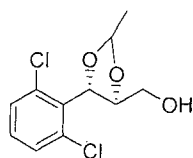


- 15 The substantially same method as described in Preparation example 146 was conducted, except that (2R,3S)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 33) was used instead of (2S,3R)-methyl-3-(2,4-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 39), to obtain the title compound (1.8g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.15(m, 2H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.17~7.36(m, 3H).

20

Preparation example 149: ((4S,5S)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol

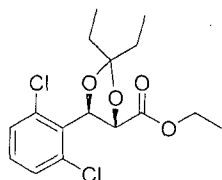


The substantially same method as described in Preparation example 147 was conducted, except that ((4R,5S)-ethyl-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 148) was used instead of ((4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2-mehtyl-1,3-dioxolane-4-

5 carboxylate(Preparation example 146), to obtain the title compound (1.3g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.18~7.39(m, 3H).

10 Preparation example 150: (4S, 5R)-ethyl-5-(2,6-dichlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-carboxylate

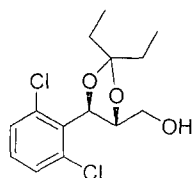


The substantially same method as described in Preparation example 130 was conducted, except that (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate(Preparation example 39) was used instead of (2S,3R)-methyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate(Preparation example 36), to obtain the title compound (1.8g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.30(t, $J=8.0$, 3H), 1.59(m, 4H), 4.12(m, 2H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.08~7.26(m, 3H)

20

Preparation example 151: ((4R,5R)-5-(2,6-dichlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-yl)methanol

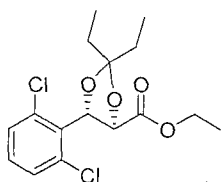


The substantially same method as described in Preparation example 147 was

conducted, except that (4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate(Preparation example 150)was used instead of ((4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 146), to obtain the title compound (1.2g, 70~95%)

5 ^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.07~7.29(m, 3H).

Preparation example 152: (4R, 5S)-ethyl-5-(2,6-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate



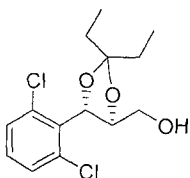
10

The substantially same method as described in Preparation example 150 was conducted, except that (2R,3S)-ethyl-3-(2,6-ichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 33) was used instead of (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 15
39), to obtain the title compound(2.5g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.30(t, $J=8.0$, 3H), 1.59(m, 4H), 4.12(m, 2H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.08~7.26(m, 3H)

Preparation example 153: ((4S,5S)-5-(2,6-chlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol

20

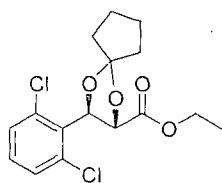


The substantially same method as described in Preparation example 151 was conducted, except that (4R,5S)-ethyl-5-(2,6-dichlorophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 152) was used instead of

(4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-carboxylate(Preparation example 150), to obtain the title compound(2.1g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 1.37(d, J=6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J=7.0, J=7.0, 1H), 5.06(m, 1H), 5.17(d, J=7.0, 1H), 7.07~7.29(m, 3H).

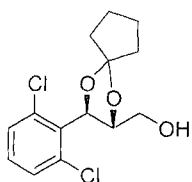
Preparation example 154: (2S, 3R)-ethyl-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



10 The substantially same method as described in Preparation example 150 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.1g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.30(t, J=7.8hz, 3H), 1.69~1.71(m, 4H), 1.73~1.86(m, 4H), 4.07~4.14(m, 2H), 5.11(d, J=7.2, 1H), 5.81(d, J=7.2, 1H), 7.07~7.31(m, 3H)

Preparation example 155: ((2R,3R)-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol

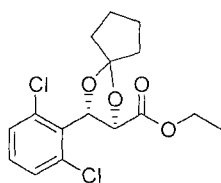


20 The substantially same method as described in Preparation example 151 was conducted, except that (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 154) was used instead of (4S,5R)-ethyl-5-(2,6-dichlorophenyl)-2,2-diehtyl-1,3-dioxolane-4-carboxylate (Preparation example 150), to obtain the title compound (1.7g,

70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 4H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.08~7.32(m, 3H)

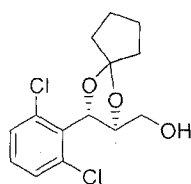
- 5 Preparation example 156: (2R, 3S)-ethyl-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



- 10 The substantially same method as described in Preparation example 152 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.5g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.30(t, $J=7.8\text{hz}$, 3H), 1.69~1.71(m, 4H), 1.73~1.86(m, 4H), 4.07~4.14(m, 2H), 5.11(d, $J=7.2$, 1H), 5.81(d, $J=7.2$, 1H), 7.07~7.31(m, 3H)

- 15 Preparation example 157: ((2S,3S)-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol

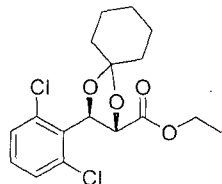


- 20 The substantially same method as described in Preparation example 155 was conducted, except that (2R,3S)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 156) was used instead of (2S, 3R)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 154), to obtain the title compound (2.0g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 4H), 3.52~3.65(m,

2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.08~7.32(m, 3H)

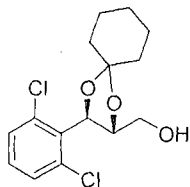
Preparation example 158: (2S, 3R)-ethyl-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 154 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (2.2g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.30(t, $J=7.6$, 3H), 1.61~1.69(m, 10H), 4.08~4.18(d, 2H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.07~7.31(m, 3H)

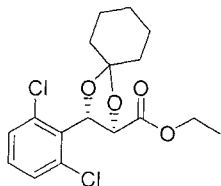
Preparation example 159: ((2R,3R)-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation example 155 was conducted, except that (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 158) was used instead of (2S, 3R)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 154), to obtain the title compound (1.7g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.05~7.30(m, 3H)

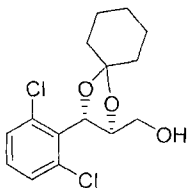
Preparation example 160: (2R, 3S)-ethyl-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



5 The substantially same method as described in Preparation example 156 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.9g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.30(t, $J=7.6$, 3H), 1.61~1.69(m, 10H), 4.08~4.18(d, 2H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.07~7.31(m, 3H)

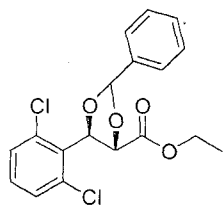
10 Preparation example 161: ((2S,3S)-3-(2,6-chlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



15 The substantially same method as described in Preparation example 159 was conducted, except that (2R,3S)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 160) was used instead of (2S, 3R)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 158), to obtain the title compound (1.5g, 70~95%)

20 ^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.05~7.30(m, 3H)

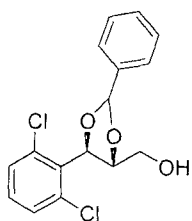
Preparation example 162: (4S, 5R)-ethyl-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 158 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (2.0g, 50~70%).

- 5 ^1H NMR (400MHz, DMSO) δ 1.30(t, $J=7.6$, 3H), 4.08~4.18(d, 2H), 5.13(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 6.18(s, 1H), 7.03~7.22(m, 8H)

Preparation example 163: ((4R,5R)-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

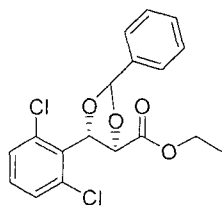


10

The substantially same method as described in Preparation example 159 was conducted, except that (4S, 5R)-ethyl-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 162) was used instead of (2S, RS)-ethyl-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate
15 (Preparation example 158), to obtain the title compound (1.6g, 70~95%)

^1H NMR (400MHz, DMSO): δ 3.50~3.79(m, 2H), 5.13(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 6.18(s, 1H), 7.03~7.22(m, 8H)

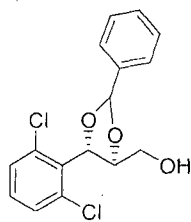
Preparation example 164: (4R, 5S)-ethyl-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate
20



The substantially same method as described in Preparation example 160 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (1.8g, 50~70%).

¹H NMR (400MHz, DMSO) δ 1.30(t, *J*=7.6, 3H), 4.08~4.18(d, 2H), 5.13(d, *J*=8.0, 1H), 5.85(d, *J*=8.0, 1H), 6.18(s, 1H), 7.03~7.22(m, 8H)

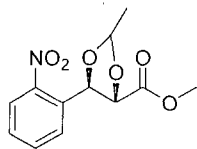
Preparation example 165: ((4S,5S)-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 163 was conducted, except that (4R, 5S)-ethyl-5-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 164) was used instead of (2S, 3R)-ethyl-3-(2,6-chlorophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 162), to obtain the title compound (1.4g, 70~95%)

¹H NMR (400MHz, DMSO): δ 3.50~3.79(m, 2H), 5.13(d, *J*=8.0, 1H), 5.85(d, *J*=8.0, 1H), 6.18(s, 1H), 7.03~7.22(m, 8H)

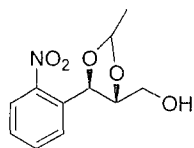
Preparation example 166: ((4S,5R)-methyl-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 60 was conducted, except that (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 44) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 433), to obtain the title compound (2.3g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.45~8.12 (m, 4H)

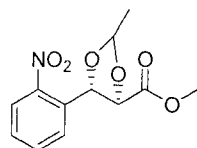
Preparation example 167: ((4R,5R)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 27 was conducted, except that (4S,5R)-methyl-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 166) was used instead of (4R,5S)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (1.9g, 70~95%).

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.47~8.11(m, 4H).

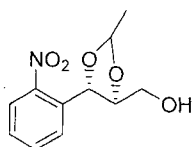
Preparation example 168: ((4R,5S)-methyl-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 160 was conducted, except that (2R,3S)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate(Preparation example 48)was used instead of (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate(Preparation example 44),
5 to obtain the title compound(2.0g, 70~95%).

^1H NMR (400MHz, CDCl_3) δ 1.36(d, $J=6.4$, 3H), 3.78(s, 3H), 4.30(d, $J=7.6$, 1H), 5.07(m, 1H), 5.62(d, $J=7.6$, 1H), 7.45~8.12 (m, 4H)

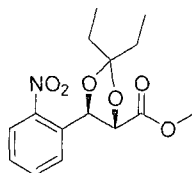
Preparation example 169: ((4S,5S)-5-(2-nitrophenyl)-2-mehtyl-1.3-dioxolane-
10 4-yl)methanol



The substantially same method as described in Preparation example 167 was conducted, except that (4R,5S)-methyl-5-(2-nitrophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 168)was used instead of
15 (4S,5R)-methyl-5-(2-nitrophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate(Preparation example 166), to obtain the title compound(1.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.47~8.11(m, 4H).

Preparation example 170: (4S, 5R)-methyl-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate

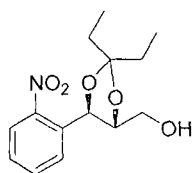


The substantially same method as described in Preparation example 150 was
25 conducted, except that (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-

dihydroxypropanoate (Preparation example 44) was used instead of (2S,3R)-ethyl-3-(2,6-dichlorophenyl)-2,3-dihydroxypropanoate (Preparation example 39), to obtain the title compound (2.4g, 60~85%).

¹H NMR (400MHz, CDCl₃) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, *J*=7.6, 1H), 5.81(d, *J*=7.6, 1H), 7.43~8.10(m, 4H)

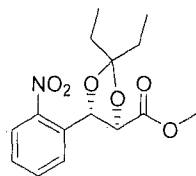
Preparation example 171: ((4R,5R)-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 167 was conducted, except that (4S,5R)-methyl-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 170) was used instead of (4S,5R)-methyl-5-(2-nitrophenyl)-2-mehtyl-1.3-dioxolane-4-carboxylate (Preparation example 166), to obtain the title compound (1.9g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 0.96(m, 6H), 1.59(m, 4H), 3.62~3.70(m, 2H), 4.36(dd, *J*=7.0, *J*=7.0, 1H), 5.17(d, *J*=7.0, 1H), 7.37~8.09(m, 4H)

Preparation example 172: (4R, 5S)-methyl-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate

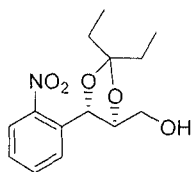


The substantially same method as described in Preparation example 170 was conducted, except that (2R,3S)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate(Preparation example 48)was used instead of (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate(Preparation example 44),

to obtain the title compound (2.5g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.43~8.10(m, 4H)

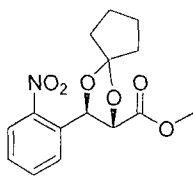
- 5 Preparation example 173: ((4S,5S)-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-yl)methanol



- The substantially same method as described in Preparation example 171 was conducted, except that (4R,5S)-methyl-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 172) was used instead of (4S,5R)-methyl-5-(2-nitrophenyl)-2,2-diehtyl-1.3-dioxolane-4-carboxylate (Preparation example 170), to obtain the title compound (2.0g, 70~95%)

- ^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.37~8.09(m, 4H)

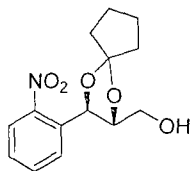
- Preparation example 174: (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



- 20 The substantially same method as described in Preparation example 170 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.5g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 4H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.44~8.06(m, 4H)

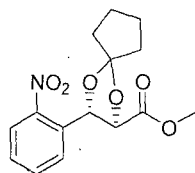
Preparation example 175: ((2R,3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



5 The substantially same method as described in Preparation example 171 was conducted, except that (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 174) was used instead of (4S,5R)-methyl-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 170), to obtain the title compound (2.1g,
10 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 4H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.46~8.09(m, 4H)

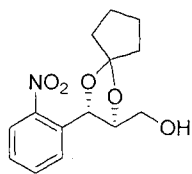
Preparation example 176: (2R, 3S)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate
15



The substantially same method as described in Preparation example 172 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.9g, 70~95%).

20 ^1H NMR (400MHz, DMSO) δ 1.69~1.71(m, 4H), 1.82~1.86(m, 4H), 3.68(s, 3H), 4.40(d, $J=7.2$, 1H), 5.39(d, $J=7.2$, 1H), 7.44~8.06(m, 4H)

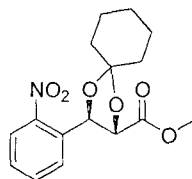
Preparation example 177: ((2S,3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 175 was conducted, except that (2R, 3S)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 176) was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 174), to obtain the title compound (2.0g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.60~1.72(m, 4H), 1.83~1.94(m, 4H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.46~8.09(m, 4H)

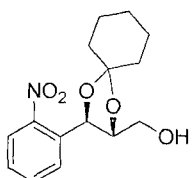
Preparation example 178: (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 174 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.7g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.45~8.12(m, 4H)

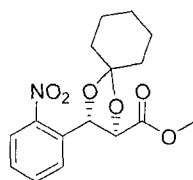
Preparation example 179: ((2R,3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation example 175 was conducted, except that (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 178) was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 174), to obtain the title compound (1.4g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.46~8.09(m, 4H)

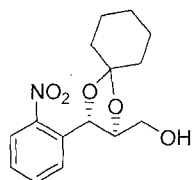
10 Preparation example 180: (2R, 3S)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 176 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (2.2g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.45~8.12(m, 4H)

Preparation example 181: ((2S,3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

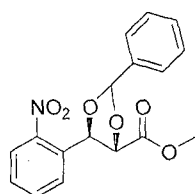


The substantially same method as described in Preparation example 179 was conducted, except that (2R, 3S)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 180) was used

instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate(Preparation example 178), to obtain the title compound(1.5g, 70~95%)

¹H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, J=8.0, 1H), 5.43(d, J=7.6, 1H), 7.19~7.49(m, 4H)

Preparation example 182: (4S, 5R)-methyl-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate

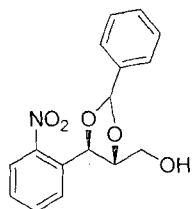


10 The substantially same method as described in Preparation example 178 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (1.9g, 50~70%).

¹H NMR (400MHz, DMSO) δ 3.67(s, 3H), 5.11(d, J=8.0, 1H), 5.81(d, J=8.0, 1H), 6.18(s, 1H), 6.96~8.12(m, 9H)

15

Preparation example 183: ((4R,5R)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

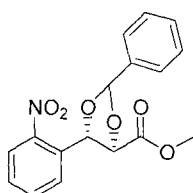


20 The substantially same method as described in Preparation example 179 was conducted, except that (4S, 5R)-methyl-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 182)was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 174), to obtain the title compound(1.5g,

70~95%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 7.06~8.14(m, 9H)

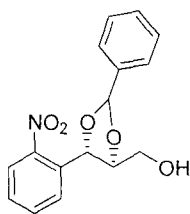
- 5 Preparation example 184: (4R, 5S)-methyl-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 180 was conducted, except benzaldehyde that was used instead of cyclohexanone, to
10 obtain the title compound (1.8g, 50~70%).

^1H NMR (400MHz, DMSO) δ 3.67(s, 3H), 5.11(d, $J=8.0$, 1H), 5.81(d, $J=8.0$, 1H), 6.18(s, 1H), 6.96~8.12(m, 9H)

- 15 Preparation example 185: ((4S,5S)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

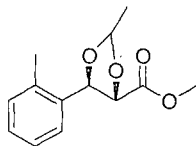


The substantially same method as described in Preparation example 183 was conducted, except that (4R, 5S)-methyl-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 184)was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 182), to obtain the title compound(1.3g,
20 70~95%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$,

1H), 6.18(s, 1H), 7.06~8.14(m, 9H)

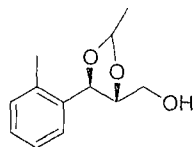
Preparation example 186: (4S,5R)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 60 was conducted, except that (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate(Preparation example 54) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate(Preparation example 433), to obtain the title compound(2.1g, 70~95%).

¹H NMR (400MHz, CDCl₃) δ 1.36(d, J=6.4, 3H), 2.35(s, 3H), 3.68(s, 3H), 5.07(m, 1H), 5.11(d, J=7.6, 1H), 5.82(d, J=7.6, 1H), 7.19~7.39 (m, 4H)

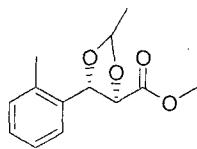
Preparation example 187: ((4R,5R)-5-(2-methylphenyl)-2-methyl-1,3dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 185 was conducted, except that (4S,5R)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 186) was used instead of (2R,3S)-methyl-3-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 184), to obtain the title compound (1.7g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 1.37(d, J=6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J=7.0, J=7.0, 1H), 5.06(m, 1H), 5.17(d, J=7.0, 1H), 7.17~7.41(m, 4H).

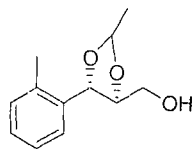
Preparation example 188: (4R,5S)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 186 was conducted, except that (2R,3S)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate(Preparation example 57) was used instead of (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate(Preparation example 54), to obtain the title compound (1.8g, 70~95%).

¹H NMR (400MHz, CDCl₃) δ 1.36(d, J=6.4, 3H), 2.35(s, 3H), 3.68(s, 3H), 5.07(m, 1H), 5.11(d, J=7.6, 1H), 5.82(d, J=7.6, 1H), 7.19~7.39 (m, 4H)

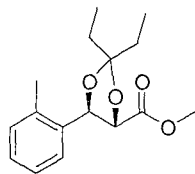
Preparation example 189: ((4S,5S)-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 187 was conducted, except that (4R,5S)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 188) was used instead of (4S,5R)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate(Preparation example 186), to obtain the title compound(1.6g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ 1.37(d, J=6.0, 3H), 3.62~3.70(m, 2H), 4.36(dd, J=7.0, J=7.0, 1H), 5.06(m, 1H), 5.17(d, J=7.0, 1H), 7.17~7.41(m, 4H).

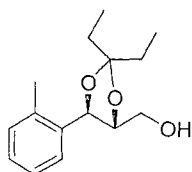
Preparation example 190: (4S, 5R)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 170 was conducted, except that (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate (Preparation example 54) was used instead of (2S,3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 44), to obtain the title compound (2.1g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 2.33(s, 1H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.00~7.17(m, 4H)

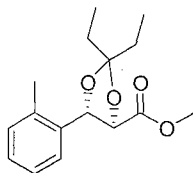
Preparation example 191: ((4R,5R)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 187 was conducted, except that (4S,5R)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 190) was used instead of (4S,5R)-methyl-5-(2-methylphenyl)-2-methyl-1,3-dioxolane-4-carboxylate (Preparation example 186), to obtain the title compound (1.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 2.37(s, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.15~7.39(m, 4H)

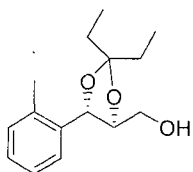
Preparation example 192: (4R, 5S)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 190 was conducted, except that (2R,3S)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate(Preparation example 57) was used instead of (2S,3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate(Preparation example 54), to obtain the title compound (2.2g, 60~85%).

^1H NMR (400MHz, CDCl_3) δ 0.96(m, 6H), 1.59(m, 4H), 2.33(s, 1H), 3.67(s, 3H), 5.11(d, $J=7.6$, 1H), 5.81(d, $J=7.6$, 1H), 7.00~7.17(m, 4H)

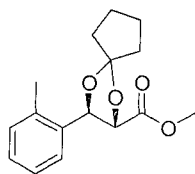
10 Preparation example 193: ((4S,5S)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 191 was conducted, except that (4R,5S)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 192) was used instead of (4S,5R)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 190), to obtain the title compound (1.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 2.37(s, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.15~7.39(m, 4H)

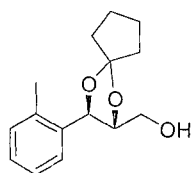
Preparation example 194: (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 190 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.1g, 70~95%).

5 ^1H NMR (400MHz, DMSO) δ 1.49~1.57(m, 4H), 1.72~1.81(m, 4H), 2.35(s, 3H), 3.68(s, 3H), 5.14(d, $J=7.2$, 1H), 5.89(d, $J=7.2$, 1H), 7.02~7.25(m, 4H)

Preparation example 195: ((2R,3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



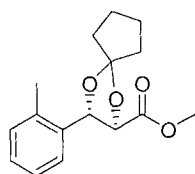
10

The substantially same method as described in Preparation example 191 was conducted, except that (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate(Preparation example 194) was used instead of (4S, 5R)-methyl-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate(Preparation example 190), to obtain the title compound(1.6g, 70~95%)

15

^1H NMR (400MHz, DMSO): δ 1.49~1.57(m, 4H), 1.72~1.81(m, 4H), 2.35(s, 3H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.02~7.25(m, 4H)

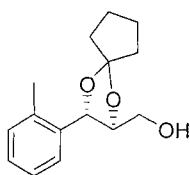
20 Preparation example 196: (2R, 3S)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 192 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.5g, 70~95%).

¹H NMR (400MHz, DMSO) δ 1.49~1.57(m, 4H), 1.72~1.81(m, 4H), 2.35(s, 3H),
5 3.68(s, 3H), 5.14(d, *J*=7.2, 1H), 5.89(d, *J*=7.2, 1H), 7.02~7.25(m, 4H)

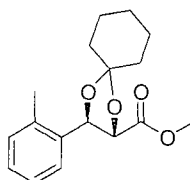
Preparation example 197: ((2S,3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



10 The substantially same method as described in Preparation example 195 was conducted, except that (2R, 3S)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 196) was used instead of (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 194), to obtain the title compound (2.0g,
15 70~95%)

¹H NMR (400MHz, DMSO): δ 1.49~1.57(m, 4H), 1.72~1.81(m, 4H), 2.35(s, 3H), 3.52~3.65(m, 2H), 4.90(t, *J*=5.2, 1H), 5.12(d, *J*=7.6, 1H), 7.02~7.25(m, 4H)

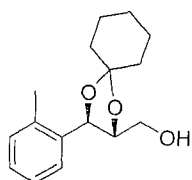
Preparation example 198: (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate
20



The substantially same method as described in Preparation example 194 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.8g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 2.34(s, 3H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.01~7.30(m, 4H)

Preparation example 199: ((2R,3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

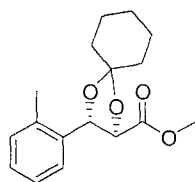


The substantially same method as described in Preparation example 195 was conducted, except that (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 198) was used instead of (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-carboxylate (Preparation example 194), to obtain the title compound (1.5g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 2.33(s, 3H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.02~7.28(m, 4H)

15

Preparation example 200: (2R, 3S)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate

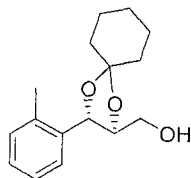


The substantially same method as described in Preparation example 196 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (2.2g, 70~95%).

^1H NMR (400MHz, DMSO) δ 1.61~1.69(m, 10H), 2.34(s, 3H), 3.79(s, 3H), 4.33(d, $J=8.0$, 1H), 5.85(d, $J=8.0$, 1H), 7.01~7.30(m, 4H)

20

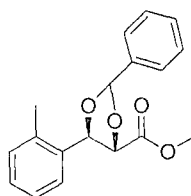
Preparation example 201: ((2S,3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation example 199 was conducted, except that (2R, 3S)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 200) was used instead of (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 198), to obtain the title compound (1.5g, 70~95%)

^1H NMR (400MHz, DMSO): δ 1.63~1.75(m, 10H), 2.33(s, 3H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.02~7.28(m, 4H)

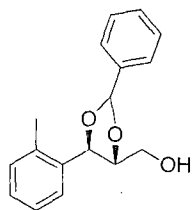
Preparation example 202: (4S, 5R)-methyl-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 198 was conducted, except that benzaldehyde was used instead of cyclohexanone, to obtain the title compound (2.2g, 50~70%).

^1H NMR (400MHz, DMSO) δ 2.33(s, 3H), 3.67(s, 3H), 5.11(d, $J=8.0$, 1H), 5.81(d, $J=8.0$, 1H), 6.18(s, 1H), 6.96~7.32(m, 9H)

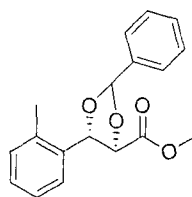
Preparation example 203: ((4R,5R)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 199 was conducted, except that (4S, 5R)-methyl-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 202) was used instead of (2S, 3R)-methyl-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decane-2-carboxylate (Preparation example 198), to obtain the title compound (1.6g, 70~95%)

^1H NMR (400MHz, DMSO): δ 2.32(s, 3H), 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 6.99~7.33(m, 9H)

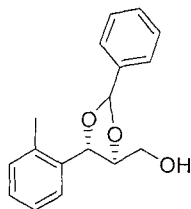
Preparation example 204: (4R, 5S)-methyl-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 200 was conducted, except benzaldehyde that was used instead of cyclohexanone, to obtain the title compound (1.9g, 50~70%).

^1H NMR (400MHz, DMSO) δ 2.33(s, 3H), 3.67(s, 3H), 5.11(d, $J=8.0$, 1H), 5.81(d, $J=8.0$, 1H), 6.18(s, 1H), 6.96~7.32(m, 9H)

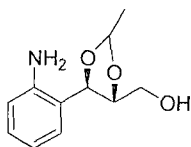
Preparation example 205: ((4S,5S)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 203 was conducted, except that (4R, 5S)-methyl-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 204) was used instead of (4S, 5R)-methyl-5-(2-methylphenyl)-2-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 202), to obtain the title compound (1.3g, 70~95%)

^1H NMR (400MHz, DMSO): δ 2.32(s, 3H), 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 6.99~7.33(m, 9H)

10 Preparation example 206: ((4R,5R)-5-(2-aminophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol

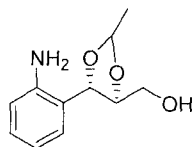


The substantially same method as described in Preparation example 47 was conducted, except that ((4R,5R)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol (Preparation example 167) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.5g, 65~85%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.57~8.08(m, 4H).

20

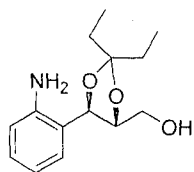
Preparation example 207: ((4S,5S)-5-(2-aminophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4S,5S)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolane-4-yl)methanol (Preparation example 169) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.1g, 65~85%)

^1H NMR (400MHz, CDCl_3): δ 1.37(d, $J=6.0$, 3H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.06(m, 1H), 5.17(d, $J=7.0$, 1H), 7.57~8.08(m, 4H).

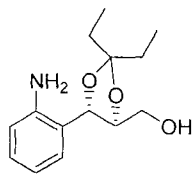
10 Preparation example 208: ((4R,5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4R,5R)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol (Preparation example 171) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.5g, 65~85%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.55~8.09(m, 4H)

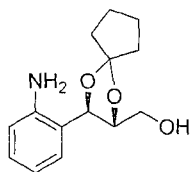
Preparation example 209: ((4S,5S)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4S,5S)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol (Preparation example 173) was used instead of ((4R,5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.4g, 65~85%)

^1H NMR (400MHz, CDCl_3): δ 0.96(m, 6H), 1.59(m, 4H), 3.62~3.70(m, 2H), 4.36(dd, $J=7.0$, $J=7.0$, 1H), 5.17(d, $J=7.0$, 1H), 7.55~8.09(m, 4H)

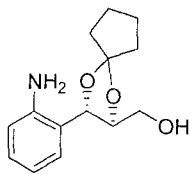
10 Preparation example 210: ((2R,3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4R,5R)-5-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol (Preparation example 175) was used instead of ((4R,5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.7g, 65~85%)

^1H NMR (400MHz, DMSO): δ 1.62~1.73(m, 4H), 1.82~1.95(m, 4H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H), 5.12(d, $J=7.6$, 1H), 7.56~8.11(m, 4H)

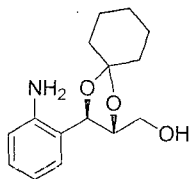
Preparation example 211: ((2S,3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4S,5S)-5-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methanol (Preparation example 177) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.6g, 65~85%)

^1H NMR (400MHz, DMSO): δ 1.62~1.73(m, 4H), 1.82~1.95(m, 4H), 3.52~3.65(m, 2H), 4.90(t, $J=5.2$, 1H); 5.12(d, $J=7.6$, 1H), 7.56~8.11(m, 4H)

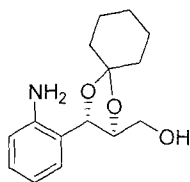
Preparation example 212: ((2R,3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4R,5R)-5-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol (Preparation example 179) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.1g, 65~85%)

^1H NMR (400MHz, DMSO): δ 1.61~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.49~8.12(m, 4H)

Preparation example 213: ((2S,3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol

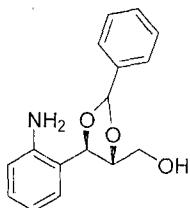


The substantially same method as described in Preparation example 47 was conducted, except that ((4S,5S)-5-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methanol (Preparation example 181) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.0g, 65~85%)

^1H NMR (400MHz, DMSO): δ 1.61~1.75(m, 10H), 3.52~3.81(m, 2H), 3.95(t, $J=8.0$, 1H), 5.43(d, $J=7.6$, 1H), 7.49~8.12(m, 4H)

10

Preparation example 214: ((4R,5R)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol

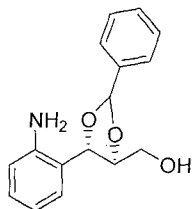


The substantially same method as described in Preparation example 47 was conducted, except that ((4R,5R)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol (Preparation example 183) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (1.2g, 65~85%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 7.06~8.14(m, 9H)

20

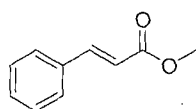
Preparation example 215: ((4S,5S)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 47 was conducted, except that ((4S,5S)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolane-4-yl)methanol (Preparation example 185) was used instead of ((4R,5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol (Preparation example 46), to obtain the title compound (0.9g, 65~85%)

^1H NMR (400MHz, DMSO): δ 3.66(d, $J=7.6$, 2H), 4.36(m, 1H), 5.17(d, $J=8.0$, 1H), 6.18(s, 1H), 7.06~8.14(m, 9H)

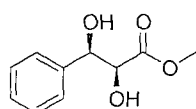
10 Preparation example 216: (E)-Methyl cinnamate



To a round-bottomed flask, *trans*-cinnamic acid (7g, 47.25mmol) and MeOH (70mL) were added. POCl_3 (0.43mL, 4.73mmol) was added dropwise. The reaction mixture was stirred under reflux for 3h. The reaction mixture was cooled to room temperature, quenched with 1N NaOH solution. The mixture was extracted by EtOAc and washed with H_2O . The aqueous layer was further extracted with EtOAc. The combined organic layer was dried over anhydrous magnesium sulfate (MgSO_4), filtered and concentrated under vacuum (7.1g, 80~95%)

20 ^1H NMR (400MHz, CDCl_3): δ 3.81(s, 3H), 6.42(d, $J=15.9$, 1H), 7.37~7.39(m, 3H), 7.50~7.53(m, 2H), 7.67(d, $J=15.9$, 1H)

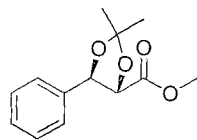
Preparation example 217: (2S, 3R)-methyl-3-phenyl-2,3-dihydroxypropanoate



The substantially same method as described in Preparation example 36 was conducted; except that (E)-Methyl cinnamate (Preparation example 216) was used instead of (E)-methyl-3-(2,4-dichlorophenyl)acrylate (Preparation example 28), to obtain the title compound(6.2g, 70~95%)

5 ^1H NMR (400MHz, CDCl_3): δ 2.70(bs, 1H), 3.08(bs, 1H), 3.82(s, 3H), 4.38(d, J=2.9, 1H), 5.03(d, J=2.9, 1H), 7.30~ 7.42(m, 5H)

Preparation example 218: (4S, 5R)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate



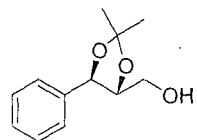
10

The substantially same method as described in Preparation example 45 was conducted, except that (2S, 3R)-methyl-3-phenyl-2,3-dihydroxypropanoate (Preparation example 217) was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 44), to obtain
15 the title compound (5.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.56(s, 3H), 1.61(s, 3H), 3.79(s, 3H), 4.36(d, J=7.8, 1H), 5.17(d, J=7.8, 1H), 7.31~7.40(m, 5H)

15

Preparation example 219: ((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolane-4-yl)methanol
20



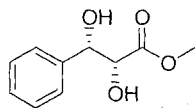
20

The substantially same method as described in Preparation example 46 was conducted, except that (4S, 5R)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 218) was used instead of (4S, 5R)-methyl-5-(2-nitrophenyl)-1,3-dioxolane-4-carboxylate (Preparation example 45), to
25 obtain the title compound(4.4g, 70~95%)

25

^1H NMR (400MHz, CDCl_3): δ 1.41(s, 3H), 1.46(s, 3H), 2.79(bs, 1H), 3.48~3.52(m, 1H), 3.68~3.76(m, 2H), 4.76(d, $J=8.8$, 1H), 7.18~7.28(m, 5H)

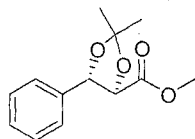
Preparation example 220: (2R, 3S)-methyl-3-phenyl-2,3-dihydroxypropanoate



The substantially same method as described in Preparation example 30 was conducted, except that (E)-Methyl cinnamate (Preparation example 216) was used instead of (E)-methyl-3-(2,4-dichlorophenyl)acrylate (Preparation example 28), to obtain the title compound (8.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 2.70(bs, 1H), 3.08(bs, 1H), 3.82(s, 3H), 4.38(d, $J=2.9$, 1H), 5.03(d, $J=2.9$, 1H), 7.30~7.42(m, 5H)

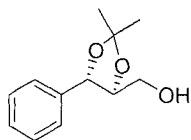
Preparation example 221: (4R, 5S)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 45 was conducted, except that (2S, 3R)-methyl-3-phenyl-2,3-dihydroxypropanoate (Preparation example 217) was used instead of (2S, 3R)-methyl-3-(2-nitrophenyl)-2,3-dihydroxypropanoate (Preparation example 44), to obtain the title compound (5.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.56(s, 3H), 1.61(s, 3H), 3.79(s, 3H), 4.36(d, $J=7.8$, 1H), 5.17(d, $J=7.8$, 1H), 7.31~7.40(m, 5H)

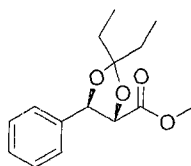
Preparation example 222: ((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 46 was conducted, except that (4R, 5S)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 221) was used instead of (4S, 5R)-methyl-5-(2-nitrophenyl)-1,3-dioxolane-4-carboxylate(Preparation example 45), to obtain the title compound(6.5g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ 1.41(s, 3H), 1.46(s, 3H), 2.79(bs, 1H), 3.48~3.52(m, 1H), 3.68~3.76(m, 2H), 4.76(d, $J=8.8$, 1H), 7.18~7.28(m, 5H)

- 10 Preparation example 223: (4S, 5R)-methyl-2,2-diethyl-5-phenyl-1,3-dioxolane-4-carboxylate

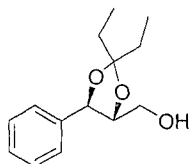


- 15 The substantially same method as described in Preparation example 190 was conducted, except that (2S, 3R)-methyl-3-phenyl-2,3-dihydroxypropanoate(Preparation example 217) was used instead of (2S, 3R)-methyl-3-(2-methylphenyl)-2,3-dihydroxypropanoate (Preparation example 54), to obtain the title compound(1.9g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.01(t, $J=7.4$, 1H), 1.06(t, $J=7.6$, 3H), 1.78~1.90(m, 4H), 3.78(s, 3H), 5.12(d, $J=8.4$, 1H), 7.32~7.45(m, 5H)

20

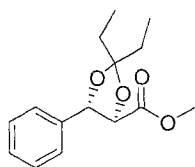
Preparation example 224: ((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolane-4-yl)methanol



The substantially same method as described in Preparation example 219 was conducted, except that (4S, 5R)-methyl-2,2-diethyl-5-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 223) was used instead of (4S, 5R)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 218), to obtain the title compound (1.3g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ = 1.00(t, J=7.6, 1H), 1.06(t, J=7.4, 1H), 1.74~1.90(m, 4H), 3.64(ddd, J=3.4, 8.4, 12.1, 1H), 3.84~3.91(m, 2H), 4.89(d, J=8.8, 1H), 7.30~7.43(m, 5H)

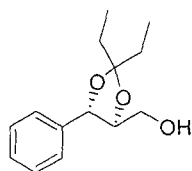
Preparation example 225: (4R, 5S)-methyl-2,2-diethyl-5-phenyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 223 was conducted, except that (2R, 3S)-methyl-3-phenyl-2,3-dihydroxypropanoate (Preparation example 220) was used instead of (2S, 3R)-methyl-3-phenyl-2,3-dihydroxypropanoate (Preparation example 217), to obtain the title compound (5.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ = 1.01(t, J=7.4, 1H), 1.06(t, J=7.6, 3H), 1.78~1.90(m, 4H), 3.78(s, 3H), 5.12(d, J=8.4, 1H), 7.32~7.45(m, 5H)

Preparation example 226: ((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolane-4-yl)methanol

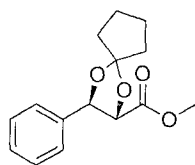


The substantially same method as described in Preparation example 224 was conducted, except that (4R, 5S)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-

4-carboxylate (Preparation example 225) was used instead of (4S, 5R)-methyl-2,2-dimethyl-5-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 218), to obtain the title compound(6.5g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.00(t, J=7.6, 1H), 1.06(t, J=7.4, 1H),
5 1.74~1.90(m, 4H), 3.64(ddd, J=3.4, 8.4, 12.1, 1H), 3.84~3.91(m, 2H), 4.89(d, J=8.8, 1H), 7.30~7.43(m, 5H)

Preparation example 227: (2S, 3R)-methyl-3-phenyl-1,4-dioxapiro[4,4]nonane-2-carboxylate

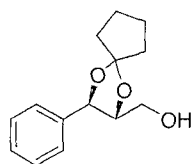


10

The substantially same method as described in Preparation example 223 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (0.9g, 50~75%)

¹H NMR (400MHz, CDCl₃): δ=1.71~1.80(m, 4H), 1.87~1.94(m, 1H),
15 2.00~2.08(m, 3H), 3.79(s, 3H), 4.35(d, J=7.2, 1H), 5.08(d, J=7.2, 1H), 7.32~7.45(m, 5H)

Preparation example 228: ((2R, 3R)-3-phenyl-1,4-dioxapiro[4,4]nonan-2-yl)methanol

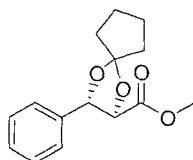


20

The substantially same method as described in Preparation example 224 was conducted, except that (2S, 3R)-methyl-3-phenyl-1,4-dioxapiro[4,4]nonane-2-carboxylate (Preparation example 227) was used instead of (4S, 5R)-methyl-2,2-diethyl-5-phenyl-1,3-dioxolane-4-carboxylate (Preparation example 223),
25 to obtain the title compound (0.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.69~1.82(m, 4H), 1.85~2.03(m, 4H), 3.66(ddd, J =3.7, 8.1, 12.1, 1H), 3.83~3.90(m, 2H), 4.84(d, J =8.4, 1H), 7.26~7.41(m, 5H)

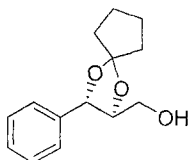
- 5 Preparation example 229: (2R, 3S)-methyl-3-phenyl-1,4-dioxapiro[4,4]nonane-2-carboxylate



The substantially same method as described in Preparation example 225 was conducted, except that cyclopentanone was used instead of 3-pentanone, to
10 obtain the title compound (0.8g, 50~75%)

^1H NMR (400MHz, CDCl_3): δ =1.71~1.80(m, 4H), 1.87~1.94(m, 1H), 2.00~2.08(m, 3H), 3.79(s, 3H), 4.35(d, J =7.2, 1H), 5.08(d, J =7.2, 1H), 7.32~7.45(m, 5H)

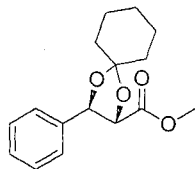
- 15 Preparation example 230: ((2S, 3S)-3-phenyl-1,4-dioxapiro[4,4]nonan-2-yl)methanol



The substantially same method as described in Preparation example 228 was conducted, except that (2R, 3S)-methyl-3-phenyl-1,4-dioxapiro[4,4]nonane-2-
20 carboxylate (Preparation example 229) was used instead (2S, 3R)-methyl-3-phenyl-1,4-dioxapiro[4,4]nonane-2-carboxylate (Preparation example 227), to obtain the title compound (0.5g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.69~1.82(m, 4H), 1.85~2.03(m, 4H), 3.66(ddd, J =3.7, 8.1, 12.1, 1H), 3.83~3.90(m, 2H), 4.84(d, J =8.4, 1H), 7.26~7.41(m,
25 5H)

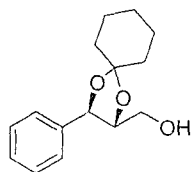
Preparation example 231: (2S,3R)-methyl 3-phenyl-1,4-dioxapiro[4,5]decane-2-carboxylate



5 The substantially same method as described in Preparation example 227 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.4g, 50~75%)

¹H NMR (400MHz, CDCl₃): δ=1.41~1.49(m, 2H), 1.58~1.76(m, 4H), 1.79~1.90(m, 4H), 3.78(s, 3H), 4.36(d, J=7.6, 1H), 5.16(d, J=7.2, 1H),
10 7.31~7.44(m, 5H)

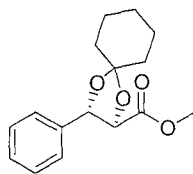
Preparation example 232: ((2R, 3R)-3-phenyl-1,4-dioxapiro[4,5]decan-2-yl)methanol



15 The substantially same method as described in Preparation example 224 was conducted, except that (2S, 3R)-methyl 3-phenyl-1,4-dioxapiro[4,5]decane-2-carboxylate (Preparation example 231) was used instead of (4S, 5R)-methyl-2,2-diethyl-5-phenyl-1,3-dioxolane-4-carboxylate(Preparation example 223), to obtain the title compound(1.0g, 70~95%)

20 ¹H NMR (400MHz, CDCl₃): δ=1.41~1.50(m, 2H), 1.61~1.89(m, 8H), 3.60~3.66(m, 1H), 3.85~3.90(m, 2H), 4.91(d, J=8.4, 1H), 7.30~7.42(m, 5H)

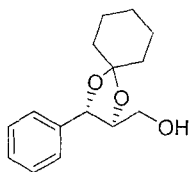
Preparation example 233: (2R, 3S)-methyl-3-phenyl-1,4-dioxapiro[4,5]decane-2-carboxylate



The substantially same method as described in Preparation example 229 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.2g, 50~75%)

5 ^1H NMR (400MHz, CDCl_3): δ =1.41~1.49(m, 2H), 1.58~1.76(m, 4H), 1.79~1.90(m, 4H), 3.78(s, 3H), 4.36(d, J =7.6, 1H), 5.16(d, J =7.2, 1H), 7.31~7.44(m, 5H)

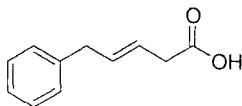
10 Preparation example 234: ((2S, 3S)-3-phenyl-1,4-dioxapero[4,5]decane-2-yl)methanol



15 The substantially same method as described in Preparation example 232 was conducted, except that (2R, 3S)-methyl-3-phenyl-1,4-dioxapero[4,5]decane-2-carboxylate(Preparation example 233) was used instead of (2S, 3R)-methyl-3-phenyl-1,4-dioxapero[4,5]decane-2-carboxylate (Preparation example 231), to obtain the title compound (0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.41~1.50(m, 2H), 1.61~1.89(m, 8H), 3.60~3.66(m, 1H), 3.85~3.90(m, 2H), 4.91(d, J =8.4, 1H), 7.30~7.42(m, 5H)

20 Preparation example 235: (E)-5-phenylpent-3-enoic acid

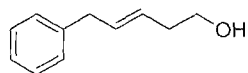


A solution of malonic acid (17.06g, 163.96mmol) in DMSO (65mL) was treated with a solution of AcOH (0.1mL, 1.49mmol) and piperidine (0.15mL,

1.49mmol) in DMSO (4mL). The reaction solution was warmed to 65°C and hydrocinnamaldehyde (10g, 74.53mmol) was added dropwise within 1.5hr. After the addition ended, the reaction mixture was stirred for further 2h at 65°C. The solution was cooled to room temperature, taken up in H₂O and extracted with Et₂O. The combined organic extracts were washed with 5% aqueous KHSO₄ and brine, dried over MgSO₄, and evaporated to dryness. The crude compound was purified by a silica gel column to produce the title compound (10.4g, 75~90%)

¹H NMR (400MHz, CDCl₃): δ=3.19(d, J=6.9, 2H), 3.46(d, J= 6.9, 2H), 5.69~5.78(m, 1H), 5.83~5.91(m, 1H), 7.01~7.56(m, 5H), 11.79(s, 1H)

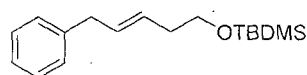
Preparation example 236: (E)-5-phenylpent-3-en-1-ol



To stirred solution of LAH (LiAlH₄, 3.3g, 86.73mmol) in THF(66mL) was added dropwise a solution (E)-5-phenylpent-3-enoic acid (Preparation example 235, 11.0g, 57.82mmol) in THF(44mL) at 0°C then stirred at room temperature for 1h. The reaction mixture was quenched with H₂O at 0°C, filtered through celite, washed with EtOAc, dried over anhydrous magnesium sulfate (MgSO₄), filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (7.2g, 70~90%)

¹H NMR (400MHz, CDCl₃): δ=1.40 (bs, 1H), 2.31(q, J=6.3, 2H), 3.37(d, J=6.8, 2H), 3.66(t, J=6.4, 2H), 5.49(dt, J=4.9, 11.0, 1H), 5.73(dt, J=4.8, 10.9, 1H), 7.17~7.31(m, 5H)

Preparation example 237: (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane

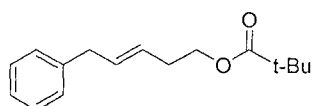


To a stirred solution of (E)-5-phenylpent-3-en-1-ol(Preparation example 236, 6.3g, 38.83mmol) in CH₂Cl₂ was added imidazole (3.4g, 50.48mmol) and

TBDMS-Cl (7.6g, 50.48mmol) at 0°C then stirred for 1h at room temperature. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound
 5 (10.6g, 80~98%)

¹H NMR (400MHz, CDCl₃): δ=0.00(s, 6H), 0.84(s, 9H), 2.21(ddd, J=6.8, 13.6, 0.8, 2H), 3.29(d, J=6.8, 2H), 3.59(t, J=6.8, 2H), 5.41~5.49(m, 1H), 5.56~5.63(m, 1H), 7.13~7.26(m, 5H)

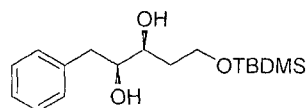
10 Preparation example 238: (E)-5-phenylpent-3-enyl pivalate



To a stirred solution of (E)-5-phenylpent-3-en-1-ol (Preparation example 236, 3.8g, 23.42mmol) in CH₂Cl₂ (40mL) was added pyridine (2.3mL, 28.1mmol) and pivaloyl chloride (3.5mL, 28.1mmol) at 0°C under N₂. The mixture was
 15 stirred for 14h. The resulting mixture was diluted with CH₂Cl₂, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (5.5g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.17(s, 9H), 2.36(q, J=6.7, 2H), 3.34(d, J=6.8, 2H), 4.09(t, J=6.8, 2H), 5.45~5.51(m, 1H), 5.64~5.69(m, 1H), 7.16~7.21(m, 3H), 7.26~7.30(m, 2H)
 20

Preparation example 239: (2S,3S)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol

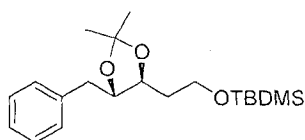


25 The substantially same method as described in Preparation example 217 was conducted, except that (E)-tert-butyldimethyl(5-phenylpent-3-

enyloxy)silane(Preparation example 237) was used instead of (E)-Methyl cinnamate (Preparation example 216), to obtain the title compound(8.7g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=0.00(s, 6H), 0.82(s, 9H), 1.57~1.62(m, 1H),
5 1.73~1.80(m, 1H), 2.51(d, J=6.0, 1H), 2.77(dq, J=6.9, 14.9, 2H), 3.50(d, J=3.6, 1H), 3.59~3.62(m, 1H), 3.66(dq, J=3.1, 5.4, 1H), 3.72~3.82(m, 2H), 7.12~7.25(m, 5H)

Preparation example 240: (2-((4S,5S)-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-yl)ethoxy)(tert-butyl)dimethylsilane
10

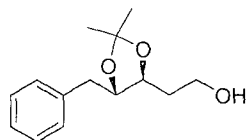


The substantially same method as described in Preparation example 218 was conducted, except that (2S,3S)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol(Preparation example 239) was used instead of (2R, 3S)-methyl-3-phenyl-2,3-dihydroxypropanoate(Preparation example 217), to
15 obtain the title compound(9.5g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=0.00(s, 6H), 0.85(s, 9H), 1.29(s, 3H), 1.34(s, 3H), 1.52~1.58(m, 2H), 2.87(dq, J=5.5, 14.2, 2H), 3.64~3.69(m, 2H), 3.80~3.88(m, 2H), 7.18~7.27(m, 5H)

20

Preparation example 241: 2-((4S,5S)-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-yl)ethanol

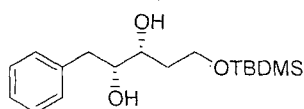


To a stirred solution of (2-((4S,5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-
25 4-yl)ethoxy)(tert-butyl)dimethylsilane (Preparation example 240, 11.5g, 32.80mmol) in THF (115mL) was slowly added tetrabutylammonium fluoride

(TBAF, 1.0M in THF, 48.8mL, 48.8mmol) at room temperature. The mixture was stirred for 5h. The resulting mixture was diluted with EtOAc, washed with water, dried over anhydrous magnesium sulfate, filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (7.3g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.38(s, 3H), 1.40(s, 3H), 1.50~1.63(m, 2H), 2.29(t, J =5.4, 1H), 2.82(dd, J =5.8, 13.8, 1H), 3.01(dd, J =6.4, 14.0, 1H), 3.72(q, J =5.5, 2H), 3.86(dt, J =3.2, 8.4, 1H), 3.92~3.97(m, 1H), 7.22~7.32(m, 5H)

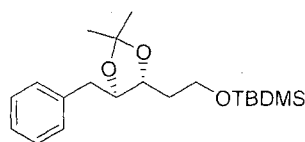
Preparation example 242: (2R,3R)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol



The substantially same method as described in Preparation example 220 was conducted, except that (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane(Preparation example 237) was used instead of (E)-Methyl cinnamate (Preparation example 216), to obtain the title compound(10.6g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.00(s, 6H), 0.82(s, 9H), 1.57~1.62(m, 1H), 1.73~1.80(m, 1H), 2.51(d, J =6.0, 1H), 2.77(dq, J =6.9, 14.9, 2H), 3.50(d, J =3.6, 1H), 3.59~3.62(m, 1H), 3.66(dq, J =3.1, 5.4, 1H), 3.72~3.82(m, 2H), 7.12~7.25(m, 5H)

Preparation example 243: (2-((4R,5R)-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-yl)ethoxy)(tert-butyl)dimethylsilane

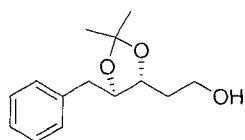


The substantially same method as described in Preparation example 221 was

conducted, except that (2R,3R)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol(Preparation example 242) was used instead of (2R,3S)-methyl-3-phenyl-2,3-dihydroxypropanoate(Preparation example 217), to obtain the title compound(11.5g, 70~95%)

5 ^1H NMR (400MHz, CDCl_3): δ =0.00(s, 6H), 0.85(s, 9H), 1.29(s, 3H), 1.34(s, 3H), 1.52~1.58(m, 2H), 2.87(dq, J =5.5, 14.2, 2H), 3.64~3.69(m, 2H), 3.80~3.88(m, 2H), 7.18~7.27(m, 5H)

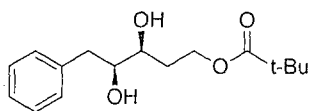
10 Preparation example 244: 2-((4R,5R)-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-yl)ethanol



The substantially same method as described in Preparation example 241 was conducted, except that (2-((4R,5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane(Preparation example 243) was used
15 instead of (2-((4S,5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane(Preparation example 240), to obtain the title compound(7.4g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.38(s, 3H), 1.40(s, 3H), 1.50~1.63(m, 2H), 2.29(t, J =5.4, 1H), 2.82(dd, J =5.8, 13.8, 1H), 3.01(dd, J =6.4, 14.0, 1H),
20 3.72(q, J =5.5, 2H), 3.86(dt, J =3.2, 8.4, 1H), 3.92~3.97(m, 1H), 7.22~7.32(m, 5H)

Preparation example 245: (3S,4S)-3,4-dihydroxy-5-phenylpentyl pivalate

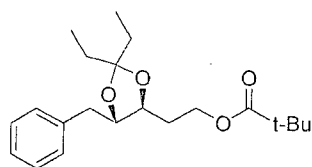


25 The substantially same method as described in Preparation example 239 was conducted, except that (E)-5-phenylpent-3-enyl pivalate (Preparation example 238) was used instead of (E)-tert-butyldimethyl(5-phenylpent-3-

enyloxy)silane(Preparation example 237), to obtain the title compound(5.5g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.16(s, 9H), 1.83~1.88(m, 2H), 2.08(d, J=4.8, 1H), 2.67(d, J=5.2, 1H), 2.80(dd, J=8.0, 13.6, 1H), 2.92(dd, J=5.2, 13.6, 1H), 3.50~3.55(m, 1H), 3.66~3.71(m, 1H), 4.09~4.19(m, 1H), 4.35~4.41(m, 1H), 7.22~7.25(m, 3H), 7.29~7.33(m, 2H)

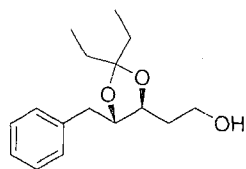
Preparation example 246: (2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolane-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 223 was conducted, except that (3S,4S)-3,4-dihydroxy-5-phenylpentyl pivalate(Preparation example 245) was used instead of (2R, 3S)-methyl-3-phenyl-2,3-dihydroxypropanoate(Preparation example 217), to obtain the title compound(0.9g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.15(s, 9H), 1.76(q, J=7.6, 2H), 1.84~1.90(m, 2H), 2.00~2.07(m, 2H), 3.85(dt, J=3.7, 8.5, 1H), 4.14~4.27(m, 2H), 5.17(d, J=8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.64(dd, J=1.4, 7.8, 1H)

Preparation example 247: 2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolane-4-yl)ethanol

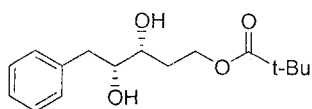


To a stirred solution of (2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 246, 1.0g, 2.87mmol) in MeOH(10mL) was added NaOMe (0.47g, 8.61mmol) and then warm to 45°C. The mixture was

stirred for 14h. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (0.7g, 80~95%);

5 ¹H NMR (400MHz, CDCl₃): δ=0.89(t, J=7.4, 6H), 1.44~1.50(m, 1H), 1.54~1.66(m, 5H), 2.37(t, J=5.6, 1H), 2.80(dd, J=5.6, 14.0, 1H), 3.03(dd, J=6.4, 14.0, 1H), 3.72(q, J=5.5, 2H), 3.80~3.85(m, 1H), 3.89~3.94(m, 1H), 7.21~7.24(m, 3H), 7.28~7.31(m, 2H)

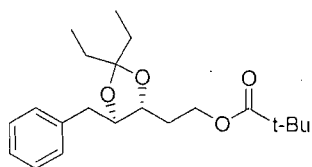
10 Preparation example 248: (3R,4R)-3,4-dihydroxy-5-phenylpentyl pivalate



The substantially same method as described in Preparation example 242 was conducted, except that (E)-5-phenylpent-3-enyl pivalate (Preparation example 238) was used instead of (E)-tert-butyl dimethyl (5-phenylpent-3-enyloxy)silane (Preparation example 237), to obtain the title compound (4.5g, 70~95%)

15 ¹H NMR (400MHz, CDCl₃): δ=1.16(s, 9H), 1.83~1.88(m, 2H), 2.08(d, J=4.8, 1H), 2.67(d, J=5.2, 1H), 2.80(dd, J=8.0, 13.6, 1H), 2.92(dd, J=5.2, 13.6, 1H), 3.50~3.55(m, 1H), 3.66~3.71(m, 1H), 4.09~4.19(m, 1H), 4.35~4.41(m, 1H),
20 7.22~7.25(m, 3H), 7.29~7.33(m, 2H)

Preparation example 249: (2-((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolane-4-yl)ethyl)ethyl pivalate

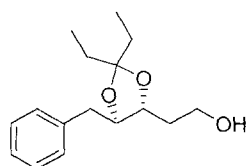


25 The substantially same method as described in Preparation example 246 was conducted, except that (3R,4R)-3,4-dihydroxy-5-phenylpentyl

pivalate(Preparation example 248) was used instead of (3S,4S)-3,4-dihydroxy-5-phenylpentyl pivalate (Preparation example 245), to obtain the title compound(1.1g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.15(s, 9H), 1.76(q, J=7.6, 2H), 1.84~1.90(m, 2H), 2.00~2.07(m, 2H), 3.85(dt, J=3.7, 8.5, 1H), 4.14~4.27(m, 2H), 5.17(d, J=8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.64(dd, J=1.4, 7.8, 1H)

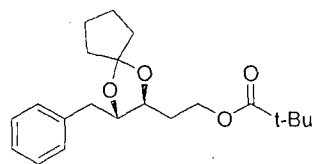
Preparation example 250: 2-((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolane-4-yl)ethanol



The substantially same method as described in Preparation example 247 was conducted, except that (2-((4R,5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 249) was used instead of (2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 246), to obtain the title compound (0.9g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=0.89(t, J=7.4, 6H), 1.44~1.50(m, 1H), 1.54~1.66(m, 5H), 2.37(t, J=5.6, 1H), 2.80(dd, J=5.6, 14.0, 1H), 3.03(dd, J=6.4, 14.0, 1H), 3.72(q, J=5.5, 2H), 3.80~3.85(m, 1H), 3.89~3.94(m, 1H), 7.21~7.24(m, 3H), 7.28~7.31(m, 2H)

Preparation example 251: 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)ethyl pivalate



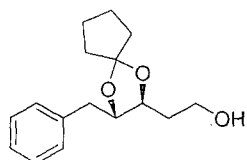
The substantially same method as described in Preparation example 246 was conducted, except that cyclopentanone was used instead of 3-pentanone, to

obtain the title compound (1.2g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.18(s, 9H), 1.53~1.80(m, 10H), 2.81(dd, J=6.0, 13.6, 1H), 3.00(dd, J=6.4, 14.0, 1H), 3.75~3.80(m, 1H), 3.84~3.89(m, 1H), 4.05~4.16(m, 2H), 7.20~7.24(m, 3H), 7.27~7.31(m, 2H)

5

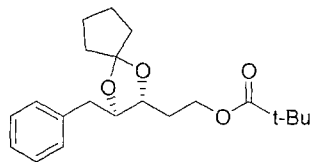
Preparation example 252: 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)ethanol



10 The substantially same method as described in Preparation example 247 was conducted, except that 2-((2S,3S)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 251) was used instead of (2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 246), to obtain the title compound (0.7g, 80~95%)

15 ¹H NMR (400MHz, CDCl₃): δ=1.44~1.51(m, 1H), 1.56~1.60(m, 1H), 1.63~1.70(m, 4H), 1.72~1.81(m, 4H), 2.26(t, J=5.4, 1H), 2.80(dd, J=6.0, 14.0, 1H), 3.03(dd, J=6.4, 14.0, 1H), 3.71(q, J=5.5, 2H), 3.81~3.92(m, 2H), 7.22~7.24(m, 3H), 7.28~7.32(m, 2H)

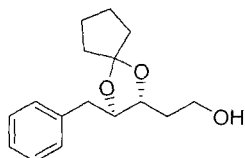
20 Preparation example 253: 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 249 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.7g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ = 1.18(s, 9H), 1.53~1.80(m, 10H), 2.81(dd, J =6.0, 13.6, 1H), 3.00(dd, J =6.4, 14.0, 1H), 3.75~3.80(m, 1H), 3.84~3.89(m, 1H), 4.05~4.16(m, 2H), 7.20~7.24(m, 3H), 7.27~7.31(m, 2H)

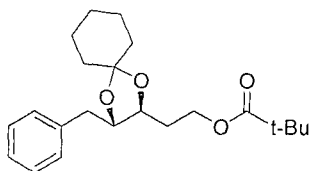
- 5 Preparation example 254: 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)ethanol



The substantially same method as described in Preparation example 252 was conducted, except that 2-((2R,3R)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 253) was used instead of 2-((2S,3S)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 251), to obtain the title compound (0.8g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ = 1.44~1.51(m, 1H), 1.56~1.60(m, 1H), 1.63~1.70(m, 4H), 1.72~1.81(m, 4H), 2.26(t, J =5.4, 1H), 2.80(dd, J =6.0, 14.0, 1H), 3.03(dd, J =6.4, 14.0, 1H), 3.71(q, J =5.5, 2H), 3.81~3.92(m, 2H), 7.22~7.24(m, 3H), 7.28~7.32(m, 2H)

Preparation example 255: 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.5]decane-2-yl)ethyl pivalate

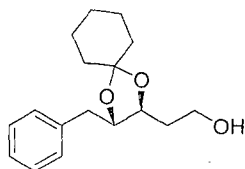


The substantially same method as described in Preparation example 251 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.4g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ = 1.18(s, 9H), 1.53~1.60(m, 10H), 1.61~1.66(m, 2H), 2.83(dd, J =5.6, 14.0, 1H), 2.98(dd, J =6.0, 14.0, 1H), 3.78(dt, J =3.5,

8.2, 1H), 3.86~3.91(m, 1H), 4.11~4.15(m, 2H), 7.20~7.31(m, 5H)

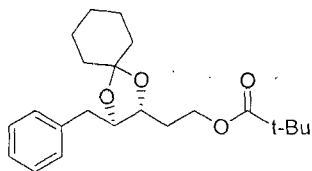
Preparation example 256: 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.5]decane-2-yl)ethanol



The substantially same method as described in Preparation example 254 was conducted, except that 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 255) was used instead of 2-((2R,3R)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 10 253), to obtain the title compound (1.0g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.34~1.43(m, 2H), 1.48~1.61(m, 10H), 2.42(t, J=5.6, 1H), 2.81(dd, J=5.6, 14.0, 1H), 3.02(dd, J=6.2, 13.8, 1H), 3.72(q, J=5.5, 2H), 3.82~3.87(m, 1H), 3.91~3.96(m, 1H), 7.21~7.31(m, 5H)

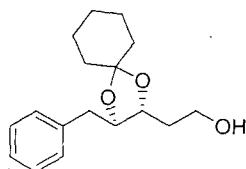
15 Preparation example 257: 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.5]decane-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 253 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.6g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.18(s, 9H), 1.53~1.60(m, 10H), 1.61~1.66(m, 2H), 2.83(dd, J=5.6, 14.0, 1H), 2.98(dd, J=6.0, 14.0, 1H), 3.78(dt, J=3.5, 8.2, 1H), 3.86~3.91(m, 1H), 4.11~4.15(m, 2H), 7.20~7.31(m, 5H)

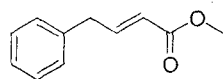
Preparation example 258: 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.5]decane-2-yl)ethanol



The substantially same method as described in Preparation example 256 was conducted, except that 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 257) was used instead of 2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 255), to obtain the title compound (1.1g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.34~1.43(m, 2H), 1.48~1.61(m, 10H), 2.42(t, J=5.6, 1H), 2.81(dd, J=5.6, 14.0, 1H), 3.02(dd, J=6.2, 13.8, 1H), 3.72(q, J=5.5, 2H), 3.82~3.87(m, 1H), 3.91~3.96(m, 1H), 7.21~7.31(m, 5H)

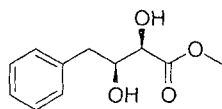
Preparation example 259: (E)-methyl-4-phenylbut-2-enoate



To a solution of phenyl acetaldehyde (5.0g, 41.61mmol) in toluene (500mL) was added methyl (triphenylphosphoranylidene) acetate (13.9g, 41.61mmol). The reaction mixture was stirred at reflux for 3 h. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was added ether/hexane(=1:1, v/v) at 0°C then stirred for 30min. The filtrate was concentrated then purified by a silica gel column to produce the title compound (5.9g, 70~90%)

¹H NMR (400MHz, CDCl₃): δ=3.47(d, J=6.8, 2H), 3.67(s, 3H), 5.79(d, J=15.4, 1H), 7.06(dt, J=15.4, 6.8, 1H), 7.28~7.12(m, 5H)

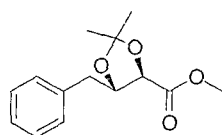
Preparation example 260: (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate



The substantially same method as described in Preparation example 245 was conducted, except that (E)-methyl-4-phenylbut-2-enoate(Preparation example 259) was used instead of (E)-5-phenylpent-3-enyl pivalate(Preparation example 238), to obtain the title compound(3.5g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=2.96(ddd, J=7.3, 13.5, 17.1, 2H), 3.10(d, J=5.2, 1H), 3.80(s, 3H), 4.08(dd, J=1.4, 5.4, 1H), 7.23~7.34(m, 5H)

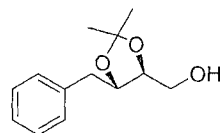
Preparation example 261: (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 240 was conducted, except that (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate(Preparation example 260) was used instead of (2S,3S)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol(Preparation example 239), to obtain the title compound(3.1g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.42(s, 3H), 1.43(s, 3H), 3.01(dd, J=6.8, 14.4, 1H), 3.12(dd, J=4.4, 14.4, 1H), 3.72(s, 3H), 4.19(d, J=7.6, 1H), 4.40(ddd, J=4.4, 7.0, 7.8, 1H), 7.22~7.33(m, 5H)

Preparation example 262: ((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methanol

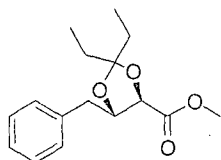


The substantially same method as described in Preparation example 234 was

conducted, except that (4R,5S)-methyl 5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 261) was used instead of (4S, 5R)-methyl-3-phenyl-1,4-dioxapiro[4,5]decane-2-carboxylate (Preparation example 233), to obtain the title compound(2.3g, 70~95%)

- 5 ^1H NMR (400MHz, CDCl_3): δ =1.41(s, 6H), 1.79(q, J =4.3, 1H), 2.83(dd, J =6.2, 13.8, 1H), 3.07(dd, J =6.4, 14.0, 1H), 3.29(ddd, J =4.7, 7.5, 12.1, 1H), 3.54(ddd, J =2.8, 5.2, 12.0, 1H), 3.83(ddd, J =3.9, 3.9, 7.1, 1H), 4.15(q, J =7.1, 1H), 7.22~7.32(m, 5H)

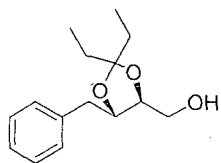
- 10 Preparation example 263: (4R,5S)-methyl-5-benzyl-2,2-diethyl-1,3-dioxolane-4-carboxylate



- 15 To a stirred solution of (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate(Preparation example 260, 2.0g, 9.51mmol) in 3-pentanone (5mL, 47.55mmol) was added a catalytic amount of H_2SO_4 (0.051mL, 0.951mmol) at room temperature. The mixture was stirred for 20h. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (1.2g, 50~75%)

- 20 ^1H NMR (400MHz, CDCl_3): δ =0.85(t, J =6.0, 3H), 0.92(t, J =7.6, 3H), 1.66(dq, J =7.6, 14.7, 4H), 3.01(dd, J =6.6, 14.2, 1H), 3.10(dd, J =4.4, 14.4, 1H), 3.71(s, 3H), 4.17(d, J =8.4, 1H), 4.32~4.37(m, 1H), 7.23~7.32(m, 5H)

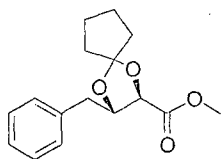
- 25 Preparation example 264: ((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 262 was conducted, except that (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 263) was used instead of (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 261), to obtain the title compound (0.8g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=0.91(dt, J=1.9, 7.5, 6H), 1.61~1.68(m, 4H), 1.77(t, J=6.2, 1H), 2.81(dd, J=6.4, 14.0, 1H), 3.09(dd, J=6.2, 13.8, 1H), 3.24~3.30(m, 1H), 3.49~3.54(m, 1H), 3.78~3.82(m, 1H), 4.08~4.13(m, 1H), 7.21~7.32(m, 5H)

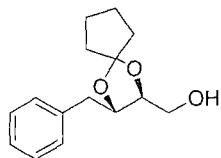
Preparation example 265: (2R, 3S)-methyl 3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate



The substantially same method as described in Preparation example 263 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.3g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.61~1.79(m, 5H), 1.85~1.92(m, 3H), 3.00~3.11(m, 2H), 3.70(s, 3H), 4.17(d, J=7.2, 1H), 4.32 (dt, J=4.9, 7.0, 1H), 7.21~7.33(m, 5H)

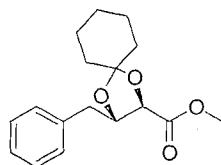
Preparation example 266: ((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)methanol



The substantially same method as described in Preparation example 264 was conducted, except that (2R, 3S)-methyl 3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 265) was used instead of (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 263), to obtain the title compound (0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.57~1.88(m, 8H), 2.82(dd, J =6.6, 13.8, 1H), 3.08(dd, J =6.4, 14.0, 1H), 3.27~3.33(m, 1H), 3.47~3.52(m, 1H), 3.79~3.83(m, 1H), 4.07(q, J =6.8, 1H), 7.21~7.32(m, 5H)

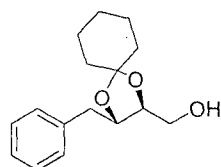
Preparation example 267: (2R,3S)-methyl-3-benzyl-1,4-dioxaspiro[4.5]decane-2-carboxylate



The substantially same method as described in Preparation example 265 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.5g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.54~1.74(m, 10H), 2.99~3.12(m, 2H), 3.70(s, 3H), 4.18(d, J =7.6, 1H), 4.36~4.41(m, 1H), 7.21~7.32(m, 5H)

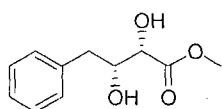
Preparation example 268: ((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.4]decan-2-yl)methanol



The substantially same method as described in Preparation example 266 was conducted, except that (2R, 3S)-methyl-3-benzyl-1,4-dioxaspiro[4.5]decane-2-carboxylate (Preparation example 267) was used instead of (2R, 3S)-methyl 3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 265),
5 to obtain the title compound (0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.53~1.65(m, 10H), 2.82(dd, J =6.2, 13.8, 1H), 3.07(dd, J =6.4, 13.6, 1H), 3.24~3.30(m, 1H), 3.52~3.56(m, 1H), 3.80~3.84(m, 1H), 4.10~4.15(m, 1H), 7.21~7.31(m, 5H)

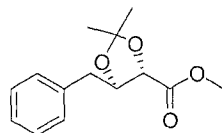
10 Preparation example 269: (2S, 3R)-methyl-2,3-dihydroxy-4-phenylbutanoate



The substantially same method as described in Preparation example 242 was conducted, except that (E)-methyl-4-phenylbut-2-enoate(Preparation example 259) was used instead of (E)-tert-butyl dimethyl(5-phenylpent-3-enyloxy)silane(Preparation example 237), to obtain the title compound(3.5g,
15 70~95%)

^1H NMR (400MHz, CDCl_3): δ =2.96(ddd, J =7.3, 13.5, 17.1, 2H), 3.10(d, J =5.2, 1H), 3.80(s, 3H), 4.08(dd, J =1.4, 5.4, 1H), 7.23~7.34(m, 5H)

20 Preparation example 270: (4S, 5R)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate

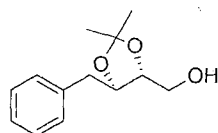


The substantially same method as described in Preparation example 261 was conducted, except that (2S, 3R)-methyl-2,3-dihydroxy-4-phenylbutanoate (Preparation example 269) was used instead of (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate (Preparation example 260), to obtain the title
25 compound(3.4g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.41(s, 6H), 1.79(q, J =4.3, 1H), 2.83(dd, J =6.2, 13.8, 1H), 3.07(dd, J =6.4, 14.0, 1H), 3.29(ddd, J =4.7, 7.5, 12.1, 1H), 3.54(ddd, J =2.8, 5.2, 12.0, 1H), 3.83(ddd, J =3.9, 3.9, 7.1, 1H), 4.15(q, J =7.1, 1H), 7.22~7.32(m, 5H)

5

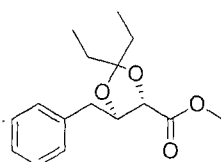
Preparation example 271: ((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 262 was conducted, except that (4S,5R)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 270) was used instead of (4R,5S)-methyl 5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 261), to obtain the title compound (2.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.41(s, 6H), 1.79(q, J =4.3, 1H), 2.83(dd, J =6.2, 13.8, 1H), 3.07(dd, J =6.4, 14.0, 1H), 3.29(ddd, J =4.7, 7.5, 12.1, 1H), 3.54(ddd, J =2.8, 5.2, 12.0, 1H), 3.83(ddd, J =3.9, 3.9, 7.1, 1H), 4.15(q, J =7.1, 1H), 7.22~7.32(m, 5H)

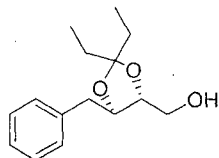
Preparation example 272: (4S, 5R)-methyl-5-benzyl-2,2-diethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 263 was conducted, except that (2S, 3R)-methyl-2,3-dihydroxy-4-phenylbutanoate (Preparation example 269) was used instead of (2,3-dihydroxy-4-phenylbutanoate (Preparation example 260), to obtain the title compound (1.5g, 50~75%)

^1H NMR (400MHz, CDCl_3): δ =0.85(t, J =6.0, 3H), 0.92(t, J =7.6, 3H), 1.66(dq, J =7.6, 14.7, 4H), 3.01(dd, J =6.6, 14.2, 1H), 3.10(dd, J =4.4, 14.4, 1H), 3.71(s, 3H), 4.17(d, J =8.4, 1H), 4.32~4.37(m, 1H), 7.23~7.32(m, 5H)

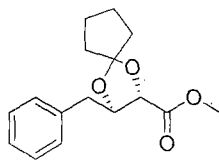
- 5 Preparation example 273: ((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 264 was conducted, except that (4S,5R)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 272) was used instead of (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 263), to obtain the title compound (1.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.91(dt, J =1.9, 7.5, 6H), 1.61~1.68(m, 4H), 1.77(t, J =6.2, 1H), 2.81(dd, J =6.4, 14.0, 1H), 3.09(dd, J =6.2, 13.8, 1H), 3.24~3.30(m, 1H), 3.49~3.54(m, 1H), 3.78~3.82(m, 1H), 4.08~4.13(m, 1H), 7.21~7.32(m, 5H)

Preparation example 274: (2S, 3R)-methyl-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate

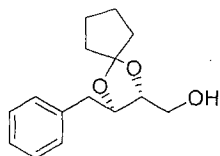


The substantially same method as described in Preparation example 272 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.2g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.61~1.79(m, 5H), 1.85~1.92(m, 3H), 3.00~3.11(m, 2H), 3.70(s, 3H), 4.17(d, J =7.2, 1H), 4.32(dt, J =4.9, 7.0, 1H),

7.21~7.33(m, 5H)

Preparation example 275: ((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-yl)methanol



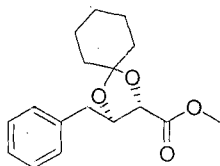
5

The substantially same method as described in Preparation example 266 was conducted, except that (2S, 3R)-methyl-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 274) was used instead of (2R, 3S)-methyl-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 265), to obtain the title compound (1.1g, 70~95%)

10

^1H NMR (400MHz, CDCl_3): δ =1.57~1.88(m, 8H), 2.82(dd, J =6.6, 13.8, 1H), 3.08(dd, J =6.4, 14.0, 1H), 3.27~3.33(m, 1H), 3.47~3.52(m, 1H), 3.79~3.83(m, 1H), 4.07(q, J =6.8, 1H), 7.21~7.32(m, 5H).

15 Preparation example 276: (2S, 3R)-methyl-3-benzyl-1,4-dioxaspiro[4.5]decane-2-carboxylate

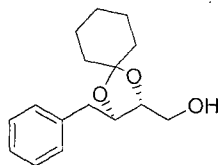


20 The substantially same method as described in Preparation example 274 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.4g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.54~1.74(m, 10H), 2.99~3.12(m, 2H), 3.70(s, 3H), 4.18(d, J =7.6, 1H), 4.36~4.41(m, 1H), 7.21~7.32(m, 5H)

Preparation example 277: ((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.4]nonane-2-

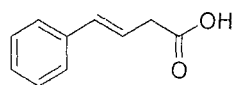
yl)methanol



The substantially same method as described in Preparation example 268 was conducted, except that (2S, 3R)-methyl-3-benzyl-1,4-dioxaspiro[4.5]decane-2-carboxylate (Preparation example 276) was used instead of (2R, 3S)-methyl-3-benzyl-1,4-dioxaspiro[4.5]decane-2-carboxylate (Preparation example 267), to obtain the title compound (1.4g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.53~1.65(m, 10H), 2.82(dd, J=6.2, 13.8, 1H), 3.07(dd, J=6.4, 13.6, 1H), 3.24~3.30(m, 1H), 3.52~3.56(m, 1H), 3.80~3.84(m, 1H), 4.10~4.15(m, 1H), 7.21~7.31(m, 5H)

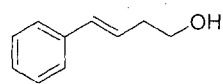
Preparation example 278: (E)-4-phenylbut-3-enoic acid



To a stirred solution of 2-phenylacetaldehyde (5.0g, 32.3mmol) and malonic acid (4.0g, 38.8mmol) in pyridine (25.0mL) was added a catalytic amount of piperidine (0.64mL, 6.46mmol) then heated to reflux. After 3h, the resulting mixture was cooled to room temperature and concentrated under reduced pressure. The crude product was slowly added 2N HCl. The white precipitate was filtered off and dried under vacuum to produce the title compound (3.5g, 55~80%)

¹H NMR (400MHz, CDCl₃): δ=3.39(d, J=8.8, 2H), 6.31(td, J=7.9, 14.8, 1H), 6.94(d, J=16, 1H), 7.17~7.45(m, 3H), 7.56~7.59(m, 1H)

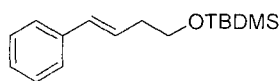
Preparation example 279: (E)-4-phenylbut-3-en-1-ol



To stirred solution of $\text{Zn}(\text{BH}_4)_2$ (40.0mL, 20.0mmol) in THF(40mL) was added dropwise a solution (E)-4-phenylbut-3-enoic acid (Preparation example 278, 2.0g, 10.0mmol) in THF(5mL) at 0°C then heated to reflux for 0.5h. The reaction mixture was quenched with H_2O at 0°C, filtered through celite, washed with EtOAc, dried over anhydrous magnesium sulfate(MgSO_4), filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (1.0g, 50~75%)

^1H NMR (400MHz, CDCl_3): δ =2.55(ddd, J = 4.1, 11.9, 21.5, 2H), 3.82(t, J =5.8, 2H), 6.24(td, J =7.2, 15.7, 1H), 6.87(d, J =14.8, 1H), 7.12~7.25(m, 3H), 7.36(dd, J =1.2, 8.0, 1H), 7.52(dd, J =1.6, 9.2, 1H)

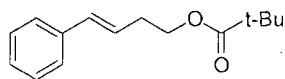
Preparation example 280: (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane



The substantially same method as described in Preparation example 237 was conducted, except that (E)-4-phenylbut-3-en-1-ol (Preparation example 279) was used instead of (E)-5-phenylpent-3-en-1-ol (Preparation example 236), to obtain the title compound(1.7g, 80~98%)

^1H NMR (400MHz, CDCl_3): δ =0.07(s, 3H), 0.10(s, 3H), 0.92(d, J =6.4, 9H), 2.51(q, J =4.5, 2H), 3.78(t, J =6.6, 2H), 6.26(td, J =7.2, 15.7, 1H), 6.84(d, J =15.6, 1H), 7.13~7.24(m, 3H), 7.36(dd, J =5.6, 12.4, 1H), 7.53(dd, J =1.4, 7.8, 1H)

Preparation example 281: (E)-4-phenylbut-3-enyl pivalate



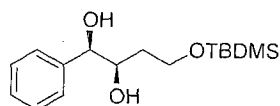
The substantially same method as described in Preparation example 238 was conducted, except that (E)-4-phenylbut-3-en-1-ol (Preparation example 279) was used instead of (E)-5-phenylpent-3-en-1-ol (Preparation example 236),

to obtain the title compound(10.8g, 75~95%)

^1H NMR (400MHz, CDCl_3): δ =1.22(s, 9H), 2.57(ddd, J =1.3, 6.7, 13.5, 2H), 4.22(t, J =6.6, 2H), 6.19(td, J =7.0, 16.0, 1H), 6.49(d, J =16.0, 1H), 7.23~7.26(m, 1H), 7.31~7.41(m, 4H)

5

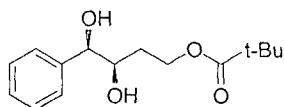
Preparation example 282: (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol



The substantially same method as described in Preparation example 239 was conducted, except that (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane(Preparation example 280) was used instead of (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane (Preparation example 237), to obtain the title compound(0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.10(s, 3H), 0.11(s, 3H), 0.92(s, 9H), 1.69~1.70(m, 1H), 1.93~2.07(m, 1H), 3.51(d, J =4.8, 1H), 3.86(d, J =3.2, 1H), 3.87(dd, J =3.2, 9.2, 1H), 3.91~3.96(m, 1H), 4.01~4.06(m, 1H), 5.05(t, J =4.6, 1H), 7.22~7.26(m, 1H), 7.31~7.37(m, 2H), 7.59(dd, J =1.2, 7.6, 1H)

Preparation example 283: (3R, 4R)-3,4-dihydroxy-4-phenylbutyl pivalate



20

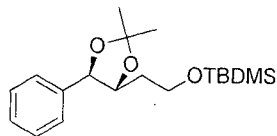
The substantially same method as described in Preparation example 282 was conducted, except that (E)-4-phenylbut-3-enyl pivalate (Preparation example 281) was used instead of (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane (Preparation example 280), to obtain the title compound(8.7g, 70~95%)

25

^1H NMR (400MHz, CDCl_3): δ =1.18(s, 9H), 1.65~1.74(m, 2H), 2.83(d, J =2.4, 1H), 2.96(d, J =3.2, 1H), 3.74~3.79(m, 1H), 4.10~4.17(m, 1H), 4.33(ddd,

J=4.0, 7.2, 12.6, 1H), 4.49(d, J=5.6, 1H), 7.31~7.41(m, 5H)

Preparation example 284: tert-butyl(2-((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane



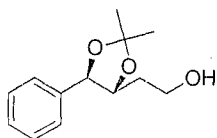
The substantially same method as described in Preparation example 218 was conducted, except that (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol (Preparation example 282) was used instead of (2R, 3S)-methyl-3-phenyl-2,3-dihydroxypropanoate(Preparation example 217), to obtain the title compound(1.6g, 70~95%)

10

^1H NMR (400MHz, CDCl_3): δ =0.02(s, 3H), 0.07(s, 3H), 0.86(s, 9H), 1.50(s, 3H), 1.58(s, 3H), 1.82~1.99(m, 2H), 3.68~3.78(m, 2H), 3.95(dt, J=3.3, 8.7, 1H), 5.16(d, J=8.4, 1H), 7.21~7.27(m, 1H), 7.31~7.38(m, 2H), 7.60(dd, J=1.6, 7.6, 1H)

15

Preparation example 285: 2-((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol



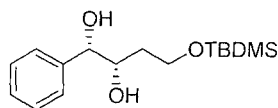
The substantially same method as described in Preparation example 244 was conducted, except that tert-butyl(2-((4R,5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane (Preparation example 284) was used instead of (2-((4R,5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane(Preparation example 243), to obtain the title compound (1.4g, 80~95%).

^1H NMR (400MHz, CDCl_3): δ =1.56(s, 3H), 1.62(s, 3H), 1.92~2.04(m, 2H), 2.26(q, J=3.7, 1H), 3.75~3.90(m, 2H), 3.94(td, J=3.9, 8.5, 1H), 5.23(d,

25

$J=15.6$, 1H), 7.22~7.27(m, 1H), 7.33~7.39(m, 2H), 7.62(dd, $J=1.6$, 7.6, 1H)

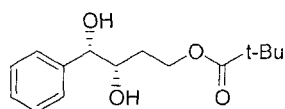
Preparation example 286: (1S, 2S)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol



The substantially same method as described in Preparation example 242 was conducted, except that (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane(Preparation example 280)was used instead of (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane (Preparation example 237), to obtain the title compound(0.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): $\delta=0.10$ (s, 3H), 0.11(s, 3H), 0.92(s, 9H), 1.69~1.70(m, 1H), 1.93~2.07(m, 1H), 3.51(d, $J=4.8$, 1H), 3.86(d, $J=3.2$, 1H), 3.87(dd, $J=3.2$, 9.2, 1H), 3.91~3.96(m, 1H), 4.01~4.06(m, 1H), 5.05(t, $J=4.6$, 1H), 7.22~7.26(m, 1H), 7.31~7.37(m, 2H), 7.59(dd, $J=1.2$, 7.6, 1H)

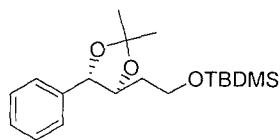
Preparation example 287: (3S, 4S)-3,4-dihydroxy-4-phenylbutyl pivalate



The substantially same method as described in Preparation example 286 was conducted, except that (E)-4-phenylbut-3-enyl pivalate (Preparation example 281) was used instead of (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane(Preparation example 280), to obtain the title compound(10.4g, 70~95%)

^1H NMR (400MHz, CDCl_3): $\delta=1.18$ (s, 9H), 1.65~1.74(m, 2H), 2.83(d, $J=2.4$, 1H), 2.96(d, $J=3.2$, 1H), 3.74~3.79(m, 1H), 4.10~4.17(m, 1H), 4.33(ddd, $J=4.0$, 7.2, 12.6, 1H), 4.49(d, $J=5.6$, 1H), 7.31~7.41(m, 5H)

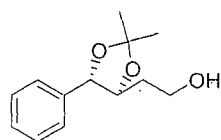
Preparation example 288: tert-butyl(2-((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane



The substantially same method as described in Preparation example 284 was conducted, except that (1S, 2S)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol (Preparation example 286) was used instead of (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol (Preparation example 282), to obtain the title compound(0.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.02(s, 3H), 0.07(s, 3H), 0.86(s, 9H), 1.50(s, 3H), 1.58(s, 3H), 1.82~1.99(m, 2H), 3.68~3.78(m, 2H), 3.95(dt, J =3.3, 8.7, 1H), 5.16(d, J =8.4, 1H), 7.21~7.27(m, 1H), 7.31~7.38(m, 2H), 7.60(dd, J =1.6, 7.6, 1H)

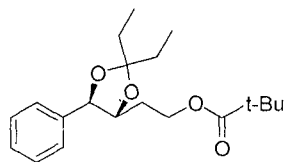
Preparation example 289: 2-((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol



The substantially same method as described in Preparation example 285 was conducted, except that tert-butyl(2-((4S,5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane (Preparation example 288) was used instead of that tert-butyl(2-((4R,5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane (Preparation example 284), to obtain the title compound(0.4g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.56(s, 3H), 1.62(s, 3H), 1.92~2.04(m, 2H), 2.26(q, J =3.7, 1H), 3.75~3.90(m, 2H), 3.94(td, J =3.9, 8.5, 1H), 5.23(d, J =15.6, 1H), 7.22~7.27(m, 1H), 7.33~7.39(m, 2H), 7.62(dd, J =1.6, 7.6, 1H)

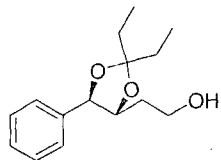
Preparation example 290: 2-((4R, 5R)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 264 was conducted, except that (3R, 4R)-3,4-dihydroxy-4-phenylbutyl pivalate (Preparation example 283) was used instead of (4R,5S)-methyl-5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 263), to obtain the title compound (1.8g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.00(t, J=7.4, 3H), 1.08(t, J=7.6, 3H), 1.14(s, 9H), 1.76(q, J=7.5, 2H), 1.81~1.89(m, 2H), 1.91~1.98(m, 2H), 3.87(td, J=5.8, 8.8, 1H), 4.13~4.18(m, 1H), 4.22~4.28(m, 1H), 4.58(d, J=8.8, 1H), 7.31~7.43(m, 5H)

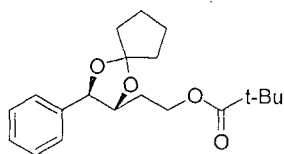
Preparation example 291: 2-((4R, 5R)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 258 was conducted, except that 2-((4R, 5R)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 290) was used instead of 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 257), to obtain the title compound (0.9g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.01(t, J=7.4, 3H), 1.07(t, J=7.6, 3H), 1.79(q, J=7.5, 2H), 1.83~1.90(m, 4H), 2.38(q, J=3.7, 1H), 3.75~3.87(m, 2H), 3.90~3.95(m, 1H), 4.63(d, J=8.8, 1H), 7.32~7.43(m, 5H)

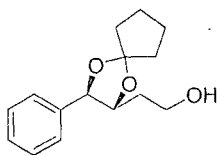
Preparation example 292: 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 290 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.8g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.14(s, 9H), 1.67~1.83(m, 4H), 1.88~2.07(m, 6H), 3.84(td, J =6.0, 8.4, 1H), 4.13(td, J =7.0, 11.1, 1H), 4.24(td, J =6.4, 11.2, 1H), 4.55(d, J =8.4, 1H), 7.31~7.39(m, 5H)

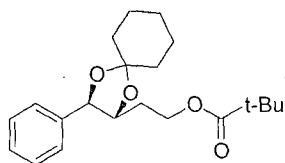
Preparation example 293: 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol



The substantially same method as described in Preparation example 291 was conducted, except that 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate(Preparation example 292) was used instead of that 2-((4S,5S)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 290), to obtain the title compound (0.9g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.71~1.81(m, 4H), 1.87~2.07(m, 6H), 2.27(q, J =3.7, 1H), 3.79~3.85(m, 2H), 3.89~3.92(m, 1H), 4.59(d, J =8.4, 1H), 7.32~7.41(m, 5H)

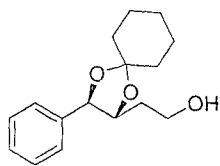
Preparation example 294: 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 292 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (2.0g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.14(s, 9H), 1.67~1.83(m, 4H), 1.88~2.07(m, 6H), 3.84(td, J=6.0, 8.4, 1H), 4.10~4.17(m, 1H), 4.21~4.27(m, 1H), 4.55(d, J=8.4, 1H), 7.31~7.39(m, 5H)

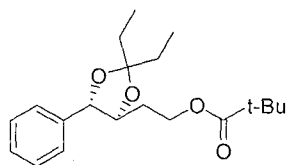
Preparation example 295: 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethanol



The substantially same method as described in Preparation example 293 was conducted, except that 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 294) was used instead of that 2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 292), to obtain the title compound (1.2g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.71~1.83(m, 4H), 1.87~2.05(m, 6H), 2.27(q, J=3.7, 1H), 3.79~3.85(m, 2H), 3.86~3.91(m, 1H), 4.59(d, J=8.4, 1H), 7.32~7.41(m, 5H)

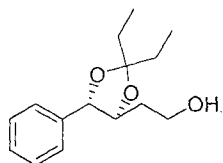
Preparation example 296: 2-((4S, 5S)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 290 was conducted, except that (3S, 4S)-3,4-dihydroxy-4-phenylbutyl pivalate(Preparation example 287) was used instead of (3R, 4R)-3,4-dihydroxy-4-phenylbutyl pivalate(Preparation example 283), to obtain the title compound(2.2g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.00(t, J=7.4, 3H), 1.08(t, J=7.6, 3H), 1.14(s, 9H), 1.76(q, J=7.5, 2H), 1.81~1.89(m, 2H), 1.91~1.98(m, 2H), 3.87(td, J=5.8, 8.8, 1H), 4.13~4.18(m, 1H), 4.22~4.28(m, 1H), 4.58(d, J=8.8, 1H), 7.31~7.43(m, 5H)

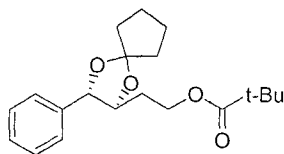
Preparation example 297: 2-(((4S, 5S)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl)ethyl pivalate



The substantially same method as described in Preparation example 295 was conducted, except 2-(((4S, 5S)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl)ethyl pivalate (Preparation example 296)was used instead of 2-(((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl)ethyl pivalate (Preparation example 294), to obtain the title compound (0.7g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.01(t, J=7.4, 3H), 1.07(t, J=7.6, 3H), 1.79(q, J=7.5, 2H), 1.83~1.90(m, 4H), 2.38(q, J=3.7, 1H), 3.75~3.87(m, 2H), 3.90~3.95(m, 1H), 4.63(d, J=8.8, 1H), 7.32~7.43(m, 5H)

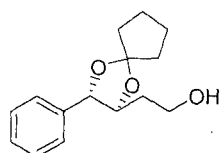
Preparation example 298: 2-(((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl)ethyl pivalate



The substantially same method as described in Preparation example 296 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (2.4g, 60~85%)

- 5 ^1H NMR (400MHz, CDCl_3): δ =1.14(s, 9H), 1.67~1.83(m, 4H), 1.88~2.07(m, 6H), 3.84(td, J =6.0, 8.4, 1H), 4.13(td, J =7.0, 11.1, 1H), 4.24(td, J =6.4, 11.2, 1H), 4.55(d, J =8.4, 1H), 7.31~7.39(m, 5H)

10 Preparation example 299: 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol

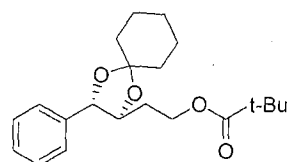


15 The substantially same method as described in Preparation example 297 was conducted, except that 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate(Preparation example 298) was used instead of that 2-((4S, 5S)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 296), to obtain the title compound (07g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.71~1.81(m, 4H), 1.87~2.07(m, 6H), 2.27(q, J =3.7, 1H), 3.79~3.85(m, 2H), 3.89~3.92(m, 1H), 4.59(d, J =8.4, 1H), 7.32~7.41(m, 5H)

20

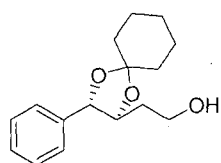
Preparation example 300: 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 298 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound(2.4g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.14(s, 9H), 1.67~1.83(m, 4H), 1.88~2.07(m, 6H), 3.84(td, J=6.0, 8.4, 1H), 4.10~4.17(m, 1H), 4.21~4.27(m, 1H), 4.55(d, J=8.4, 1H), 7.31~7.39(m, 5H)

Preparation example 301: 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethanol



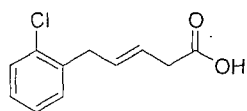
10

The substantially same method as described in Preparation example 299 was conducted, except that 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate(Preparation example 300) was used instead of that 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate(Preparation example 298), to obtain the title compound (1.2g, 80~95%)

15

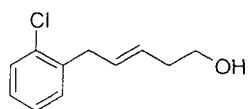
¹H NMR (400MHz, CDCl₃): δ=1.71~1.83(m, 4H), 1.87~2.05(m, 6H), 2.27(q, J=3.7, 1H), 3.79~3.85(m, 2H), 3.86~3.91(m, 1H), 4.59(d, J=8.4, 1H), 7.32~7.41(m, 5H)

20 Preparation example 302: (E)-5-(2-chlorophenyl)pent-3-enoic acid



25 ¹H NMR (400MHz, CDCl₃): δ=3.15(dd, J=0.8, 6.8, 2H), 3.53(d, J=6.4, 2H), 5.61~5.69(m, 1H), 5.75~5.82(m, 1H), 7.16~7.28(m, 3H), 7.36~7.38(m, 1H)

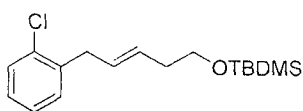
Preparation example 303: (E)-5-(2-chlorophenyl)pent-3-en-1-ol



The substantially same method as described in Preparation example 236 was conducted, except that (E)-5-(2-chlorophenyl)pent-3-enoic acid(Preparation example 302) was used instead of that (E)-5-phenylpent-3-enoic acid(Preparation example 235), to obtain the title compound (4.6g, 70~90%)

^1H NMR (400MHz, CDCl_3): δ =2.33(dq, J =1.0, 6.5, 2H), 3.50(dd, J =1.8, 5.0, 2H), 3.67(q, J =6.0, 2H), 5.45~5.53(m, 1H), 5.70~5.77(m, 1H), 7.15~7.37(m, 4H)

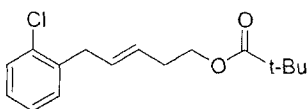
Preparation example 304: (E)-tert-butyl(5-(2-chlorophenyl)pent-3-enyloxy)dimethylsilane



The substantially same method as described in Preparation example 237 was conducted, except that (E)-5-(2-chlorophenyl)pent-3-en-1-ol (Preparation example 303) was used instead of that (E)-5-phenylpent-3-en-1-ol (Preparation example 236), to obtain the title compound (4.9g, 75~95%)

^1H NMR (400MHz, CDCl_3): δ =0.60(s, 6H), 0.90(s, 9H), 2.28(dq, J =1.0, 6.7, 2H), 3.47(d, J =6.4, 2H), 3.65(t, J =6.8, 2H), 5.49~5.56(m, 1H), 5.62~5.70(m, 1H), 7.14~7.36(m, 4H)

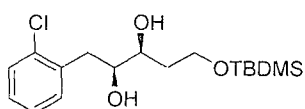
Preparation example 305: (E)-5-(2-chlorophenyl)pent-3-enyl pivalate



The substantially same method as described in Preparation example 238 was conducted, except that (E)-5-(2-chlorophenyl)pent-3-en-1-ol (Preparation example 303) was used instead of that (E)-5-phenylpent-3-en-1-ol (Preparation example 236), to obtain the title compound (7.2g, 75~95%)

5 ^1H NMR (400MHz, CDCl_3): δ =1.18(s, 9H), 2.36(q, J=6.7, 2H), 3.45(d, J=6.4, 2H), 4.08(t, J=6.6, 2H), 5.43~5.50(m, 1H), 5.63~5.70(m, 1H), 7.12~7.35(m, 4H)

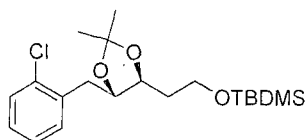
10 Preparation example 306: (2S, 3S)-5-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)pentane-2,3-diol



The substantially same method as described in Preparation example 239 was conducted, except that (E)-tert-butyl(5-(2-chlorophenyl)pent-3-enyloxy)dimethylsilane (Preparation example 304) was used instead of that (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane (Preparation example 237), to obtain the title compound (2.8g, 90%)

15 ^1H NMR (400MHz, CDCl_3): δ =0.11(s, 6H), 0.92(s, 9H), 1.68~1.77(m, 1H), 1.87~1.96(m, 1H), 2.64(d, J=6.0, 1H), 2.93(dd, J=8.2, 13.4, 1H), 3.07(dd, J=4.8, 13.6, 1H), 3.68(d, J=3.2, 1H), 3.76~3.96(m, 4H), 7.17~7.25(m, 2H),
20 7.35~7.39(m, 2H)

Preparation example 307: (2-(4S, 5S)-5-(2chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane

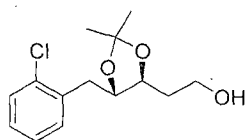


25 The substantially same method as described in Preparation example 240 was conducted, except that (2S, 3S)-5-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)pentane-2,3-diol (Preparation example 306) was used instead of

that (2S,3S)-5-(tert-butyldimethylsilyloxy)-1-phenylpentane-2,3-diol (Preparation example 239), to obtain the title compound (3.6g, 75~90%)

¹H NMR (400MHz, CDCl₃): δ=0.06(s, 6H), 0.91(s, 9H), 1.39(s, 3H), 1.40(s, 3H), 1.69(q, J=6.5, 2H), 3.05(dq, J=5.8, 15.1, 2H), 3.70~3.80(m, 2H),
5 3.86~3.93(m, 1H), 3.97~4.02(m, 1H), 7.17~7.25(m, 2H), 7.36~7.38(m, 2H)

Preparation example 308: 2-((4S,5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol

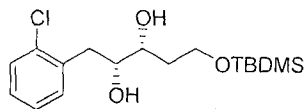


10 The substantially same method as described in Preparation example 241 was conducted, except that (2-(4S, 5S)-5-(2chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane (Preparation example 307) was used instead of that (2-(4S,5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl) dimethylsilane (Preparation example 240), to obtain
15 the title compound (3.2g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.38(s, 3H), 1.40(s, 3H), 1.50~1.63(m, 2H), 2.29(t, J=5.4, 1H), 2.82(dd, J=5.8, 13.8, 1H), 3.01(dd, J=6.4, 14.0, 1H), 3.72(q, J=5.5, 2H), 3.86(dt, J=3.2, 8.4, 1H), 3.92~3.97(m, 1H), 7.17~7.25(m, 2H), 7.36~7.38(m, 2H)

20

Preparation example 309: (2R, 3R)-5-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)pentane-2,3-diol

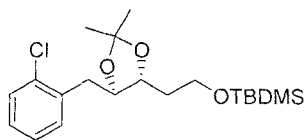


25 The substantially same method as described in Preparation example 242 was conducted, except that (E)-tert-butyl(5-(2-chlorophenyl)pent-3-enyloxy)dimethylsilane (Preparation example 304) was used instead of that (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane(Preparation example

237), to obtain the title compound (4.4g, 90%)

¹H NMR (400MHz, CDCl₃): δ=0.11(s, 6H), 0.92(s, 9H), 1.68~1.77(m, 1H), 1.87~1.96(m, 1H), 2.64(d, J=6.0, 1H), 2.93(dd, J=8.2, 13.4, 1H), 3.07(dd, J=4.8, 13.6, 1H), 3.68(d, J=3.2, 1H), 3.76~3.96(m, 4H), 7.17~7.25(m, 2H),
5 7.35~7.39(m, 2H)

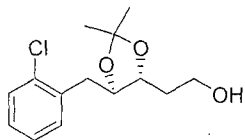
Preparation example 310: (2-(4R, 5R)-5-(2chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane



10 The substantially same method as described in Preparation example 307 was conducted, except that (2R, 3R)-5-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)pentane-2,3-diol(Preparation example 309) was used instead of (2S, 3S)-5-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)pentane-2,3-diol (Preparation example 306), to obtain the title compound (4.6g, 70~95%)

15 ¹H NMR (400MHz, CDCl₃): δ=0.06(s, 6H), 0.91(s, 9H), 1.39(s, 3H), 1.40(s, 3H), 1.69(q, J=6.5, 2H), 3.05(dq, J=5.8, 15.1, 2H), 3.70~3.80(m, 2H), 3.86~3.93(m, 1H), 3.97~4.02(m, 1H), 7.17~7.25(m, 2H), 7.36~7.38(m, 2H)

20 Preparation example 311: 2-((4R,5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol

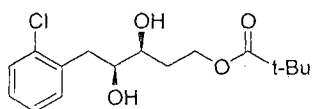


The substantially same method as described in Preparation example 241 was conducted, except that (2-(4S, 5S)-5-(2chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane (Preparation example 307)
25 was used instead of that (2-(4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)(tert-butyl)dimethylsilane (Preparation example 240), to obtain

the title compound (3.0g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.38(s, 3H), 1.40(s, 3H), 1.50~1.63(m, 2H), 2.29(t, J=5.4, 1H), 2.82(dd, J=5.8, 13.8, 1H), 3.01(dd, J=6.4, 14.0, 1H), 3.72(q, J=5.5, 2H), 3.86(dt, J=3.2, 8.4, 1H), 3.92~3.97(m, 1H), 7.17~7.25(m, 2H), 7.36~7.38(m, 2H)

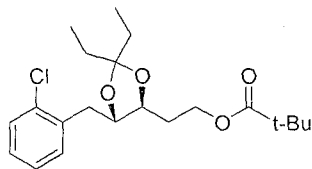
Preparation example 312: (3S,4S)-3,4-dihydroxy-5-(2-chlorophenyl)pentyl pivalate



The substantially same method as described in Preparation example 306 was conducted, except that (E)-5-(2-chlorophenyl)pent-3-enyl pivalate (Preparation example 305) was used instead of (E)-tert-butyl(5-(2-chlorophenyl)pent-3-enyloxy)dimethylsilane (Preparation example 304), to obtain the title compound(6.0g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.16(s, 9H), 1.85~1.91(m, 2H), 2.17(d, J=6.0, 1H), 2.73(d, J=5.2, 1H), 2.91(dd, J=8.4, 13.6, 1H), 3.08(dd, J=5.6, 13.6, 1H), 3.52~3.55(m, 1H), 3.77~3.80(m, 1H), 4.11~4.19(m, 1H), 4.37~4.41(m, 1H), 7.18~7.23(m, 2H), 7.31(dd, J=2.2, 7.0, 1H), 7.36(dd, J=1.8, 7.4, 1H)

Preparation example 313: 2-((4S,5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate



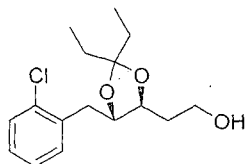
The substantially same method as described in Preparation example 246 was conducted, except that (3S,4S)-3,4-dihydroxy-5-(2-chlorophenyl)pentyl pivalate(Preparation example 312) was used instead of (3S,4S)-3,4-dihydroxy-5-phenylpentyl pivalate (Preparation example 245), to obtain the

title compound(1.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.90(t, J =7.4, 6H), 1.21(s, 9H), 1.58~1.66(m, 4H), 1.70~1.77(m, 2H), 3.06(d, J =5.6, 2H), 3.81~3.86(m, 1H), 3.94~3.99(m, 1H), 4.15~4.25(m, 2H), 7.18~7.24(m, 2H), 7.36~7.38(m, 2H)

5

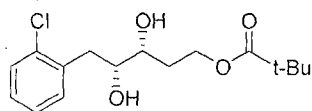
Preparation example 314: 2-((4S,5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol



The substantially same method as described in Preparation example 247 was conducted, except that 2-((4S,5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 313) was used instead of 2-((4S,5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 246), to obtain the title compound (0.9g, 80~95%);

^1H NMR (400MHz, CDCl_3): δ =0.91(dt, J =2.5, 7.5, 6H), 1.46~1.79(m, 6H), 2.42(t, J =5.6, 1H), 3.01~3.12(m, 2H), 3.79(q, J =5.6, 2H), 3.88~3.93(m, 1H), 3.98~4.06(m, 1H), 7.18~7.25(m, 2H), 7.35~7.39(m, 2H)

Preparation example 315: (3R,4R)-3,4-dihydroxy-5-(2-chlorophenyl)pentyl pivalate



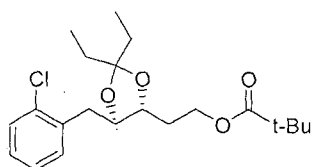
The substantially same method as described in Preparation example 309 was conducted, except that (E)-5-(2-chlorophenyl)pent-3-enyl pivalate (Preparation example 305) was used instead of (E)-tert-butyl(5-(2-chlorophenyl)pent-3-enyloxy)dimethylsilane (Preparation example 304), to obtain the title compound (4.4g, 70~95%)

25

^1H NMR (400MHz, CDCl_3): δ =0.11(s, 6H), 0.92(s, 9H), 1.68~1.77(m, 1H), 1.87~1.96(m, 1H), 2.64(d, J =6.0, 1H), 2.93(dd, J =8.2, 13.4, 1H), 3.07(dd, J =4.8, 13.6, 1H), 3.68(d, J =3.2, 1H), 3.76~3.96(m, 4H), 7.17~7.25(m, 2H), 7.35~7.39(m, 2H)

5

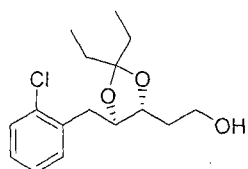
Preparation example 316: 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 313 was conducted, except that (3R, 4R)-3,4-dihydroxy-5-(2chlorophenyl)pentyl pivalate (Preparation example 315) was used instead of (3S, 4S)-3,4-dihydroxy-5-(2chlorophenyl)pentyl pivalate (Preparation example 312), to obtain the title compound(1.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.90(t, J =7.4, 6H), 1.21(s, 9H), 1.58~1.66(m, 4H), 1.70~1.77(m, 2H), 3.06(d, J =5.6, 2H), 3.81~3.86(m, 1H), 3.94~3.99(m, 1H), 4.15~4.25(m, 2H), 7.18~7.24(m, 2H), 7.36~7.38(m, 2H)

Preparation example 317: 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol



20

The substantially same method as described in Preparation example 314 was conducted, except that 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 316) was used instead of 2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate(Preparation example 313), to obtain the title compound (0.9g,

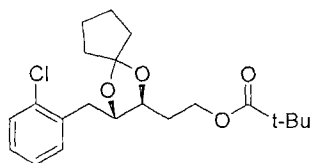
25

80~95%)

^1H NMR (400MHz, CDCl_3): δ =0.91(dt, J =2.5, 7.5, 6H), 1.46~1.79(m, 6H), 2.42(t, J =5.6, 1H), 3.01~3.12(m, 2H), 3.79(q, J =5.6, 2H), 3.88~3.93(m, 1H), 3.98~4.06(m, 1H), 7.18~7.25(m, 2H), 7.35~7.39(m, 2H)

5

Preparation example 318: 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate

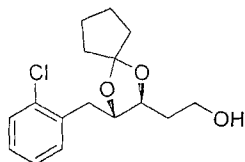


10 The substantially same method as described in Preparation example 313 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.2g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.21(s, 9H), 1.64~1.74(m, 5H), 1.75~1.88(m, 5H), 3.03~3.11(m, 2H), 3.81~3.86(m, 1H), 3.97(q, J =6.5, 1H), 4.12~4.22(m, 2H), 7.18~7.25(m, 2H); 7.34~7.39(m, 2H)

15

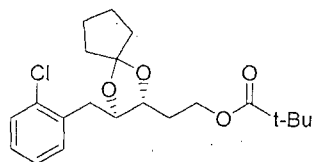
Preparation example 319: 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol



20 The substantially same method as described in Preparation example 317 was conducted, except that 2-((2S,3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 318) was used instead of 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 316), to obtain the title compound (0.7g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.62~1.74(m, 6H), 1.75~1.88(m, 4H), 2.28(t, J =5.6, 1H), 3.03~3.12(m, 2H), 3.78(q, J =5.6, 1H), 3.88~3.95(m, 1H), 3.97~4.06(m, 1H), 7.18~7.26(m, 2H), 7.34~7.39(m, 2H)

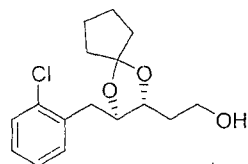
- 5 Preparation example 320: 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate



- 10 The substantially same method as described in Preparation example 316 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (1.4g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.21(s, 9H), 1.64~1.74(m, 5H), 1.75~1.88(m, 5H), 3.03~3.11(m, 2H), 3.81~3.86(m, 1H), 3.97(q, J =6.5, 1H), 4.12~4.22(m, 2H), 7.18~7.25(m, 2H), 7.34~7.39(m, 2H)

- 15 Preparation example 321: 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol

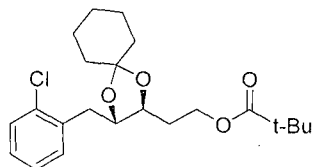


- 20 The substantially same method as described in Preparation example 319 was conducted, except that 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 320) was used instead of 2-((2S,3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 318), to obtain the title compound (0.8g, 80~95%)

- 25 ^1H NMR (400MHz, CDCl_3): δ =1.62~1.74(m, 6H), 1.75~1.88(m, 4H), 2.28(t, J =5.6, 1H), 3.03~3.12(m, 2H), 3.78(q, J =5.6, 1H), 3.88~3.95(m, 1H),

3.97~4.06(m, 1H), 7.18~7.26(m, 2H), 7.34~7.39(m, 2H)

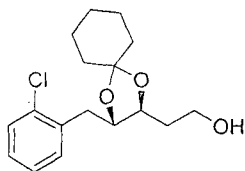
Preparation example 322: 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 318 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.1g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.21(s, 9H), 1.58~1.61(m, 8H), 1.77(q, J=6.8, 2H), 3.07(d, J=6.0, 2H), 3.81~3.88(m, 1H), 3.96~4.01(m, 1H), 4.16~4.22(m, 2H), 7.17~7.25(m, 2H), 7.36~7.39(m, 2H)

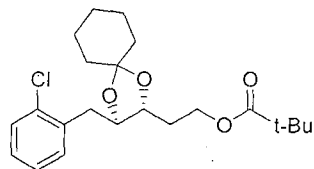
Preparation example 323: 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethanol



The substantially same method as described in Preparation example 321 was conducted, except that 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 322) was used instead of 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 320), to obtain the title compound (0.7g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.51~1.64(m, 8H), 1.65~1.74(m, 2H), 2.59~2.63(m, 1H), 3.06(d, J=6.0, 2H), 3.76~3.78(m, 2H), 3.89~3.94(m, 1H), 3.99~4.04(m, 1H), 7.16~7.24(m, 2H), 7.35~7.38(m, 2H)

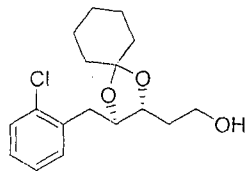
Preparation example 324: 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate



5 The substantially same method as described in Preparation example 320 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (1.5g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.21(s, 9H), 1.58~1.61(m, 8H), 1.77(q, J=6.8, 2H), 3.07(d, J=6.0, 2H), 3.81~3.88(m, 1H), 3.96~4.01(m, 1H), 4.16~4.22(m, 10 2H), 7.17~7.25(m, 2H), 7.36~7.39(m, 2H)

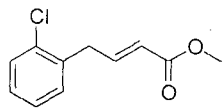
Preparation example 325: 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethanol



15 The substantially same method as described in Preparation example 323 was conducted, except that 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 324) was used instead of 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 322), to obtain the title compound 20 (0.9g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.51~1.64(m, 8H), 1.65~1.74(m, 2H), 2.59~2.63(m, 1H), 3.06(d, J=6.0, 2H), 3.76~3.78(m, 2H), 3.89~3.94(m, 1H), 3.99~4.04(m, 1H), 7.16~7.24(m, 2H), 7.35~7.38(m, 2H)

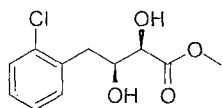
Preparation example 326: (E)-methyl-4-(2-chlorophenyl)but-2-enoate



The substantially same method as described in Preparation example 259 was conducted, except that 2-chlorophenyl acetaldehyde was used instead of phenyl acetaldehyde, to obtain the title compound (5.0g, 65~85%)

^1H NMR (400MHz, CDCl_3): δ =3.47(d, J =6.8, 2H), 3.67(s, 3H), 5.79(d, J =15.4, 1H), 7.06(dt, J =15.4, 6.8, 1H), 7.12~7.28(m, 4H)

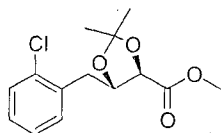
Preparation example 327: (2R, 3S)-methyl-4-(2chlorophenyl)-2,3-dihydroxybutanoate



The substantially same method as described in Preparation example 260 was conducted, except that (E)-methyl-4-(2-chlorophenyl)but-2-enoate(Preparation example 326) was used instead of (E)-methyl-4-phenylbut-2-enoate(Preparation example 259), to obtain the title compound(3.0g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =3.08~3.17(m, 2H), 3.84(s, 3H), 4.12(dd, J =1.6, 5.2, 1H), 4.28~4.34(m, 1H), 7.20~7.27(m, 2H), 7.33~7.36(m, 1H), 7.39~7.41(m, 1H)

Preparation example 328: (4R, 5S)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate

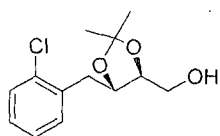


The substantially same method as described in Preparation example 261 was

conducted, except that (2R, 3S)-methyl-4-(2-chlorophenyl)-2,3-dihydroxybutanoate(Preparation example 327) was used instead of (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate(Preparation example 260), to obtain the title compound(0.6g, 70~95%)

- 5 ^1H NMR (400MHz, CDCl_3): δ =1.45(s, 3H), 1.49(s, 3H), 3.11(dd, J=7.6, 14.4, 1H), 3.35(dd, J=4.4, 14.4, 1H), 3.74(s, 3H), 4.30(d, J=7.6, 1H), 4.50(dt, J=4.0, 7.6, 1H), 7.19~7.26(m, 2H), 7.36~7.40(m, 2H)

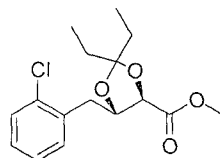
10 Preparation example 329: ((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 262 was conducted, except that (4R,5S)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 328) was used instead of
15 (4R,5S)-methyl 5-benzyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 261), to obtain the title compound(0.5g, 70~95%)

- 20 ^1H NMR (400MHz, CDCl_3): δ =1.43(s, 6H), 1.83(q, J=4.3, 1H), 3.06~3.17(m, 2H), 3.45(ddd, J=4.6, 7.4, 12.0, 1H), 3.68(ddd, J=3.2, 5.2, 12.0, 1H), 3.91(ddd, J=3.3, 4.7, 8.0, 1H), 4.22~4.27(m, 1H), 7.20~7.26(m, 2H), 7.35~7.40(m, 2H)

Preparation example 330: (4R,5S)-methyl-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate

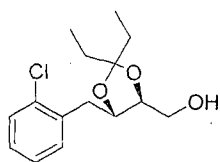


25 The substantially same method as described in Preparation example 263 was

conducted, except that (2R, 3S)-methyl-4-(2-chlorophenyl)-2,3-dihydroxybutanoate(Preparation example 327) was used instead of (2R, 3S)-methyl 2,3-dihydroxy-4-phenylbutanoate(Preparation example 260), to obtain the title compound(0.8g, 50~75%)

5 ^1H NMR (400MHz, CDCl_3): δ = 0.93(t, J=7.4, 6H), 1.67~1.74(m, 4H), 3.10(dd, J=8.0, 14.4, 1H), 3.35(dd, J=4.0, 14.4, 1H), 3.73(s, 3H), 4.27(d, J=8.4, 1H), 4.42~4.47(m, 1H), 7.18~7.26(m, 2H), 7.37~7.40(m, 2H)

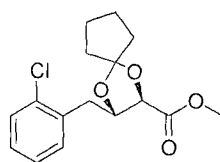
Preparation example 331: ((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 329 was conducted, except that (4R,5S)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 330) was used instead of (4R,5S)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 328), to obtain the title compound(0.6g, 70~95%)

20 ^1H NMR (400MHz, CDCl_3): δ = 0.93(dt, J=2.1, 7.5, 6H), 1.62~1.70(m, 4H), 1.83(q, J=4.3, 1H), 3.11(ddd, J=6.0, 14.2, 28.0, 2H), 3.44(ddd, J=4.8, 7.2, 12.0, 1H), 3.64~3.69(m, 1H), 3.88(ddd, J=3.3, 4.9, 8.3, 1H), 4.18~4.24(m, 1H), 7.19~7.26(m, 2H), 7.36~7.39(m, 2H)

Preparation example 332: (2R, 3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate

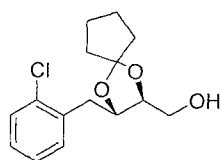


25

The substantially same method as described in Preparation example 330 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (0.8g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.65~1.80(m, 5H), 1.89~2.00(m, 3H), 3.13(dd, J=7.8, 14.2, 1H), 3.32(dd, J=4.6, 14.2, 1H), 3.72(s, 3H), 4.28(d, J=7.2, 1H), 4.41~4.46(m, 1H), 7.19~7.26(m, 2H), 7.35~7.40(m, 2H)

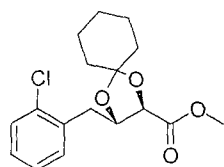
Preparation example 333: ((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methanol



The substantially same method as described in Preparation example 331 was conducted, except that (2R, 3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 332) was used instead of (4R,5S)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 330), to obtain the title compound (0.6g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.69~1.74(m, 3H), 1.77~1.85(m, 5H), 3.11(ddd, J=6.3, 14.1, 31.3, 2H), 3.42~3.48(m, 1H), 3.61~3.66(m, 1H), 3.87~3.91(m, 1H), 4.19(q, J=6.8, 1H), 7.19~7.26(m, 2H), 7.34~7.40(m, 2H)

Preparation example 334: (2R,3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decane-2-carboxylate



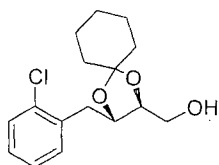
The substantially same method as described in Preparation example 332 was conducted, except that cyclohexanone was used instead of cyclopentanone, to

obtain the title compound (0.5g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.54~1.77(m, 10H), 3.12(dd, J =7.6, 14.4, 1H), 3.32(dd, J =4.4, 14.4, 1H), 3.72(s, 3H), 4.30(d, J =7.6, 1H), 4.46~4.51(m, 1H), 7.18~7.26(m, 2H), 7.37~7.39(m, 2H)

5

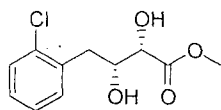
Preparation example 335: ((2S, 3S)-3-(-2chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-yl)methanol



10 The substantially same method as described in Preparation example 333 was conducted, except that (2R, 3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decan-2-carboxylate(Preparation example 334) was used instead of (2R, 3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate(Preparation example 332), to obtain the title compound(0.5g, 70~95%)

15 ^1H NMR (400MHz, CDCl_3): δ =1.38~1.45(m, 2H), 1.58~1.63(m, 8H), 1.84(q, J =4.3, 1H), 3.11(ddd, J =7.9, 15.9, 22.1, 2H), 3.43(ddd, J =4.6, 7.6, 12.1, 1H), 3.66~3.71(m, 1H), 3.88~3.92(m, 1H), 4.21~4.26(m, 1H), 7.18~7.26(m, 2H), 7.37~7.39(m, 2H)

20 Preparation example 336: (2S, 3R)-methyl-4-(2chlorophenyl)-2,3-dihydroxybutanoate



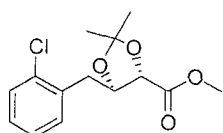
25 The substantially same method as described in Preparation example 269 was conducted, except that (E)-methyl-4-(2-chlorophenyl)but-2-enoate(Preparation example 326) was used instead of (E)-methyl-4-phenylbut-2-enoate(Preparation example 259), to obtain the title compound(3.5g,

70~95%)

^1H NMR (400MHz, CDCl_3): δ =3.08~3.17(m, 2H), 3.84(s, 3H), 4.12(dd, J =1.6, 5.2, 1H), 4.28~4.34(m, 1H), 7.20~7.27(m, 2H), 7.33~7.36(m, 1H), 7.39~7.41(m, 1H)

5

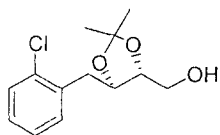
Preparation example 337: (4S, 5R)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 328 was conducted, except that (2S, 3R)-methyl-4-(2-chlorophenyl)-2,3-dihydroxybutanoate (Preparation example 336) was used instead of (2R, 3S)-methyl-4-(2-chlorophenyl)-2,3-dihydroxybutanoate (Preparation example 327), to obtain the title compound (3.4g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.41(s, 6H), 1.79(q, J =4.3, 1H), 2.83(dd, J =6.2, 13.8, 1H), 3.07(dd, J =6.4, 14.0, 1H), 3.29(ddd, J =4.7, 7.5, 12.1, 1H), 3.54(ddd, J =2.8, 5.2, 12.0, 1H), 3.83(ddd, J =3.9, 3.9, 7.1, 1H), 4.15(q, J =7.1, 1H), 7.22~7.32(m, 5H)

Preparation example 338: ((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol

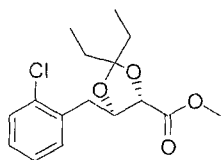


The substantially same method as described in Preparation example 335 was conducted, except that (4S,5R)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 337) was used instead of (2R, 3S)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decane-2-carboxylate (Preparation example 334), to obtain the title compound (2.7g,

70~95%).

¹H NMR (400MHz, CDCl₃): δ=1.41(s, 6H), 1.79(q, J=4.3, 1H), 2.83(dd, J=6.2, 13.8, 1H), 3.07(dd, J=6.4, 14.0, 1H), 3.29(ddd, J=4.7, 7.5, 12.1, 1H), 3.54(ddd, J=2.8, 5.2, 12.0, 1H), 3.83(ddd, J=3.9, 3.9, 7.1, 1H),
5 4.15(q, J=7.1, 1H), 7.22~7.32(m, 5H)

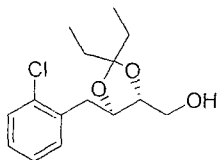
Preparation example 339: (4S, 5R)-methyl-(5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate



10 The substantially same method as described in Preparation example 330 was conducted, except that (2S, 3R)-methyl-2,3-dihydroxy-4-phenylbutanoate (Preparation example 336) was used instead of that (2R, 3S)-methyl-4-(2-chlorophenyl)-2,3-dihydroxybutanoate (Preparation example 327), to obtain the title compound (0.6g, 50~75%)

15 ¹H NMR (400MHz, CDCl₃): δ=0.93(t, J=7.4, 6H), 1.67~1.74(m, 4H), 3.10(dd, J=8.0, 14.4, 1H), 3.35(dd, J=4.0, 14.4, 1H), 3.73(s, 3H), 4.27(d, J=8.4, 1H), 4.42~4.47(m, 1H), 7.18~7.26(m, 2H), 7.37~7.40(m, 2H)

20 Preparation example 340: ((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methanol

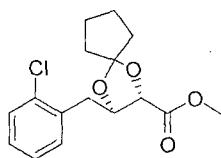


The substantially same method as described in Preparation example 338 was conducted, except that (4S, 5R)-methyl-(5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 339) was used instead of
25 (4S,5R)-methyl-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate

(Preparation example 337), to obtain the title compound (0.5g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=0.93(dt, J=2.1, 7.5, 6H), 1.62~1.70(m, 4H), 1.83(q, J=4.3, 1H), 3.11(ddd, J=6.0, 14.2, 28.0, 2H), 3.44(ddd, J=4.8, 7.2, 12.0, 1H), 3.64~3.69(m, 1H), 3.88(ddd, J=3.3, 4.9, 8.3, 1H), 4.18~4.24(m, 1H), 7.19~7.26(m, 2H), 7.36~7.39(m, 2H)

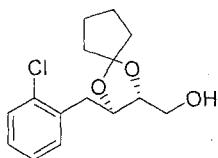
Preparation example 341: (2S, 3R)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate



The substantially same method as described in Preparation example 339 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (0.5g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.65~1.80(m, 5H), 1.89~2.00(m, 3H), 3.13(dd, J=7.8, 14.2, 1H), 3.32(dd, J=4.6, 14.2, 1H), 3.72(s, 3H), 4.28(d, J=7.2, 1H), 4.41~4.46(m, 1H), 7.19~7.26(m, 2H), 7.35~7.40(m, 2H)

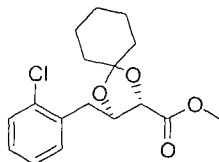
Preparation example 342: ((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methanol



The substantially same method as described in Preparation example 340 was conducted, except that (2S, 3R)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 341) was used instead of that (4S, 5R)-methyl-(5-2-chlorobenzyl)-2,2-diethyl-1,3-dioxolane-4-carboxylate (Preparation example 339), to obtain the title compound (0.4g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.69~1.74(m, 3H), 1.77~1.85(m, 5H), 3.11(ddd, J =6.3, 14.1, 31.3, 2H), 3.42~3.48(m, 1H), 3.61~3.66(m, 1H), 3.87~3.91(m, 1H), 4.19(q, J =6.8, 1H), 7.19~7.26(m, 2H), 7.34~7.40(m, 2H)

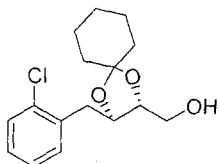
- 5 Preparation example 343: (2S, 3R)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decane-2-carboxylate



- 10 The substantially same method as described in Preparation example 341 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (0.9g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.54~1.77(m, 10H), 3.12(dd, J =7.6, 14.4, 1H), 3.32(dd, J =4.4, 14.4, 1H), 3.72(s, 3H), 4.30(d, J =7.6, 1H), 4.46~4.51(m, 1H), 7.18~7.26(m, 2H), 7.37~7.39(m, 2H)

- 15 Preparation example 344: ((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decane-2-yl)methanol

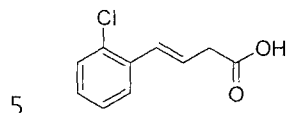


- 20 The substantially same method as described in Preparation example 342 was conducted, except that (2S, 3R)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.5]decane-2-carboxylate (Preparation example 343) was used instead of (2S, 3R)-methyl-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonane-2-carboxylate (Preparation example 341), to obtain the title compound (0.7g, 70~95%)

- 25 ^1H NMR (400MHz, CDCl_3): δ =1.38~1.45(m, 2H), 1.58~1.63(m, 8H), 1.84(q, J =4.3, 1H), 3.11(ddd, J =7.9, 15.9, 22.1, 2H), 3.43(ddd, J =4.6, 7.6, 12.1,

1H), 3.66~3.71(m, 1H), 3.88~3.92(m, 1H), 4.21~4.26(m, 1H), 7.18~7.26(m, 2H), 7.37~7.39(m, 2H)

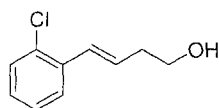
Preparation example 345: (E)-4-(2-chlorophenyl)but-3-enoic acid



The substantially same method as described in Preparation example 278 was conducted, except that 2-(2-chlorophenyl)acetaldehyde was used instead of phenylacetaldehyde, to obtain the title compound (4.0g, 55~80%)

10 ^1H NMR (400MHz, CDCl_3): δ =3.39(d, J =8.8, 2H), 6.31(td, J =7.9, 14.8, 1H), 6.94(d, J =16, 1H), 7.17~7.45(m, 3H), 7.56~7.59(m, 1H)

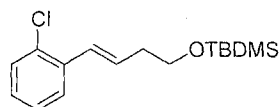
Preparation example 346: (E)-4-(2-chlorophenyl)but-3-en-1-ol



15 The substantially same method as described in Preparation example 279 was conducted, except that (E)-4-(2-chlorophenyl)but-3-enoic acid(Preparation example 345) was used instead of (E)-4-phenylbut-3-enoic acid(Preparation example 278), to obtain the title compound (1.2g, 55~80%)

20 ^1H NMR (400MHz, CDCl_3): δ =2.55(ddd, J = 4.1, 11.9, 21.5, 2H), 3.82(t, J =5.8, 2H), 6.24(td, J =7.2, 15.7, 1H), 6.87(d, J =14.8, 1H), 7.12~7.25(m, 3H), 7.36(dd, J =1.2, 8.0, 1H), 7.52(dd, J =1.6, 9.2, 1H)

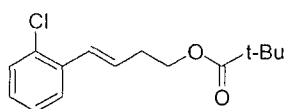
Preparation example 347: (E)-tert-butyldimethyl(4-(2-chlorophenyl)but-3-enyloxy)silane



The substantially same method as described in Preparation example 280 was conducted, except that (E)-4-(2-chlorophenyl)but-3-en-1-ol (Preparation example 346) was used instead of (E)-4-phenylbut-3-en-1-ol (Preparation example 279), to obtain the title compound (1.1g, 80~98%)

- 5 ^1H NMR (400MHz, CDCl_3): δ =0.07(s, 3H), 0.10(s, 3H), 0.92(d, J=6.4, 9H), 2.51(q, J=4.5, 2H), 3.78(t, J=6.6, 2H), 6.26(td, J=7.2, 15.7, 1H), 6.84(d, J=15.6, 1H), 7.13~7.24(m, 3H), 7.36(dd, J=5.6, 12.4, 1H), 7.53(dd, J=1.4, 7.8, 1H)

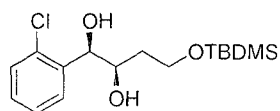
- 10 Preparation example 348: (E)-4-(2-chlorophenyl)but-3-enyl pivalate



- 15 The substantially same method as described in Preparation example 281 was conducted, except that (E)-4-(2-chlorophenyl)but-3-en-1-ol (Preparation example 346) was used instead of (E)-4-phenylbut-3-en-1-ol (Preparation example 279), to obtain the title compound (3.5g, 75~95%)

^1H NMR (400MHz, CDCl_3): δ =1.21(s, 9H), 2.55~2.64(m, 2H), 4.24(t, J=6.4, 2H), 6.18(td, J=7.9, 14.8, 1H), 6.86(d, J=16.0, 1H), 7.22~7.26(m, 2H), 7.38(dd, J=3.6, 10.8, 1H), 7.51(dd, J=1.6, 7.6, 1H)

- 20 Preparation example 349: (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)butane-1,2-diol

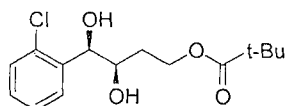


- 25 The substantially same method as described in Preparation example 282 was conducted, except that (E)-tert-butyldimethyl(4-(2-chlorophenyl)but-3-enyloxy)silane (Preparation example 347) was used instead of (E)-tert-butyldimethyl(5-phenylpent-3-enyloxy)silane (Preparation example 237), to obtain the title compound (0.7g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.10(s, 3H), 0.11(s, 3H), 0.92(s, 9H), 1.69~1.70(m, 1H), 1.93~2.07(m, 1H), 3.51(d, J =4.8, 1H), 3.86(d, J =3.2, 1H), 3.87(dd, J =3.2, 9.2, 1H), 3.91~3.96(m, 1H), 4.01~4.06(m, 1H), 5.05(t, J =4.6, 1H), 7.22~7.26(m, 1H), 7.31~7.37(m, 2H), 7.59(dd, J =1.2, 7.6, 1H)

5

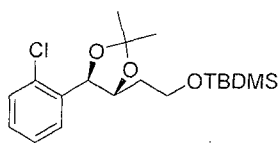
Preparation example 350: (3R, 4R)-3,4-dihydroxy-4-(2-chlorophenyl)butyl pivalate



The substantially same method as described in Preparation example 349 was conducted, except that (E)-4-(2-chlorophenyl)but-3-enyl pivalate (Preparation example 348) was used instead of (E)-tert-butyl dimethyl(4-(2-chlorophenyl)but-3-enyloxy)silane (Preparation example 347), to obtain the title compound (3.2g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.19(s, 9H), 1.76~1.84(m, 1H), 1.90~1.98(m, 1H), 2.70(d, J =4.4, 1H), 2.86(d, J =5.2, 1H), 3.84~3.90(m, 1H), 4.14~4.21(m, 1H), 4.35~4.41(m, 1H), 5.05(t, J =5.0, 1H), 7.23~7.39(m, 3H), 7.54(dd, J =1.6, 7.6, 1H)

Preparation example 351: tert-butyl(2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane

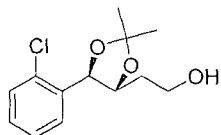


The substantially same method as described in Preparation example 284 was conducted, except that (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)butane-1,2-diol (Preparation example 349) was used instead of (1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-phenylbutane-1,2-diol (Preparation example 282), to obtain the title compound (0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =0.02(s, 3H), 0.07(s, 3H), 0.86(s, 9H), 1.50(s,

3H), 1.58(s, 3H), 1.82~1.99(m, 2H), 3.68~3.78(m, 2H), 3.95(dt, J=3.3, 8.7, 1H), 5.16(d, J=8.4, 1H), 7.21~7.27(m, 1H), 7.31~7.38(m, 2H), 7.60(dd, J=1.6, 7.6, 1H)

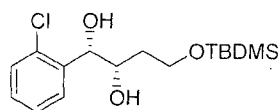
- 5 Preparation example 352: 2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol



The substantially same method as described in Preparation example 285 was conducted, except tert-butyl(2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane (Preparation example 351) was used instead of tert-butyl(2-((4R,5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane (Preparation example 284), to obtain the title compound(0.7g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.56(s, 3H), 1.62(s, 3H), 1.92~2.04(m, 2H), 2.26(q, J=3.7, 1H), 3.75~3.90(m, 2H), 3.94(td, J=3.9, 8.5, 1H), 5.23(d, J=15.6, 1H), 7.22~7.27(m, 1H), 7.33~7.39(m, 2H), 7.62(dd, J=1.6, 7.6, 1H)

Preparation example 353: (1S, 2S)-4-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)butane-1,2-diol

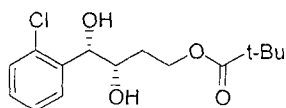


The substantially same method as described in Preparation example 286 was conducted, except that (E)-tert-butyldimethyl(4-(2-chlorophenyl)but-3-enyloxy)silane (Preparation example 347) was used instead of (E)-tert-butyldimethyl(4-phenylbut-3-enyloxy)silane (Preparation example 280), to obtain the title compound(0.7g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.19(s, 9H), 1.76~1.84(m, 1H), 1.90~1.98(m, 1H), 2.70(d, J=4.4, 1H), 2.86(d, J=5.2, 1H), 3.84~3.90(m, 1H), 4.14~4.21(m,

1H), 4.35-4.41(m, 1H), 5.05(t, J=5.0, 1H), 7.23-7.39(m, 3H), 7.54(dd, J=1.6, 7.6, 1H)

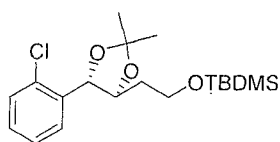
Preparation example 354: (3S, 4S)-3,4-dihydroxy-4-(2-chlorophenyl)butyl
5 pivalate



The substantially same method as described in Preparation example 353 was conducted, except that (E)-4-(2-chlorophenyl)but-3-enyl pivalate (Preparation example 348) was used instead of ((E)-tert-butyldimethyl(4-(2-chlorophenyl)but-3-enyloxy)silane (Preparation example 347), to obtain the
10 title compound(3.0g, 70~95%)

¹H NMR (400MHz, CDCl₃): δ=1.19(s, 9H), 1.76-1.84(m, 1H), 1.90-1.98(m, 1H), 2.70(d, J=4.4, 1H), 2.86(d, J=5.2, 1H), 3.84-3.90(m, 1H), 4.14-4.21(m, 1H), 4.35-4.41(m, 1H), 5.05(t, J=5.0, 1H), 7.23-7.39(m, 3H), 7.54(dd, J=1.6,
15 7.6, 1H)

Preparation example 355: tert-butyl(2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane

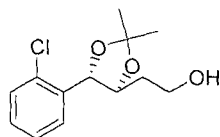


20 The substantially same method as described in Preparation example 351 was conducted, except that (1S, 2S)-4-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)butane-1,2-diol (Preparation example 353) was used instead of 1R, 2R)-4-(tert-butyldimethylsilyloxy)-1-(2-chlorophenyl)butane-1,2-diol (Preparation example 349), to obtain the title compound(0.7g, 70~95%)

25 ¹H NMR (400MHz, CDCl₃): δ=0.02(s, 3H), 0.07(s, 3H), 0.86(s, 9H), 1.50(s, 3H), 1.58(s, 3H), 1.82-1.99(m, 2H), 3.68-3.78(m, 2H), 3.95(dt, J=3.3, 8.7, 1H), 5.16(d, J=8.4, 1H), 7.21-7.27(m, 1H), 7.31-7.38(m, 2H), 7.60(dd, J=1.6,

7.6, 1H)

Preparation example 356: 2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethanol

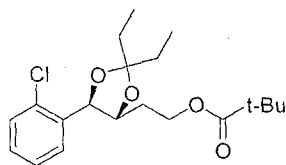


The substantially same method as described in Preparation example 352 was conducted, except that tert-butyl(2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane(Preparation example 355) was used instead of that tert-butyl(2-((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethyl silane (Preparation example 351),
10 to obtain the title compound (0.3g, 80~95%).

^1H NMR (400MHz, CDCl_3): δ =1.56(s, 3H), 1.62(s, 3H), 1.92~2.04(m, 2H), 2.26(q, J=3.7, 1H), 3.75~3.90(m, 2H), 3.94(td, J=3.9, 8.5, 1H), 5.23(d, J=15.6, 1H), 7.22~7.27(m, 1H), 7.33~7.39(m, 2H), 7.62(dd, J=1.6, 7.6, 1H)

15

Preparation example 357: 2-((4R, 5R)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate

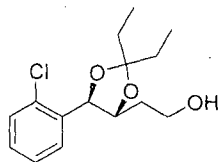


The substantially same method as described in Preparation example 290 was conducted, except that (3R, 4R)-3,4-dihydroxy-4-(2-chlorophenyl)butyl pivalate (Preparation example 350) was used instead of (3R, 4R)-3,4-dihydroxy-4-phenylbutyl pivalate(Preparation example 283), to obtain the title compound(0.8g, 70~95%)

^1H NMR (400MHz, CDCl_3): δ =1.15(s, 9H), 1.76(q, J=7.6, 2H), 1.84~1.90(m, 2H), 2.00~2.07(m, 2H), 3.85(dt, J=3.7, 8.5, 1H), 4.14~4.27(m, 2H), 5.17(d,
25

J=8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.64(dd, J=1.4, 7.8, 1H)

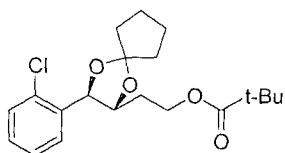
Preparation example 358: 2-((4R, 5R)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate



The substantially same method as described in Preparation example 291 was conducted, except that 2-((4R, 5R)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 357) was used instead of 2-((4R, 5R)-2,2-diethyl-5-phenyl-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 290), to obtain the title compound (0.6g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.02(t, J=7.4, 3H), 1.08(t, J=7.4, 3H), 1.80(q, J=7.5, 2H), 1.86~1.91(m, 2H), 1.96~2.00(m, 2H), 2.37(q, J=3.7, 1H), 3.76~3.95(m, 3H), 5.23(d, J=8.4, 1H), 7.25~7.27(m, 1H), 7.32~7.39(m, 2H), 7.65(dd, J=1.8, 7.8, 1H)

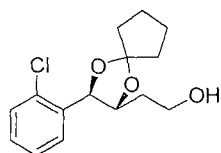
Preparation example 359: 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 357 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (0.8g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.17(s, 9H), 1.58~2.02(m, 10H), 3.86(ddd, J=3.8, 8.2, 8.2, 1H), 4.11~4.28(m, 2H), 5.13(d, J=8.0, 1H), 7.20~7.39(m, 3H), 7.58(dd, J=1.6, 8.0, 1H)

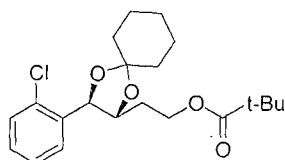
Preparation example 360: 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol



5 The substantially same method as described in Preparation example 358 was conducted, except that 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 359) was used instead of that 2-((4R, 5R)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 357), to obtain the title compound
10 (0.5g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.72~1.90(m, 4H), 1.93~1.98(m, 6H), 2.28(q, J =3.7, 1H), 3.76~3.93(m, 3H), 5.18(d, J =8.0, 1H), 7.24~7.29(m, 1H), 7.32~7.38(m, 2H), 7.60(dd, J =1.8, 7.8, 1H)

15 Preparation example 361: 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate

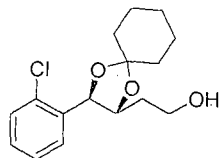


The substantially same method as described in Preparation example 359 was conducted, except that cyclohexanone was used instead of cyclopentanone, to
20 obtain the title compound (1.0g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.15(s, 9H), 1.70~1.94(m, 10H), 2.06~2.09(m, 2H), 3.86(dt, J =3.5, 8.5, 1H), 4.16~4.26(m, 2H), 5.18(d, J =8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.61(dd, J =1.4, 7.8, 1H)

25 Preparation example 362: 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-

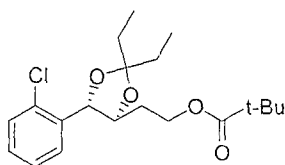
dioxaspiro[4.5]decan-2-yl)ethanol



The substantially same method as described in Preparation example 360 was conducted, except that 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 361) was used instead of that 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 359), to obtain the title compound (0.6g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.42~1.50(m, 2H), 1.63~1.77(m, 5H), 1.82~1.89(m, 5H), 2.41(q, J=3.9, 1H), 3.78~3.96(m, 3H), 5.25(d, J=8.4, 1H), 7.21~7.28(m, 1H), 7.32~7.38(m, 2H), 7.63(dd, J=1.4, 7.8, 1H)

Preparation example 363: 2-((4S, 5S)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate

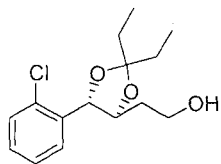


The substantially same method as described in Preparation example 357 was conducted, except that (3S, 4S)-3,4-dihydroxy-4-(2-chlorophenyl)butyl pivalate (Preparation example 354) was used instead of (3R, 4R)-3,4-dihydroxy-4-(2-chlorophenyl)butyl pivalate (Preparation example 350), to obtain the title compound (0.7g, 70~95%).

^1H NMR (400MHz, CDCl_3): δ =1.15(s, 9H), 1.76(q, J=7.6, 2H), 1.84~1.90(m, 2H), 2.00~2.07(m, 2H), 3.85(dt, J=3.7, 8.5, 1H), 4.14~4.27(m, 2H), 5.17(d, J=8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.64(dd, J=1.4, 7.8, 1H)

Preparation example 364: 2-((4S, 5S)-2,2-diethyl-5-(2-chlorophenyl)-1,3-

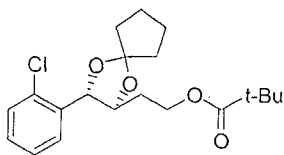
dioxolan-4-yl)ethanol



The substantially same method as described in Preparation example 358 was conducted, except that 2-((4S, 5S)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 363) was used instead of 2-((4R, 5R)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 357), to obtain the title compound (0.5g, 80~95%)

¹H NMR (400MHz, CDCl₃): δ=1.02(t, J=7.4, 3H), 1.08(t, J=7.4, 3H), 1.80(q, J=7.5, 2H), 1.86~1.91(m, 2H), 1.96~2.00(m, 2H), 2.37(q, J=3.7, 1H), 3.76~3.95(m, 3H), 5.23(d, J=8.4, 1H), 7.25~7.27(m, 1H), 7.32~7.39(m, 2H), 7.65(dd, J=1.8, 7.8, 1H)

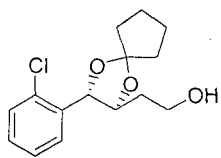
Preparation example 365: 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 363 was conducted, except that cyclopentanone was used instead of 3-pentanone, to obtain the title compound (0.6g, 60~85%)

¹H NMR (400MHz, CDCl₃): δ=1.17(s, 9H), 1.58~2.02(m, 10H), 3.86(ddd, J=3.8, 8.2, 8.2, 1H), 4.11~4.28(m, 2H), 5.13(d, J=8.0, 1H), 7.20~7.39(m, 3H), 7.58(dd, J=1.6, 8.0, 1H)

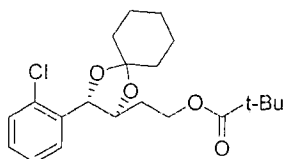
Preparation example 366: 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethanol



The substantially same method as described in Preparation example 364 was conducted, except that 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 365) was used instead of that 2-((4S, 5S)-2,2-diethyl-5-(2-chlorophenyl)-1,3-dioxolan-4-yl)ethyl pivalate (Preparation example 363), to obtain the title compound (0.4g, 80~95%)

^1H NMR (400MHz, CDCl_3): δ =1.72~1.90(m, 4H), 1.93~1.98(m, 6H), 2.28(q, J =3.7, 1H), 3.76~3.93(m, 3H), 5.18(d, J =8.0, 1H), 7.24~7.29(m, 1H), 7.32~7.38(m, 2H), 7.60(dd, J =1.8, 7.8, 1H)

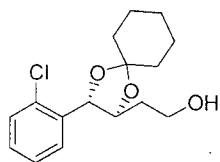
Preparation example 367: 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate



The substantially same method as described in Preparation example 366 was conducted, except that cyclohexanone was used instead of cyclopentanone, to obtain the title compound (0.7g, 60~85%)

^1H NMR (400MHz, CDCl_3): δ =1.15(s, 9H), 1.70~1.94(m, 10H), 2.06~2.09(m, 2H), 3.86(dt, J =3.5, 8.5, 1H), 4.16~4.26(m, 2H), 5.18(d, J =8.4, 1H), 7.22~7.28(m, 1H), 7.32~7.38(m, 2H), 7.61(dd, J =1.4, 7.8, 1H)

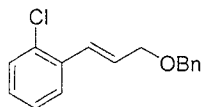
Preparation example 368: 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethanol



The substantially same method as described in Preparation example 366 was conducted, except that 2-((2S,3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.5]decan-2-yl)ethyl pivalate (Preparation example 367) was used instead of that 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl pivalate (Preparation example 365), to obtain the title compound (0.4g, 80~95%).

¹H NMR (400MHz, CDCl₃): δ=1.42~1.50(m, 2H), 1.63~1.77(m, 5H), 1.82~1.89(m, 5H), 2.41(q, J=3.9, 1H), 3.78~3.96(m, 3H), 5.25(d, J=8.4, 1H), 7.21~7.28(m, 1H), 7.32~7.38(m, 2H), 7.63(dd, J=1.4, 7.8, 1H)

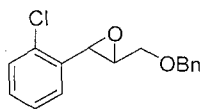
Preparation example 369: (E)-1-(3(benzyloxy)prop-1-enyl)2-chlorobenzene



To a solution of (E)-3-(2-chlorophenyl) prop-2-en-1-ol (Preparation example 1, 5.3 g, 31.6 mmole) in THF was added NaH (60 % in mineral oil, 0.91g, 37.7 mmole) and Benzyl bromide (4.12 mL, 34.8 mmole), sequentially at 0°C. The reaction mixture was stirred at room temperature for 18 hr. The TLC showed complete consumption of SM. The reaction mixture was quenched with H₂O at 0°C then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with H₂O, then dried over MgSO₄ and evaporated under reduced pressure. The crude compound was purified by silica gel column to produce the title compound (4.94 g, 70~90%).

¹H NMR (400 MHz, CDCl₃) δ 7.57 (dd, J = 7.76, 2, 1H), 7.42~7.13 (m, 3H), 7.05 (d, J = 16 Hz, 1H), 6.37~6.30 (m, 1H), 4.62 (s, 2H), 4.26 (dd, J = 6, 1.6, 2H).

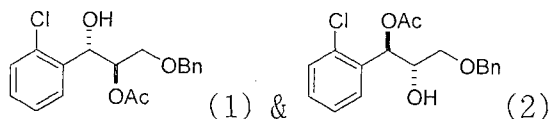
Preparation example 370: (±)-2-(benzyloxymethyl)-3-(2-chlorophenyl)oxirane



To a solution of (E)-1-(3-(benzyloxy)prop-1-enyl)-2-chlorobenzene (Preparation example 369, 4.94 g, 22 mmole) in CH_2Cl_2 (110 mL) was added 3-chloroperoxybenzoic acid (70~75 %, 8 g, 33 mmole) portionwise at 0°C . The mixture was stirred for 18 hr at room temperature. The TLC showed complete consumption of SM. The reaction mixture was quenched with H_2O at 0°C then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with sat' NaHCO_3 , H_2O , then dried over MgSO_4 and evaporated under reduced pressure. The crude compound was purified by silica gel column to produce the title compound (4.3 g, 60~80%).

^1H NMR (400 MHz, CDCl_3) δ 7.42~7.24 (m, 9H), 4.68 (d, $J = 14.8$, 2H), 4.18 (d, $J = 2$ Hz, 1H), 3.96 (dd, $J = 11.6$, 2.8 Hz, 1H), 3.69~3.64 (m, 1H), 3.14 (qt, $J = 2.4$ Hz, 1H)

Preparation example 371: (±)-3-(benzyloxy)-1-(2-chlorophenyl)-2-hydroxypropyl & (±)-3-(benzyloxy)-1-(2-chlorophenyl)-1-hydroxypropan-2-yl acetate



To a solution of (±)-2-(benzyloxymethyl)-3-(2-chlorophenyl)oxirane (Preparation example 370, 4.3 g, 15.6 mmole) in Acetic acid (78 mL) was added Cerium Ammonium Nitrate (1.71 g, 3.1 mmole) at room temperature. The mixture was stirred for 18 hr at room temperature. The TLC showed complete consumption of SM. The reaction mixture was quenched with sat' NaHCO_3 to pH7 at 0°C then extracted with EtOAc. The aqueous layer was

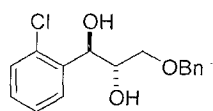
extracted with EtOAc and separated. The combined organic layer was washed with H₂O, then dried over MgSO₄ and evaporated under reduced pressure. The crude compound was purified by silica ge column to produce the title compound (1) (1.2 g, 23 %). (2)(1.8 g, 34 %).

5 (1)¹H NMR (400 MHz, CDCl₃) δ 7.55-7.22 (m, 9H), 5.41 (t, *J* = 5 Hz, 1H), 5.33-5.29 (m, 1H), 4.61-4.47 (m, 2H), 3.70-3.63 (m, 2H, -OH), 2.09 (s, 3H).

(2)¹H NMR (400 MHz, CDCl₃) δ 7.46-7.24 (m, 9H), 6.31 (d, *J* = 5.6 Hz, 1H), 4.55 (d, *J* = 9.6 Hz, 2H), 4.24-4.22 (m, 1H), 3.67-3.55 (m, 2H), 2.52 (d, *J* = 5.2 Hz, -OH), 2.10 (s, 3H).

10

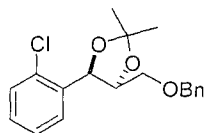
Preparation example 372: (±)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol(Anti mixture)



To a solution of (±)-3-(benzyloxy)-1-(2-chlorophenyl)-2-hydroxypropyl
15 and (±)-3-(benzyloxy)-1-(2-chlorophenyl)-1-hydroxypropan-2-yl acetate
(Preparation example 371, 3 g, 8.9 mmole) in MeOH (36 mL) and H₂O (4 mL)
was added K₂CO₃ (3.69 g, 26.7 mmole) at 0 °C. The mixture was stirred for
1.5 hr at 0°C. The TLC showed complete consumption of SM. The reaction
mixture was quenched with H₂O at 0°C then extracted with EtOAc. The aqueous
20 layer was extracted with EtOAc and separated. The combined organic layer
was washed with H₂O, then dried over MgSO₄ and evaporated under reduced
pressure. The crude compound was purified by silica ge column to produce
the title compound (2.4 g, 80-95 %).

¹H NMR (400 MHz, CDCl₃) δ 7.50 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.35-7.19 (m,
25 8H), 5.28 (t, *J* = 4.8 Hz, 1H), 4.46 (d, *J* = 6 Hz, 2H), 4.18-4.13 (m, 1H),
3.55-3.42 (m, 3H, -OH), 3.02 (d, *J* = 5.2 Hz, -OH).

Preparation example 373: (±)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane

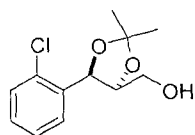


To a solution of (±)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol (Preparation example 372, 2.4 g, 8.2 mmole) in CH₂Cl₂ (40 mL) was added p-toluenesulfonyl chloride (15.2 g, 0.08 mmole), and 2,2-dimethoxypropan
 5 (8.4mL, 9.84mmole) at 0 °C sequently. The mixture was stirred for 1.5 hr at room temperature. The TLC showed complete consumption of SM. The reaction mixture was quenched with H₂O then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with H₂O, then dried over MgSO₄ and evaporated under reduced
 10 pressure. The crude compound was purified by silica gel column to produce the title compound (2.2 g, 75~90 %).

¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, J = 7.4, 1.6 Hz, 1H), 7.35-7.16 (m, 8H), 5.63 (d, J = 6.8, 1H), 4.83-4.78 (m, 1H). 4.26 (d, J = 12 Hz, 2H), 3.14-3.06 (m, 2H), 1.66 (s, 3H), 1.53 (s, 3H).

15

Preparation example 374: 5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol(SR & RS mixture)



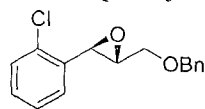
To a solution of (±)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3 -dioxolane (Preparation example 375, 2.2 g, 6.6 mmole) in EtOAc (33 mL) was added 10% Pd/C on carbon (0.11 g) at room temperature. The mixture was stirred for 1 hr at room temperature under H₂ (g). The TLC showed complete consumption of SM. The reaction mixture was filtered through celite pad then evaporated under reduced pressure. The crude
 20 compound was purified by silica gel column to produce the title compound (1.5 g, 80~95 %).

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¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, J = 7.4, 1.6, 1H), 7.35-7.16 (m, 8H), 5.63 (d, J = 6.8 Hz, 1H), 4.83-4.78 (m, 1H), 4.26 (d, J = 12, 2H), 3.14-

3.06 (m, 2H), 1.66 (s, 3H), 1.53 (s, 3H).

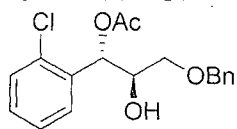
Preparation example 375: (2R,3R)-2-(benzyloxymethyl)-3-(2-chlorophenyl)oxirane



To a solution of (*E*)-1-(3-(benzyloxy)prop-1-enyl)-2-chlorobenzene (Preparation example 369, 4.16 g, 18.58 mmole) and 1,2:4,5-di-*O*-isopropylidene- β -*D*-erythro-2,3-hexodiulo-2,6-pyranose (5.76 g, 22.30 mmole) in ACN-DMM (3:1, v/v) (185 mL) was added buffer (0.2M K₂CO₃-AcOH in 4 X 10⁻⁴ M aq. EDTA, buffer pH = 8.0) (185 mL) and Bu₄NHSO₄ (0.26 g, 0.75 mmole). After the mixture was cooled to 0 °C, a solution of Oxone (15.76 g, 25.64 mmole) in 4 X 10⁻⁴ M aq. EDTA (100 mL) and a solution of K₂CO₃ (13.6 g, 98.47 mmole) in H₂O (100 mL) were added dropwise separately over a period of 3.5hr via a syringe pump at 0 °C. The reaction mixture was stirred for 14hr at 0 °C. The reaction mixture was quenched with H₂O then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with H₂O then dried over MgSO₄ and evaporated under reduced pressure. The crude compound was purified by silica ge column to produce the title compound (2.9 g, 50~65 %).

¹H NMR (400 MHz, CDCl₃) δ 3.14 (qt, *J* = 2.4 Hz, 1H), 3.69-3.64 (m, 1H), 3.96 (dd, *J* = 11.6, 2.8 Hz, 1H), 4.18 (d, *J* = 2 Hz, 1H), 4.68 (d, *J* = 14.8, 2H), 7.42-7.24 (m, 9H),

Preparation example 376: (1S, 2R)-3-(benzyloxy)-1-(2-chlorophenyl)-2-hydroxypropyl acetate

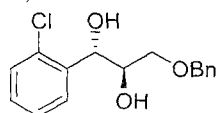


To a solution of (2R,3R)-2-(benzyloxymethyl)-3-(2-chlorophenyl)oxirane (Preparation example 375, 2.9 g, 10.55 mmole) in Acetic acid (55 mL) was added Cerium Ammonium Nitrate (1.15 g, 2.11 mmole) at room temperature. The mixture was stirred for 18 hr at room temperature. The TLC showed complete consumption of SM. The reaction mixture was quenched with sat' NaHCO₃ to

pH7 at 0°C then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with H₂O, then dried over MgSO₄ and evaporated under reduced pressure. The crude compound was purified by silica ge column to produce the title compound(1.2 g, 30~50 %).

¹H NMR (400 MHz, CDCl₃) δ 2.10 (s, 3H), 2.52 (d, J = 5.2 Hz, -OH), 3.67-3.55 (m, 2H), 4.24-4.22 (m, 1H), 4.55 (d, J = 9.6 Hz, 2H), 6.31 (d, J = 5.6 Hz, 1H), 7.46-7.24 (m, 9H).

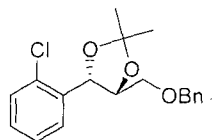
- 10 Preparation example 377: (1S, 2R)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol



- To a solution of (1S, 2R)-3-(benzyloxy)-1-(2-chlorophenyl)-2-hydroxypropyl acetate (Preparation example 376, 1.2 g, 3.58 mmole) in MeOH (16.2 mL) and H₂O (1.8 mL) was added K₂CO₃ (1.48 g, 10.74 mmole) at 0 °C. The mixture was stirred for 1.5 hr at 0°C. The TLC showed complete consumption of SM. The reaction mixture was quenched with H₂O at 0°C then extracted with EtOAc. The aqueous layer was extracted with EtOAc and separated. The combined organic layer was washed with H₂O, then dried over MgSO₄ and evaporated under reduced pressure. The crude compound was purified by silica ge column to produce the title compound (1.0 g, 80~100 %).

¹H NMR (400 MHz, CDCl₃) δ 3.02 (d, J = 5.2 Hz, 1H), 3.55-3.42 (m, 3H, -OH), 4.18-4.13 (m, 1H), 4.46 (d, J = 6 Hz, 2H), 5.28 (t, J = 4.8 Hz, 1H), 7.35-7.19 (m, 8H), 7.50 (dd, J = 7.6, 1.2 Hz, 1H).

- 25 Preparation example 378: (4R, 5S)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane

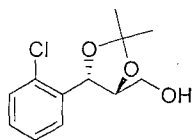


- The substantially same method as described in Preparation example 373 was conducted, except that (1S, 2R)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol(Preparation example 377) was used instead of that (±)-3-

(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol (Preparation example 372), to obtain the title compound (0.77 g, 80~100 %).

¹H NMR (400 MHz, CDCl₃) δ 1.53 (s, 3H), 1.66 (s, 3H), 3.14-3.06 (m, 2H), 4.26 (d, J = 12 Hz, 2H), 4.83-4.78 (m, 1H), 5.63 (d, J = 6.8, 1H), 7.35-7.16 (m, 8H), 7.61 (dd, J = 7.4, 1.6 Hz, 1H).

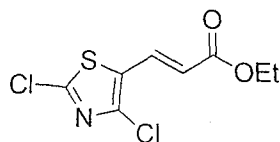
Preparation example 379: ((4R, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 374 was conducted, except that ((4R, 5S)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane (Preparation example 378) was used instead of that (±)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane (Preparation example 373), to obtain the title compound (0.58 g, 80~100 %).

¹H NMR (400 MHz, CDCl₃) δ 1.66 (s, 3H), 1.53 (s, 3H), 3.14-3.06 (m, 2H), 4.26 (d, J = 12, 2H), 4.83-4.78 (m, 1H), 5.63 (d, J = 6.8 Hz, 1H), 7.35-7.16 (m, 8H), 7.61 (dd, J = 7.4, 1.6, 1H).

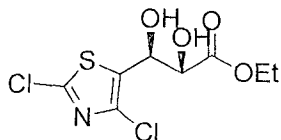
Preparation example 380: (E)-ethyl 3-(2,4-dichlorothiazol-5-yl)acrylate



To a stirred solution of 2,4-dichlorothiazole-5-carbadehyde (5.0g, 27.5mmol) in THF (200mL) was added triethylphosphonoacetate (6.6mL, 32.9mmol) and Lithiumhydroxide (0.79mL, 32.9mmol), 4A molecular sieve 5g at room temperature under N₂. The mixture was stirred for 3h. The resulting mixture was diluted with EtOAc, washed with water, dried over anhydrous magnesium sulfate (MgSO₄), filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (6.1g, 80~95%)

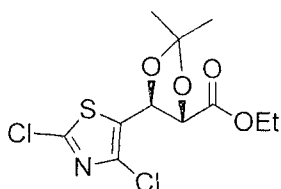
^1H NMR (400MHz, DMSO): δ = 1.22(q, J =12.5, 3H), 4.23(q, J =7.0, 2H), 6.54(d, J = 16, 1H), 7.54(d, J = 16, 1H).

Preparation example 381: (2S,3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 3 was conducted, except that (E)-ethyl 3-(2,4-dichlorothiazol-5-yl)acrylate (Preparation example 380) was used instead of (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (3.94g, 50~70%); ^1H NMR (400MHz, DMSO): δ = 1.22(q, J =12.5, 3H), 4.18(q, J =7.0, 2H), 4.20(dd, J = 2.4, J = 7.6, 1H), 5.19(dd, J = 2.6, J = 5.8, 1H), 6.03(d, J = 7.6, 1H), 6.37(d, J = 5.6, 1H).

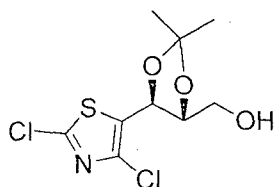
Preparation example 382: (4S,5S)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation example 26 was conducted, except that (2S,3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate (Preparation example 381) was used instead of (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate (Preparation example 25), to obtain the title compound (0.13g, 65~80%)

^1H NMR (400MHz, DMSO): δ = 1.20(t, J =7.2, 3H), 1.42(s, 3H), 1.49(s, 3H), 4.18(m, 2H), 4.66(d, J = 6.8, 1H), 5.44(d, J = 6.8, 1H).

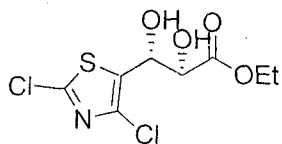
Preparation example 383: ((4R,5S)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 27 was conducted, except that (4S,5S)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 382) was used instead of (4S,5R)-methyl-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 26), to obtain the title compound (0.05g, 50~70%)

^1H NMR (400MHz, DMSO): δ = 1.42(d, J =6.0, 6H), 3.59(m, 1H), 3.67(m, 1H), 3.97(m, 1H), 5.04(t, J = 5.4, 1H), 5.10(d, J = 8.4, 1H).

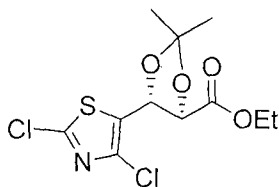
Preparation example 384: (2R, 3R)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 381 was conducted, except that (DHQ)₂-PHAL was used instead of (DHQD)₂-PHAL, to obtain the title compound (3.9g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.22(q, J =12.5, 3H), 4.18(q, J =7.0, 2H), 4.20(dd, J = 2.4, J = 7.6, 1H), 5.19(dd, J = 2.6, J = 5.8, 1H), 6.03(d, J = 7.6, 1H), 6.37(d, J = 5.6, 1H).

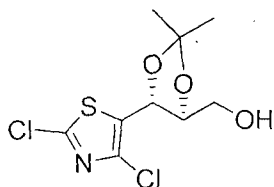
Preparation example 385: (4R, 5R)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 382 was conducted, except that (2R, 3R)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 384) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 381), to obtain the title compound(0.13g, 65~80%).

^1H NMR (400MHz, DMSO): δ = 1.20(t, J =7.2, 3H), 1.42(s, 3H), 1.49(s, 3H), 4.18(m, 2H), 4.66(d, J = 6.8, 1H), 5.44(d, J = 6.8, 1H).

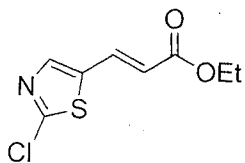
Preparation example 386: ((4S, 5R)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 383 was conducted, except that (4R, 5R)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385) was used instead of (4S, 5S)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 382), to obtain the title compound(0.05g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.42(d, J =6.0, 6H), 3.59(m, 1H), 3.67(m, 1H), 3.97(m, 1H), 5.04(t, J = 5.4, 1H), 5.10(d, J = 8.4, 1H).

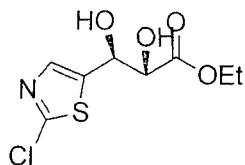
Preparation example 387: (E)-ethyl 3-(2-chlorothiazol-5-yl)acrylate



The substantially same method as described in Preparation Example 380 was conducted, except that 2-chlorothiazole-5-carbadehyde was used instead of 2,4-dichlorothiazole-5-carbadehyde, to obtain the title compound (4.7g, 80~95%)

^1H NMR (400MHz, DMSO): δ = 1.25(t, J =7.0, 3H), 4.19(q, J =7.2, 2H), 6.40(d, J = 16, 1H), 7.81(d, J = 16, 1H), 8.11(s, 1H)

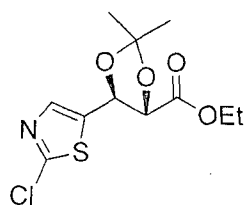
Preparation example 388: (2S,3S)-ethyl-3-(2-chlorothiazol-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 381 was conducted, except that (E)-ethyl 3-(2-chlorothiazol-5-yl)acrylate(Preparation example 387) was used instead of (E)-ethyl 3-(2,4-dichlorothiazol-5-yl)acrylate(Preparation example 380), to obtain the title compound(4.1g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.20(t, J =7.0, 3H), 4.12(q, J =7.2, 2H), 5.18(d, J = 1.6, 1H), 5.87(s, 1H), 6.12(s, 1H), 7.63(s, 1H).

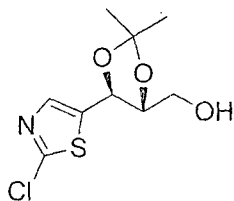
Preparation example 389: (4S,5S)-ethyl-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 382 was conducted, except that (2S, 3S)-ethyl 3-(2-chlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 388) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 381), to obtain the title compound(1.0g, 65~80%).

^1H NMR (400MHz, DMSO): δ = 1.44(d, J =16.8, 3H), 4.18(m, 2H), 4.62(d, J =7.6, 1H), 5.50(d, J = 7.2, 1H), 7.74(s, 1H).

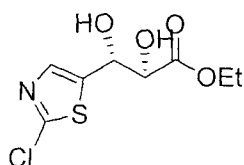
10 Preparation example 390: (4R, 5S)-5-(2-chlorothiazol-5-yl)2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 386 was conducted, except that (4S, 5S)-ethyl 5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 389) was used instead of (4R, 5R)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385), to obtain the title compound(0.84g, 70~90%)..

^1H NMR (400MHz, DMSO): δ = 1.40(d, J =2.0, 6H), 3.59(q, J =4.7, 2H), 3.94(m, 1H), 5.06(t, J =6.6, 1H), 5.09(d, J = 0.8, 1H), 7.69(s, 1H).

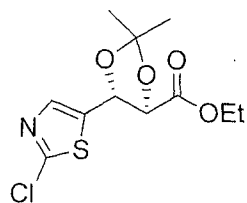
Preparation example 391: (2R, 3R)-ethyl 3-(2-chlorothiazol-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 384 was conducted, except that (E)-ethyl-3-(2-chlorothiazol-5-yl)acrylate(Preparation example 387) was used instead of (E)-ethyl 3-(2,4-dichlorothiazol-5-yl)acrylate(Preparation example 380), to obtain the title compound(3.9g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.20(t, J =7.0, 3H), 4.12(q, J =7.2, 2H), 5.18(d, J = 1.6, 1H), 5.87(s, 1H), 6.12(s, 1H), 7.63(s, 1H).

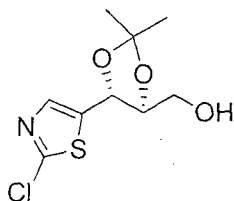
Preparation example 392: (4R, 5R)-ethyl-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 382 was conducted, except that (2R, 3R)-ethyl-3-(2-chlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 391) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 381), to obtain the title compound(0.73g, 65~80%).

^1H NMR (400MHz, DMSO): δ = 1.44(d, J =16.8, 3H), 4.18(m, 2H), 4.62(d, J = 7.6, 1H), 5.50(d, J = 7.2, 1H), 7.74(s, 1H).

Preparation example 393: (4S, 5R)-5-(2-chlorothiazol-5-yl)2,2-dimethyl-1,3-dioxolan-4-yl)methanol

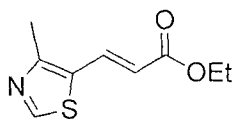


The substantially same method as described in Preparation Example 386 was

conducted, except that (4R, 5R)-ethyl-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 392) was used instead of (4R, 5R)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385), to obtain the title compound(0.60g, 70~90%)..

^1H NMR (400MHz, DMSO): δ = 1.40(d, J =2.0, 6H), 3.59(q, J =4.7, 2H), 3.94(m, 1H), 5.06(t, J =6.6, 1H), 5.09(d, J = 0.8, 1H), 7.69(s, 1H).

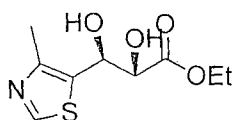
Preparation example 394: (E)-ethyl-3-(4-methylthiazol-5-yl)acrylate



The substantially same method as described in Preparation Example 380 was conducted, except that 4-methylthiazole-5-carbadehyde was used instead of 2,4-dichlorothiazole-5-carbadehyde, to obtain the title compound (15g, 80~95%)

^1H NMR (400MHz, DMSO): δ = 1.25(t, J =7.0, 3H), 1.45(s 3H), 4.19(q, J =7.0, 2H), 6.12(d, J = 16, 1H), 7.77(d, J = 16, 1H), 9.09(s, 1H).

Preparation example 395: (2S,3S)-ethyl-3-(4-methylthiazol-5-yl)-2,3-dihydroxypropanoate

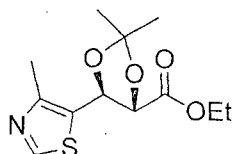


The substantially same method as described in Preparation Example 2 was conducted, except that (E)-ethyl-3-(4-methlythiazol-5-yl)acrylate(Preparation example 394) was used instead of (E)-ethyl-3-(2,4-dichlorothiazol-5-yl)acrylate(Preparation example 381), to obtain the title compound(4.0g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.11(t, J =7.0, 3H), 1.43(s, 3H), 4.04(m, 2H),

5.11(t, $J=3.8$, 1H), 5.70(d, $J=20.7$, 1H), 5.92(d, $J=4.0$, 1H), 6.81(s, 1H), 8.86(s, 1H).

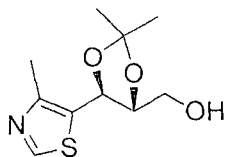
Preparation example 396: (4S,5S)-ethyl-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 382 was conducted, except that (2S, 3S)-ethyl-3-(4-methylthiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 395) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 381), to obtain the title compound(2.6g, 55~70%).

^1H NMR (400MHz, DMSO): δ = 1.17(t, $J=3.6$, 3H), 1.43(s, 3H), 1.49(s, 3H), 2.34(s, 3H), 4.17(q, $J=7.0$ 2H), 4.40(d, $J=14.0$, 1H), 5.53(d, $J=7.2$, 1H), 9.01(s, 1H).

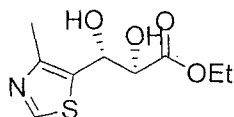
Preparation example 397: (4R, 5S)-5-(4-methylthiazol-5-yl)2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 386 was conducted, except that (4S, 5S)-ethyl-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 396) was used instead of (4R, 5R)-ethyl 5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385), to obtain the title compound(1.7g, 70~90%)..

^1H NMR (400MHz, DMSO): δ = 1.42(d, J =7.6, 6H), 2.36(s, 3H), 3.58(m, 2H), 3.80(d, J =3.2, 1H), 5.02(t, J =5.4, 1H), 5.17(d, J = 8.4, 1H), 8.98(s, 1H).

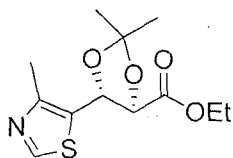
Preparation example 398: (2R, 3R)-ethyl-3-(4-methylthiazol-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 384 was conducted, except that (E)-ethyl-3-(4-methylthiazol-5-yl)acrylate(Preparation example 394) was used instead of (E)-ethyl-3-(2,4-dichlorothiazol-5-yl)acrylate(Preparation example 380), to obtain the title compound(6.0g, 50~70%).

^1H NMR (400MHz, DMSO): δ = 1.11(t, J =7.0, 3H), 1.43(s, 3H), 4.04(m, 2H), 5.11(t, J = 3.8, 1H), 5.70(d, J =20.7, 1H), 5.92(d, J = 4.0, 1H), 6.81(s, 1H), 8.86(s, 1H).

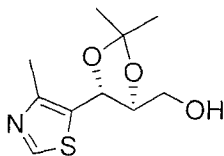
Preparation example 399: (4R, 5R)-ethyl-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 382 was conducted, except that (2R, 3R)-ethyl-3-(4-methylthiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 398) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate(Preparation example 381), to obtain the title compound(5.0g, 65~80%).

^1H NMR (400MHz, DMSO): δ = 1.17(t, J =3.6, 3H), 1.43(s, 3H), 1.49(s, 3H), 2.34(s, 3H), 4.17(q, J =7.0 2H), 4.40(d, J = 14.0, 1H), 5.53(d, J = 7.2, 1H), 9.01(s, 1H).

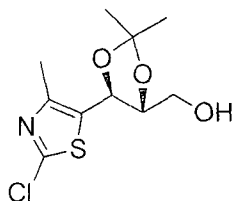
Preparation example 400: (4S, 5R)-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



5 The substantially same method as described in Preparation Example 386 was conducted, except that (4R, 5R)-ethyl-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example399) was used instead of (4R, 5R)-ethyl-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385), to obtain the title
10 compound(4.1g, 70~90%).

^1H NMR (400MHz, DMSO): δ = 1.42(d, J =7.6, 6H), 2.36(s, 3H), 3.58(m, 2H), 3.80(d, J =3.2, 1H), 5.02(t, J =5.4, 1H), 5.17(d, J = 8.4, 1H), 8.98(s, 1H).

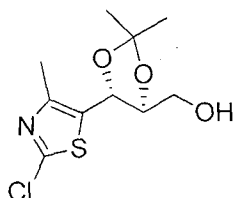
Preparation example 401: (4R, 5S)-ethyl-5-(2-chloro-4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate
15



To a stirred solution of (4R, 5S)-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol(Preparation example 397, 3.1g, 14.3mmol) in THF (20mL) was added n-Buthyllithium (14.3mL, 35.7mmol) and CCl_4 (4.1mL, 42.8mmol) at -78°C . The mixture was stirred for 0.5h. The resulting mixture
20 was diluted with EtOAc, washed with water, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (2.8g, 70~90%)

^1H NMR (400MHz, DMSO): δ = 1.40(d, J =5.6, 6H), 2.28(s, 3H), 3.58(m, 2H),
25 3.80(m, 1H), 5.06(m, 1H), 5.13(d, J = 8.4, 1H).

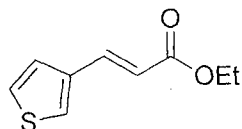
Preparation example 402: (4S, 5R)-ethyl-5-(2-chloro-4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



5 The substantially same method as described in Preparation Example 401 was conducted, except that (4S, 5R)-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol(Preparation example 400) was used instead of (4R, 5S)-5-(4-methylthiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-yl)methanol(Preparation example 397), to obtain the title compound(1.5g, 10 70~90%).

^1H NMR (400MHz, DMSO): δ = 1.40(d, J =5.6, 6H), 2.28(s, 3H), 3.58(m, 2H), 3.80(m, 1H), 5.06(m, 1H), 5.13(d, J = 8.4, 1H).

Preparation example 403: (E)-ethyl 3-(thiophen-3-yl)acrylate

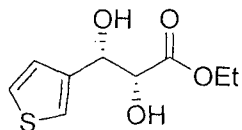


15 To a stirred solution of triethylphosphonoacetate(5.36ml, 26.7mmol) in THF(40ml) was added to t-BuOK(3g,26.7mmol) dropwise at rt and stirred at this temperature for 30min. Then thiophene-3-carbaldehyde (3g, 26.7mmol)was added and stirred at 90° C and stirred at this temperature for 20 30min. The product was quenched with 1M HCl solution. The resulting mixture was extracted with ethyl acetate from water. The combined organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was purified by silica gel column to produce the title compound (3.9g, 70~90%).

25 ^1H NMR (400MHz, CDCl_3): δ =1.34(t, J =7.2, 3H), 4.26(q, J =7.2, 2H), 6.31(d, J =15.6, 1H), 6.89 (d, J =4, 1H), 7.69(s, 1H), 7.73(d, J =4, 1H), 7.80(d,

$J=15.6$, 1H)

Preparation example 404: (2R,3S)-ethyl 2,3-dihydroxy-3-(thiophen-3-yl)propanoate



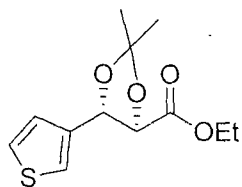
The substantially same method as described in Preparation Example 384 was conducted, except that (E)-ethyl 3-(thiophen-3-yl)acrylate (Preparation example 403) was used instead of (E)-ethyl 13-(2,4-dichlorothiazol-5-yl)acrylate (Preparation example 380), to obtain the title compound (6.0g, 60~80%).

10

^1H NMR (400MHz, CDCl_3): δ =1.34(t, $J=7.2$, 3H), 4.26(q, $J=7.2$, 2H), 4.65(d, $J=5.5$, 1H), 5.13(d, $J=5.5$, 1H), 6.93(dd, $J=6.09$, $J=1.32$, 1H), 7.47(dd, $J=6.09$, $J=1.73$, 1H), 7.88(dd, $J=1.73$, $J=1.32$, 1H)

Preparation example 405: (4R,5S)-ethyl 2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolane-4-carboxylate

15

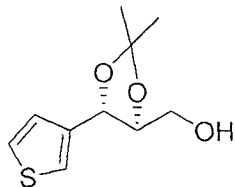


The substantially same method as described in Preparation Example 382 was conducted, except that (2R,3S)-ethyl 2,3-dihydroxy-3-(thiophen-3-yl)propanoate (Preparation example 404) was used instead of (2S, 3S)-ethyl 3-(2,4-dichlorothiazol-5-yl)-2,3-dihydroxypropanoate (Preparation example 381), to obtain the title compound (3.0g, 65~80%).

^1H NMR (400MHz, CDCl_3): δ =1.18(t, $J=7.1$, 3H), 1.41(s, 3H), 1.43(s, 3H), 4.16(q, $J=7.1$, 2H), 4.21(d, $J=7.0$, 1H), 4.94(d, $J=7.0$, 1H), 6.95(dd, $J=6.0$, $J=1.3$, 1H), 7.48(dd, $J=6.0$, $J=1.7$, 1H), 7.90(dd, $J=1.7$, $J=1.3$, 1H)

25

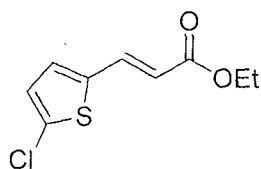
Preparation example 406: ((4S,5S)-2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methanol



- 5 The substantially same method as described in Preparation Example 386 was conducted, except that (4R, 5R)-ethyl 2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolane-4-carboxylate(Preparation example 405) was used instead of (4R, 5R)-ethyl-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 385), to obtain the title compound(2.2g, 10 70~90%).

^1H NMR (400MHz, CDCl_3): δ =1.39 (s, 3H), 1.42 (s, 3H), 3.47~3.6 (m, 2H,) 3.84~3.88(m, 1H) 4.82 (d, J =7.0, 1H), 6.93 (dd, J =6.1, J =1.3, 1H), 7.47 (dd, J =6.1, J =1.7, 1H,), 7.89 (dd, J =1.7, J =1.3, 1H)

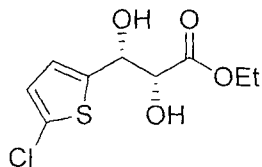
- 15 Preparation example 407: (E)-ethyl 3-(5-chlorothiophen-2-yl)acrylate



The substantially same method as described in Preparation Example 403 was conducted, except that 5-chlorothiophene-2-carbaldehyde was used instead of thiophene-3-carbaldehyde, to obtain the title compound (4.0g, 70~90%).

- 20 ^1H NMR (400MHz, CDCl_3): δ =1.36(t, J =7.2, 3H), 4.20(q, J =7.2, 2H), 6.13(d, J =15.6, 1H), 6.89 (d, J =4, 1H), 7.65(d, J =15.6, 1H), 7.83(d, J =4.2, 1H)

Preparation example 408: (2R,3S)-ethyl 2,3-dihydroxy-3-(5-chlorothiophen-2-yl)propanoate

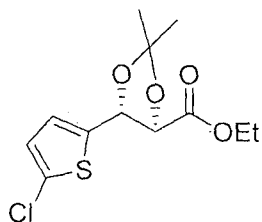


The substantially same method as described in Preparation Example 404 was conducted, except that (E)-ethyl 3-(5-chlorothiophen-2-yl)acrylate (Preparation example 407) was used instead of (E)-ethyl 3-(thiophen-3-yl)acrylate (Preparation example 403), to obtain the title compound (2.8g, 60~80%).

^1H NMR (400MHz, CDCl_3) δ 1.34(t, $J=7.2$, 3H), 2.76(d, $J=8.4$, 1H), 3.32(d, $J=5.6$, 1H), 4.33(q, $J=7.2$, 2H), 4.4(dd, $J=2.4$, $J=5.2$, 1H), 5.16(dd, $J=2$, $J=8$, 1H), 6.82(d, $J=4$, 1H), 6.88(dd, $J=0.8$, $J=3.6$, 1H)

10

Preparation example 409: (4R,5S)-ethyl 2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolane-4-carboxylate

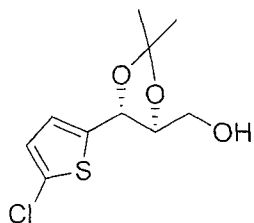


The substantially same method as described in Preparation Example 405 was conducted, except that (2R,3S)-ethyl 2,3-dihydroxy-3-(5-chlorothiophen-2-yl)propanoate (Preparation example 408) was used instead of (2R,3S)-ethyl 2,3-dihydroxy-3-(thiophen-3-yl)propanoate (Preparation example 404), to obtain the title compound (0.85g, 65~80%).

^1H NMR (400MHz, CDCl_3): δ = 1.31(t, $J=7.2$, 3H), 1.54(s, 3H), 1.58(s, 3H), 4.29~4.36 (m, 2H), 4.42(d, $J=7.2$, 1H), 5.29(d, $J=7.2$, 1H), 6.81(q, $J=4$, 1H), 6.88(d, $J=3.2$, 1H)

20

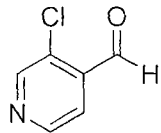
Preparation example 410: ((4S,5S)-2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 406 was conducted, except that (4R, 5R)-ethyl 2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolane-4-carboxylate(Preparation example 409) was used instead of (4R, 5R)-ethyl 2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolane-4-carboxylate(Preparation example 405), to obtain the title compound(0.8g, 70~90%).

^1H NMR (400MHz, CDCl_3): δ =1.39 (s, 3H), 1.42 (s, 3H), 3.54~3.79 (m, 2H,) 4.28~4.42(m, 1H), 5.17(d, J =7.2, 1H), 6.47 (d, J =6.1, 1H,), 6.51(d, J =6.1,1H)

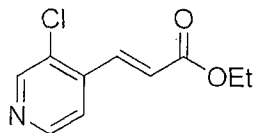
Preparation example 411: 3-chloroisonicotinaldehyde



To a 250 ml round-bottomed flask, LDA (11ml, 22.02mmol) was added to 3-chloropyridine(1g, 8.80mmol) in THF(20 ml) dropwise at -78°C and stirred at same temperature for 1~2hr. Then DMF(822 μl , 10.56mmol)was added and stirred at room temperature for 1hr. EA (Ethyl acetate) and water were added to the reaction mixture, and after the separation of the layers, the aqueous phase was further extracted with the organic solvent. The combined organic extracts were dried over anhydrous Sodium sulfate (Na_2SO_4), filtered and concentrated under vacuum. The crude compound was purified by a silica gel column to produce the title compound (0.33g, 30~65%)

^1H NMR (400MHz, CDCl_3) δ 7.73 (d, J = 8.0, 1H) 8.71 (d, J = 4.0, 1H) 8.81 (s, 1H) 10.52 (s, 1H)

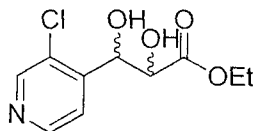
Preparation example 412: (E)-ethyl 3-(3-chloropyridin-4-yl)acrylate



3-chloroisonicotinaldehyde (Preparation example 411, 0.54g, 3.79mmol) was dissolved in benzene. At the room temperature, triethyl phosphoacetate (753 μ l, 3.79mmol) and potassium tert-butoxide (468 mg, 4.17 mmol) were added and stirred. When the reaction was completed, the obtained product was washed with water and ethylacetate (EA). Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgSO_4), filtrated, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (0.57g, 70~90%).

^1H NMR (400MHz, CDCl_3) δ 1.40 (t, $J = 12$, 3H) 4.13 (q, $J = 6.6$, 2H) 6.61(d, $J = 16.0$, 1H) 7.46 (d, $J = 16.0$, 1H) 7.97 (d $J = 8.0$, 1H) 8.51 (d, $J = 4.0$, 1H) 8.66 (s, 1H)

Preparation example 413: Ethyl 3-(3-chloropyridin-4-yl)-2,3-dihydroxypropanoate

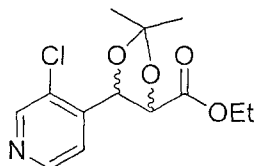


(E)-ethyl 3-(3-chloropyridin-4-yl)acrylate(Preparation example 412, 0.57g, 2.69mmol) was dissolved in the mixture of actone(11.4ml)/water(2.3ml)/t-BuOH(2.3ml). NMO(0.47g, 4.03mmol), Osmium tetroxide (13.6mg, 0.05mmol) were added thereto and stirred at 40°C. When the reaction was completed, the obtained product was washed with water and ethylacetate (EA). Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgSO_4), filtrated, and concentrated under reduced pressure. The crude compound was purified by a silica gel column to produce the title compound (0.44g, 60~80%).

^1H NMR (400MHz, CDCl_3) δ 1.28 (t, $J = 12.0$, 3H) 4.15 (q, $J = 6.6$, 2H) 4.26

(d, $J = 4.0$, 1H) 5.24 (d, $J = 4.0$, 1H) 5.44 (br s, 1H) 5.98 (br s, 1H)
7.59(d, $J = 8.0$, 1H) 8.52 (d, $J = 4.0$, 1H) 8.56 (s, 1H)

Preparation example 414: Ethyl 5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-
5 dioxolane-4-carboxylate

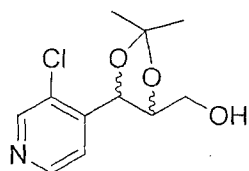


The substantially same method as described in Preparation Example 405 was
conducted, except that Ethyl 3-(3-chloropyridin-4-yl)-2,3-
dihydroxypropanoate(Preparation example 413) was used instead of (2R,3S)-
10 ethyl 2,3-dihydroxy-3-(thiophen-3-yl)propanoate(Preparation example 404),
to obtain the title compound(5.26g, 70~90%).

^1H NMR (400MHz, CDCl_3) δ 1.28 (t, $J = 12.0$, 3H) 1.61 (s, 3H) 1.65 (s, 3H)
4.23 (q, $J = 6.0$ 2H) 4.38 (d, $J = 7.2$ 1H) 5.67 (d, $J = 8.0$,1H) 7.55 (d, $J =$
8.0 ,1H) 8.56 (d, $J = 4.0$,1H) 8.57 (s, 1H)

15

Preparation example 415: (5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-
dioxolan-4-yl)methanol

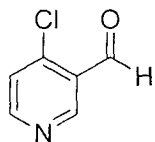


The substantially same method as described in Preparation Example 406 was
20 conducted, except that Ethyl 5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-
dioxolane-4-carboxylate(Preparation example 414) was used instead of (4R,
5R)-ethyl 2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolane-4-
carboxylate(Preparation example 405), to obtain the title compound(0.18g,
70~90%).

25 ^1H NMR (400MHz, CDCl_3) δ 1.56 (s, 3H) 1.59 (s, 3H) 3.79~3.67 (m, 1H)

3.85 (dd, $J = 8.0, 6.0$, 1H) 4.06~3.90 (m, 1H) 4.14 (dd, $J = 8.0, 6.0$, 1H)
5.37 (d, $J = 8.0$, 1H) 7.57(d, $J = 6.0$, 1H) 8.57 (d, $J = 12$, 2H)

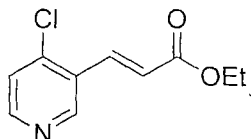
Preparation example 416: 4-chloroisonicotinaldehyde



The substantially same method as described in Preparation Example 411 was conducted, except that Ethyl 4-chloropyridine was used instead of 3-chloropyridine, to obtain the title compound(3.0g, 60~80%).

^1H NMR (400MHz, CDCl_3): δ =7.45(d, J =5.2, 1H), 8.70(d, J =5.2, 1H), 9.06(s, 1H), 10.52(s, 1H)

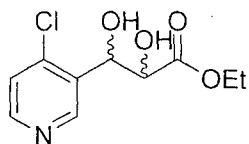
Preparation example 417: (E)-ethyl 3-(4-chloropyridin-3-yl)acrylate



The substantially same method as described in Preparation Example 412 was conducted, except that Ethyl 4-chloronicotinaldehyde(Preparation example 416) was used instead of 3-chloroisonicotinaldehyde(Preparation example 411), to obtain the title compound(4.0g, 70~90%).

^1H NMR (400MHz, CDCl_3): δ =1.37(t, J =7.0, 3H), 4.33(q, J =6.6, 2H), 6.57(d, J =16.4, 1H), 7.39 (d, J =5.2, 1H), 7.98(d, J =16.0, 1H), 8.49(d, J =5.2, 1H), 8.82(s, 1H)

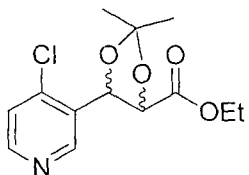
Preparation example 418: Ethyl 3-(4-chloropyridin-3-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 413 was conducted, except that (E)-ethyl 3-(4-chloropyridin-3-yl)acrylate (Preparation example 417) was used instead of (E)-ethyl 3-(3-chloropyridin-4-yl)acrylate (Preparation example 412), to obtain the title compound (2.4g, 60~80%).

^1H NMR (400MHz, CDCl_3): δ = 1.34(t, J =7.2, 3H), 4.35(q, J =7.0, 2H), 4.45(d, J =2.4, 1H), 5.49 (d, J =2.0, 1H), 7.32(d, J =5.2, 1H), 8.46(d, J =4.4, 1H), 8.79(s, 1H)

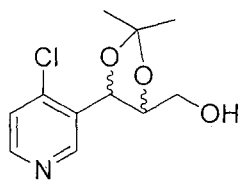
Preparation example 419: Ethyl 5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 414 was conducted, except that Ethyl 3-(4-chloropyridin-3-yl)-2,3-dihydroxypropanoate (Preparation example 418) was used instead of Ethyl 3-(3-chloropyridin-4-yl)-2,3-dihydroxypropanoate (Preparation example 413), to obtain the title compound (1.3g, 70~90%).

^1H NMR (400MHz, CDCl_3): δ = 1.25(t, J =7.2 3H), 1.59(s, 3H), 1.64(s, 3H), 4.22 (q, J =8.27 2H), 4.37(d, J =7.6, 1H); 5.56(d, J =7.6, 1H), 7.31(d, J =5.2, 1H), 8.48(d, J =5.2, 1H), 8.78(s, 1H)

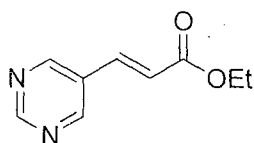
Preparation example 420: (5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 415 was conducted, except that Ethyl 5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 419) was used instead of Ethyl 5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate(Preparation example 414), to obtain the title compound(0.8g, 70~90%).

^1H NMR (400MHz, CDCl_3): δ = 1.56(s, 3H), 1.63(s, 3H), 1.64(s, 3H), 3.73~3.77(m, 1H), 3.95~3.99(m, 2H), 5.39(d, J =8.4, 1H), 7.32(d, J =5.6, 1H), 8.46(d, J =5.2, 1H), 8.82(s, 1H)

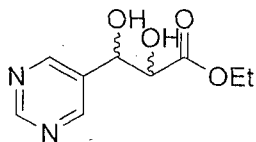
Preparation example 421: (E)-ethyl 3-(pyrimidin-5-yl)acrylate



5-bromopyrimidine (5 g, 31.4 mmol) in DMF (75 ml) was added ethyl acrylate (9.5 ml, 94.4 mmol) at room temperature. Diisopropylamine (7.5 ml, 42.8 mmol), trimethyl phosphate (0.19 ml, 1.6 mmole), $\text{Pd}(\text{Pac})_2$ (0.18g, 0.78 mmol) were added. The reaction mixture was heated at 110 °C for 2hr. The reaction mixture was cooled to room temperature and quenched with H_2O then extracted with EA(Ethyl acetate). The aqueous layer was extracted with EA and separated. The combined organic layer was washed with H_2O , then dried over anhydrous magnesium sulfate(MgSO_4)and evaporated under reduced. The crude compound was purified by a silica gel column to produce the title compound (3.9g, 70~90%).

^1H NMR (400 MHz, CDCl_3) δ 1.38 (t, J = 6.8, 3H), 4.29-4.35 (m, 1H), 6.61 (d, J = 17.2, 1H), 7.63 (d, J = 16.4, 1H), 8.90 (s, 2H), 9.22 (s, 1H).

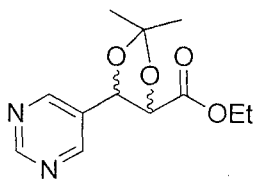
Preparation example 422: Ethyl 3-(pyrimidin-5-yl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation Example 418 was conducted, except that (E)-ethyl 3-(pyrimidin-5-yl)acrylate (Preparation example 421) was used instead of (E)-ethyl 3-(4-chloropyridin-3-yl)acrylate (Preparation example 417), to obtain the title compound (1.6g, 40~60%).

^1H NMR (400 MHz, CDCl_3) δ 1.07-1.39 (m, 3H), 4.16-4.34 (m, 2H), 4.39 (s, 1H), 4.69 (s, 1H), 5.04 (s, 1H), 5.10 (s, 1H), 8.98 (s, 2H), 9.01 (s, 1H).

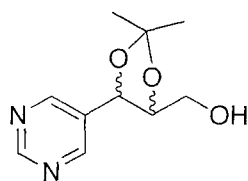
Preparation example 423: Ethyl 2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 419 was conducted, except that Ethyl 3-(pyrimidin-5-yl)-2,3-dihydroxypropanoate (Preparation example 422) was used instead of Ethyl 3-(4-chloropyridin-3-yl)-2,3-dihydroxypropanoate (Preparation example 418), to obtain the title compound (0.97g, 40~60%).

^1H NMR (400 MHz, CDCl_3) δ 1.30 (t, $J = 7.2$, 3H), 1.55 (s, 3H), 1.61 (s, 3H), 4.25-4.32 (m, 1H), 4.35 (d, $J = 8.0$, 1H), 5.18 (d, $J = 7.6$, 1H), 8.82 (s, 2H), 9.20 (s, 1H).

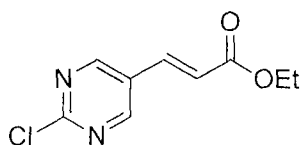
Preparation example 424: (2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 420 was conducted, except that Ethyl 2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolane-4-carboxylate (Preparation example 423) was used instead of Ethyl 5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (Preparation example 419), to obtain the title compound (0.65g, 70~90%).

^1H NMR (400 MHz, CDCl_3) δ 1.53 (s, 3H), 1.56 (s, 3H), 2.75 (s, -OH), 3.68-3.73 (m, 1H), 3.69-3.64 (m, 1H), 3.89-3.93 (m, 2H), 5.0 (d, $J = 8.4$, 1H), 8.79 (s, 2H), 9.18 (s, 1H).

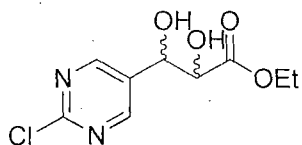
Preparation example 425: (E)-ethyl 3-(2-chloropyrimidin-5-yl)acrylate



The substantially same method as described in Preparation Example 421 was conducted, except that 2-chloro-5-bromopyrimidine was used instead of 5-bromopyrimidine, to obtain the title compound (9.7g, 50~70%).

^1H NMR (400 MHz, CDCl_3) δ 1.37 (t, $J = 6.8$, 3H), 4.32 (qt, $J = 7.2$, 2H), 6.59 (d, $J = 16.4$, 1H), 7.60 (d, $J = 16.4$, 1H), 8.77 (s, 2H).

Preparation example 426: Ethyl 3-(2-chloropyrimidin-5-yl)-2,3-dihydroxypropanoate

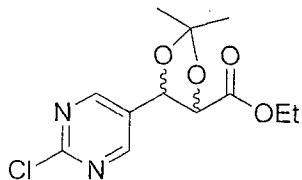


The substantially same method as described in Preparation Example 422 was conducted, except that (E)-ethyl 3-(2-chloropyrimidin-5-yl)acrylate (Preparation example 425) was used instead of (E)-ethyl 3-(pyrimidin-5-yl)acrylate (Preparation example 421), to obtain the title compound (2.1g,

40~60%).

^1H NMR (400 MHz, CDCl_3) δ 1.33-1.37 (m, 3H), 2.97 (d, $J = 7.2$, 1H), 3.31 (d, $J = 18.4$, 1H), 4.34-4.55 (m, 3H), 5.10 (d, $J = 7.2$, 1H), 8.72 (s, 2H).

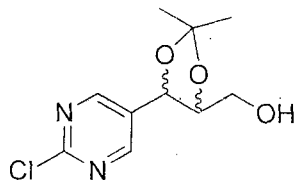
- 5 Preparation example 427: Ethyl 2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolane-4-carboxylate



The substantially same method as described in Preparation Example 423 was conducted, except that Ethyl 3-(2-chloropyrimidin-5-yl)-2,3-dihydroxypropanoate (Preparation example 426) was used instead of Ethyl 3-(pyrimidin-5-yl)-2,3-dihydroxypropanoate (Preparation example 422), to obtain the title compound (0.98g, 40~60%).

^1H NMR (400 MHz, CDCl_3) δ 1.32 (t, $J = 7.2$ 3H), 1.55 (s, 3H), 1.60 (s, 3H), 4.27-4.34 (m, 3H), 5.19 (d, $J = 7.6$, 1H), 8.71 (s, 2H).

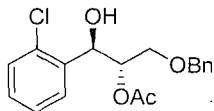
- 15 Preparation example 428: (2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation Example 424 was conducted, except that Ethyl 2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolane-4-carboxylate (Preparation example 427) was used instead of Ethyl 2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolane-4-carboxylate (Preparation example 423), to obtain the title compound (0.71g, 70~90%).

^1H NMR (400 MHz, CDCl_3) δ 1.54 (s, 3H), 1.56 (s, 3H), 2.21 (s, -OH), 3.71-3.76 (m, 1H), 3.69-3.64 (m, 1H), 3.88-3.96 (m, 2H), 5.02 (d, $J = 8.0$, 1H), 8.68 (s, 2H).

Preparation example 429: (1R, 2S)-3-(benzyloxy)-1-(2-chlorophenyl)-1-hydroxypropan-2-yl acetate

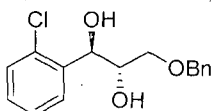


- 5 A regioisomer of acetate was separated and purified by conducting the silica gel column chromatography as described in Preparation example 376, to obtain the title compound (0.42g, yield 10~30%)

^1H NMR (400 MHz, CDCl_3) δ 2.09 (s, 3H), 3.63-3.70 (m, 2H), 4.47-4.61 (m, 2H), 5.29-5.33(m, 1H), 5.41(t, J = 5.0 Hz, 1H), 7.22-7.55 (m, 9H).

10

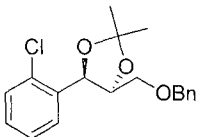
Preparation example 430: (1R, 2S)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol



- 15 The substantially same method as described in Preparation Example 377 was conducted, except that (1R, 2S)-3-(benzyloxy)-1-(2-chlorophenyl)-1-hydroxypropan-2-yl acetate (Preparation example 429) was used instead of (1S, 2R)-3-(benzyloxy)-1-(2-chlorophenyl)-2-hydroxypropyl acetate (Preparation example 376), to obtain the title compound (0.31 g, 80~95 %).

20 ^1H NMR (400 MHz, CDCl_3) δ 3.02 (d, J = 5.2 Hz, 1H), 3.55-3.42 (m, 3H, -OH), 4.18-4.13 (m, 1H), 4.46 (d, J = 6 Hz, 2H), 5.28 (t, J = 4.8 Hz, 1H), 7.35-7.19 (m, 8H), 7.50 (dd, J = 7.6, 1.2 Hz, 1H).

Preparation example 431: (4S, 5R)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane



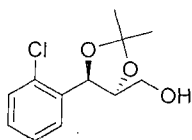
25

The substantially same method as described in Preparation example 373 was conducted, except that (1R, 2S)-3-(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol(Preparation example 430) was used instead of that ($\pm$)-3-

(benzyloxy)-1-(2-chlorophenyl)propane-1,2-diol (Preparation example 372), to obtain the title compound (0.84 g, 80~100 %).

¹H NMR (400 MHz, CDCl₃) δ 1.53 (s, 3H), 1.66 (s, 3H), 3.14-3.06 (m, 2H), 4.26 (d, J = 12 Hz, 2H), 4.83-4.78 (m, 1H), 5.63 (d, J = 6.8, 1H), 7.35-7.16 (m, 8H), 7.61 (dd, J = 7.4, 1.6 Hz, 1H).

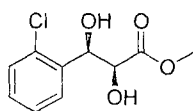
Preparation example 432: ((4S, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol



The substantially same method as described in Preparation example 374 was conducted, except that ((4S, 5R)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane (Preparation example 431) was used instead of that (±)-4-(benzyloxymethyl)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolane (Preparation example 373), to obtain the title compound (0.82 g, 80~100 %).

¹H NMR (400 MHz, CDCl₃) δ 1.66 (s, 3H), 1.53 (s, 3H), 3.14-3.06 (m, 2H), 4.26 (d, J = 12, 2H), 4.83-4.78 (m, 1H), 5.63 (d, J = 6.8 Hz, 1H), 7.35-7.16 (m, 8H), 7.61 (dd, J = 7.4, 1.6, 1H).

Preparation example 433: (2S,3R)-methyl-3-(2-chlorophenyl)-2,3-dihydroxypropanoate



The substantially same method as described in Preparation example 3 was conducted, except that (E)-methyl-3-(2-chlorophenyl)acrylate (Preparation example 24) was used instead of that (E)-1-chloro-2-(3-(methoxymethoxy)prop-1-enyl)benzene (Preparation example 2), to obtain the title compound (14.2g, 70~90%)

¹H NMR (400MHz, CDCl₃) δ 2.79(d, j=7.2, 1H), 3.13(d, J=6.0, 1H), 3.86(s, 3H), 4.50(dd, J=5.6, 2.4, 1H), 5.51(dd, J=7.2, 2.4, 1H), 7.62~7.26 (m, 4H)

Table 1: Example of sulfamate compound (A = Phenyl)

No	A = Phenyl	n	l	m	R ¹	R ²	R ³	R ⁴	Chiral-1	Chiral-2
1	2-Cl	1	0	0	Me	Me	H	H	R	R
2	2-Cl	1	0	0	Me	Me	H	H	S	S
3	2-Cl	1	0	0	Me	Me	H	H	Rac.(syn)	Rac.(syn)
4	2-Cl	1	0	0	Me	Me	H	H	Rac.(anti)	Rac.(anti)
5	2-Cl	1	0	0	Me	H	H	H	R	R
6	2-Cl	1	0	0	Me	H	H	H	S	S
7	2-Cl	1	0	0	Et	Et	H	H	R	R
8	2-Cl	1	0	0	Et	Et	H	H	S	S
9	2-Cl	1	0	0	Cyclopentyl		H	H	R	R
10	2-Cl	1	0	0	Cyclopentyl		H	H	S	S
11	2-Cl	1	0	0	Cyclohexyl		H	H	R	R
12	2-Cl	1	0	0	Cyclohexyl		H	H	S	S
13	2-Cl	1	0	0	Methylbenzene		H	H	R	R
14	2-Cl	1	0	0	Methylbenzene		H	H	S	S
15	2-F	1	0	0	Me	Me	H	H	R	R
16	2-F	1	0	0	Me	Me	H	H	S	S
17	2-F	1	0	0	Me	H	H	H	R	R

18	2-F	1	0	0	Me	H	H	H	S	S
19	2-F	1	0	0	Et	Et	H	H	R	R
20	2-F	1	0	0	Et	Et	H	H	S	S
21	2-F	1	0	0	Cyclopentyl		H	H	R	R
22	2-F	1	0	0	Cyclopentyl		H	H	S	S
23	2-F	1	0	0	Cyclohexyl		H	H	R	R
24	2-F	1	0	0	Cyclohexyl		H	H	S	S
25	2-F	1	0	0	Methylbenzene		H	H	R	R
26	2-F	1	0	0	Methylbenzene		H	H	S	S
27	2-I	1	0	0	Me	Me	H	H	R	R
28	2-I	1	0	0	Me	Me	H	H	S	S
29	2-I	1	0	0	Me	H	H	H	R	R
30	2-I	1	0	0	Me	H	H	H	S	S
31	2-I	1	0	0	Et	Et	H	H	R	R
32	2-I	1	0	0	Et	Et	H	H	S	S
33	2-I	1	0	0	Cyclopentyl		H	H	R	R
34	2-I	1	0	0	Cyclopentyl		H	H	S	S
35	2-I	1	0	0	Cyclohexyl		H	H	R	R
36	2-I	1	0	0	Cyclohexyl		H	H	S	S
37	2-I	1	0	0	Methylbenzene		H	H	R	R

38	2-I	1	0	0	Methylbenzen e		H	H	S	S
39	2,4-Cl	2	0	0	Me	Me	H	H	R	R
40	2,4-Cl	2	0	0	Me	Me	H	H	S	S
41	2,4-Cl	2	0	0	Me	H	H	H	R	R
42	2,4-Cl	2	0	0	Me	H	H	H	S	S
43	2,4-Cl	2	0	0	Et	Et	H	H	R	R
44	2,4-Cl	2	0	0	Et	Et	H	H	S	S
45	2,4-Cl	2	0	0	Cyclopentyl		H	H	R	R
46	2,4-Cl	2	0	0	Cyclopentyl		H	H	S	S
47	2,4-Cl	2	0	0	Cyclohexyl		H	H	R	R
48	2,4-Cl	2	0	0	Cyclohexyl		H	H	S	S
49	2,4-Cl	2	0	0	Methylbenzen e		H	H	R	R
50	2,4-Cl	2	0	0	Methylbenzen e		H	H	S	S
51	2,6-Cl	2	0	0	Me	Me	H	H	R	R
52	2,6-Cl	2	0	0	Me	Me	H	H	S	S
53	2,6-Cl	2	0	0	Me	H	H	H	R	R
54	2,6-Cl	2	0	0	Me	H	H	H	S	S
55	2,6-Cl	2	0	0	Et	Et	H	H	R	R
56	2,6-Cl	2	0	0	Et	Et	H	H	S	S
57	2,6-Cl	2	0	0	Cyclopentyl		H	H	R	R

58	2,6-Cl	2	0	0	Cyclopentyl		H	H	S	S
59	2,6-Cl	2	0	0	Cyclohexyl		H	H	R	R
60	2,6-Cl	2	0	0	Cyclohexyl		H	H	S	S
61	2,6-Cl	2	0	0	Methylbenzene		H	H	R	R
62	2,6-Cl	2	0	0	Methylbenzene		H	H	S	S
63	2-NH ₂	1	0	0	Me	Me	H	H	R	R
64	2-NH ₂	1	0	0	Me	Me	H	H	S	S
65*	2-NH ₂	1	0	0	Me	Me	H	H	R	R
66*	2-NH ₂	1	0	0	Me	Me	H	H	S	S
67	2-NH ₂	1	0	0	Me	H	H	H	R	R
68	2-NH ₂	1	0	0	Me	H	H	H	S	S
69	2-NH ₂	1	0	0	Et	Et	H	H	R	R
70	2-NH ₂	1	0	0	Et	Et	H	H	S	S
71	2-NH ₂	1	0	0	Cyclopentyl		H	H	R	R
72	2-NH ₂	1	0	0	Cyclopentyl		H	H	S	S
73	2-NH ₂	1	0	0	Cyclohexyl		H	H	R	R
74	2-NH ₂	1	0	0	Cyclohexyl		H	H	S	S
75	2-NH ₂	1	0	0	Methylbenzene		H	H	R	R
76	2-NH ₂	1	0	0	Methylbenzene		H	H	S	S
77	2-NO ₂	1	0	0	Me	Me	H	H	R	R

78	2-NO2	1	0	0	Me	Me	H	H	S	S
79	2-NO2	1	0	0	Me	H	H	H	R	R
80	2-NO2	1	0	0	Me	H	H	H	S	S
81	2-NO2	1	0	0	Et	Et	H	H	R	R
82	2-NO2	1	0	0	Et	Et	H	H	S	S
83	2-NO2	1	0	0	Cyclopentyl		H	H	R	R
84	2-NO2	1	0	0	Cyclopentyl		H	H	S	S
85	2-NO2	1	0	0	Cyclohexyl		H	H	R	R
86	2-NO2	1	0	0	Cyclohexyl		H	H	S	S
87	2-NO2	1	0	0	Methylbenzene		H	H	R	R
88	2-NO2	1	0	0	Methylbenzene		H	H	S	S
89	2-NO2	1	0	0	Cyclocarbonyl		H	H	R	R
90	2-NO2	1	0	0	Cyclocarbonyl		H	H	S	S
91	2-Me	1	0	0	Me	Me	H	H	R	R
92	2-Me	1	0	0	Me	Me	H	H	S	S
93	2-Me	1	0	0	Me	H	H	H	R	R
94	2-Me	1	0	0	Me	H	H	H	S	S
95	2-Me	1	0	0	Et	Et	H	H	R	R
96	2-Me	1	0	0	Et	Et	H	H	S	S
97	2-Me	1	0	0	Cyclopentyl		H	H	R	R

98	2-Me	1	0	0	Cyclopentyl		H	H	S	S
99	2-Me	1	0	0	Cyclohexyl		H	H	R	R
100	2-Me	1	0	0	Cyclohexyl		H	H	S	S
101	2-Me	1	0	0	Methylbenzene		H	H	R	R
102	2-Me	1	0	0	Methylbenzene		H	H	S	S
103	2-MeNH	1	0	0	Me	Me	Me	H	R	R
104	2-MeNH	1	0	0	Me	Me	Me	H	S	S
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107	H	1	0	0	Et	Et	H	H	R	R
108	H	1	0	0	Et	Et	H	H	S	S
109	H	1	0	0	Cyclopentyl		H	H	R	R
110	H	1	0	0	Cyclopentyl		H	H	S	S
111	H	1	0	0	Cyclohexyl		H	H	R	R
112	H	1	0	0	Cyclohexyl		H	H	S	S
113	H	1	1	1	Me	Me	H	H	R	R
114	H	1	1	1	Me	Me	H	H	S	S
115	H	1	1	1	Et	Et	H	H	R	R
116	H	1	1	1	Et	Et	H	H	S	S
117	H	1	1	1	Cyclopentyl		H	H	R	R
118	H	1	1	1	Cyclopentyl		H	H	S	S

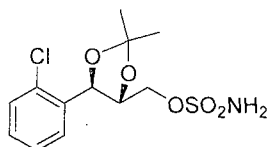
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121	H	1	1	0	Me	Me	H	H	R	R
122	H	1	1	0	Me	Me	H	H	S	S
123	H	1	1	0	Et	Et	H	H	R	R
124	H	1	1	0	Et	Et	H	H	S	S
125	H	1	1	0	Cyclopentyl		H	H	R	R
126	H	1	1	0	Cyclopentyl		H	H	S	S
127	H	1	1	0	Cyclohexyl		H	H	R	R
128	H	1	1	0	Cyclohexyl		H	H	S	S
129	H	1	0	1	Me	Me	H	H	R	R
130	H	1	0	1	Me	Me	H	H	S	S
131	H	1	0	1	Et	Et	H	H	R	R
132	H	1	0	1	Et	Et	H	H	S	S
133	H	1	0	1	Cyclopentyl		H	H	R	R
134	H	1	0	1	Cyclopentyl		H	H	S	S
135	H	1	0	1	Cyclohexyl		H	H	R	R
136	H	1	0	1	Cyclohexyl		H	H	S	S
137	2-Cl	1	1	1	Me	Me	H	H	R	R
138	2-Cl	1	1	1	Me	Me	H	H	S	S
139	2-Cl	1	1	1	Et	Et	H	H	R	R
140	2-Cl	1	1	1	Et	Et	H	H	S	S

141	2-Cl	1	1	1	Cyclopentyl		H	H	R	R
142	2-Cl	1	1	1	Cyclopentyl		H	H	S	S
143	2-Cl	1	1	1	Cyclohexyl		H	H	R	R
144	2-Cl	1	1	1	Cyclohexyl		H	H	S	S
145	2-Cl	1	1	0	Me	Me	H	H	R	R
146	2-Cl	1	1	0	Me	Me	H	H	S	S
147	2-Cl	1	1	0	Et	Et	H	H	R	R
148	2-Cl	1	1	0	Et	Et	H	H	S	S
149	2-Cl	1	1	0	Cyclopentyl		H	H	R	R
150	2-Cl	1	1	0	Cyclopentyl		H	H	S	S
151	2-Cl	1	1	0	Cyclohexyl		H	H	R	R
152	2-Cl	1	1	0	Cyclohexyl		H	H	S	S
153	2-Cl	1	0	1	Me	Me	H	H	R	R
154	2-Cl	1	0	1	Me	Me	H	H	S	S
155	2-Cl	1	0	1	Et	Et	H	H	R	R
156	2-Cl	1	0	1	Et	Et	H	H	S	S
157	2-Cl	1	0	1	Cyclopentyl		H	H	R	R
158	2-Cl	1	0	1	Cyclopentyl		H	H	S	S
159	2-Cl	1	0	1	Cyclohexyl		H	H	R	R
160	2-Cl	1	0	1	Cyclohexyl		H	H	S	S
161	2-Cl	1	0	0	Me	Me	H	H	R	S
162	2-Cl	1	0	0	Me	Me	H	H	S	R

177*	2-Cl	1	0	0	Me	Me	H	H	S	S	
*: Sodium salt											
Table 2: Example of sulfamate compound(A = Heterocyclic ring)											
No	A	X	n	l	m	R ¹	R ²	R ³	R ⁴	Chiral-1	Chiral-2
16 3	Thiazole	2,4-Cl	2	0	0	Me	Me	H	H	R	S
16 4	Thiazole	2,4-Cl	2	0	0	Me	Me	H	H	S	R
16 5	Thiazole	2-Cl	1	0	0	Me	Me	H	H	R	S
16 6	Thiazole	2-Cl	1	0	0	Me	Me	H	H	S	R
16 7	Thiazole	4-Me	1	0	0	Me	Me	H	H	R	S
16 8	Thiazole	4-Me	1	0	0	Me	Me	H	H	S	R
16 9	Thiazole	2-Cl, 4-Me	2	0	0	Me	Me	H	H	R	S
17 0	Thiazole	2-Cl, 4-Me	2	0	0	Me	Me	H	H	S	R
17 1	Thiophene	H	1	0	0	Me	Me	H	H	S	S
17 2	Thiophene	2-Cl	1	0	0	Me	Me	H	H	S	R

17 3	Pyridine	3-Cl	1	0	0	Me	Me	H	H	Rac.(syn)	Rac.(syn)
17 4	Pyridine	4-Cl	1	0	0	Me	Me	H	H	Rac.(syn)	Rac.(syn)
17 5	Pyrimidin e	H	1	0	0	Me	Me	H	H	Rac.(syn)	Rac.(syn)
17 6	Pyrimidin e	2-Cl	1	0	0	Me	Me	H	H	Rac.(syn)	Rac.(syn)

Example 1-1: ((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate



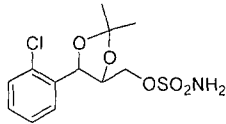
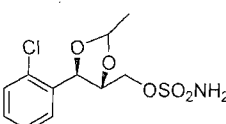
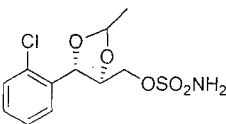
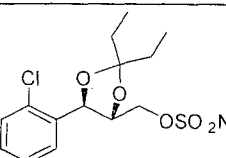
- 5 To a 100ml flask, Acetonitrile (2.26ml, 43.2mmol) was added and cooled to 0°C. Chlorosulfonyl isocyanate (1.5ml, 17.3mmol), and formic acid (0.65ml, 17.3mmol) was added dropwise and stirred at room temperature for 6 hours. ((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (Preparation example 6, 1.05g, 4.3mmol) in N,N-dimethyl acetamide (13.2ml, 142.7mmol) was slowly added at 0°C and stirred at room temperature for 1
- 10 hours. The reaction mixture was quenched with H₂O, extracted with EtOAc, and washed with H₂O. The organic layer was dried over anhydrous magnesium sulfate (MgSO₄), filtered and concentrated. The crude compound was purified by a silica gel column to produce the title compound (1.00g, 50~80%).
- 15 ¹H NMR (400MHz, CDCl₃) δ 1.57 (s, 3H), 1.63 (s, 3H), 4.11~4.10 (m, 1H), 4.53~4.42 (m, 2H), 4.88 (s, 2H), 5.37 (d, J = 8.4, 1H), 7.28~7.56 (m, 4H)

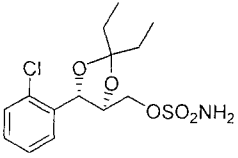
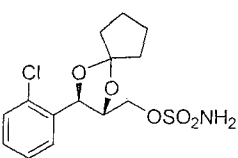
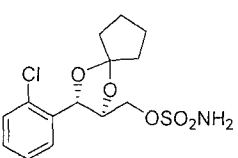
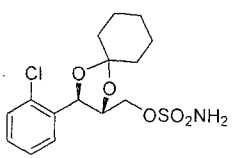
Example 1-2: ((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate

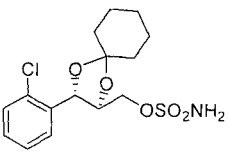
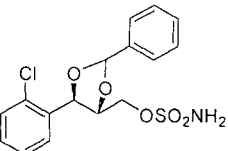
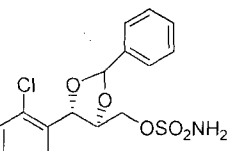
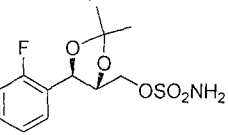
- To a 100 mL RB flask, ((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (Preparation example 6, 10.0 g, 41.2mmol), 50 ml of toluene, 7.92 g (82.4 mmol) of sulfamide and 13.0 g (165 mmol) of pyridine were added at RT. The mixture was refluxed for 1.5 hr (bath temperature 135 °C). The reaction mixture cooled to room temperature then solution was extracted with 27.5 ml (82.4 mmol) of 3N NaOH solution. The aqueous layer was washed with 50 mL of toluene. To the mixture 50 ml of methanol and 35 ml of water was added then acidified to pH 6.0 by slow adding acetic acid to give title compound.(9.9g 60~80%).
- According to the method described in Preparation example 1, the following compounds of Examples 2 to 64, 67 to 88, 91 to 102, 105 to 176 were prepared:

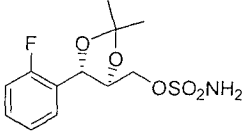
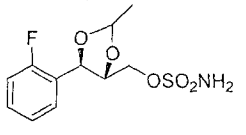
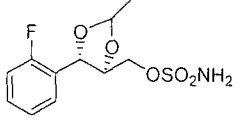
[Table 3] Characterization of the examples of sulfamate compounds

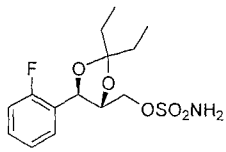
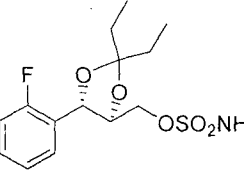
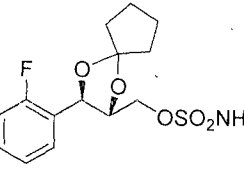
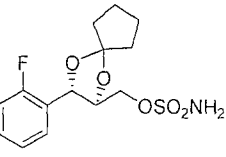
Example No.	Structure	Name	Starting material	¹ H NMR (400MHz)
2		((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 7, 27	¹ H NMR (400MHz) δ 1.59 (s, 3H), 1.65 (s, 3H), 4.12~4.07 (m, 1H), 4.54~4.42 (m, 2H), 4.91 (s, 2H), 5.37 (d, J = 8.8, 1H), 7.29~7.65 (m, 4H)
3		(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SS & RR mixture)	Preparation example 8	¹ H NMR (400MHz) δ 1.57 (s, 3H), 1.63 (s, 3H), 4.11~4.10 (m, 1H), 4.53~4.42 (m, 2H), 4.88 (s, 2H), 5.37 (d, J = 8.4, 1H), 7.28~7.65 (m, 4H)

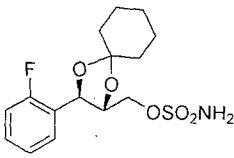
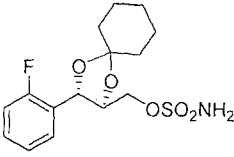
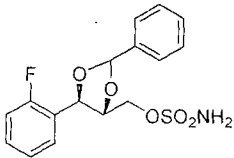
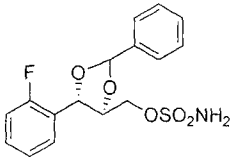
4		(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SR & RS mixture)	Preparation example 374	^1H δ 1.59 (s, 3H), 1.65 (s, 3H), 4.11~4.10 (m, 1H), 4.50~4.42 (m, 2H), 4.85 (s, 2H), 5.35 (d, J = 8.4, 1H) 7.28~7.65 (m, 4H)
5		((4R,5R)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 61	^1H δ 1.40 (d, J = 6.4, 3H), 4.22 (dt, J = 7.0, J = 3.3, 1H), 4.7 (d, J = 3.2, 2H), 5.08 (d, J = 7.0, 1H), 5.46 (m, J = 6.4, 1H), 7.26~7.40 (m, 3H), 7.49 (s, 2H), 7.61 (dd, J = 1.2, J = 7.6, 1H).
6		((4S,5S)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 63	^1H δ 1.40 (d, J = 6.4, 3H), 4.22 (dt, J = 7.0, J = 3.3, 1H), 4.7 (d, J = 3.2, 2H), 5.08 (d, J = 7.0, 1H), 5.46 (m, J = 6.4, 1H), 7.26~7.40 (m, 3H), 7.49 (s, 2H), 7.61 (dd, J = 1.2, J = 7.6, 1H).
7		((4R,5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 65	^1H δ 1.59 (s, 10H), 4.17 (m, 3H), 4.98 (d, J = 8.4, 1H), 5.08 (s, 2H), 6.59 (t, J = 8.4,

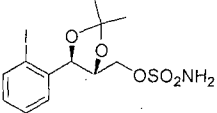
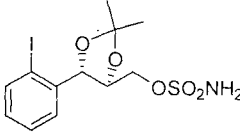
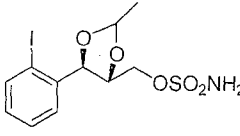
		sulfamate		1H), 6.68 (d, J = 8.4, 1H), 7.04~7.56 (m, 4H)
8		((4S, 5S)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 67	^c δ 1.59 (s, 10H), 4.17 (m, 3H), 4.96 (d, J = 8.4, 1H), 5.08 (s, 2H), 6.59 (t, J = 8.4, 1H), 6.68 (d, J = 8.4, 1H), 7.04~7.56 (m, 4H)
9		((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 69	^D δ 1.64~1.72 (m, 4H), 1.85~19.8 (m, 4H), 4.10~4.16 (m, 2H), 4.17~4.25 (m, 1H), 5.20 (d, J = 7.2, 1H), 7.34~7.62 (m, 6H)
10		((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 71	^D δ 1.64~1.75 (m, 4H), 1.85~19.9 (m, 4H), 4.10~4.16 (m, 2H), 4.17~4.25 (m, 1H), 5.20 (d, J = 7.2, 1H), 7.34~7.62 (m, 6H)
11		((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 73	^D δ 1.51~1.67 (m, 10H), 4.11~4.23 (m, 3H), 4.98 (d, J = 8.0, 2H), 5.08 (s, 1H), 6.59 (t, J = 8.0, 1H), 6.68 (d, J = 8.0, 1H), 7.04~7.56 (m, 4H)

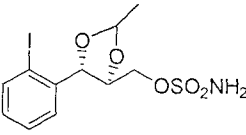
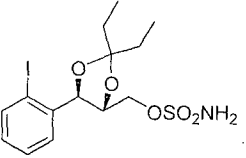
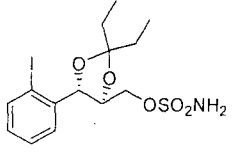
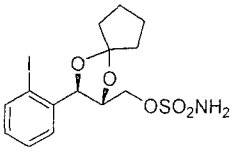
12		((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 75	^D δ 1.51~1.67 (m, 10H), 4.11~4.23 (m, 3H), 4.98 (d, J = 8.0, 2H), 5.08 (s, 1H), 6.59 (t, J = 8.0, 1H), 6.68 (d, J = 8.0, 1H), 7.04~7.56 (m, 4H)
13		((4R,5R)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 77	^D δ 4.25 (dt, J = 3.3, J = 5.7, 1H), 4.55 (d, J = 5.7, 1H), 4.75 (d, J = 3.3, 2H), 5.59 (m, 1H), 6.72~7.75 (m, 2H), 6.92~7.33 (m, 5H), 7.29 (m, 1H), 7.76 (m, 1H)
14		((4S,5S)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 79	^D δ 4.28 (dt, J = 3.3, J = 5.7, 1H), 4.58 (d, J = 5.7, 1H), 4.75 (d, J = 3.3, 2H), 5.62 (m, 1H), 6.72~7.75 (m, 2H), 6.92~7.33 (m, 5H), 7.29 (m, 1H), 7.76 (m, 1H)
15		((4R,5R)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 13	^D δ 1.47 (d, J=11.6, 6H), 3.35~3.94 (m, 1H), 4.02~4.20 (m, 1H), 4.23 (d, J=2.0 1H), 5.07 (d, J = 8.4, 1H), 7.21~7.58 (m,

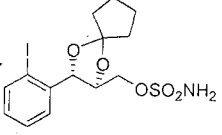
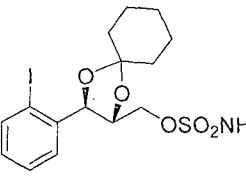
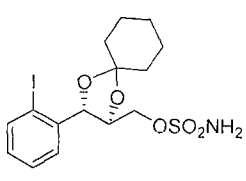
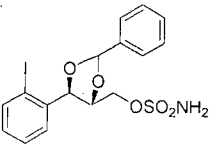
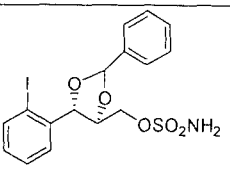
				4H)
16		((4S,5S)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 15	$^D\delta$ 1.47 (d, J=11.6, 6H), 3.35~3.94 (m, 1H), 4.02~4.20 (m, 1H), 4.23(d, J=2.0 1H), 5.07 (d, J = 8.4, 1H), 7.21~7.58 (m, 4H)
17		((4R,5R)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 84	$^D\delta$ 1.40 (d, J = 6.4, 3H), 4.7 (d, J = 3.2, 2H), 5.46 (m, J = 6.4, 1H), 4.22 (dt, J = 3.3, J = 7.0, 1H), 5.08 (d, J = 7.0, 1H), 7.26~7.40 (m, 3H), 7.49 (s, 2H), 7.61 (dd, J = 1.2, J = 7.6, 1H).
18		((4S,5S)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 86	$^D\delta$ 1.40 (d, J = 6.4, 3H), 4.7 (d, J = 3.2, 2H), 5.46 (m, J = 6.4, 1H), 4.22 (dt, J = 3.3, J = 7.0, 1H), 5.18 (d, J = 7.0, 1H), 7.26~7.40 (m, 3H), 7.52 (s, 2H), 7.61 (dd, J = 1.2, J = 7.6, 1H).

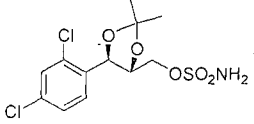
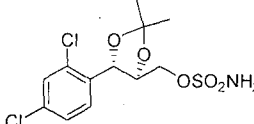
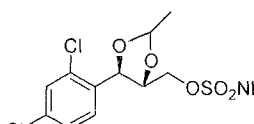
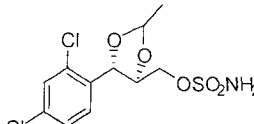
19		((4R,5R)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 88	^1H δ 1.59 (s, 10H), 4.17 (m, 3H), 4.98 (d, J = 8.4, 1H), 5.08 (s, 2H), 6.59 (t, J = 8.4, 1H), 6.68 (d, J = 8.4, 1H), 7.04~7.56 (m, 4H)
20		((4S,5S)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 90	^1H δ 1.59 (s, 10H), 4.14 (m, 3H), 4.98 (d, J = 8.4, 1H), 5.05 (s, 2H), 6.59 (t, J = 8.4, 1H), 6.65 (d, J = 8.4, 1H), 7.04~7.60 (m, 4H)
21		((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 92	^1H δ 1.64~1.72 (m, 4H), 1.84~19.8 (m, 4H), 4.10~4.16 (m, 2H), 4.19~4.25 (m, 1H), 5.25 (d, J = 7.2, 1H), 7.34~7.62 (m, 6H)
22		((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 94	^1H δ 1.64~1.72 (m, 4H), 1.85~19.8 (m, 4H), 4.10~4.16 (m, 2H), 4.17~4.25 (m, 1H), 5.20 (d, J = 7.2, 1H), 7.34~7.62 (m, 6H)

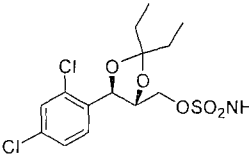
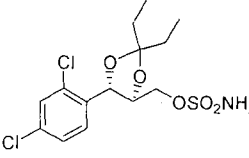
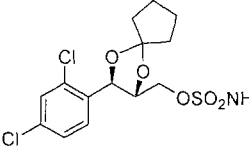
23		((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 96	$^D\delta$ 1.51~1.67 (m, 10H), 4.11~4.23 (m, 3H), 4.98 (d, J = 8.0, 2H), 5.08 (s, 1H), 6.59 (t, J = 8.0, 1H), 6.68 (d, J = 8.0, 1H), 7.04~7.56 (m, 4H)
24		((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 98	$^D\delta$ 1.51~1.67 (m, 10H), 4.11~4.23 (m, 3H), 4.98 (d, J = 8.0, 2H), 5.08 (s, 1H), 6.59 (t, J = 8.0, 1H), 6.68 (d, J = 8.0, 1H), 7.04~7.56 (m, 4H)
25		((4R,5R)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 100	$^D\delta$ 4.25(dt, J=5.7, J=3.3, 1H), 4.59(d, J=5.7, 1H), 4.75(d, J=3.3, 2H), 5.59(m, 1H), 6.72~7.75(m, 2H), 6.92~7.33(m, 5H), 7.25 (m, 1H), 7.76(m, 1H)
26		((4S,5S)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 102	$^D\delta$ 4.25(dt, J=5.7, J=3.3, 1H), 4.59(d, J=5.7, 1H), 4.75(d, J=3.3, 2H), 5.59(m, 1H), 6.72~7.75(m, 2H), 6.92~7.33(m, 5H),

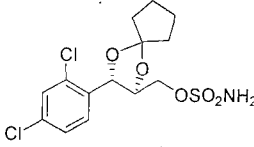
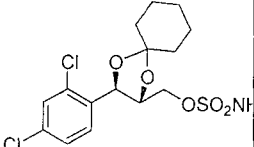
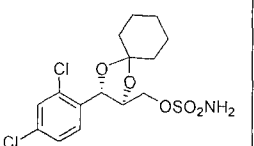
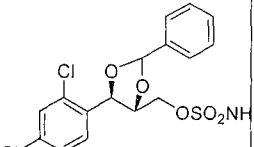
				7.25 (m, 1H), 7.76(m, 1H)
27		((4R,5R)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 21	$^D\delta$ 1.55 (s, 3H), 1.47 (s, 3H) 4.21~4.11 (m, 3H),), 5.10(d, J = 7.6, 1H), 7.56~7.13(m, 3H) 7.60 (s, 2H), 7.91 (d, J = 8.0, 1H)
28		((4S,5S)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 23	$^D\delta$ 1.55 (s, 3H), 1.47 (s, 3H) 4.21~4.11 (m, 3H),), 5.10(d, J = 7.6, 1H), 7.56~7.13(m, 3H) 7.60 (s, 2H), 7.91 (d, J = 8.0, 1H)
29		((4R,5R)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 107	$^D\delta$ 1.40 (d, J = 6.4, 3H), 4.7 (d, J = 3.2, 2H), 5.46 (m, J = 6.4, 1H), 4.22 (dt, J = 3.3, J = 7.0, 1H), 5.10 (d, J = 7.0, 1H), 7.26~7.40 (m, 3H), 7.49 (s, 2H), 7.61 (dd, J = 1.2, J = 7.6, 1H).

30		((4S, 5S)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 109	$^D\delta$ 1.40 (d, J = 6.4, 3H), 4.7 (d, J = 3.2, 2H), 5.46 (m, J = 6.4, 1H), 4.22 (dt, J = 3.3, J = 7.0, 1H), 5.08 (d, J = 7.0, 1H), 7.30-7.40 (m, 3H), 7.61 (s, 2H), 7.65 (dd, J = 1.2, J = 7.6, 1H).
31		((4R, 5R)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 111	$^C\delta$ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 3.96-4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.88(s, 2H), 5.17(d, J = 7.0, 1H), 7.13-7.56(m, 4H)
32		((4S, 5S)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 113	$^C\delta$ 1.46-1.90(m, 8H), 3.96-4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.88(s, 2H), 5.17(d, J = 7.0, 1H), 7.13-7.56(m, 4H)
33		((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 115	$^D\delta$ 1.46-1.90(m, 8H), 3.96-4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.88(s, 2H), 5.17(d, J = 7.0, 1H),

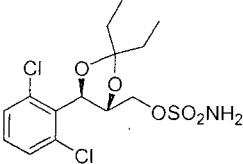
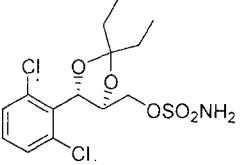
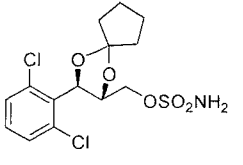
				7.13~7.56(m, 4H)
34		((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 117	$^D\delta$ 1.46~1.92(m, 8H), 3.96~4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.88(s, 2H), 5.22(d, J = 7.0, 1H), 7.13~7.59(m, 4H)
35		((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 119	$^D\delta$ 1.33~1.72(m, 10H), 4.02~4.31(m, 2H), 4.51(q, J = 7.0, 1H), 4.97(s, 2H), 5.25(d, J = 7.0, 1H), 7.19~7.65(m, 4H)
36		((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 121	$^D\delta$ 1.33~1.72(m, 10H), 4.02~4.31(m, 2H), 4.51(q, J = 7.0, 1H), 4.97(s, 2H), 5.25(d, J = 7.0, 1H), 7.19~7.6m, 4H)
37		((4R, 5R)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 123	$^D\delta$ 3.96~4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.92(s, 2H), 5.20(d, J = 7.0, 1H), 5.97(s, 1H), 7.14~7.38(m, 9H)
38		((4S, 5S)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example	$^D\delta$ 3.96~4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.92(s, 2H), 5.20(d, J =

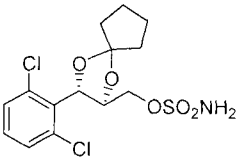
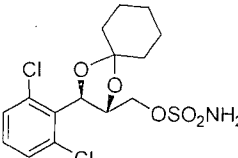
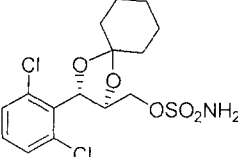
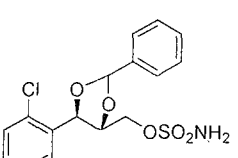
		yl)methyl sulfamate	125	7.0 (s, 1H), 5.97(s, 1H), 7.14~7.38(m, 9H)
39		((4R,5R)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 38	^1H 1.27(s, 6H), 3.90~4.15(m, 2H), 4.37(q, J = 7.0 (s, 1H), 4.79(s, 2H), 5.12(d, J = 7.0 (s, 1H), 7.29~7.42 (m, 2H), 7.79(s, 1H).
40		((4S,5S)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 31	^1H 1.27(s, 6H), 3.90~4.15(m, 2H), 4.37(q, J = 7.0 (s, 1H), 4.79(s, 2H), 5.12(d, J = 7.0 (s, 1H), 7.29~7.42 (m, 2H), 7.79(s, 1H).
41		((4R,5R)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 127	^1H 1.40(s, 3H), 3.81~4.08(m, 2H), 4.25(q, J = 7.0 (s, 1H), 4.81(s, 2H), 5.03(q, J = 6.8 (s, 1H), 5.12(d, J = 7.0 (s, 1H), 7.21~7.27(m, 2H), 7.70(s, 1H).
42		((4S,5S)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 129	^1H 1.40(s, 3H), 3.81~4.08(m, 2H), 4.25(q, J = 7.0 (s, 1H), 4.81(s,

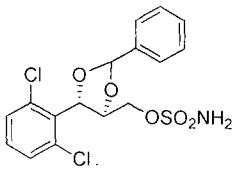
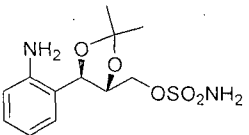
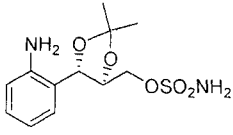
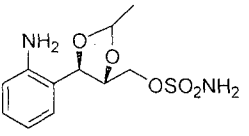
		yl)methyl sulfamate		2H), 5.03(q, $J = 6.8$, 1H), 5.12(d, $J = 7.0$, 1H), 7.21~7.27(m, 2H), 7.70(s, 1H).
43		((4R,5R)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 131	$^c\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 3.96~4.21(m, 2H), 4.42(q, $J = 7.0$, 1H), 4.88(s, 2H), 5.17(d, $J = 7.0$, 1H), 7.24~7.30(m, 2H), 7.73(s, 1H).
44		((4S,5S)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 133	$^c\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 3.96~4.21(m, 2H), 4.42(q, $J = 7.0$, 1H), 4.88(s, 2H), 5.17(d, $J = 7.0$, 1H), 7.24~7.30(m, 2H), 7.73(s, 1H).
45		((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 135	$^d\delta$ 1.46~1.90(m, 8H), 3.79~4.05(m, 2H), 4.25(q, $J = 7.0$, 1H), 4.80(s, 2H), 5.11(d, $J = 7.0$, 1H), 7.28~7.34(m, 2H),

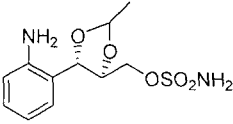
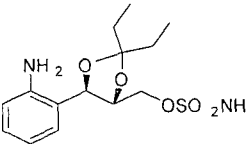
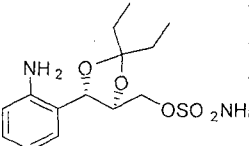
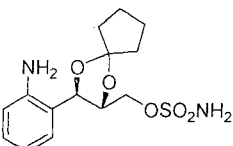
				7.76(s, 1H).
46		((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 137	$^D\delta$ 1.46~1.90(m, 8H), 3.79~4.05(m, 2H), 4.25(q, J = 7.0, 1H), 4.80(s, 2H), 5.11(d, J = 7.0, 1H), 7.28~7.34(m, 2H), 7.76(s, 1H).
47		((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methyl sulfamate	Preparation example 139	$^D\delta$ 1.33~1.72(m, 10H), 3.78~4.03(m, 2H), 4.22(q, J = 7.0, 1H), 4.78(s, 2H), 5.07(d, J = 7.0, 1H), 7.26~7.32(m, 2H), 7.77(s, 1H).
48		((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decane-2-yl)methyl sulfamate	Preparation example 141	$^D\delta$ 1.33~1.72(m, 10H), 3.78~4.03(m, 2H), 4.22(q, J = 7.0, 1H), 4.78(s, 2H), 5.07(d, J = 7.0, 1H), 7.26~7.32(m, 2H), 7.77(s, 1H).
49		((4R, 5R)-5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 143	$^D\delta$ 3.96~4.21(m, 2H), 4.42(q, J = 7.0, 1H), 4.88(s, 2H), 5.17(d, J = 7.0, 1H), 5.97(s, 1H), 7.14~7.39(m, 8H)

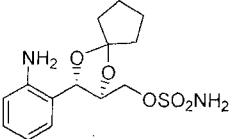
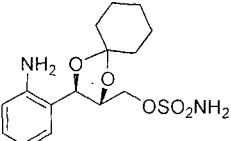
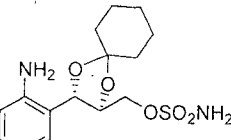
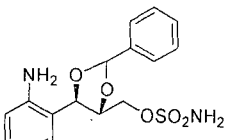
50		((4S,5S)-5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 145	$^D\delta$ 3.96-4.21(m, 2H), 4.42(q, J = 7.0 ,1H), 4.88(s, 2H), 5.17(d, J = 7.0 ,1H), 5.97(s, 1H), 7.14~7.39(m, 8H)
51		((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 41	$^C\delta$ 1.27(s, 6H), 3.96-4.21(m, 2H), 4.42(q, J = 7.0 ,1H), 4.88(s, 2H), 5.17(d, J = 7.0 ,1H), 7.45~7.58(m, 3H).
52		((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 35	$^C\delta$ 1.27(s, 6H), 3.96-4.21(m, 2H), 4.42(q, J = 7.0 ,1H), 4.88(s, 2H), 5.17(d, J = 7.0 ,1H), 7.45~7.58(m, 3H).
53		((4R, 5R)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 147	$^D\delta$ 1.40(s, 3H), 3.88~4.13(m, 2H), 4.42(q, J = 7.0 ,1H), 4.88(s, 2H), 5.07(q, J = 6.8 , 1H), 5.21(d, J = 7.0 ,1H), 5.97(s, 1H), 7.45~7.58(m, 3H).
54		((4S, 5S)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example	$^D\delta$ 1.40(s, 3H), 3.88~4.13(m, 2H), 4.42(q,

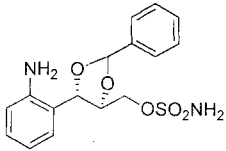
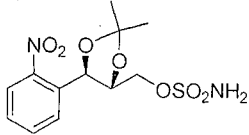
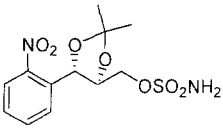
		dioxolan-4-yl)methyl sulfamate	149	$J=7.0$,1H), 4.88(s, 2H), 5.07(q, $J=6.8$, 1H), 5.21(d, $J=7.0$,1H), 5.97(s, 1H), 7.45~7.58(m, 3H).
55		((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 151	$^c\delta$ 0.90(t, $J=8.0$,6H), 1.59(q, $J=8.0$,4H), 3.86~4.11(m, 2H), 4.49(q, $J=7.0$,1H), 4.88(s, 2H), 5.15(d, $J=7.0$,1H), 7.45~7.58(m, 3H).
56		((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 153	$^c\delta$ 0.90(t, $J=8.0$,6H), 1.59(q, $J=8.0$,4H), 3.86~4.11(m, 2H), 4.49(q, $J=7.0$,1H), 4.88(s, 2H), 5.15(d, $J=7.0$,1H), 7.45~7.58(m, 3H).
57		((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 155	$^d\delta$ 1.46~1.90(m, 8H), 3.98~4.24(m, 2H), 4.45(q, $J=7.0$,1H), 4.88(s, 2H), 5.20(d, $J=7.0$,1H),

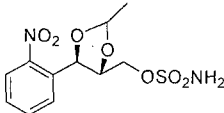
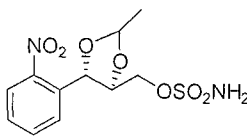
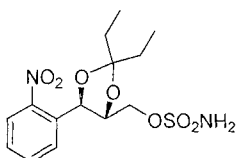
				7.45~7.58(m, 3H).
58		((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 157	^D δ 1.46~1.90(m, 8H), 3.98~4.24(m, 2H), 4.45(q, <i>J</i> =7.0, 1H), 4.88(s, 2H), 5.20(d, <i>J</i> =7.0, 1H), 7.45~7.58(m, 3H).
59		((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 159	^D δ 1.33~1.72(m, 10H), 3.96~4.21(m, 2H), 4.42(q, <i>J</i> =7.0, 1H), 4.88(s, 2H), 5.17(d, <i>J</i> =7.0, 1H), 7.45~7.58(m, 3H).
60		((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 161	^D δ 1.33~1.72(m, 10H), 3.96~4.21(m, 2H), 4.42(q, <i>J</i> =7.0, 1H), 4.88(s, 2H), 5.17(d, <i>J</i> =7.0, 1H), 7.45~7.58(m, 3H).
61		((4R, 5R)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 163	^D δ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dd, <i>J</i> =7.0, <i>J</i> =7.0, 1H), 5.17(d, <i>J</i> =7.0, 1H), 5.79(s, 1H), 7.36~7.38(m, 5H), 7.57~7.58(m, 3H).

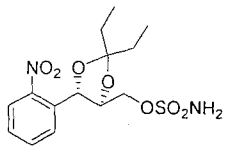
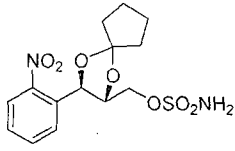
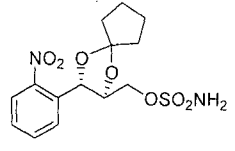
62		((4S, 5S)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 165	$^D\delta$ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dd, $J = 7.0$, $J = 7.0$, 1H), 5.17(d, $J = 7.0$, 1H), 5.79(s, 1H), 7.36~7.38(m, 5H), 7.57~7.58(m, 3H).
63		((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 47	$^D\delta$ 1.27(s, 6H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 6.27(s, 2H), 6.73~7.13(m, 4H).
64		((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 51	$^D\delta$ 1.27(s, 6H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 6.27(s, 2H), 6.73~7.13(m, 4H).
67		((4R, 5R)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 206	$^D\delta$ 1.40(d, $J = 6.8$, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(q, $J = 7.0$, 1H), 5.07(q, $J = 7.0$, 1H), 5.17(d, $J = 7.0$, 1H), 6.27(s, 2H), 6.73~7.13(m, 4H).

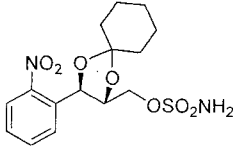
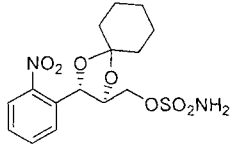
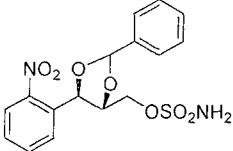
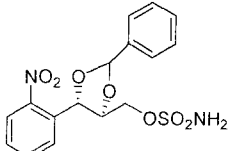
68		((4S, 5S)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 207	$^D\delta$ 1.40(d, J = 6.8, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(q, J = 7.0, 1H), 5.07(q, J = 7.0, 1H), 5.17(d, J = 7.0, 1H), 6.27(s, 2H), 6.73~7.13(m, 4H)
69		((4R, 5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 208	$^C\delta$ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 6.27(s, 2H), 6.71~7.14(m, 4H).
70		((4S, 5S)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 209	$^C\delta$ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 6.27(s, 2H), 6.71~7.14(m, 4H).
71		((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4.4]non-2-yl)methyl sulfamate	Preparation example 210	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02,

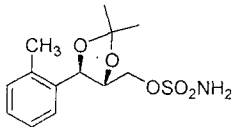
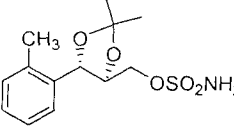
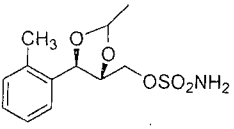
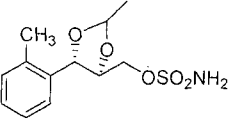
		sulfamate		$J = 3.27, 1\text{H}$), 5.17(d, $J = 7.0$, 1H), 6.27(s, 2H), 6.70~7.11(m, 4H)
72		((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 211	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27, 1\text{H}$), 5.17(d, $J = 7.0$, 1H), 6.27(s, 2H), 6.70~7.11(m, 4H)
73		((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4.5]decane-2-yl)methyl sulfamate	Preparation example 212	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.43(dt, $J = 7.02$, $J = 3.27, 1\text{H}$), 5.17(d, $J = 7.0$, 1H), 6.25(s, 2H), 6.71~7.12(m, 4H).
74		((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4.5]decane-2-yl)methyl sulfamate	Preparation example 213	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.43(dt, $J = 7.02$, $J = 3.27, 1\text{H}$), 5.17(d, $J = 7.0$, 1H), 6.25(s, 2H), 6.71~7.12(m, 4H)
75		((4R, 5R)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 214	$^D\delta$ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27, 1\text{H}$),

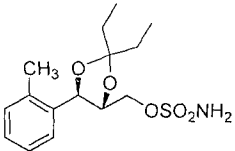
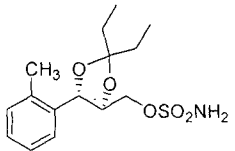
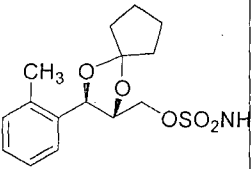
		yl)methyl sulfamate		5.17(d, $J = 7.0$, 1H), 5.79(s, 1H), 6.27(s, 2H), 6.73~6.74(m, 2H), 7.11~7.13(m, 2H), 7.36~7.38(m, 5H).
76		((4S, 5S)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 215	$^D\delta$ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 5.79(s, 1H), 6.27(s, 2H), 6.73~6.74(m, 2H), 7.11~7.13(m, 2H), 7.36~7.38(m, 5H).
77		((4R, 5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 46	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
78		((4S, 5S)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 50	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m,

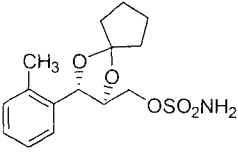
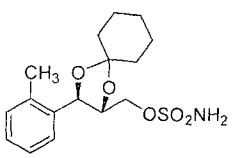
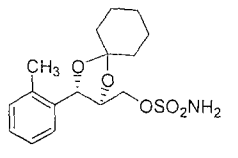
				2H), 7.77~7.90(m, 2H).
79		((4R, 5R)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 167	^D δ 1.40(d, <i>J</i> = 6.8, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(q, <i>J</i> = 7.0, 1H), 5.07(q, <i>J</i> = 7.0, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
80		((4S, 5S)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 169	^D δ 1.40(d, <i>J</i> = 6.8, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(q, <i>J</i> = 7.0, 1H), 5.07(q, <i>J</i> = 7.0, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
81		((4R, 5R)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 171	^C δ 0.90(t, <i>J</i> = 8.0, 6H), 1.59(q, <i>J</i> = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

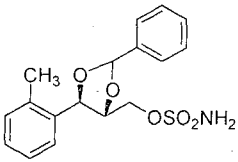
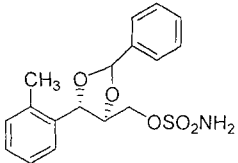
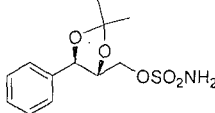
82		((4S,5S)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 173	$^c\delta$ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
83		((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate	Preparation example 175	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
84		((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate	Preparation example 177	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

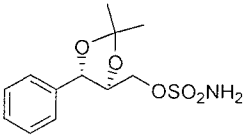
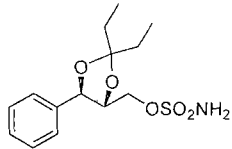
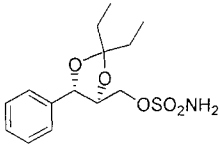
85		((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 179	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
86		((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 181	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
87		((4R, 5R)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 183	$^D\delta$ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 5.79(s, 1H), 6.73~6.74(m, 2H), 7.11~7.13(m, 2H), 7.36~7.38(m, 5H).
88		((4S, 5S)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 185	$^D\delta$ 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 5.79(s, 1H), 6.73~6.74(m, 2H),

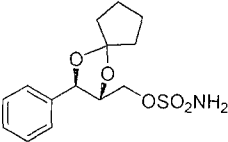
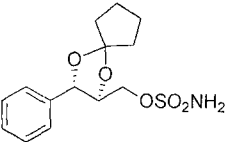
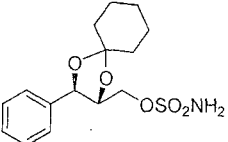
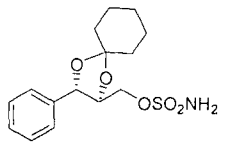
				7.11~7.13(m, 2H), 7.36~7.38(m, 5H).
91		((4R, 5R)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 56	^c δ 1.38(s, 3H), 1.40(s, 3H), 2.24(s, 3H), 4.29(d, <i>J</i> =3.3, 2H), 4.74(dt, <i>J</i> =7.0, <i>J</i> =3.3, 1H), 5.06 (d, <i>J</i> =7.0, 1H), 5.52(s, 2H), 7.13~7.29(m, 4H)
92		((4S, 5S)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 59	^c δ 1.38(s, 3H), 1.40(s, 3H), 2.24(s, 3H), 4.29(d, <i>J</i> =3.3, 2H), 4.74(dt, <i>J</i> =7.0, <i>J</i> =3.3, 1H), 5.06 (d, <i>J</i> =7.0, 1H), 5.52(s, 2H), 7.13~7.29(m, 4H)
93		((4R, 5R)-5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 187	^c δ 1.40(d, <i>J</i> =6.4, 3H), 2.24(s, 3H), 4.27(dt, <i>J</i> =7.0, <i>J</i> =3.3, 1H), 4.70(d, <i>J</i> =3.3, 2H), 5.13(d, <i>J</i> =7.0, 1H), 5.40(q, <i>J</i> =6.4, 1H), 5.52(s, 2H), 7.13~7.29(m, 4H)
94		((4S, 5S)-5-(2-methylphenyl)-2-methyl-1,3-	Preparation example	^c δ 1.40(d, <i>J</i> =6.4, 3H), 2.24(s, 3H), 4.27(dt, <i>J</i> =7.0,

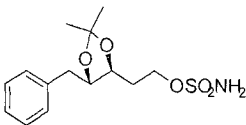
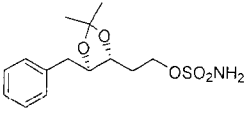
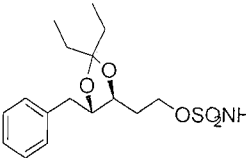
		dioxolan-4-yl)methyl sulfamate	189	$J=3.3$, 1H), 4.70(d, $J=3.3$, 2H), 5.13(d, $J=7.0$, 1H), 5.40(q, $J=6.4$, 1H), 5.52(s, 2H), 7.13~7.29(m, 4H)
95		((4R, 5R)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 191	$^c \delta$ 1.05(t, $J=6.8$, 3H), 1.15(t, $J=6.8$, 3H), 1.77~1.85(m, 4H), 2.24(s, 3H), 4.35(d, $J=3.3$, 2H), 4.75(dt, $J=7.0$, $J=3.3$, 1H), 5.10(d, $J=7.0$, 1H), 5.52(s, 2H), 7.18~7.30(m, 4H)
96		((4S, 5S)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 193	$^c \delta$ 1.05(t, $J=6.8$, 3H), 1.15(t, $J=6.8$, 3H), 1.77~1.85(m, 4H), 2.24(s, 3H), 4.35(d, $J=3.3$, 2H), 4.75(dt, $J=7.0$, $J=3.3$, 1H), 5.10(d, $J=7.0$, 1H), 5.52($\overline{s}$, 2H), 7.18~7.30(m, 4H)
97		((2R, 3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4.4]nonane-2-yl)methyl sulfamate	Preparation example 195	$^c \delta$ 1.60~1.70(m, 4H), 1.74~1.99(m, 4H), 2.24(s, 3H), 4.75(d, $J=3.267$, 2H), 4.36(dt,

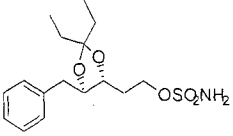
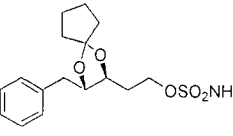
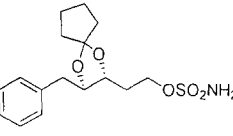
		sulfamate		$J=7.1$, $J=3.3$, 1H), 5.13(d, $J=7.0$, 1H), 5.52(s, 2H), 7.13~7.30(m, 4H)
98		((2S, 3S)-3-(2-methylphenyl)- 1,4- dioxaspiro[4,4]nonane-2-yl)methyl sulfamate	Prepara tion example 197	$^c \delta$ 1.60~1.70(m, 4H), 1.74~1.99(m, 4H), 2.24(s, 3H), 4.75(d, $J=3.267$, 2H), 4.36(dt, $J=7.1$, $J=3.3$, 1H), 5.13(d, $J=7.0$, 1H), 5.52(s, 2H), 7.13~7.30(m, 4H)
99		((2R, 3R)-3-(2-methylphenyl)- 1,4- dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Prepara tion example 199	$^c \delta$ 1.40~1.49(m, 2H), 1.53~1.60(m, 4H), 1.61~2.09(m, 4H), 2.24(s, 3H), 4.23(d, $J=3.3$, 2H), 4.75(dt, $J=7.0$, $J=3.3$, 1H), 5.10(d, $J=7.0$, 1H), 5.62(s, 2H), 7.13~7.30(m, 4H)
100		((2S, 3S)-3-(2-methylphenyl)- 1,4- dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Prepara tion example 201	$^c \delta$ 1.40~1.49(m, 2H), 1.53~1.60(m, 4H), 1.61~2.09(m, 4H), 2.24(s, 3H), 4.23(d, $J=3.3$, 2H), 4.75(dt, $J=7.0$, $J=3.3$, 1H), 5.10(d, $J=7.0$, 1H), 5.62(s, 2H), 7.13~7.30(m, 4H)

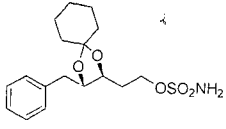
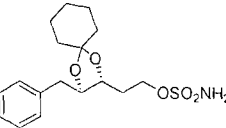
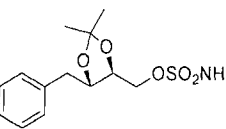
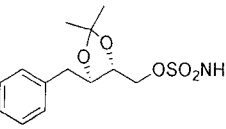
101		((4R, 5R)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 203	^c δ 2.24(s, 3H), 4.35(d, <i>J</i> =3.3, 2H), 4.64(d, <i>J</i> =5.7, 1H), 4.75(dt, <i>J</i> =5.7, <i>J</i> =3.3, 1H), 5.59(m, 1H), 5.78(s, 2H), 7.13~7.29(m, 4H), 7.33(ddt, <i>J</i> =7.7, <i>J</i> =7.5, <i>J</i> =1.5, 1H), 7.40~7.75(m, 4H)
102		((4S, 5S)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 205	^c δ 2.24(s, 3H), 4.35(d, <i>J</i> =3.3, 2H), 4.64(d, <i>J</i> =5.7, 1H), 4.75(dt, <i>J</i> =5.7, <i>J</i> =3.3, 1H), 5.59(m, 1H), 5.78(s, 2H), 7.13~7.29(m, 4H), 7.33(ddt, <i>J</i> =7.7, <i>J</i> =7.5, <i>J</i> =1.5, 1H), 7.40~7.75(m, 4H)
105		((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 219	^d δ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)

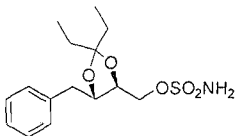
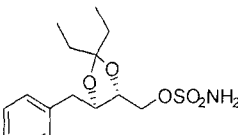
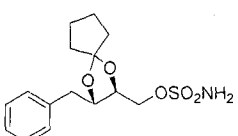
106		((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 222	^D δ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
107		((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 224	^C δ 0.90(t, <i>J</i> = 8.0, 6H), 1.59(q, <i>J</i> = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
108		((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 226	^C δ 0.90(t, <i>J</i> = 8.0, 6H), 1.59(q, <i>J</i> = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)

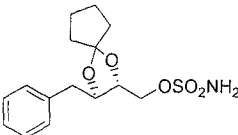
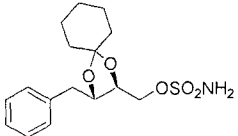
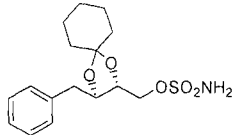
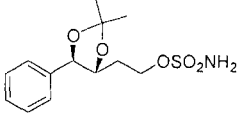
109		((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 228	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
110		((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 230	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
111		((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)methyl sulfamate	Preparation example 232	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
112		((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)methyl sulfamate	Preparation example 234	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H),

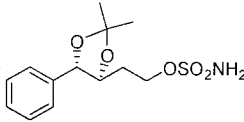
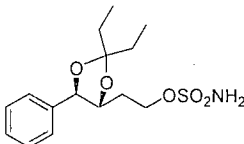
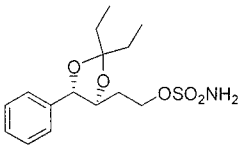
		sulfamate		5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
113		2-((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 241	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
114		2-((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 244	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
115		2-((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 247	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m,

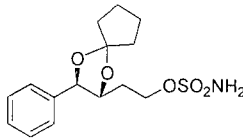
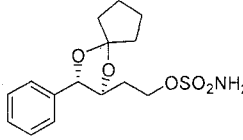
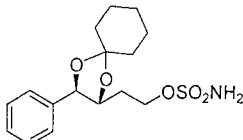
				2H).
116		2-((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 250	^1H δ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
117		2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate	Preparation example 252	^1H δ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
118		2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate	Preparation example 254	^1H δ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

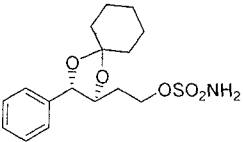
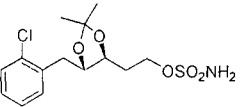
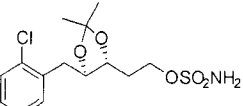
119		2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,5]decane-2-yl)ethyl sulfamate	Preparation example 256	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
120		2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,5]decane-2-yl)ethyl sulfamate	Preparation example 258	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
121		((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 262	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
122		((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 271	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H),

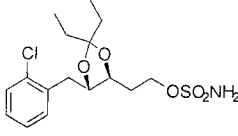
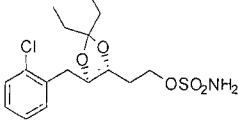
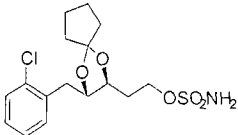
		sulfamate		5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
123		((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 264	$^c\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
124		((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 273	$^c\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
125		((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 266	$^d\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m,

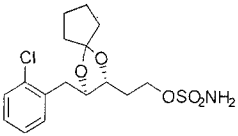
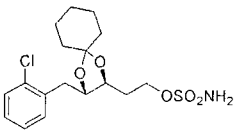
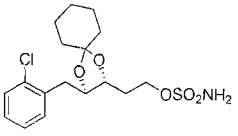
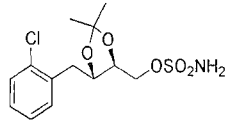
				2H), 7.77~7.90(m, 2H).
126		((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.4]nonan-2-yl)methyl sulfamate	Preparation example 275	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
127		((2S, 3S)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)methyl sulfamate	Preparation example 268	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
128		((2R, 3R)-3-benzyl-1,4-dioxaspiro[4.5]decan-2-yl)methyl sulfamate	Preparation example 277	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
129		2-((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolane-4-yl)methyl sulfamate	Preparation example	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H),

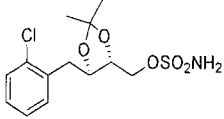
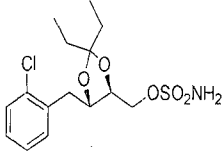
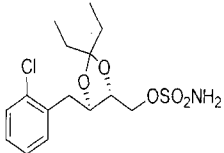
		dioxolan-4-yl)ethyl sulfamate	285	3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
130		2-((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 289	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
131		2-((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 291	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
132		2-((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl	Preparation example 297	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$,

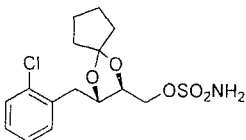
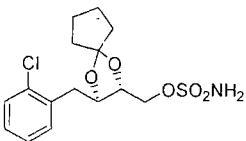
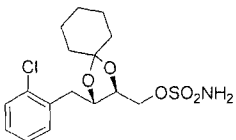
		sulfamate		$J = 3.27, 1\text{H}),$ 5.17(d, $J = 7.0,$ 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
133		2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl sulfamate	Preparation example 293	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02,$ $J = 3.27, 1\text{H}),$ 5.17(d, $J = 7.0, 1\text{H}),$ 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
134		2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl sulfamate	Preparation example 299	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02,$ $J = 3.27, 1\text{H}),$ 5.17(d, $J = 7.0, 1\text{H}),$ 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
135		2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4.5]decan-2-yl)ethyl sulfamate	Preparation example 295	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02,$ $J = 3.27, 1\text{H}),$ 5.17(d, $J = 7.0, 1\text{H}),$ 7.62~7.64(m, 2H), 7.77~7.90(m,

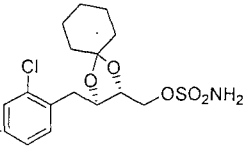
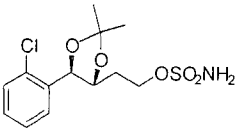
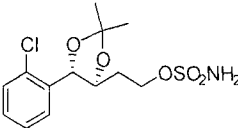
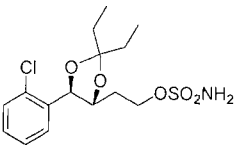
				2H).
136		2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate	Preparation example 301	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
137		2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 308	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
138		2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 311	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

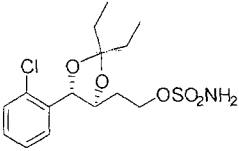
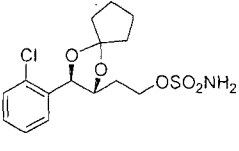
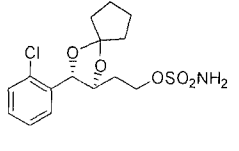
139		2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 314	^1H δ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
140		2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 317	^1H δ 0.90(t, J = 8.0, 6H), 1.59(q, J = 8.0, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
141		2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4.4]nonan-2-yl)ethyl sulfamate	Preparation example 319	^1H δ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, J = 7.02, J = 3.27, 1H), 5.17(d, J = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

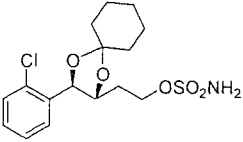
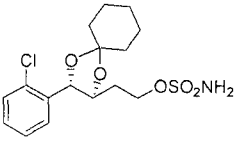
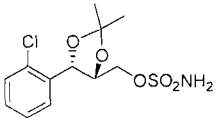
142		2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate	Preparation example 321	$^D\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H)
143		2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate	Preparation example 323	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
144		2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate	Preparation example 325	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
145		((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 329	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H),

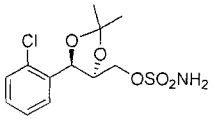
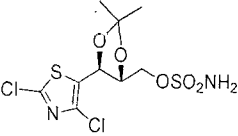
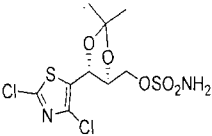
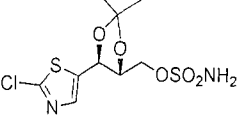
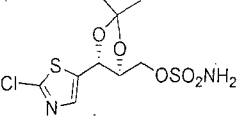
		sulfamate		5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
146		((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 338	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
147		((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 331	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
148		((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 340	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H).

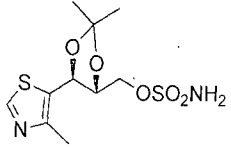
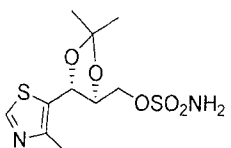
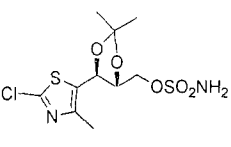
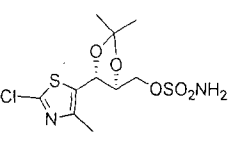
				2H), 7.77~7.90(m, 2H).
149		((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 333	^D δ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
150		((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate	Preparation example 342	^D δ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
151		((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 335	^D δ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

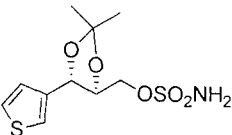
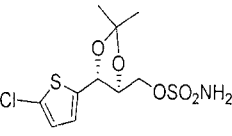
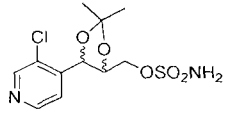
152		((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate	Preparation example 344	$^D\delta$ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
153		2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 352	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
154		2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 356	$^D\delta$ 1.27(s, 6H), 1.40(s, 3H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
155		2-((4R, 5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate	Preparation example 358	$^C\delta$ 0.90(t, $J = 8.0$, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H),

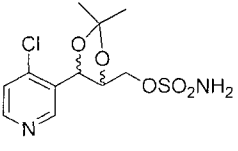
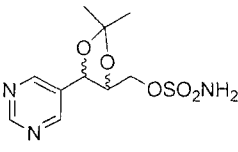
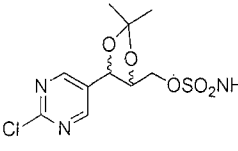
		sulfamate		4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
156		2-((4S, 5S)-5-(2-chlorophenyl)- 2,2-diethyl-1,3- dioxolan-4- yl)ethyl sulfamate	Prepara tion example 364	$^c\delta$ 0.90(t, $J =$ 8.0, 6H), 1.59(q, $J = 8.0$, 4H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
157		2-((2R, 3R)-3-(2- chlorophenyl)- 1,4- dioxaspiro[4.4]no nan-2-yl)ethyl sulfamate	Prepara tion example 360	$^d\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
158		2-((2S, 3S)-3-(2- chlorophenyl)- 1,4- dioxaspiro[4.4]no nan-2-yl)ethyl sulfamate	Prepara tion example 366	$^d\delta$ 1.46~1.56(m, 6H), 1.65~1.90(m, 2H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, $J = 7.02$, $J = 3.27$, 1H), 5.17(d, $J = 7.0$,

				1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
159		2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate	Preparation example 362	^D δ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
160		2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate	Preparation example 368	^D δ 1.33~1.72(m, 10H), 2.0(s, 2H), 3.96~4.21(m, 2H), 4.42(dt, <i>J</i> = 7.02, <i>J</i> = 3.27, 1H), 5.17(d, <i>J</i> = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).
161		((4R, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 379	^C δ 1.53 (s, 3H), 1.66 (s, 3H), 3.14~3.06 (m, 2H), 4.26 (d, <i>J</i> = 12, 2H), 4.83~4.78 (m, 1H), 5.63 (d, <i>J</i> = 6.8 Hz, 1H), 7.35~7.16 (m, 8H), 7.61 (dd, <i>J</i> = 7.4, 1.6, 1H)

162		((4S, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 432	$^c\delta$ 1.58 (s, 3H), 1.70 (s, 3H), 3.68-3.88 (m, 2H), 4.61 (s, 2H), 4.88-4.93 (m, 1H), 5.64 (d, J = 6.8 Hz, 1H), 7.29-7.66 (m, 4H)
163		((4R, 5S)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 383	$^d\delta$ 1.44(s, 3H), 1.45(s, 3H), 4.21~4.24(m, 1H), 4.25~4.27(m, 2H), 5.17(d, J = 7.6, 1H), 7.64(brs, 2H).
164		((4S, 5R)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 386	$^d\delta$ 1.44(s, 3H), 1.45(s, 3H), 4.21~4.24(m, 1H), 4.25~4.27(m, 2H), 5.17(d, J = 7.6, 1H), 7.64(brs, 2H).
165		((4R, 5S)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 390	$^d\delta$ 1.42(s, 3H), 1.43(s, 3H), 4.16~4.19(m, 1H), 4.20~4.22(m, 2H), 5.20(d, J =8.4, 1H), 7.65(brs, 2H), 7.74(s, 1H).
166		((4R, 5S)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 393	$^d\delta$ 1.42(s, 3H), 1.43(s, 3H), 4.16~4.19(m, 1H), 4.20~4.22(m, 2H),

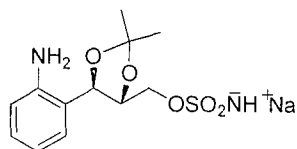
		yl)methylsulfamate		5.20(d, $J=8.4$, 1H), 7.65(brs, 2H), 7.74(s, 1H).
167		((4R, 5S)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 397	$^D\delta$ 1.43(s, 3H), 1.47(s, 3H), 2.39(s, 3H), 4.06~4.10(m, 1H), 4.13(d, $J=4.0$, 2H), 5.27(d, $J=8.0$, 1H), 7.62(brs, 2H), 9.04(s, 1H)
168		((4S, 5R)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 400	$^D\delta$ 1.42(s, 3H), 1.47(s, 3H), 2.39(s, 3H), 4.08~4.11(m, 1H), 4.13(d, $J=4.0$, 2H), 5.27(d, $J=8.0$, 1H), 7.62(brs, 2H), 9.04(s, 1H).
169		((4R, 5S)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 401	$^D\delta$ 1.43(s, 3H), 1.44(s, 3H), 2.33(s, 3H), 4.11~4.25(m, 1H), 4.15(d, $J=4.4$, 2H), 5.22(d, $J=8.0$, 1H), 7.62(br s, 2H).
170		((4S, 5R)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)methylsulfamate	Preparation example 402	$^D\delta$ 1.43(s, 3H), 1.44(s, 3H), 2.33(s, 3H), 4.11~4.25(m, 1H),

		yl)-1,3-dioxolan-4-yl)methylsulfamate		4.15(d, $J=4.4$, 2H), 5.22(d, $J=8.0$, 1H), 7.62(br s, 2H).
171		((4S, 5S)-2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 406	$^D\delta$ 1.41(s, 3H), 1.45(s, 3H), 4.05~4.15(m, 2H), 4.54~4.71(m, 1H), 4.94(d, $J=7.6$, 1H), 7.03(d, $J=3.6$, 1H), 7.14(s, 1H), 7.22(brs, 2H), 7.42(d, $J=3.6$, 1H)
172		((4S, 5R)-2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 410	$^D\delta$ 1.51(s, 3H), 1.54(s, 3H), 4.11~4.14(m, 2H), 4.16~4.18(m, 1H), 5.10(d, $J=7.6$, 1H), 7.05(dd, $J=3.6$, $J=10.0$, 2H), 7.63(brs, 2H)
173		(5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate	Preparation example 415	$^D\delta$ 1.39(s, 3H), 1.48(s, 3H), 4.16~4.21(m, 2H), 4.27~4.22(m, 1H), 5.23(d, $J=8.0$, 1H), 7.37(br s, 2H), 7.62(d, $J=4.0$, 1H), 8.59(d, $J=4.0$, 1H), 8.66(s, 1H)

174		(5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 420	^D δ 1.47(s, 3H), 1.54(s, 3H), 4.23~4.30(m, 2H), 4.40(s, 1H), 5.25(d, , J=8.0, 1H), 7.58(brs, 2H), 7.59(s, 1H), 8.53(d, J=5.2, 1H), 8.75(s, 1H)
175		2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 424	^C δ 1.32(s, 3H), 1.35(s, 3H), 3.86-3.90(m, 1H), 4.06-4.14(m, 2H), 4.82(d, J = 8.0, 2H), 6.92(brs, 2H), 8.63(s, 2H), 8.95(s, 1H).
176		(2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolan-4-yl)methyl sulfamate	Preparation example 428	^C δ 1.29(s, 3H), 1.33(s, 3H), 3.86-3.90(m, 1H), 4.10-4.18(m, 2H), 4.62(d, J = 8.0, 2H), 6.92(brs, 2H), 8.67(s, 2H).

^C: CDCl₃, ^D: DMSO

Example 65: Sodium (((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfonyl)amide

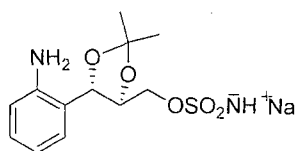


- 5 To stirred solution of ((4R,5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 63, 5.5g) in distilled water(55ml)

was added 1N NaOH(23ml) then heated. After 30min, the resulting mixture cooled to room temperature and concentrated under reduced pressure. The crude product in EA (ethyl acetate, 16.5ml) was slowly added to Ether(200ml) at low temperature. The precipitate was filtered off, washed with Hexane, and dried under vacuum to obtain the title compound (4.7g, 65~85%)

^1H NMR (400MHz, DMSO) δ 1.42(s, 3H), 1.46(s, 3H), 3.79~3.81(m, 2H), 3.99~4.00(m, 1H), 4.94(d, $J=8.4$, 1H), 6.59~7.16(m, 4H).

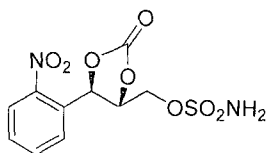
Example 66: Sodium (((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfonyl)amide



The substantially same method as described in example 65 was conducted, except that (((4R,5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 64) was used instead of (((4R,5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 63), to obtain the title compound(4.23g, 65~85%).

^1H NMR (400MHz, DMSO) δ 1.42(s, 3H), 1.46(s, 3H), 3.79~3.81(m, 2H), 3.99~4.00(m, 1H), 4.94(d, $J=8.4$, 1H), 6.59~7.16(m, 4H).

Example 89: (((4R, 5R)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate

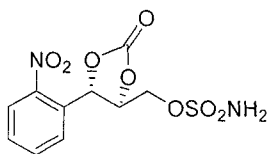


To a stirred solution of (((4R, 5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 77, 5.2g, 16mmol) in EtOAc (50mL)

was added 3N HCl (24.6mL, 80.0mmol) at room temperature. The mixture was stirred for 5h. The resulting mixture was diluted with EtOAc, washed with sat. NaHCO₃, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product stirred in THF (35mL) was added CDI (2.91g, 17.9mmol) at room temperature. The mixture was stirred for 1h. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by SiO₂ gel column chromatography to produce the title compound (2.6g, 60~80%)

¹H NMR (400MHz, CDCl₃) δ 2.0(s, 2H), 4.08~4.33(m, 2H), 4.72(dt, *J* = 7.02, *J* = 3.27, 1H), 5.47(d, *J* = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

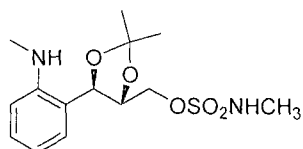
Example 90: ((4S, 5S)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate



The substantially same method as described in example 89 was conducted, except that ((4S, 5S)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 78) was used instead of ((4R, 5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 77), to obtain the title compound(0.9g, 50~80%)

¹H NMR (400MHz, CDCl₃) δ 2.0(s, 2H), 4.08~4.33(m, 2H), 4.72(dt, *J* = 7.02, *J* = 3.27, 1H), 5.47(d, *J* = 7.0, 1H), 7.62~7.64(m, 2H), 7.77~7.90(m, 2H).

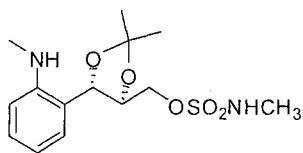
Example 103: ((4R, 5R)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate



To a stirred solution of ((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 63, 0.68g, 2.25mmol) and benzotriazole (0.27g, 2.25mmol) in EtOH (10mL) was slowly added formaldehyde (10wt% in H₂O, 0.62mL, 2.25mmol) and NaBH₄ (0.085g, 2.25mmol) at 0°C. The resulting mixture was diluted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by SiO₂ gel column chromatography to obtain the title compound (0.3g, 30~50%)

¹H NMR (400MHz, CDCl₃) δ 1.40(s, 6H), 2.62(s, 3H), 2.96(s, 3H), 4.25(dt, J=7.0, J=3.3, 1H), 4.75(d, J=3.3, 2H), 4.84(d, J=7.0, 1H), 6.99~7.20(m, 4H)

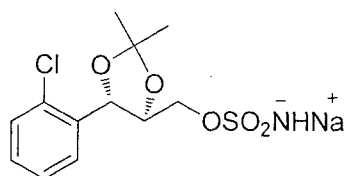
Example 104: ((4S, 5S)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate



The substantially same method as described in example 103 was conducted, except that ((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 64) was used instead of ((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(Example 63), to obtain the title compound(0.5g, 50~80%)

¹H NMR (400MHz, CDCl₃) δ 1.40(s, 6H), 2.62(s, 3H), 2.96(s, 3H), 4.25(dt, J=7.0, J=3.3, 1H), 4.75(d, J=3.3, 2H), 4.84(d, J=7.0, 1H), 6.99~7.20(m, 4H)

Example 177: sodium (((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)sulfonyl)amide



To a stirred solution of ((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate (Example 2, 5.0g, 15.5mmol) in a mixture of MTBE and IPA (50mL, 3:1, v/v) was added 6 N NaOH aqueous solution (2.5mL, 14.2mmol) at room temperature then stirred for 1 hr at 0°C. The resulting mixture was removed solvent. The concentrated residue was added a mixture of H₂O and IPA (15mL, 1:2, v/v) at room temperature then stirred for 30 min. The mixture was added MTBE (75mL) then stirred for 1 hr at 0°C. Solid product was filtered and air-dried to give a title compound. (4.76g, 70~90%).

10 Water content: 1.54%, MP: 1st 67.6~67.7 °C, 2nd 126.9 °C

¹H NMR (400 MHz, DMSO-d₆) δ 1.43 (s, 3H), 1.50 (s, 3H), 3.77 (dd, *J*=7.2, 11.2, 1H), 3.87 (dd, *J*=2.8, 11.2, 1H), 3.99~4.03 (m, 1H), 5.09 (d, *J*=8.4, 1H), 7.35~7.47 (m, 3H), 7.61 (dd, *J*=1.8, 7.4, 1H)

15 Biological Experimental Example. 1: Measurement of Anti-epilepsy activity (MES-test)

In the MES test (Ref., G. Villetti et al. Neuropharmacology 40(2001) 866-878), an electrical stimulus (mice: 50mA, 60Hz, 0.2sec, and rats: 150mA, 60Hz, 0.2sec in the test animal) supplied by an 11A Shocker (IITC Life Science Company) was delivered through corneal electrodes. All mice or rats assigned to any electroshock at peak time were treated with each test compound sample which was dissolved in 20% tween 80 prepared by saline solvent applied orally before the test. If the test animal's stretching of its hind limb in a straight line wasn't observed in the MES test, this results indicated that the test sample had anti-epilepsy activity. Three doses of the test sample were administered orally to 9-18 animals (3-6 mice per dose) for evaluating the respective doses at which 50% of the animals were protected from seizure (ED₅₀). The ED₅₀ value (median effective dose) was calculated by Litchfield and Wicoxon log-probit method which is a dose-response relationship. The test results are shown in the following Table 4~5. Experimental animals, male ICR mice and male SD rats, were purchased from OrientBio, Samtako, or Nara Biotech, Korea, and housed in cages (4-5 mice or 3 rats per cage) for 4-5 days. The range of mice body weight was between 19 and 25 grams and range of rats body weight was between 100 and 130 grams.

[Statistical Analysis]

The obtained results are shown as mean $\pm$ sem. The difference between the groups was statistically analyzed by ANOVA, and then further examined by Dunnett's test or Bonferroni test. If p is less than 0.05, it was determined that the difference between the groups had statistical significance.

[Results]

The results of anti-epileptic activity of the sulfamate derivative compounds measured in the above Experimental Example are shown in the following Tables 4 and 5. In Tables 4 and 5, the ED50 is represented by the concentration where the compound shows 50% of anti-epileptic activity compared to the vehicle only (100%).

[Table 4] Results of the measurements of anti-epileptic activity of the sulfamate derivative compounds

Example No.	mMES(po)	
	ED50(mg/kg)	Peak Time
1	6.5	0.5hr
2	9.0	1hr
3	14.0	4hr
4	50 ^a (33%)	1hr
6	50 ^a (33%)	1hr
8	50 ^b (100%)	1,2,4hr
10	30 ^a (66%)	1,2hr

12	50 ^b (100%)	1,2,4hr
15	50 ^b (100%)	1,2,4hr
16	50 ^a (100%)	1,2,4hr
27	27.6	1hr
28	15.0	1hr
40	49.2	4hr
52	50 ^a (100%)	1,2,4hr
66	12.3	1hr
70	50 ^a (100%)	1,2,4hr
72	14.2	2hr
74	14.5	2hr
76	50 ^a (66%)	1hr
90	9.2	2hr
92	50 ^a (100%)	1,2hr
104	50 ^a (66.6%)	4h
106	30 ^a (100%)	4h
108	50 ^a (100%)	2,4h
110	9 ^a (33.3%)	4h
112	50 ^a (100%)	1,2h
114	80 ^a (33.3%)	2h
116	150 ^a (33.3%)	1h
118	80 ^a (66.6%)	2h

120	80 ^a (66.6%)	1, 2, 4h
122	50 ^a (100%)	1, 2h
124	50 ^a (100%)	1h
126	50 ^a (100%)	2h
128	50 ^a (100%)	4h
130	50 ^a (33.3%)	2h
132	80 ^a (33.3%)	1, 2h
134	50 ^a (100%)	1, 2, 4h
136	50 ^a (100%)	4h
138	80 ^a (33.3%)	4h
140	50 ^a (33.3%)	1h
142	80 ^a (33.3%)	1h
144	100 ^a (33.3%)	1, 2, 4h
146	50 ^a (66.6%)	2, 4h
148	50 ^a (33.3%)	1h
150	50 ^a (100%)	2h
152	50 ^a (66.6%)	2h
154	50 ^a (100%)	4h
156	80 ^a (100%)	1, 2h
158	50 ^a (100%)	2h
160	80 ^a (66.6%)	4h
161	100 ^a (100%)	2, 4h

162	100 ^a (100%)	1,2h
163	50 ^b (50%)	1,2h
164	50 ^a (100%)	4h
165	100 ^a (100%)	2,4h
166	100 ^a (100%)	1,2h
167	100 ^a (100%)	1,2,4h
168	100 ^a (100%)	1,2,4h
169	30 ^a (100%)	1h
170	100 ^a (100%)	1,2,4h
171	43.3	4h
172	30.2	4h
173	100 ^a (100%)	1,2,4h
174	100 ^a (100%)	1,4h
175	100 ^a (100%)	1,2h
176	100 ^a (100%)	2h

a: Injection amount(mg/kg), Protection%(3 mice); b: Injection amount(mg/kg), Protection%(4 mice), %= the percentage of anti-epileptic activity compared to the vehicle only (100%), respectively.

- 5 [Table 5] Results of the measurements of anti-epileptic activity of the sulfamate derivative compounds

Example No.	rMES(po)	
	ED50(mg/kg)	Peak Time

1	1.2	1h
2	3.5	4h
4	5.2	1h
15	50 ^b (66.6%)	
16	7.7	1h
28	32.7	4h
66	11.8	4h
72	1.0	4h
90	1.1	2h
163	6.5	4h
164	13.2	2h
166	1.9	4h
168	4.9	4h
169	15 ^a (100%)	
172	4.7	4h
177	3.5 ^a (100%)	

a: Injection amount(mg/kg), Protection%(3 rats); b: Injection amount(mg/kg), Protection%(6 rats), %= the percentage of anti-epileptic activity compared to the vehicle only (100%), respectively.

5

Biological Experimental Example 2: Lithium-pilocarpine induced epilepsy test(LI-PILO test)

Prevention test

Male Sprague-Dawley rats (purchased from Orient Bio Inc. Korea) of body weight 175 grams were used for these studies and 3 rats per cage were housed for 4-5 days. On the day prior to SE, rats received 127 mg/kg lithium chloride (Sigma, St. Louis, MO, U.S.A.) intraperitoneally (i.p.).

5 Approximately 18-20 h following this treatment, rats were given an i.p. injection of 43 mg/kg pilocarpine (Sigma). An i.p. injection of 2 mg/kg methyl-scopolamine (Sigma) was administered 30 min prior to pilocarpine to block the effects of the muscarinic agonist on peripheral cholinergic receptors. Test drugs were dissolved in 20% tween80 (Sigma).

10 The drugs were administered intraperitoneally (i.p.) in a volume of 2ul/g body weight. Pharmacological effects of all of the test materials were evaluated to compare test groups (n=6) with a control group (n=6). Control group was administered vehicle only. The efficacy was measured 0.5, 1, 2, or 4 hours after the administration of the test material. The time point

15 that the most animals were protected was defined as peak time and the ED50 was determined at peak time. The animals were then transferred to observation cages and observed continuously for 90 min. Seizure was elicited in approximately 95% of the control group. Protection was defined as complete absence of seizure grade 3-5 (Racine scale; Racine, 1972) over

20 the 90-min observation period. The effective dose of the compound necessary to protect 50% of the animals against seizures compared to controls (i.e. ED50) was determined by a curve fitting program (Excel 2007, Microsoft).

Intervention

25 Male Sprague-Dawley rats (purchased from Orient Bio Inc. Korea) of body weight 175 grams were used for these studies and 3 rats per cage were housed for 4-5 days. On the day prior to SE, rats received 127 mg/kg lithium chloride (Sigma, St. Louis, MO, U.S.A.) intraperitoneally (i.p.).

Approximately 18-20 h following this treatment, rats were given an i.p.

30 injection of 43 mg/kg pilocarpine (Sigma). An i.p. injection of 2 mg/kg methyl-scopolamine (Sigma) was administered 30 min prior to pilocarpine to block the effects of the muscarinic agonist on peripheral cholinergic receptors. Test drugs were dissolved in 20% tween80 (Sigma).

The drugs were administered intravenously (i.v.) in a volume of 2ul/g body weight at SE onset. Pharmacological effects of all of the test materials were evaluated to compare test groups (n=3-6) with a control group (n=3-6). Control group was administered vehicle only. The animals were then transferred to observation cages and observed continuously for 90 min. Seizure was elicited in approximately 95% of the control group. Protection was defined as complete absence of seizure grade 3-5 (Racine scale; Racine, 1972) over the 90-min observation period. The effective dose of the compound necessary to protect 50% of the animals against seizures compared to controls (i.e. ED50) was determined by a curve fitting program (Excel 2007, Microsoft).

[Results]

The results of Lithium-pilocarpine induced epilepsy test of the sulfamate derivative compounds measured in the above Experimental Example are shown in the following Tables 6. In Tables 6, the ED50 is represented by the concentration where the compound shows 50% of Lithium-pilocarpine induced epilepsy test compared to the vehicle only (100%).

[Table 6] Results of test compounds' efficacy against lithium-pilocarpine induced seizure (Rats)

Example No.	Anti-epileptogenesis (rat/ip)		Therapeutic effect (min, rat/Iv)
	ED50(mg/kg)	Peak Time(h)	ED50(mg/kg)
1	150 ^b (50%)	2h	
2	97.1	4h	89.0
15	100 ^b (66.6%)	0.5h	

	100 ^b (16.6%)	1h	
	100 ^b (33.3%)	0.5h	
	100 ^b (50%)	2h	
	150 ^b (16.6%)	2h	
28	154.4	1h	
167	30 ^a (100%)	1h	

a: Injection amount(mg/kg), Protection%(3 rats); b: Injection amount(mg/kg), Protection%(6 rats), %= the percentage of anti-epileptic activity compared to the vehicle only (100%), respectively.

5 [Statistical Analysis]

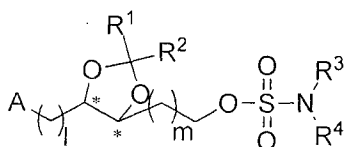
The obtained results are shown as mean±sem. The difference between the groups was statistically analyzed by ANOVA, and then further examined by Dunnett' s test or Bonferroni test. If p is less than 0.05, it was determined that the difference between the groups had statistical significance.

【CLAIMS】

【Claim 1】

A method of preventing or treating epilepsy comprising administering
 5 a pharmaceutically effective amount of a sulfamate derivative compound
 represented by Chemical Formula 1 or a pharmaceutically acceptable salt
 thereof, to a subject in need of preventing or treating epilepsy:

[Chemical formula 1]



10

wherein R^1 and R^2 are each independently selected from the group
 consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl and C_6 - C_{10} aryl, R^1 and R^2
 together with the carbon atom to which they attach form a C_3 - C_{12} cycloalkyl
 group, or R^1 and R^2 are bond and they together with the oxygen atom to
 15 which they attach form a carbonyl group;

A is an aryl moiety or a heterocyclic moiety optionally substituted
 by one or more substituents selected from the group consisting of hydrogen,
 hydroxyl, C_1 - C_5 alkoxy, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_6 - C_{10} aryl, C_1 - C_5
 alkoxy carbonyl, carboxyl, C_2 - C_5 acyl, C_1 - C_5 alkylthio, cyano, nitro, amine,
 20 C_1 - C_5 alkylamine and halogen;

R^3 and R^4 are each independently hydrogen or C_1 - C_3 alkyl; and

l and m are each independently an integer of 0-4

【Claim 2】

The method according to Claim 1, wherein A is the aryl moiety
 25 representing a C_6 - C_{10} aryl group.

【Claim 3】

The method according to Claim 1, wherein A is the heterocyclic
 moiety representing a C_3 - C_{10} heterocyclic group.

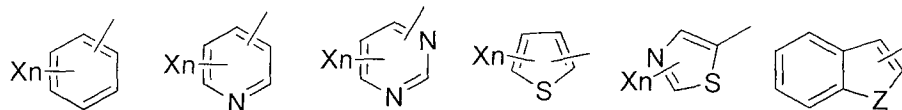
【Claim 4】

The method according to Claim 1, wherein A is a phenyl optionally
 30 substituted by one or more substituents selected from the group consisting
 of hydrogen, halogen, C_1 - C_5 alkyl, nitro, amine and C_1 - C_5 alkylamine or C_3 -
 C_{10} heterocyclic group optionally substituted by one or more substituents

selected from the group consisting of hydrogen, halogen, C₁-C₅ alkyl, and C₆-C₁₀ aryl.

【Claim 5】

The method according to Claim 4, wherein A is selected from the group consisting of:



and

wherein

X is each independently selected from the group consisting of halogen, nitro, amine, and C₁-C₅ alkyl; n is an integer of 0~5; and Z is selected from S, O or NH.

【Claim 6】

The method according to Claim 5, wherein n is an integer of 0~2.

【Claim 7】

The method according to Claim 1, wherein R³ and R⁴ are each independently hydrogen or methyl.

【Claim 8】

The method according to Claim 1, wherein l and m are each independently an integer of 0~2.

【Claim 9】

The method according to Claim 1, wherein the compound is selected from the group consisting of:

- (1) (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
- (2) (5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (3) (5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (4) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (5) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (6) (5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (7) (5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (8) (5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (9) (5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- (10) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (11) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 5 (12) (5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (13) (5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (14) (5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (15) (5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 10 (16) (3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (17) (3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 15 (18) (5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (19) (5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (20) (5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 20 (21) (5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (22) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (23) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 25 (24) (5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (25) (5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 30 (26) (5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (27) (5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (28) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 35 (29) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (30) (5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 40 (31) (5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- (32) (5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
(33) (5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(34) (3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
5 (35) (3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(36) (5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
(37) (5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 (38) (5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
(39) (5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(40) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
15 (41) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(42) (5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
(43) (5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
20 (44) (5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(45) (5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
(46) (5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
25 (47) (3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
(48) (3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(49) (5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
30 (50) (5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methyl sulfamate;
(51) (5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(52) (5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(53) (3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
35 (54) (3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(55) 2-(5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(56) 2-(5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(57) 2-(3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
(58) 2-(3-benzyl-1,4-dioxaspiro[4,5]decane-2-yl)ethyl sulfamate;
40 (59) (5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
(60) (5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- (61) (3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
(62) (3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
(63) (5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
(64) (5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
5 (65) (3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
(66) (3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
(67) 2-(5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
(68) 2-(5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
10 sulfamate;
(69) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
sulfamate;
(70) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
sulfamate;
15 (71) (5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(72) (5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(73) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
20 sulfamate;
(74) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
(75) (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
25 (76) (5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;
(77) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
sulfamate;
(78) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
30 sulfamate;
(79) (5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
yl)methyl sulfamate;
(80) (5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
yl)methylsulfamate;
35 (81) (2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-
yl)methylsulfamate;
(82) (2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-
yl)methylsulfamate;
(83) (2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methylsulfamate;
40 (84) (2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-

yl)methylsulfamate;

(85) (5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;

(86) (5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;

(87) (2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;
and

(88) (2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolan-4-yl)methylsulfamate.

10 **【Claim 10】**

The method according to Claims 1 or 9, wherein the compound is in the form of a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers.

【Claim 11】

15 The method according to Claim 1, wherein the compound is selected from the group consisting of:

((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SS & RR
20 mixture);

(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SR & RS
mixture);

((4R,5R)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S, 5S)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

25 ((4R, 5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S, 5S)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

- ((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R,5R)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
5 ((4R,5R)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((4R,5R)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
15 ((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R,5R)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
20 ((4R,5R)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
5 ((4R,5R)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
((4S,5S)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
10 sulfamate;
((4R,5R)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl
sulfamate;
((4R,5R)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
15 sulfamate;
((4S,5S)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;
20 ((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;
((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
25 sulfamate;
((4R, 5R)-5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl
sulfamate;

- ((4S,5S)-5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 5 ((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 10 ((4S, 5S)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 15 ((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 20 ((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- ((4R, 5R)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 25 ((4S,5 S)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((4R, 5R)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
5 ((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R, 5R)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((4S, 5S)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
15 ((4R, 5R)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
20 ((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;

- ((4S, 5S)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 5 ((4S, 5S)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 10 ((2R, 3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
- ((2R, 3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 15 ((2S, 3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate;
- 20 ((4S, 5S)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate;
- ((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 25 ((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
5 2-((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
10 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,5]decane-2-yl)ethyl sulfamate;
2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
15 ((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
20 ((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
2-((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;

- 2-((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
5 2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
10 2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
15 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
20 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
25 ((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 5 2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
10 sulfamate;
2-((4S, 5S)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
15 2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
20 sulfamate;
((4S, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 25 ((4R,5S)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5R)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-

yl)methyl sulfamate;

((4R,5S)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;

5 ((4S, 5R)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;

((4R, 5S)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

((4S, 5R)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

10 ((4R, 5S)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

((4S, 5R)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

((4S, 5S)-2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methylsulfamate;

15 ((4S, 5R)-2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-yl)methylsulfamate;

Sodium (((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfonyl)amide ;

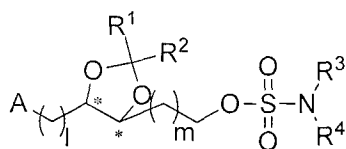
20 Sodium (((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfonyl)amide and

sodium (((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)sulfonyl)amide.

【Claim 12】

25 A pharmaceutical composition for preventing or treating epilepsy comprising a pharmaceutically effective amount of a sulfamate derivatives compound represented by Chemical Formula 1 or a pharmaceutically acceptable salt thereof:

[Chemical formula 1]



wherein R^1 and R^2 are each independently selected from the group consisting of hydrogen, C_1 - C_5 alkyl, C_2 - C_5 alkenyl and C_6 - C_{10} aryl, R^1 and R^2 together with the carbon atom to which they attach form a C_3 - C_{12} cycloalkyl group, or R^1 and R^2 are bond and they together with the oxygen atom to which they attach form a carbonyl group;

A is an aryl moiety or a heterocyclic moiety optionally substituted by one or more substituents selected from the group consisting of hydrogen, hydroxyl, C_1 - C_5 alkoxy, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_6 - C_{10} aryl, C_1 - C_5 alkoxycarbonyl, carboxyl, C_2 - C_5 acyl, C_1 - C_5 alkylthio, cyano, nitro, amine, C_1 - C_5 alkylamine and halogen;

R^3 and R^4 are each independently hydrogen or C_1 - C_3 alkyl; and

l and m are each independently an integer of 0-4.

【Claim 13】

The pharmaceutical composition according to Claim 12, wherein A is an aryl moiety representing a C_6 - C_{10} aryl group.

【Claim 14】

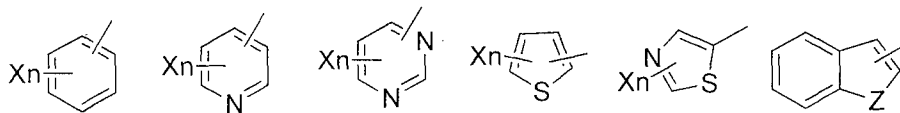
The pharmaceutical composition according to Claim 12, wherein A is a heterocyclic moiety representing a C_3 - C_{10} heterocyclic group.

【Claim 15】

The pharmaceutical composition according to Claim 12, wherein A is a phenyl optionally substituted by one or more substituents selected from the group consisting of hydrogen, halogen, C_1 - C_5 alkyl, nitro, amine and C_1 - C_5 alkylamine or C_3 - C_{10} heterocyclic group optionally substituted by one or more substituents selected from the group consisting of hydrogen, halogen, C_1 - C_5 alkyl, and C_6 - C_{10} aryl.

【Claim 16】

The pharmaceutical composition according to Claim 15, wherein A is selected from the group consisting of:



and

wherein

X is each independently selected from the group consisting of halogen, nitro, amine, and C₁-C₅ alkyl; n is an integer of 0-5; and Z is selected from S, O or NH.

【Claim 17】

5 The pharmaceutical composition according to Claim 16, wherein n is an integer of 0-2.

【Claim 18】

The pharmaceutical composition according to Claim 12, wherein R³ and R⁴ are each independently hydrogen or methyl.

10 【Claim 19】

The pharmaceutical composition according to Claim 12, wherein l and m are each independently an integer of 0-2.

【Claim 20】

15 The pharmaceutical composition according to Claim 12, wherein the compound is selected from the group consisting of:

- (1) (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
- (2) (5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (3) (5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 20 (4) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (5) (3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 25 (6) (5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (7) (5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (8) (5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (9) (5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 30 (10) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (11) (3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 35 (12) (5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (13) (5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (14) (5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;
- (15) (5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl) methyl sulfamate;
- 40 (16) (3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl) methyl sulfamate;

- sulfamate;
(17) (3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
(18) (5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
5 (19) (5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(20) (5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(21) (5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
10 sulfamate;
(22) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;
(23) (3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
15 (24) (5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(25) (5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
(26) (5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl
20 sulfamate;
(27) (5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(28) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;
25 (29) (3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
(30) (5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(31) (5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
30 sulfamate;
(32) (5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
(33) (5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
(34) (3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
35 sulfamate;
(35) (3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;
(36) (5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
(37) (5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
40 sulfamate;
(38) (5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl) methyl sulfamate;

- (39) (5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (40) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 5 (41) (3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (42) (5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (43) (5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
- (44) (5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 10 (45) (5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (46) (5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (47) (3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 15 (48) (3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (49) (5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (50) (5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methyl sulfamate;
- 20 (51) (5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (52) (5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (53) (3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (54) (3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 25 (55) 2-(5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- (56) 2-(5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- (57) 2-(3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
- (58) 2-(3-benzyl-1,4-dioxaspiro[4,5]decane-2-yl)ethyl sulfamate;
- (59) (5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 30 (60) (5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- (61) (3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- (62) (3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- (63) 2-(5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- (64) 2-(5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 35 (65) 2-(3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
- (66) 2-(3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
- (67) 2-(5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- (68) 2-(5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 40 (69) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl

- sulfamate;
 (70) 2-(3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
 sulfamate;
 (71) (5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
 5 sulfamate;
 (72) (5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
 sulfamate;
 (73) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
 sulfamate;
 10 (74) (3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
 sulfamate;
 (75) 2-(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl
 sulfamate;
 (76) 2-(5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
 15 sulfamate;
 (77) 2-(3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
 sulfamate;
 (78) 2-(3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
 sulfamate;
 20 (79) (5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
 (80) (5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
 (81) (2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;
 25 (82) (2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;
 (83) (2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methylsulfamate;
 (84) (2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-yl)methylsulfamate;
 30 (85) (5-(3-chloropyridin-4-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
 (86) (5-(4-chloropyridin-3-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfamate;
 35 (87) (2,2-dimethyl-5-(pyrimidin-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;
 and

(88) (2,2-dimethyl-5-(2-chloropyrimidin-5-yl)-1,3-dioxolan-4-yl)methylsulfamate.

21. The pharmaceutical composition according to Claim 12 or 20, wherein the compound is in the form of a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers.

22. The pharmaceutical composition according to Claim 12, wherein the compound is selected from the group consisting of:

((4R,5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S,5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

10 (5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SS & RR mixture);

(5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate(SR & RS mixture);

((4R,5R)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

15 ((4S, 5S)-5-(2-chlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4R, 5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S, 5S)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;

((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

20 ((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;

((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;

((4R,5R)-5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4S,5S)- 5-(2-chlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;

((4R,5R)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

25 ((4S,5S)-5-(2-fluorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((4R,5R)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-fluorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-fluorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
5 ((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-fluorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R,5R)-5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((4S,5S)- 5-(2-fluorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-iodophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
15 ((4R,5R)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
20 ((2S, 3S)-3-(2-iodophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R,5R)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S,5S)-5-(2-iodophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R,5R)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl

sulfamate;

((4S,5S)-5-(2,4-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R,5R)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

5 ((4S, 5S)-5-(2,4-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R,5R)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

10 ((4S,5S)-5-(2,4-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;

((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl
sulfamate;

15 ((2R, 3R)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;

((2S, 3S)-3-(2,4-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl
sulfamate;

20 ((4R, 5R)-5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4S,5S)- 5-(2,4-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

25 ((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R, 5R)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl
sulfamate;

- ((4S, 5S)-5-(2,6-dichlorophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 5 ((4S, 5S)-5-(2,6-dichlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- 10 ((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- ((2R, 3R)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2,6-dichlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 15 ((4R, 5R)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2,6-dichlorophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 20 ((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-aminophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-aminophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 25 ((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;

- ((2R, 3R)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-aminophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R, 5R)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-aminophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
5 ((4R, 5R)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((4S, 5S)-5-(2-nitrophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-nitrophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
15 ((4R, 5R)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-nitrophenyl)-2-oxo-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
20 sulfamate;
((4S, 5S)-5-(2-methylphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;
((4R, 5R)-5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-methylphenyl)-2-methyl-1,3-dioxolan-4-yl)methyl sulfamate;

- ((4R, 5R)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-(2-methylphenyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
5 ((2S, 3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,4]nonane-2-yl)methyl sulfamate;
((2R, 3R)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-(2-methylphenyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((4R, 5R)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((4S, 5S)-5-(2-methylphenyl)-2-phenyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate;
((4S, 5S)-5-(2-methylaminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl methylsulfamate;
15 ((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
20 ((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
2-((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
25 2-((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;

- 2-((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
5 2-((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
((4S, 5S)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-benzyl-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4S, 5S)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
((4R, 5R)-5-benzyl-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
10 ((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
((2S, 3S)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
((2R, 3R)-3-benzyl-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
2-((4R, 5R)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
15 2-((4S, 5S)-5-phenyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4R, 5R)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((4S, 5S)-5-phenyl-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
2-((2R, 3R)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
20 2-(2R, 3R)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
2-((2S, 3S)-3-phenyl-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;

- 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 2-((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 5 2-((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
- 10 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl sulfamate;
- 2-((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
- 2-((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl sulfamate;
- 15 ((4S, 5S)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4R, 5R)-5-(2-chlorobenzyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((4S, 5S)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- 20 ((4R, 5R)-5-(2-chlorobenzyl)-2,2-diethyl-1,3-dioxolan-4-yl)methyl sulfamate;
- ((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- ((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,4]nonan-2-yl)methyl sulfamate;
- ((2S, 3S)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- ((2R, 3R)-3-(2-chlorobenzyl)-1,4-dioxaspiro[4,5]decan-2-yl)methyl sulfamate;
- 25 2-((4R, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl sulfamate;
- 2-((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl

sulfamate;

2-((4R, 5R)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
sulfamate;

2-((4S, 5S)-5-(2-chlorophenyl)-2,2-diethyl-1,3-dioxolan-4-yl)ethyl
5 sulfamate;

2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
sulfamate;

2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,4]nonan-2-yl)ethyl
sulfamate;

10 2-((2R, 3R)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
sulfamate;

2-((2S, 3S)-3-(2-chlorophenyl)-1,4-dioxaspiro[4,5]decan-2-yl)ethyl
sulfamate;

15 ((4S, 5R)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

((4R,5S)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl
sulfamate;

20 ((4S, 5R)-5-(2,4-dichlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
yl)methyl sulfamate;

((4R,5S)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
yl)methylsulfamate;

25 ((4S, 5R)-5-(2-chlorothiazol-5-yl)-2,2-dimethyl-1,3-dioxolan-4-
yl)methylsulfamate;

((4R, 5S)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-
yl)methylsulfamate;

((4S, 5R)-2,2-dimethyl-5-(4-methylthiazol-5-yl)-1,3-dioxolan-4-

yl)methylsulfamate;

((4R, 5S)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

5 ((4S, 5R)-2,2-dimethyl-5-(2-chloro-4-methylthiazol-5-yl)-1,3-dioxolan-4-yl)methylsulfamate;

((4S, 5S)-2,2-dimethyl-5-(thiophen-3-yl)-1,3-dioxolan-4-yl)methylsulfamate;

((4S, 5R)-2,2-dimethyl-5-(5-chlorothiophen-2-yl)-1,3-dioxolan-4-yl)methylsulfamate;

10 Sodium (((((4R, 5R)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfonyl)amide ;

Sodium (((((4S, 5S)-5-(2-aminophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methylsulfonyl)amide ; and

sodium (((((4S, 5S)-5-(2-chlorophenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)sulfonyl)amide.

15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2014/012259**A. CLASSIFICATION OF SUBJECT MATTER****A61K 31/357(2006.01)i, A61K 31/18(2006.01)i, A61P 25/00(2006.01)i**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K 31/357; A61K 31/335; C07D 311/94; C07C 143/68; C07D 317/00; C07D 309/06; C07D 319/16; C07D 319/20; A61K 31/255; A61K 31/18; A61P 25/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: sulfamate derivative compound, epilepsy, antiepileptic

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 8084490 B2 (MCCOMSEY, D. F. et al.) 27 December 2011 See abstract; examples 1-17; and claims 15-20.	12-22
A	US 4591601 A (MARYANOFF, B. E. et al.) 27 May 1986 See abstract; table 1; and examples 1-3.	12-22
A	US 2010-0063138 A1 (MCCOMSEY, D. F. et al.) 11 March 2010 See abstract; examples 1-3; and claims 1-17.	12-22
A	US 4582916 A (MARYANOFF, B. E. et al.) 15 April 1986 See the whole document.	12-22
A	US 4792569 A (MARYANOFF, B. E. et al.) 20 December 1988 See the whole document.	12-22
PX	WO 2013-187727 A1 (BIO-PHARM SOLUTIONS CO., LTD.) 19 December 2013 See abstract; formula (I); examples; claims 1-19	12-22



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

25 March 2015 (25.03.2015)

Date of mailing of the international search report

26 March 2015 (26.03.2015)

Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2014/012259

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-11
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 1-11 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2014/012259

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2014/012259

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