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(54) **Title:** PHENYL CARBAMATE COMPOUNDS FOR USE IN PREVENTING OR TREATING ALS

Compound 1 Survival
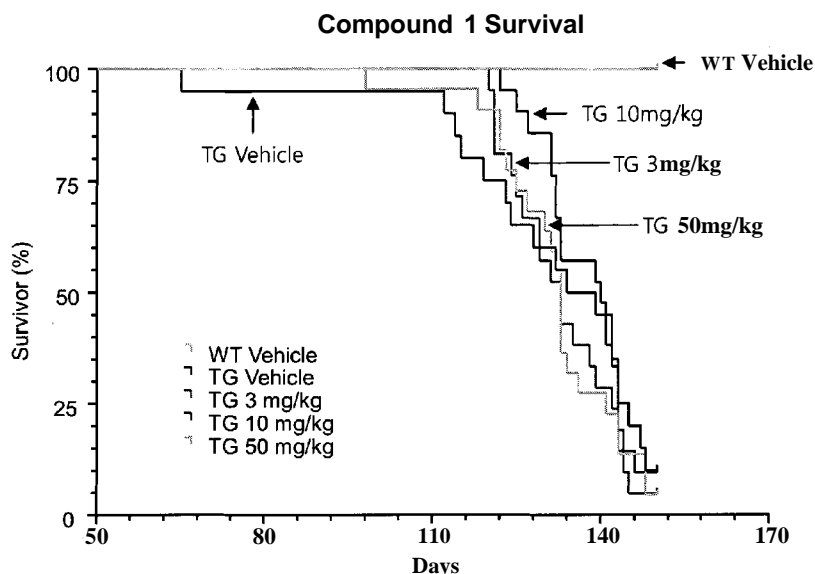
(57) **Abstract:** A composition for treating and/or preventing ALS containing the phenyl carbamate compound or a pharmaceutically
acceptable salt thereof as an active ingredient; a method of treating and/or preventing ALS comprising administering the phenyl car-
bamate compound or a pharmaceutically acceptable salt thereof to a patient in need of ALS treatment; and a use of the phenyl car-
bamate compound or a pharmaceutically acceptable salt thereof in treating and/or preventing ALS, are provided.

[Title of the Invention]

PHENYL CARBAMATE COMPOUNDS FOR USE IN PREVENTING OR TREATING ALS

[Technical Field]

5   A phenyl carbamate compound; a composition for treating and/or preventing amyotrophic lateral sclerosis (ALS) containing the phenyl carbamate compound or a pharmaceutically acceptable salt thereof as an active ingredient; a method of treating and/or preventing ALS comprising administering the phenyl carbamate compound or a pharmaceutically acceptable salt thereof to a patient in need of ALS treatment; and a use of the

10   phenyl carbamate compound or a pharmaceutically acceptable salt thereof in treating and/or preventing ALS, are provided.

[Background Art]

        Amyotrophic lateral sclerosis (ALS), which is also called as a Lou Gehrig disease, is

15   accompanied by degeneration of both upper motor neurons (UMN) and lower motor neurons(LMN) and marked by neurogenic atrophy, weakness, and fasciculation. While the pathogenesis of ALS remains to be resolved, excitotoxicity has been expected to participate in the process of ALS. In particular, ALS patients show increased levels of extracellular glutamate and defects in glutamate transport. Administration of excitotoxins mimicked pathological

20   changes in the spinal cord of ALS patients [Rothstein. Clin. Neurosci.3:348-359 (1995); Ikonomidou, Qin, Labruyere, and Olney J. Neuropathol. Exp. Neurol.55:21 1-224 (1996)].

        UMN signs include hyperreflexia, extensor plantar response and weakness in a topographic representation. LMN signs include weakness, hyporeflexia, and fasciculations. Initial presentation varies. Affected individuals typically present with either asymmetric focal

25   weakness of the extremities (stumbling or poor handgrip) or bulbar findings (dysarthria, dysphagia). Regardless of initial symptoms, atrophy and weakness eventually affect other muscles. The mean age of onset is 56 years in individuals with no known family history and 46 years in individuals with more than one affected family member (familial ALS or FALS). Average disease duration is about three years, but it can vary significantly. Death usually results

30   from compromise of the respiratory muscles.

        The diagnosis of ALS is based on clinical features, electrodiagnostic testing, and exclusion of other health conditions with related symptoms. Molecular genetic testing, available in clinical laboratories for several genes associated with ALS, plays a prominent role in diagnosis of the genetic subtype and genetic counseling.

35   Amyotrophic lateral sclerosis can be inherited in an autosomal dominant, autosomal

[Title of the Invention]

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[Technical Field]

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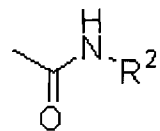30   from compromise of the respiratory muscles.

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35   Amyotrophic lateral sclerosis can be inherited in an autosomal dominant, autosomal
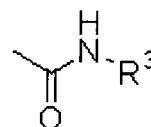
n, that means the number of substituent X, is an integer from 1 to 5, for example, 1 or 2,

R1 is a linear or branched alkyl group of C1-C4, for example, methyl group, ethyl group, isopropyl group, or butyl group,

A is hydrogen or a carbamoyl derivative represented by ,

B is hydrogen, a carbamoyl derivative represented by , trialkyl silyl groups (e.g., a trimethyl silyl (TMS) group, a triethyl silyl (TES) group, a triisopropyl silyl (TIPS) group, t-butyl dimethyl silyl (TBDMS) group, and the like), trialkylaryl silyl groups (wherein the total number of alkyl and aryl groups is three; e.g., a t-butyl diphenyl silyl (TBDPS) group and the like), or a trialkyl silyl ether group, wherein each alkyl group may be independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups, and each aryl group may be independently selected from the group consisting of C5-C8 aryl groups, preferably a phenyl group,

A and B are not the carbamoyl derivative at same time, and

R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, a linear or branched alkyl group of C1-C4, for example C1-C3, a cycloalkyl group of C3-C8, for example C3-C7, and benzyl group, and more specifically, R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, methyl group, propyl group, isopropyl group, cyclopropyl group, cyclohexyl group, bicycloheptane group, and benzyl group.

The compound has remarkably excellent treatment and/or prevention effect on amyotrophic lateral sclerosis (ALS) as well as very low toxicity. Therefore, the compounds of formula I may be useful as a drug for the treatment and/or prevention of ALS.

Another embodiment provides a pharmaceutical composition for of preventing and/or treating amyotrophic lateral sclerosis (ALS) containing a compound of Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof, as an active ingredient

Another embodiment provides a method of preventing and/or treating ALS comprising administering a therapeutically effective amount of a phenyl carbamate compound represented by Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof, to a subject in need of preventing and/or treating ALS.
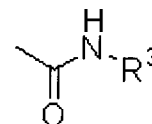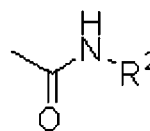
Another embodiment provides a use of a phenyl carbamate compound represented by Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof, in the prevention and/or treatment of ALS or in the manufacture of a medicament for preventing and/or treating ALS.

[DETAILED DESCRIPTION OF THE EMBODIMENTS]

Continuing its research work in the field of ALS, the present inventors, as results of studies on the development of anti-ALS drugs, found that a phenyl carbamate compounds of the following Chemical Formula 1 exhibits remarkably excellent anti-ALS activity in various emulation models and simultaneously has very low toxicity, to complete the invention.

An embodiment provides an organic compound, particularly, a phenyl carbamate compound, more particularly, a phenyl carbamate compound represented by following Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof:

[Chemical Formula 1]
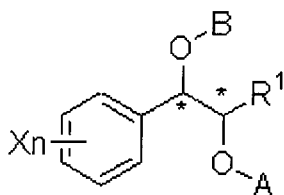
wherein,

X is a halogen, for example, chlorine, fluorine, iodine, or bromine,

n, that means the number of substituent X, is an integer from 1 to 5, for example, 1 or 2,

R1 is a linear or branched alkyl group of C1-C4, for example, methyl group, ethyl group, isopropyl group, or butyl group,

A is hydrogen or a carbamoyl derivative represented by ,

B is hydrogen, a carbamoyl derivative represented by , trialkyl silyl groups (e.g., a trimethyl silyl (TMS) group, a triethyl silyl (TES) group, a triisopropyl silyl (TIPS) group, t-butyl dimethyl silyl (TBDMS) group, and the like), trialkylaryl silyl groups (wherein the total number of alkyl and aryl groups is three; e.g., a t-butyl diphenyl silyl (TBDPS)

group and the like), or a trialkyl silyl ether group, wherein each alkyl group may be independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups, and each aryl group may be independently selected from the group consisting of C5-C8 aryl groups, preferably a phenyl group,

A and B are not the carbamoyl derivative at same time, and

R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, a linear or branched alkyl group of C1-C4, for example C1-C3, a cycloalkyl group of C3-C8, for example C3-C7, and benzyl group, and more specifically, R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, methyl group, propyl group, isopropyl group, cyclopropyl group, cyclohexyl group, bicycloheptane group, and benzyl group.

In a concrete embodiment, the phenyl carbamate compound may be selected from the group consisting of:

1-(2-chlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-methyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-propylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-isopropylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclopropylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclohexylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-benzyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-bicyclo[2,2, 1]heptanecarbamate,

1-(2,4-dichlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2,4-dichlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,4-dichlorophenyl)- 1-hydroxy-3-methyl-butyl-2-carbamate,

l-(2,6-dichlorophenyl)-l-hydroxy-3-methyl-butyl-2-carbamate,

1-(2,4-dichlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-methylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-propylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-isopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclohexylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-benzylcarbamate,

1-(2,4-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxy-3 -methyl-butyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxy-3-methyl -butyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2-fluorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,3-dichlorophenyl)- 1-hydroxypropyl-2-carbamate, and

1-(2,3-dichlorophenyl)-2-hydroxypropyl-1 -carbamate.

In this compound, 2 chiral carbons exist at positions 1 and 2 from phenyl group substituted with X; thus, the compound may exist in the form of an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers, as well as a racemate.

Alternatively, the compound may be in the form of a pharmaceutically acceptable salt. The pharmaceutically acceptable salt may include an additional salt of acid or base, and its stereochemical isomer.   For example, the compound may be in the form of an additional salt of an organic or inorganic acid.   The salt may not be specially limited, and include any salts that maintain the activities of their parent compounds, with no undesirable effects, in the subject, when they are administered to the subject.   Such salts may include inorganic and organic salts, such as salts of acetic acid, nitric acid, aspartic acid, sulfonic acid, sulfuric acid, maleic acid, glutamic acid, formic acid, succinic acid, phosphoric acid, phthalic acid, tannic acid, tartaric acid, hydrobromic acid, propionic acid, benzene sulfonic acid, benzoic acid, stearic acid, lactic acid, bicarbonic acid, bisulfuric acid, bitartaric acid, oxalic acid, butyric acid, calcium edetate,

carbonic acid, chlorobezoic acid, citric acid, edetic acid, toluenesulfonic acid, fumaric acid, gluceptic acid, esilic acid, pamoic acid, gluconic acid, methyl nitric acid, malonic acid, hydrochloric acid, hydroiodic, hydroxynaphtholic acid, isethionic acid, lactobionic acid, mandelic acid, mucic acid, naphthylic acid, muconic acid, p-nitromethanesulfonic acid, hexamic acid, pantothenic acid, monohydrogen phosphoric acid, dihydrogen phosphoric acid, salicylic acid, sulfamic acid, sulfanilic acid, methane sulfonic acid, and the like. The additional salts of base may include salts of akali metal or alkaline earth metal, such as salts of ammonium, lithium, sodium, potassium, magnesium, calcium, and the like; salts having an organic base, such as benzathine, N-methyl-D- glucamine, hydrabamine, and the like; and salts having an amino acid such as arginine, lysine, and the like. In addition, these salts may be converted to a released form by treating with a proper base or acid.

As demonstrated in the following experimental examples, the compound of Chemical Formula 1, a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof, or pharmaceutically acceptable salt thereof exhibits an excellent effect on preventing and/or treating ALS.

Therefore, another embodiment provides a pharmaceutical composition for preventing and/or treating ALS containing a phenyl carbamate compound represented by Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof, as an active ingredient.

Another embodiment provides a method of preventing and/or treating ALS comprising administering a therapeutically effective amount of a phenyl alkyl carbamate compound represented by Chemical Formula 1; a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof; or a pharmaceutically acceptable salt thereof, to a subject in need of preventing and/or treating ALS. The method may further comprise a step of identifying the subject in need of preventing and/or treating ALS prior to the step of administering. The term "therapeutically effective amount" may refer to an amount of the active gradient capable of exhibiting the effect of preventing and/or treating ALS.

Another embodiment provides a phenyl carbamate compound represented by Chemical Formula 1, a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof, or a pharmaceutically acceptable salt thereof, for use in the prevention and/or treatment of ALS or in the manufacture of a medicament for preventing and/or treating ALS. Another embodiment provides a use of a phenyl carbamate compound represented by Chemical Formula 1, a racemate, an enantiomer, a diastereomer, a mixture of enantiomers, or a mixture of diastereomers thereof, or a pharmaceutically acceptable salt thereof, in the prevention

and/or treatment of ALS or in the manufacture of a medicament for preventing and/or treating ALS.

Amyotrophic lateral sclerosis (ALS) is involving both upper motor neurons (UMNs) and lower motor neurons (LMNs). Upper motor neurons, located in the motor cortex of the frontal lobe, send their axons through the great corticofugal tracts to the brain stem (corticobulbar neurons) and the spinal cord (corticospinal neurons) to influence patterned activity of the lower motor neurons (LMS). Additional UMN influences on the LMN are carried over descending pathways of the brain stem. UMN signs in ALS include hyperreflexia and extensor plantar response. Lower motor neurons, located in the brain stem and spinal cord, innervate striated muscle. LMN signs in ALS include weakness, muscle wasting (atrophy), hyporeflexia and fasciculations.

Symptoms present in early disease may vary. Affected individuals most often present with either asymmetric focal weakness of the extremities (stumbling or poor handgrip) or bulbar findings (dysarthria, dysphagia). Other findings may include lability of affect, but not necessarily mood. A diagnostic feature of ALS, typically not seen in other disorders, is the presence of hyperreflexia in segmental regions of muscle atrophy, unaccompanied by sensory disturbance.

Limb involvement occurs more often than bulbar involvement. Onset in the lower extremities is most common for familial ALS [Mulder et al 1986, Siddique 1991]. Various subtypes of ALS may be identified:

- "Progressive bulbar palsy," which presents with speech disturbance and swallowing difficulties;
- Limb-onset ALS;
- Progressive muscular atrophy in which only lower motor neurons are involved; and
- UMN-predominant ALS.

Regardless of initial symptoms, atrophy and weakness eventually spread to affect other muscles.

Oculomotor neurons are generally resistant to degeneration in ALS, but may be affected in individuals with a long disease course, especially when life span is extended by ventilatory support. Once all muscles of communication and expression are paralyzed, the individual is "locked in." In some instances, eye movements remain intact, allowing communication by way of special devices. Death usually results from compromise of the respiratory muscles.

In a concrete embodiment, the ALS may include a neurodegeneration associated ALS. In another concrete embodiment, the ALS may not be a muscle spasm associated ALS.

The pharmaceutical composition may be formulated in various forms for oral or parenteral administration. For example, the pharmaceutical composition may be formulated in

the oral administration form, such as a tablet, pill, soft or hard capsule, liquid, suspension, emulsion, syrup, granules, elixirs, and the like. In addition to the active ingredient, the oral administration form may further include pharmaceutically acceptable and conventional components, for example, a diluent such as lactose, dextrose, sucrose, mannitol, sorbitol, cellulose, glycine, and the like; a lubricant such as silica, talc, stearic acid, magnesium or calcium salt thereof, polyethyleneglycol, and the like.

In the case that the oral administration form is a tablet, it may further include a binder such as magnesium aluminium silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, polyvinylpirrolidine, and the like; and optionally include one or more additives selected from the group consisting of a disintegrant such as starch, agar, arginic acid or sodium salt thereof, an absorbent, a colorant, a flavoring, a sweetener, and the like.

Alternatively, the pharmaceutical composition may also be formulated in a parenteral administration form, which can be administered by subcutaneous injection, intravenous injection, intramuscular injection, injection into thoracic cavity, and the like. In order to formulate the parenteral administration form, the pharmaceutical composition may be prepared as a solution or suspension wherein the active ingredient is dissolved in water together with a stabilizer and/or a buffering agent, and such solution or suspension formulation may be prepared as a dosage form in ample or vial.

The pharmaceutical composition may be sterilized, and/or include further additives such as a preservative, a stabilizer, a hydrating agent, an emulsification accelerator, a salt and/or buffering agent for osmoregulation, and the like, and/or further therapeutically effective ingredients. The pharmaceutical composition may be formulated by any conventional method for mixing, granulating, coating, and the like.

The pharmaceutical composition may be administered to a mammal including human, in the therapeutically effective amount of 0.01 to 750 mg/kg(body weight), preferably 0.1 to 500 mg/kg(body weight) per one day, based on the active ingredient. The therapeutically effective amount may be administered through oral or parenteral pathway, one or two or more times per one day.

The therapeutically effective amount and the administration pathway of the present pharmaceutical composition may be properly adjusted by a person skilled in the relevant field considering the conditions of the subject (patient), desired effects, and the like.

The subject may be a mammal including human or cells and/or tissues separated

therefrom.

The phenyl carbamate compound of the present invention may prepared by the following reaction formula.

Reaction Formula I: Synthesis of Diol-1
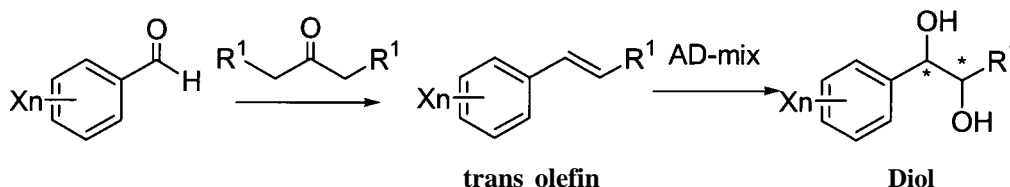
trans olefin   **Diol**

5

A diol compound used in the synthesis of the carbamate compound may be synthesized by dihydroxylation of a trans-olefin compound.   A diol compound having optical activity may be synthesized using a sharpless asymmetric dihydroxylation catalyst.

Reaction Formula II : Synthesis of Diol-2

Haloro-Mandelic acid

PG = Protecting Group

Protected alcohol   Diol
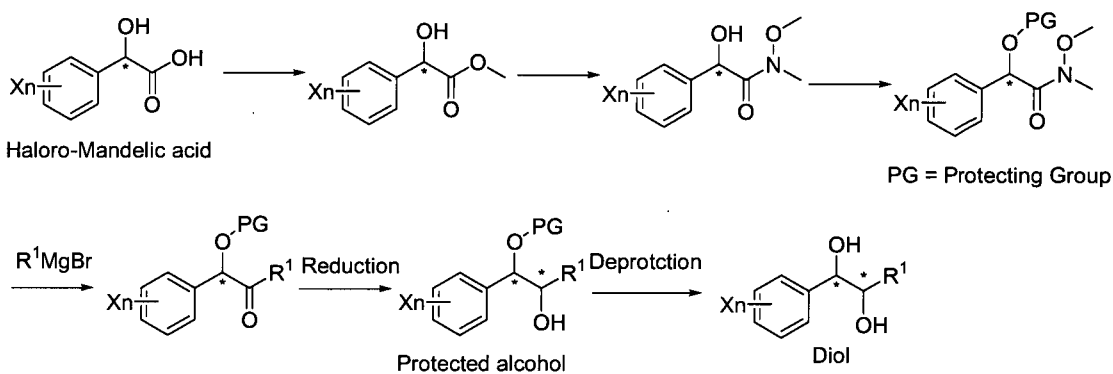
10

As indicated in the Reaction Formula II, the optically active substance of diol may also be synthesized using a reduction reagent after synthesizing a hydroxy-ketone compound using Haloro-Mandelic acid.   In the Reaction Formula II, PG may be Trialkyl Silyl group(TMS, TES, TIPS, TBDMS, TBDPS), Ether group [BOM(Benzyloxymethyl ether). MTM(Methylthiomethyl ether),   SEM(2-(Trimethylsilyl)ethoxymethyl   ether),   PMBM(p-Methoxybenzyl   ether),

15   THP(Tetrahydropyranyl ether), Allyl ether, Trityl ether, Ester group[Ac(acetate), Bz(Benzoate), Pv(Pivaloate),   Cbz(Benzyl   carbonate),   BOC(t-Butyl   carbonate),   Fmoc(9-Fulorenylmethyl)carbaonate, Alloc(Allyl Carbonate), Troc(Trichloroehtyl carbonate), or p-Methoxybenzoate, Methyl carbonate, and so on.

20   Reaction Formula III : Carbamation reaction- 1
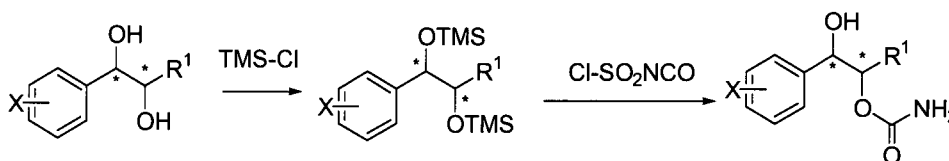
As a highly selectivity form of regioisomer of single carbamate of diol having halogen substituent at phenyl ring. (Example 1-14 and 36-67 are synthesized by reaction formula III)

Reaction Formula IV : Carbamation reaction-2
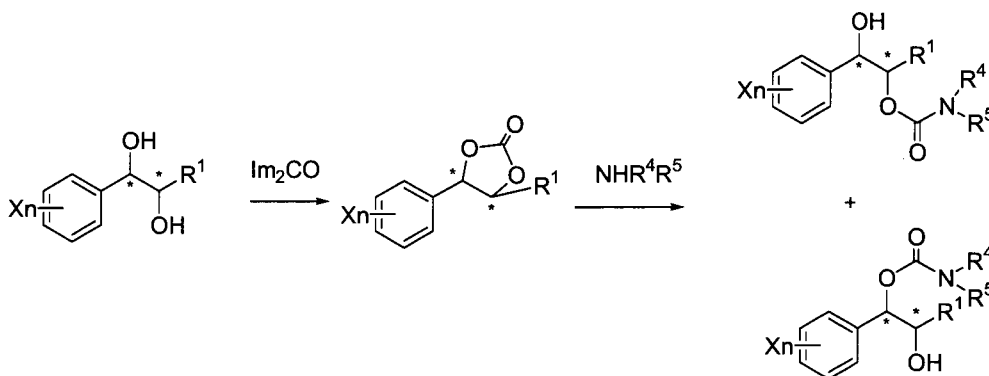
5   Two substances in the form of regioisomers of a single carbamate of diol having halogen substituent at phenyl ring may be separated by flash column chromatography to obtain two kinds of single carbamate compounds. (Example 15-35 and 68-1 15 are synthesized by reaction formula IV)

Reaction Formula V : Protection reaction
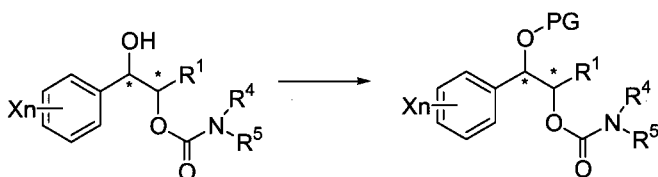
10   In the Reaction Formula V, PG may be Trialkyl Silyl group(TMS, TES, TIPS, TBDMS, TBDPS), Ether group[BOM(Benzyloxymethyl ether). MTM(Methylthiomethyl ether), SEM(2-(Trimethylsilyl)ethoxymethyl ether), PMBM(p-Methoxybenzyl ether), THP(Tetrahydropyranyl ether), Allyl ether, Trityl ether, Ester group[Ac(acetate), Bz(Benzoate), Pv(Pivaloate),

15   Cbz(Benzyl carbonate), BOC(t-Butyl carbonate), Fmoc(9-Fulorenylmethyl)carbaonate, Alloc(Allyl Carbonate), Troc(Trichloroehtyl carbonate), or p-Methoxybenzoate, Methyl carbonate, and so on.

[BREIF DESCRIPTION OF DRAWINGS]

20   Fig. 1 is a graph illustrating the rate (%) of survivor according to survival time.

Fig. 2 is a graph illustrating the rate (%) of survivor according to disease onset time.

Fig. 3 is a graph illustrating the body weight (g) of each group.

Fig. 4 is a graph illustrating the clinical score of each group.

Fig. 5 is a graph illustrating the distance moved of each group, wherein the term

25   "JBPOS0101" refers to Compound 1.

[EXAMPLE]

The present invention is further explained in more detail with reference to the following examples. These examples, however, should not be interpreted as limiting the scope of the present invention in any manner.

Preparation Example 1: Synthesis of l-(2-chlorophenyl)-trans-l-propene
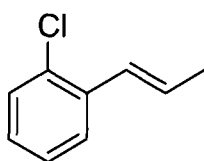
48ml of 2-chlorobenzenaldehyde (0.42mol) and 49.7ml of 3-pentanone (0.47mol) were dissolved in 600mL of hexane in flask, and then stirred with raising the temperature. 53.6ml of Boron trifluoride etherate (BF_3OEt_2, 0.42mol) was added to the resultant under reflux conditions. When the reaction was completed, water was added thereto. After layer separation, the obtained organic layer was washed twice with IM sodium hydroxide solution (IM NaOH), and then the separated organic layer was washed with water. The separated organic layer was dehydrated with anhydrous magnesium sulfate ($MgSO_4$) and concentrated. The concentrated residue was purified by a silica gel column chromatography to produce the title compound (38g, yield 58%). H NMR(400MHz, $CDCl_3$) 61.94(d, *J*=4.8Hz, 3H), 6.24(m, 1H), 6.78(d, *J*=14Hz, 1H), 7.1 1-7.5 l(m, 4H)
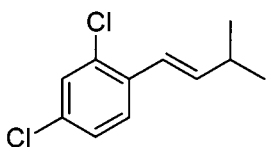
Preparation Example 2: Synthesis of l-(2-chlorophenyl)-trans-l-butene
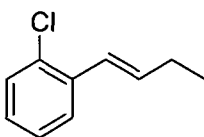
The substantially same method as described in Preparation Example 1 was conducted, except that 3-heptanone was used instead of 3-pentanone, to obtain the title compound (2.9g, yield 83%).

H NMR(400MHz, $CDCl_3$) 51.14(d, *J*=7.6Hz, 3H), 2.29~2.33(m, 2H), 6.28(dt, *J*=16Hz, 6.4Hz, 1H), **6.78(d, *J*=l**5.6Hz, 1H), 7.13~7.54(m, 4H)

Preparation Example 3: Synthesis of l-(2-chlorophenyl)-3-methyl-trans-l-butene
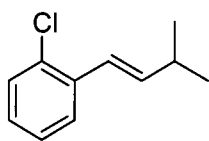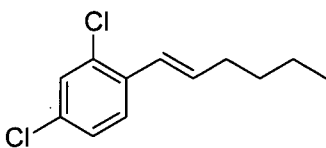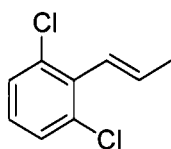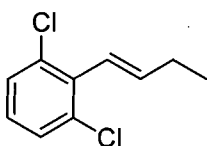
12

The substantially same method as described in Preparation Example 1 was conducted, except that 2,6-dimethyl-heptan-4-one was used instead of 3-pentanone, to obtain the title compound (8.0g, yield 50-90%).

H NMR(400MHz, CDCl$_3$) 51.14(d, J=6.8Hz, 6H), 2.25~2.57(m, 1H), 6.20(dd, J=16Hz, 7.2Hz, 1H), 7.64(d, J=16Hz, 1H), 7.12~7.54(m, 4H)

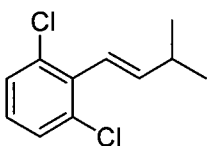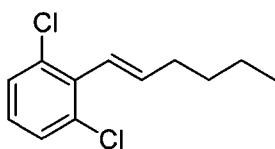**Preparation Example 4: Synthesis of l-(2-chlorophenyI)-trans-l-hexene**
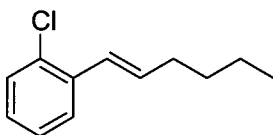
The substantially same method as described in Preparation Example 1 was conducted, except that 6-undecanone was used instead of 3-pentanone, to obtain the title compound (lOg, yield 85%).

^{1}H NMR(400MHz, CDCl$_3$) 50.96(t, J=7.2Hz, 3H), 1.33~1.56(m, 4H), 2.26~2.32(m, 4H), **6.24(dt, J=1**5.6Hz, 7Hz, 1H), 6.78(d, J=16Hz, 1H), 7.13~7.54(m, 4H)

Preparation Example 5: Synthesis of l-(2,4-dichlorophenyl)-trans-l-propene
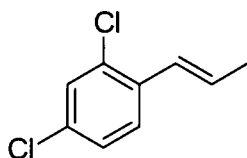
The substantially same method as described in Preparation Example 1 was conducted, except that 2,4-dichlorobenzenaldehyde was used instead of 2-chlorobenzenaldehyde, to obtain the title compound (2.4g, yield 57%).

H NMPv(400MHz, CDCl$_3$) 51.95(dd, J=6.8Hz, 1.6Hz, 3H), 6.24(m, 1H), 6.72(d, J=1 5.6Hz, 1H), 7.18~7.44(m, 3H)

Preparation Example 6: Synthesis of l-(2,4-dichlorophenyl)-trans-l-butene
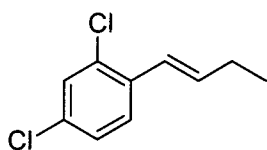
13

The substantially same method as described in Preparation Example 5 was conducted, except that 3-heptanone was used instead of 3-pentanone, to obtain the title compound (2.1g, yield 90%).

H NMR(400MHz, CDCl$_3$) 61.14(d, *J*=7.6Hz, 3H), 2.20~2.33(m, 2H), 6.26(dt, *J*=16Hz, 6.8Hz, 1H), 6.70(d, *J*=15.6Hz, 1H), 7.18~7.46(m, 3H)

Preparation Example 7: Synthesis of l-(2,6-dichlorophenyl)-3-methyl-trans-l-butene

The substantially same method as described in Preparation Example 5 was conducted, except that 2,6-dimethyl-heptan-4-one was used instead of 3-pentanone, to obtain the title compound (0.23g, yield 10-40%).

[1]H **NMPv**(400MHz, CDCl$_3$) 61.15(d, *J*=6.8Hz, 6H), 2.53~2.58(m, 1H), 6.19(dd, *J*=16.4Hz, 6.8Hz, 1H), 6.31(d, *J*=16.4Hz, 1H), 7.18~7.46(m, 3H)
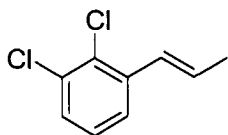
Preparation Example 8: Synthesis of l-(2,4-dichlorophenyl)-trans-l-hexene

The substantially same method as described in Preparation Example 5 was conducted, except that 6-undecanone was used instead of 3-pentanone, to obtain the title compound (3.2g, yield 40-80%).

H NMR(400MHz, CDCl$_3$) 50.96(t, *J*=7.2Hz, 3H), 1.38~1.52(m, 4H), 2.25-2.3 l(m, 2H), 6.22(dt, *J*=15.6Hz, 6.8Hz, 1H), 6.70(d, *J*=15.6Hz, 1H), 7.18~7.46(m, 3H)

**Preparation Example 9: Synthesis of l-(2,6-dichlorophenyl)-trans-l-propene**

The substantially same method as described in Preparation Example 1 was conducted, except that 2,6-dichlorobenzenaldehyde was used instead of 2-chlorobenzenaldehyde, to obtain the title compound (0.4g, yield 10-40%).

H NMR(400MHz, CDCl$_3$) 61.98(d, J=8Hz, 3H), 6.23-6.3 l(m, 1H), 6.40(d, J=16Hz, 1H), 7.05~7.32(m, 3H)

Preparation Example 10: Synthesis of l-(2,6-dichlorophenyl)-trans-l-butene

The substantially same method as described in Preparation Example 9 was conducted, except that 3-heptanone was used instead of 3-pentanone, to obtain the title compound (1.2g, yield 10-40%).

H NMR(400MHz, CDCl$_3$) 51.17(t, J=7.6Hz, 3H), 2.30-2.37(m, 2H), 6.29(dt, J=16.4Hz, 6Hz, 1H), 6.37(d, J=16.4Hz, 1H), 7.05~7.32(m, 3H)

Preparation Example 11: Synthesis of l-(2,6-dichlorophenyl)-3-methyl-trans-l-butene

The substantially same method as described in Preparation Example 9 was conducted, except that 2,6-dimethyl-heptan-4-one was used instead of 3-pentanone, to obtain the title compound (0.23g, yield 10-40%).

^{1}H NMR(400MHz, CDCl$_3$) 51.15(d, J=6.8Hz, 6H), 2.53~2.58(m, 1H), 6.19(dd, J=16.4Hz, 6.8Hz, 1H), 6.31(d, J=16.4Hz, 1H), 7.05~7.32(m, 3H)

Preparation Example 12: Synthesis of l-(2,6-dichlorophenyl)-trans-l-hexene

The substantially same method as described in Preparation Example 9 was conducted, except that 6-undecanone was used instead of 3-pentanone, to obtain the title compound (0.2g, yield 10-40%).

H NMR(400MHz, CDC1$_3$) 50.99(t, *J*=7.2Hz, 3H),1.14~1.59(m, 4H), 2.30~2.36(m, 2H), 6.24(dt, *J*=16Hz, 6.6Hz, 1H), 6.38(d, *J*=16.4Hz, 1H), 7.05~7.33(m, 3H)

Preparation Example 13: Synthesis of l-(2,3-dichlorophenyl)-trans-l-propene

The substantially same method as described in Preparation Example 1 was conducted, except that 2,3-dichlorobenzenaldehyde was used instead of 2-chlorobenzenaldehyde, to obtain the title compound (0.2g, yield 10-40%).

H NMR(400MHz, CDC1$_3$) δ1.94(d, *J*=4.8Hz, 3H), 6.24(m, 1H), 6.78(d, *J*=14Hz, 1H), 7.1 1-7.5 l(m, 3H)

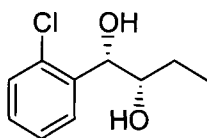**Preparation Example 14: Synthesis of l-(2-chlorophenyl)-(S,S)-l,2-propanediol**
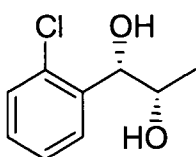
l-(2-chlorophenyl)-trans-l-propene(1.5g, Preparation Example 1) was dissolved in 30mL of the mixture of t-BuOH/H$_2$0 (1:1 (V/V)). At 0℃, AD-mix-a (Aldrich, U.S.A.) (13.7g) and methane sulfone amide·(CH$_3$S0$_2$NH$_2$, 0.76g, 0.0080mol) were added thereto and stirred for overnight. When the reaction was completed, the obtained product was washed with an aqueous solution of sodium sulfite (Na$_2$S0$_3$) and ethylacetate (EA). Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgS0$_4$), filtrated, and concented under reduced pressure. The concentrated residue was purified by a silica gel column chromatography to produce the title compound (1.65g, yield 90%).

^{1}H NMR(400MHz, CDC1$_3$) 51.20(d, *J*=6.4Hz, 3H), 2.48(d, *J*=4.0Hz 1H), 2.92(d,

16

J=4.4Hz, 1H), 3.93~3.97(m, 1H), 4.97(t, J=4.8Hz, 1H), 7.22~7.51(m, 4H)

^{13}CNMR(100MHz,CDCl$_3$) 518.8, 71.5, 74.4, 127.1, 128.1, 128.9, 129.5, 132.6, 138.9

Preparation Example 15: Synthesis of l-(2-chlorophenyl)-(R,R)-l,2-propanediol
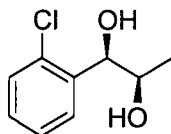
l-(2-chlorophenyl)-trans-l-propene   (2.5g, Preparation Example 1) was dissolved in 50mL of the mixture of t-BuOH/H$_2$0 (1:1 (V/V)).   At 0℃, AD-mix-a (Aldrich, U.S.A.) (23.5g) and methane sulfone amide (CH$_3$S0$_2$NH$_2$, 1.27g, 0.013mol) were added thereto and stirred for overnight.   When the reaction was completed, the obtained product was washed with an aqueous solution of sodium sulfite (Na$_2$S0$_3$) and ethylacetate (EA).   Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgS0$_4$), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography to produce the title compound (2.96g, yield 90%).

H   NMR(400MHz, CDCl$_3$) 51.20(d, J=6.4Hz, 3H), 2.48(d, J=4.0Hz, 1H), 2.92(d, J=4.4Hz, 1H), 3.93~3.97(m, 1H), 4.97(t, J=4.8Hz, 1H), 7.22~7.51(m, 4H)

Preparation Example 16: Synthesis of the mixture of l-(2-chlorophenyl)-(S,S)-l,2-propanediol and l-(2-chlorophenyl)-(R,R)-l,2-propanediol

l-(2-chlorophenyl)-trans-l-propene(6.53g,   Preparation Example 1) was dissolved in 45mL of the mixture of acetone/t-BuOH/H$_2$0(5:l:l   V/V). At the room temperature, N-methylmorpholine-N-oxide (7.5lg) and Os0$_4$ (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 (MgS0$_4$), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography to produce the title compound (6.42g, yield 80%).

^{1}H NMR(400MHz, CDCl$_3$) 51.20(d, J=6.4Hz, 3H), 2.48(d, J=4.0Hz, 1H), 2.92(d,

*J*=4.4Hz, 1H), 3.93~3.97(m, 1H), 4.97(t, *J*=4.8Hz, 1H), 7.22~7.51(m, 4H)

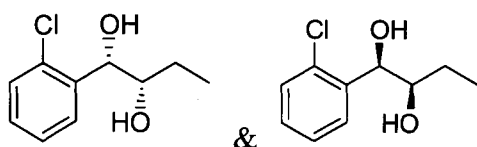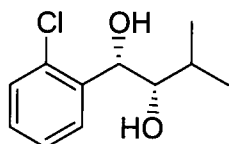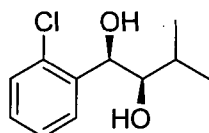## Preparation Example 17: Synthesis of l-(2-chlorophenyl)-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2-chlorophenyl)-trans-l-butene(Preparation   Example 2) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.36g, yield 95%).

ᴴ NMR(400MHz, CDCl₃) 61.01(t, *J*=7.4Hz, 3H), 1.52~1.65(m, 2H), 2.01(d, *J*=4.4Hz, 1H), 2.74(d, *J*=5.2Hz, 1H), 3.69~3.75(m, 1H), 5.05(t, *J*=5.0Hz, 1H), 7.23~7.54(m, 4H)

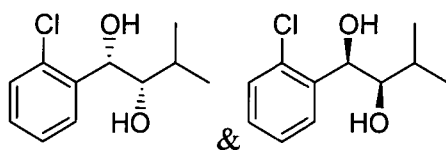## Preparation Example 18: Synthesis of l-(2-chlorophenyl)-(R,R)-l,2-butanediol
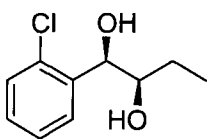
The substantially same method as described in Preparation Example 15 was conducted, except that l-(2-chlorophenyl)-trans-l-butene(Preparation   Example 2) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.84g, yield 60-95%).

ᴴ NMR(400MHz, CDCl₃) 51.01(t, *J*=7.4Hz, 3H), 1.52~1.65(m, 2H), 2.01(d, *J*=4.4Hz, 1H), 2.74(d, *J*=5.2Hz, 1H), 3.69~3.75(m, 1H), 5.05(t, *J*=5.0Hz, 1H), 7.23~7.54(m, 4H)

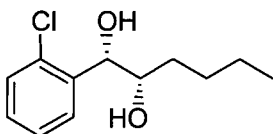## Preparation Example 19: Synthesis of the mixture of l-(2-chlorophenyl)-(S,S)-l,2-butanediol and l-(2-chlorophenyl)-(R,R)-l,2-butanediol
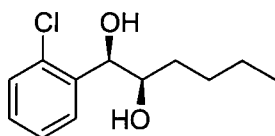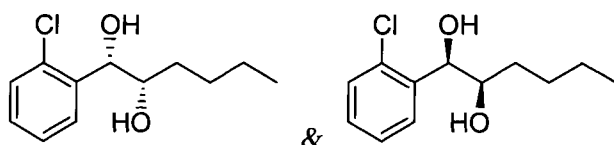

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2-chlorophenyl)-trans-l-butene(Preparation   Example 2) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (5.1g, yield

60-90%).

H NMR(400MHz, CDC1$_3$) 61.01(t, *J*=7.4Hz, 3H), 1.52~1.65(m, 2H), 2.01(d, *J*=4.4Hz, 1H), 2.74(d, *J*=5.2Hz, 1H), 3.69~3.75(m, 1H), 5.05(t, *J*=5.0Hz, 1H), 7.23~7.54(m, 4H)

Preparation Example 20: Synthesis of l-(2-chlorophenyl)-3-methyI-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2-chlorophenyl)-3-methyl-trans-l-butene(Preparation Example 3) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.96g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) 61.07(t, *J*=7.2Hz, 6H), 1.83~1.89(m, 1H), 1.92(d, *J*=5.6Hz, 1H), 2.69(d, *J*=6.4Hz, 1H), 3.53~3.56(m, 1H), 5.22~5.25(m, 1H), 7.23~7.55(m, 4H)

Preparation Example 21: Synthesis of l-(2-chIorophenyI)-3-methyl-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2-chlorophenyl)-3 -methyl-trans- l-butene(Preparation Example 3) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (4.2g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) 51.07(t, *J*=7.2Hz, 6H), 1.82~1.90(m, 1H), 1.93(d, *J*=5.6Hz, 1H), 2.79(d, *J*=6Hz, 1H), 3.53~3.57(m, 1H), 5.23~5.25(m, 1H), 7.23~7.54(m, 4H)

Preparation Example 22: Synthesis of the mixture of l-(2-chlorophenyl)-3-methyl-(S,S)-l,2-butanediol and l-(2-chlorophenyl)-3-methyl-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2-chlorophenyl)-3-methyl-trans-l-butene(Preparation Example 3) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.8g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) 51.07(t, J=7.2Hz, 6H), 1.83~1.90(m, 1H), 1.92(d, J=5.6Hz, 1H), 2.69(d, J=6.4Hz, 1H), 3.53~3.56(m, 1H), 5.22~5.25(m, 1H), 7.23~7.55(m, 4H)

Preparation Example 23: Synthesis of l-(2-chlorophenyI)-(S,S)-l,2-hexanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2-chlorophenyl)-trans-l-hexene(Preparation Example 4) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.37g, yield 90%).

H NMR(400MHz, CDC1$_3$) 50.90(t, J=7.2Hz, 3H), 1.35~1.65(m, 6H), 2.08(d, J=4.4Hz, 1H), 2.71(d, J=5.2Hz, 1H), 3.78~3.83(m, 1H), 5.04(t, J=5.0Hz, 1H), 7.23~7.53(m, 4H)

Preparation Example 24:   Synthesis of l-(2-chlorophenyl)-(R,R)-l,2-hexanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2-chlorophenyl)-trans-l-hexene(Preparation Example 4) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (4.2g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) δ0.91(ï, J=6.6Hz, 3H), 1.35~1.65(m, 6H), 2.08(d, J=4.8Hz, 1H), 2.70(d, J=5.2Hz, 1H), 3.80~3.83(m, 1H), 5.05(t, J=5.0Hz, 1H), 7.24~7.56(m, 4H)

Preparation Example 25: Synthesis of the mixture of 1-(2-chlorophenyl)-(S,S)-1,2-hexanediol and 1-(2-chlorophenyl)-(R,R)-1,2-hexanediol
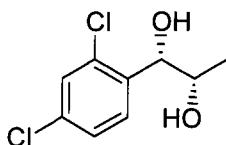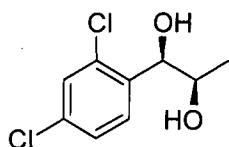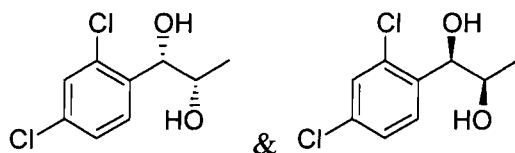

The substantially same method as described in Preparation Example 16 was conducted, except that 1-(2-chlorophenyl)-trans-1-hexene(Preparation   Example 4) was used instead of 1-(2-chlorophenyl)-trans-1-propene(Preparation   Example 1), to obtain the title compound (7.9g, yield 60-90%).

H NMPv (400MHz, CDC1$_3$) 50.90(t, *J*=7.2Hz, 3H), 1.26~1.55(m, 6H), 2.08(d, *J*=4.4Hz, IH), 2.71(d, *J*=5.6Hz, IH), 3.78~3.84(m, IH), 5.04(t, *J*=3.2Hz, IH), 7.24~7.55(m, 4H)

Preparation Example 26: Synthesis of 1-(2,4-dichlorophenyl)-(S,S)-1,2-propanediol

.The substantially same method as described in Preparation Example 14 was conducted, except that 1-(2,4-ichlorophenyl)-trans-1-propene(Preparation   Example 5) was used instead of 1-(2-chlorophenyl)-trans-1-propene(Preparation   Example 1), to obtain the title compound (0.33g, yield 60-95%).

^{1}H NMR(400MHz,   CDC1$_3$) 51.22(d, *J*=6.4Hz, 3H), 2.10(d, *J*=4.4Hz, IH), 2.71(d, *J*=4.8Hz, IH), 3.90~3.95(m, IH), 4.94(t, *J*=5.0Hz, IH), 7.31(dd, *J*=2.0Hz, *J*=8.0Hz, IH), 7.40(d, *J*=2.0Hz, IH), 7.49(d, *J*=8.4Hz, IH)

Preparation Example 27: Synthesis of 1-(2,4-dichlorophenyl)-(R,R)-1,2-propanediol

The substantially same method as described in Preparation Example 15 was conducted, except that 1-(2,4-ichlorophenyl)-trans-1-propene(Preparation   Example 5) was used instead of 1-(2-chlorophenyl)-trans-1-propene(Preparation   Example 1), to obtain the title compound (0.45g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 61.22(d, *J*=6.4Hz, 3H), 2.10(d, *J*=4.4Hz, 1H), 2.71(d, *J*=4.8Hz, 1H), 3.90~3.95(m, 1H), 4.94(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)
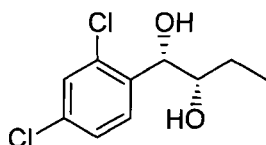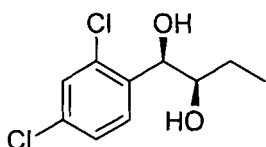
Preparation Example 28: Synthesis of the mixture of l-(2,4-dichlorophenyl)-(S,S)-1,2-propanediol and l-(2,4-dichlorophenyI)-(R,R)-l,2-propanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,4-ichlorophenyl)-trans-l-propene(Preparation Example 5) was used instead of 1-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.45g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 51.22(d, *J*=6.4Hz, 3H), 2.10(d, *J*=4.4Hz, 1H), 2.71(d, *J*=4.8Hz, 1H), 3.90~3.95(m, 1H), 4.94(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)

Preparation Example 29: Synthesis of l-(2,4-dichlorophenyl)-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-butene(Preparation Example 6) was used instead of 1-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.32g, yield 90%).

H NMR(400MHz, CDCl$_3$) 51.02(t, *J*=7.4Hz, 3H), 1.54~1.61(m, 2H), 2.07(d, *J*=4.8Hz, 1H), 2.74(d, *J*=4.8Hz, 1H), 3.65~3.68(m, 1H), 5.01(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)

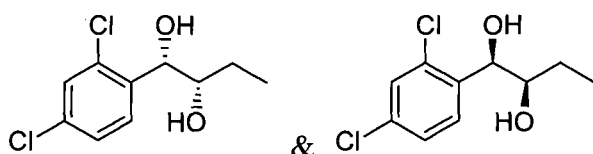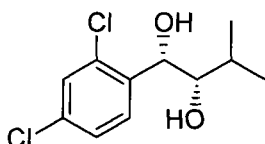**Preparation Example 30: Synthesis of l-(2,4-dichlorophenyl)-(R,R)-l,2-butanediol**
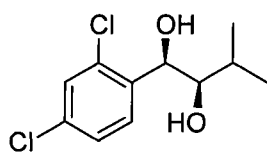

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-butene(Preparation Example 6) was used instead of 1-

(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.43g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 51.02(t, *J*=7.4Hz, 3H), 1.54-1. 6 1(m, 2H), 2.07(d, *J*=4.8Hz, 1H), 2.74(d, *J*=4.8Hz, 1H), 3.65~3.68(m, 1H), 5.01(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)

Preparation Example 31: Synthesis of the mixture of l-(2,4-dichlorophenyl)-(S,S)-1,2-butanediol and l-(2,4-dich!orophenyl)-(R,R)-1.2-butanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-butene(Preparation   Example 6) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.33g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 51.02(t, *J*=7.4Hz, 3H), 1.54-1. 6 1(m, 2H), 2.07(d, *J*=4.8Hz, 1H), 2.74(d, *J*=4.8Hz, 1H), 3.65~3.68(m, 1H), 5.01(t, *J*=5.0Hz, 1H), 77.31~7.49(m, 3H)

Preparation Example 32: Synthesis of l-(2,4-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,4-dichlorophenyl)-3 -methyl -trans- l-butene(Preparation   Example 7) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.25g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 81.00(d, *J*=6.8Hz, 6H), 1.60~1.65(m, 1H), 2.35(d, *J*=4.0Hz, 1H), 3.12(d, *J*=8.4Hz, 1H), 4.13-4.18(m, 1H), 5.36(t, *J*=7.6Hz, 1H), 7.17~7.35(m, 3H)
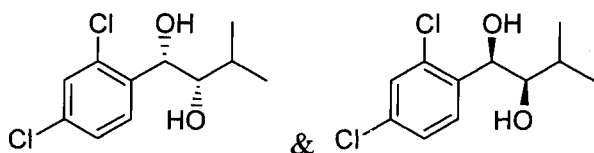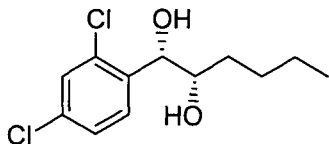
Preparation Example 33: Synthesis of l-(2,4-dichlorophenyl)-3-methyl-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,4-dichlorophenyl)-3 -methyl-trans- 1-butene(Preparation Example 7) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.36g, yield 60-95%).

H NMR(400MHz, CDC1$_3$) 61.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 2.35(d, J=4.0Hz, 1H), 3.12(d, J=8.4Hz, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 34: Synthesis of the mixture of l-(2,4-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol and l-(2,4-dichlorophenyl)-3-methyl-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-trans-l-butene(Preparation Example 7) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.26g, yield 60-95%).

H NMR(400MHz, CDC1$_3$) 51.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 2.35(d, J=4.0Hz, 1H), 3.12(d, J=8.4Hz, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 35: Synthesis of l-(2,4-dichlorophenyl)-(S,S)-l,2-hexanediol
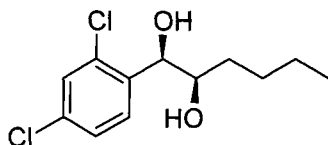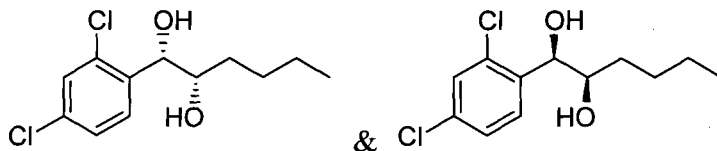

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-hexene(Preparation Example 8) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (l.lg, yield 60-90%).

^{1}H NMR(400MHz, CDC1$_3$) 60.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H), 1.56~1.62(m, 2H), 2.05(d, J=5.2Hz, 1H), 2.74(d, J=5.2Hz, 1H), 3.72-3.77(m, 1H), 4.98(t,
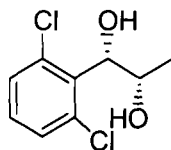
J=4.8Hz, 1H), 7.28~7.50(m, 3H)

Preparation Example 36: Synthesis of l-(2,4-dichlorophenyl)-(R,R)-l,2-hexanediol

5   The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-propene(Preparation   Example 8) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (1.2g, yield 60-95%).

          H NMR(400MHz, CDCl$_3$) 60.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H),
10   1.56~1.62(m, 2H), 2.05(d, *J*=5.2Hz, 1H), 2.74(d, *J*=5.2Hz, 1H), 3.72~3.77(m, 1H), 4.98(t, *J*=4.8Hz, 1H), 7.28~7.50(m, 3H)

Preparation Example 37: Synthesis of the mixture of l-(2,4-dichlorophenyl)-(S,S)-1,2-hexanediol and l-(2,4-dichlorophenyl)-(R,R)-l,2-hexanediol
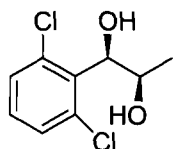

15   The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,4-dichlorophenyl)-trans-l-propene(Preparation   Example 8) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.67g, yield 60-95%).

20   ^{1}H NMR(400MHz, CDCl$_3$) 50.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H), 1.56~1.62(m, 2H), 2.05(d, *J*=5.2Hz, 1H), 2.74(d, *J*=5.2Hz, 1H), 3.72~3.77(m, 1H), 4.98(t, *J*=4.8Hz, 1H), 7.28~7.50(m, 3H)

Preparation Example 38: Synthesis of l-(2,6-dichlorophenyl)-(S,S)-l,2-propanediol
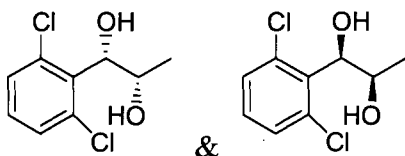

25   The substantially same method as described in Preparation Example 14 was conducted,

except that l-(2,6-dichlorophenyl)-trans-l-propene(Preparation Example 9) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.9g, yield 60-90%).

^{1}H NMR(400MHz, CDC1$_3$) 61.10(d, *J*=6.4Hz, 3H), 2.72(d, *J*=2.4Hz, 1H), 3.10(d, *J*=8.4Hz, 1H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.36(m, 3H)

Preparation Example 39: Synthesis of l-(2,6-dichlorophenyl)-(R,R)-l,2-propanedioI
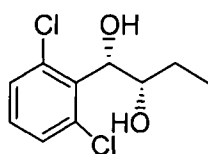

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-propene(Preparation Example 9) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.84g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) 51.10(d, *J*=6.4Hz, 3H), 2.72(d, *J*=2.4Hz, 1H), 3.10(d, *J*=8.4Hz, 1H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.36(m, 3H)

Preparation Example 40: Synthesis of the mixture of l-(2,6-dichlorophenyI)-(S,S)-1,2-propanediol and l-(2,6-dichlorophenyl)-(R,R)-l,2-propanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-propene(Preparation Example 9) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.9lg, yield 60-90%).

[1]H **NMPv**(400MHz, CDC1$_3$) 51.10(d, *J*=6.4Hz, 3H), 2.72(d, *J*=2.4Hz, 1H), 3.10(d, *J*=8.4Hz, 1H), 4.47-4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.36(m, 3H)
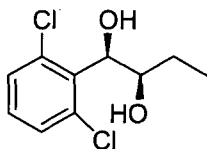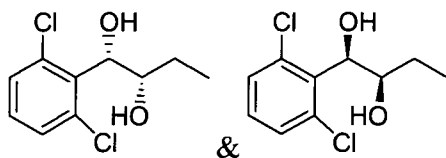
Preparation Example 41: Synthesis of l-(2,6-dichlorophenyl)-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-butene(Preparation   Example 10) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (1.23g, yield 60-95%).

^{1}H NMR(400MHz, CDCl$_3$) 50.97(t, *J*=7.6Hz, 3H), 1.26~1.53(m, 2H), 2.64(dd, *J*=0.8Hz, *J*=4.0Hz, 1H), 3.14(d, *J*=8.4Hz, 1H), 4.22~4.26(m, 1H), 5.26(t, *J*=8.4Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 42: Synthesis of l-(2,6-dichlorophenyl)-(R,R)-1.2-butanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-butene(Preparation   Example 10) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.96g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 50.97(t, *J*=7.6Hz, 3H), 1.26~1.53(m, 2H), 2.64(dd, *J*=0.8Hz, *J*=4.0Hz, 1H), 3.14(d, *J*=8.4Hz, 1H), 4.22~4.26(m, 1H), 5.26(t, *J*=8.4Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 43: Synthesis of the mixture of l-(2,6-dichlorophenyl)-(S,S)-1,2-butanediol and l-(2,6-dichlorophenyl)-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-butene(Preparation   Example 10) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.86g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 50.97(t, *J*=7.6Hz, 3H), 1.26~1.53(m, 2H), 2.64(dd, *J*=0.8Hz, *J*=4.0Hz, 1H), 3.14(d, *J*=8.4Hz, 1H), 4.22-4.26(m, 1H), 5.26(t, *J*=8.4Hz, 1H), 7.17-7.35(m, 3H)
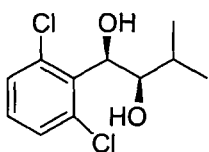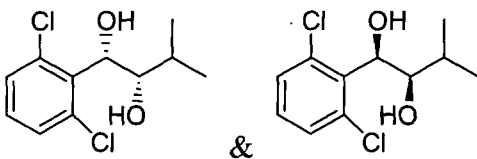
Preparation Example 44: Synthesis of l-(2,6-dichlorophenyl)-3-mefhyl-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,6-dichlorophenyl)-3 -methyl-trans- 1-butene(Preparation Example 11) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.25g, yield 60-95%).

H NMR(400MHz, CDCl$_3$) 61.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 2.35(d, J=4.0Hz, 1H), 3.12(d, J=8.4Hz, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 45: Synthesis of l-(2,6-dichlorophenyl)-3-methyI-(R,R)-l,2-butanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,6-dichlorophenyl)-3 -methyl-trans- l-butene(Preparation Example 11) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation Example 1), to obtain the title compound (0.3 7g, yield 60-95%).

^{1}H NMR(400MHz, CDCl$_3$) 51.00(d, J=6.8Hz, 6H), 1.60-1 .65(m, 1H), 2.35(d, J=4.0Hz, 1H), 3.12(d, J=8.4Hz, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 46: Synthesis of the mixture of l-(2,6-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol and l-(2,6-dichlorophenyl)-3-methyl-(R,R)-l,2-butanediol
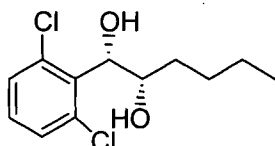

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,6-dichlorophenyl)-3-methyl-trans-l-butene(Preparation Example 11) was used

instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.47g, yield 60-95%).

^{1}H NMR(400MHz, CDC1$_3$) 61.00(d, J=6.8Hz, 6H), 1.60~1.65(m, IH), 2.35(d, J=4.0Hz, IH), 3.12(d, J=8.4Hz, IH), 4.13~4.18(m, IH), 5.36(t, J-7.6Hz, IH), 7.17~7.35(m, 3H)

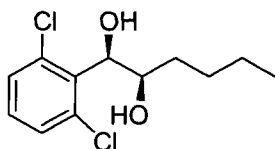**Preparation Example 47: Synthesis of l-(2,6-dichlorophenyl)-(S,S)-l,2-hexanediol**
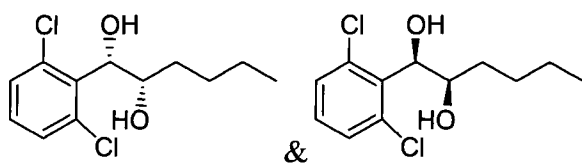

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-hexene(Preparation   Example 12) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.36g, yield 60-90%).

н NMR(400MHz, CDC1$_3$) 60.85(t, J=6.8Hz, 3H), 1.20-1. 3l(m, 4H), 1.45~1.53(m, 2H), 2.61~2.62(m, IH), 3.12(d, J=8.4Hz, IH), 4.28-4.33(m, IH), 5.25(t, J=8.4Hz, IH), 7.18~7.35(m, 3H)

Preparation Example 48: Synthesis of l-(2,6-dichlorophenyl)-(R,R)-l,2-hexanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,6-dichlorophenyl)-trans-l-hexene(Preparation   Example 12) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.58g, yield 60-90%).

^{1}H NMR(400MHz, CDC1$_3$) 60.85(t, J=6.8Hz, 3H), 1.20~1.31(m, 4H), 1.45~1.53(m, 2H), 2.61~2.62(m, IH), 3.12(d, J=8.4Hz, IH), 4.28~4.33(m, IH), 5.25(t, J=8.4Hz, IH), 7.18~7.35(m, 3H)

Preparation Example 49: Synthesis of the mixture of l-(2,6-dichlorophenyl)-(S,S)-1,2-hexanediol and l-(2,6-dichlorophenyl)-(R,R)-l,2-hexanediol

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The substantially same method as described in Preparation Example 16 was conducted, except that 1-(2,6-dichlorophenyl)-trans-1-hexene(Preparation   Example 12) was used instead of 1-(2-chlorophenyl)-trans-1-propene(Preparation   Example 1), to obtain the title compound (0.62g, yield 60-90%).

H NMR(400MHz, CDC1$_3$) 50.85(t, *J*=6.8Hz, 3H), 1.20-1. 3l(m, 4H), 1.45~1.53(m, 2H), 2.61~2.62(m, 1H), 3.12(d, *J*=8.4Hz, 1H), 4.28~4.33(m, 1H), 5.25(t, *J*=8.4Hz, 1H), 7.18~7.35(m, 3H)

Preparation   Example   50:   Synthesis   of   methyl   2-(2-chlorophenyl)-(R)-2-hydroxyacetate
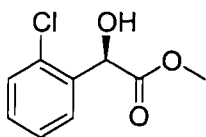
15g of (R)-2-chloromandelic acid was mixed with methanol (CH$_3$OH, 150ml) and phosphorus chloride oxide (POCl$_3$, 0.76ml) in a flask by stirring using a magnetic stirrer at the room temperature for 6 hours.   When the reaction was completed, the obtained product was washed with an aqueous solution of sodium sulfite (Na$_2$S0$_3$) and ethylacetate (EA).   Then, the organic layer was dehydrated with anhydrous magnesium sulfate (MgS0$_4$), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography to produce the title compound (15.64g, yield 95%).

^{1}H NMR(400MHz, CDC1$_3$) δ 3.59(d, *J*=5.2, 1H), 3.79(t, *J*=6.0, 3H), 5.59(d, *J*=5.2, 1H), 7.28~7.43(m, 4H)

Preparation   Example   51:   Synthesis   of   2-(2-chlorophenyl)-(R)-2-hydroxy-N-methoxy-N-methylacetamide
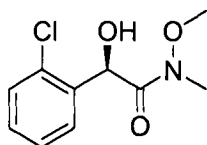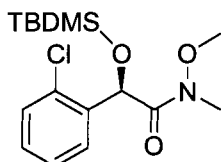

N,O-dimethylhydroxylamine hydrochloride (N,O-dimethylhydroxylamine.HCl,   15.2g)

was dissolved in dichloromethane (DCM, 150ml), and cooled to 0℃ using an ice-bath.   Then, 77.7ml of 2.0M trimethylaluminium in hexane was slowly added thereto in drop-wise manner for 30 minutes.   Thereafter, the ice-bath was removed, and the obtained product was stirred at the room temperature for 2 hours.   Methyl-2-(2-chlorophenyl)-(R)-2-hydroxyacetate(15.64g) dissolved in dichloromethane(DCM, 150ml) was added in drop-wise manner thereto at the room temperature for 30 minutes, and subjected to reflux for 12 hours. When the reaction was completed, the obtained product was cooled to 0℃, and washed by a slow drop-wise addition of hydrochloric acid (HC1, 200ml).   The obtained organic layer was washed with distilled water and brine, dehydrated with anhydrous magnesium sulfate (MgS0$_4$), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography to produce the title compound (14.68g, yield 82%).

^{1}H NMR(400MHz, CDC1$_3$) 53.23(s, 3H), 3.28(s, 3H), 4.33(d, J=6.0Hz, 1H), 5.81(d, J=5.6Hz, 1H), 7.23~7.42(m, 4H)
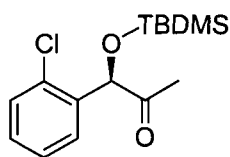

Preparation Example 52: Synthesis of 2-(2-chlorophenyl)-N-methoxy-(R)-2-(t-butyl dimethlysiloxy)-N-methylacetamide

2-(2-chlorophenyl)-(R)-2-hydroxy-N-methoxy-N-methylacetamide   (0.81 g,   3.52mmol) obtained in Preparation Example 5 1 was dissolved in dichloromethane (DCM), and cooled to 0℃. Imedazole (0.36g, 5.28mmol) was slowly added, and stirred. TBDMS-C1 (t-butyldimethylsily chloride, 0.79g, 5.28mmol) was slowly added. When the reaction was completed, the reaction mixture was quenched with H$_2$0 . The organic layer was separated and collected. The aqueous layer was extracted with CH$_2$C l$_2$ (300mL), dried over MgS0$_4$. Concentration under vacuum provided a title compound.(0.97g, 80~95%).

H NMR(400MHz, CDC1$_3$) 5-0.03(s, 3H), 0.14(s, 3H), 0.94(s, 9H), 2.97(s, 3H), 3.02(s, 3H), 5.83(s, 1H), 7.25~7.60(m, 4H)

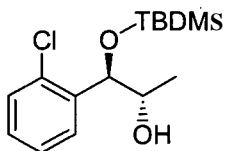**Preparation Example 53: Synthesis of l-(2-chlorophenyl)-(R)-l-(t-butyldimethyl-siloxy)propane-2-on**

2-(2-chlorophenyl)-N-methoxy-(R)-2-(t-butyldimethylsiloxy)-N-methylacetamide(0.9g)

obtained in Preparation Example 52 was dissolved in tetrahydrofuran(THF), and cooled to 0 ℃.

3.0M methyl magnesium bromide (MeMgBr, 2.18ml) solution in ether was added thereto in

drop-wise manner for 30 minutes, and the obtained product was stirred at 0 ℃. When the

reaction was completed, diethylether was added thereto. The obtained product was washed

with 10%(w/v) potassium hydrogen sulfate (KHS0$_4$, 100ml) and then, washed again with brine.

The obtained organic layer was dehydrated with anhydrous magnesium sulfate (MgS0$_4$),

filtrated, and concentrated under reduced pressure. The concentrated residue was purified by a

silica gel column chromatography to produce the title compound (0.69g, yield 85-95%).

^{1}H NMR(400MHz, CDC1$_3$) 8-0.3(**s,** 3H), 0.14(s, 3H), 0.94(s, 9H), 2.18(s, 3H), 5.50(s,

1H), 7.27~7.56(m, 4H)

Preparation Example 54: Synthesis of l-(2-chlorophenyl)-(R)-l-(t-butyldimethyl-siloxy)-(S)-2-propanol

1-(2-chlorophenyl)-(R)- 1-(t-butyldimethyl-siloxy)propane-2-on(0. 14g) obtained in

Preparation Example 53 was dissolved in ether, and cooled to -78 ℃. Zinc

borohydride(Zn(BH$_4$)$_2$) was slowly added thereto and the obtained product was stirred. When the

reaction was completed, the obtained product was washed by H$_2$0. The obtained organic layer

was washed with H$_2$0, dehydrated with anhydrous magnesium sulfate (MgS0$_4$), filtrated, and

concentrated under reduced pressure. The concentrated residue was purified by a silica gel

column chromatography to produce the title compound (0.04g, yield 25-33%, cis : trans = 2 : 1).

H NMR(400MHz, CDC1$_3$) 8-0.11(s, 3H), 0.11(s, 3H), 0.93(S, 9H), 1.07(d, J=6.4 3H),

2.05(d, J=6.4 1H), 4.01~4.05(m, 1H), 5.18(d, *J*=4.0, 1H), 7.20~7.56(m, 4H))

Preparation Example 55: Synthesis of l-(2-chlorophenyI)-(R,S)-l,2-propanediol
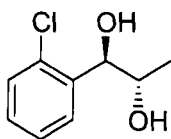
1-(2-chlorophenyl)-(R)-1 -(t-butyldimethyl-siloxy)-(S)-2-propanol(10.3 8g) obtained in Preparation Example 54 was dissolved in methanol (CH$_3$OH, 100ml), and then, cooled to 0℃. 8M hydrochloric acid(HCl, 56.2ml) was slowly added in drop-wise manner to the obtained product, and then, the obtained product was warmed to the room temperature, and stirred for 15 hours.   When the reaction was completed, the obtained product was cooled to 0℃.   5N sodium hydroxide (NaOH, 30ml) was slowly added thereto, and the obtained product was subjected to vacuum concentration.   The obtained product was diluted with ethylacetate.   The obtained organic layer was washed with distilled water, dehydrated with anhydrous magnesium sulfate **(MgS04),** filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography to produce the title compound (7.05g, yield 60-90%).

H   NMR(400MHz, CDCl$_3$) 81.07(d, *J*=6.8, 3H), 2.01(d, *J*=5.6, 1H), 2.61(s, 1H), 4.21~4.27(m, 1H), 5.24(d, *J*=3.6, 1H), 7.22~7.64(m, 4H)

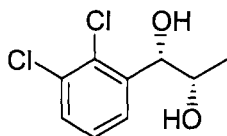**Preparation Example 56: Synthesis of l-(2-chlorophenyl)-(S,R)-l,2-propanediol**
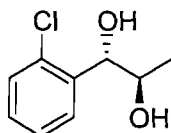
The substantially same method as described in Preparation Example 50-55 was conducted, except that (S)-2-chloromandelic acid was used instead of (R)-2-chloromandelic acid, to obtain the title compound (5.04g, yield 84%).

H   NMR(400MHz, CDCl$_3$) 51.07(d, *J*=6.8, 3H), 2.00(d, *J*=5.6, 1H), 2.54(d, *J*=3.6, 1H), 4.22~4.26(m, 1H), 5.25(t, *J*=3.2, 1H), 7.22~7.65(m, 4H)

Preparation Example 57: Synthesis of l-(2,3-dichlorophenyl)-(S,S)-l,2-propanediol
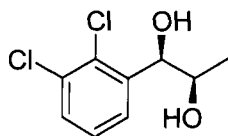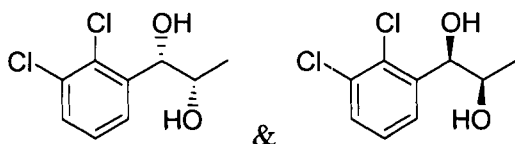

The substantially same method as described in Preparation Example 14 was conducted,

except that l-(2,3-dichlorophenyl)-trans-l-propene(Preparation   Example 13) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.9g, yield 60-90%).

H   NMR(400MHz,   CDCl$_3$)   61.10(d,   *J*=6.4Hz,   3H),   2.72(d,   *J*=2.4Hz,   1H),   3.10(d, *J*=8.4Hz, 1H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18- (m, 3H)

Preparation Example 58: Synthesis of l-(2,3-dichlorophenyI)-(R,R)-l,2-propanediol
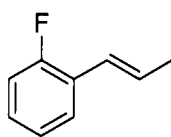

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2,3-dichlorophenyl)-trans-l-propene(Preparation   Example 13) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.84g, yield 60-90%).

H   NMR(400MHz,   CDCl$_3$)   51.10(d,   *J*=6.4Hz,   3H),   2.72(d,   *J*=2.4Hz,   1H),   3.10(d, *J*=8.4Hz, 1H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18- (m, 3H)

Preparation Example 59: Synthesis of the mixture of l-(2,3-dichlorophenyl)-(S,S)-1,2-propanediol and l-(2,3-dichlorophenyl)-(R,R)-l,2-propanediol

The substantially same method as described in Preparation Example 16 was conducted, except that l-(2,3-dichlorophenyl)-trans-l-propene(Preparation   Example 13) was used instead of l-(2-chlorophenyl)-trans-l-propene(Preparation   Example 1), to obtain the title compound (0.91g, yield 60-90%).

H   NMR(400MHz,   CDCl$_3$)   51.10(d,   *J*=6.4Hz,   3H),   2.72(d,   *J*=2.4Hz,   1H),   3.10(d, *J*=8.4Hz, 1H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~(m, 3H)
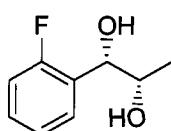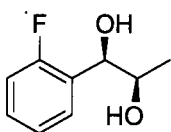
Preparation Example 60: Synthesis of l-(2-fluorophenyl)-trans-l-propene

The substantially same method as described in Preparation Example 1 was conducted, except that 2-fluorobenzenaldehyde was used instead of 2-chlorobenzenealdehyde, to obtain the title compound (6.67g, yield 61%).

^{1}H NMR(400MHz, CDC1$_3$) 51.94(d, *J*=6.8Hz, 3H), 6.30~6.38(m, 1H), 6.57(d, *J*=16Hz, 1H), 7.00-7.4 l(m, 4H)

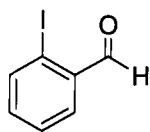**Preparation Example 61: Synthesis of l-(2-fluorophenyl)-(S,S)-l,2-propanediol**

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2-fluorophenyl)-trans-l-propene (Preparation Example 60) was used instead of 1-(2-chlorophenyl)-trans-l-propene (Preparation Example 1), to obtain the title compound (6.46g, yield 78%).

H NMR(400MHz, CDC1$_3$) 51.15(d, *J*=6.4Hz, 3H), 2.43(d, *J*=3.6Hz, 1H), 2.69(d, *J*=4.8Hz, 1H), 3.90~3.98(m, 1H), 4.78(dd, *J*=4.4, 7.2Hz, 1H), 7.04~7.50(m, 4H)

Preparation Example 62: Synthesis of l-(2-fluorophenyl)-(R,R)-l ,2-propanediol

The substantially same method as described in Preparation Example 15 was conducted, except that l-(2-fluorophenyl)-trans-l-propene (Preparation Example 60) was used instead of 1-(2-chlorophenyl)-trans-l-propene (Preparation Example 1), to obtain the title compound (3.29g, yield 79%).

H NMR(400MHz, CDC1$_3$) 51.15(d, *J*=6.4Hz, 3H), 2.43(d, *J*=3.6Hz, 1H), 2.69(d, *J*=4.8Hz, 1H), 3.90~3.98(m, 1H), 4.78(dd, *J*=4.4, 7.2Hz, 1H), 7.04~7.50(m, 4H)
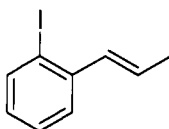
Preparation Example 63: Synthesis of 2-iodobenzcnealdehyde

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 the reflux condition. When the reaction was completed, the obtained reaction product was cooled to the room temperature, and then, fiteated and concentrated using celite, to obtain the title compound (3.6g, yield 91%).

H NMR(400MHz, CDCl$_3$)57.30~7.99(m, 4H), 10.10(s, 1H)

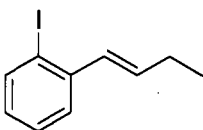**Preparation Example 64: Synthesis of l-(2-iodophenyl)-trans-l-propene**

The substantially same method as described in Preparation Example 1 was conducted, except that 2-iodobenzenealdehyde (Preparation Example 63) was used instead of 2-chlorobenzenealdehyde, to obtain the title compound (3.4g, yield 65%).

H NMR(400MHz, CDCl$_3$)51.95(dd, *J*=6.8Hz, 1.6Hz, 3H), 6.09-6. 18(m, 1H), 6.60(dd, *J*=l5.66Hz, 1.8Hz, 1H), 6.89~7.84(m, 4H)

Preparation Example 65: Synthesis of l-(2-iodophenyl)-trans-l-butene
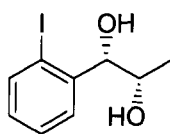

The substantially same method as described in Preparation Example 64 was conducted, except that 3-heptanone was used instead of 3-pentanone, to obtain the title compound (8.5g, yield 75%).

H NMR(400MHz, CDCl$_3$)81.46(t, *J*=7.6Hz, 3H), 2.26~2.34(m, 2H), 6.17(dt, *J*=15.6Hz, 6.6Hz 1H), 6.57(d, *J*=15.6Hz, 1H), 6.89~7.85(m, 4H)
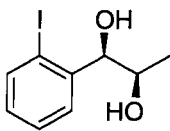

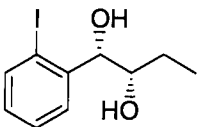**Preparation Example 66: Synthesis of l-(2-iodophenyl)-(S,S)-l,2-propanediol**

The substantially same method as described in Preparation Example 14 was conducted, except that l-(2-iodophenyl)-trans-l-propene (Preparation Example 64) was used instead of 1-(2-chlorophenyl)-trans-l-propene (Preparation Example 1), to obtain the title compound (3.4g, yield 88%).

ʜ NMR(400MHz, CDCl$_3$)51.27(d, J=6.4Hz, 3H), 2.26(br s, 1H), 2.74(br s, 1H), 3.99(t, J=6.0Hz, 1H), 4.8 1(d, J=4.0Hz, 1H), 7.01~7.87(m, 4H)

Preparation Example 67: Synthesis of l-(2-iodorophenyl)-(R,R)-l,2-propanediol

The substantially same method as described in Preparation Example 15 was conducted was conducted, except that l-(2-iodophenyl)-trans-l-propene (Preparation Example 64) was used instead of l-(2-chlorophenyl)-trans-l-propene (Preparation Example 1), to obtain the title compound (7.4g, yield 84%).

ʜ NMR(400MHz, CDCl$_3$)51.26(d, J=6.4Hz, 3H), 2.35(br s, 1H), 2.85(br d, J=4.0Hz, 1H), 3.98(t, J=6.2Hz, 1H), 4.80(dd, J=5.0, 4.4Hz, 1H), 7.00~7.87(m, 4H)

Preparation Example 68: Synthesis of l-(2- iodophenyl)-(S,S)-l,2-butanediol

The substantially same method as described in Preparation Example 14 was conducted was conducted, except that l-(2-iodophenyl)-trans-l-butene (Preparation Example 65) was used instead of l-(2-chlorophenyl)-trans-l-propene (Preparation Example 1), to obtain the title compound (9.5g, yield 84%»).

ʜ NMR(400MHz, CDCl$_3$)51.04(t, J=7.6Hz, 3H), 1.60-1.7l(m, 2H), 2.07(br s, 1H), 2.74(br s, 1H), 3.71~3.76(m, 1H), 4.87(d, J=4.8Hz, 1H), 7.01~7.87(m, 4H)
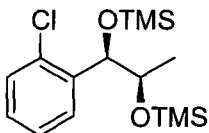

Preparation Example 69 : Preparation of l-(2-chIorophenyl)-(S,S)-l,2-(Bis-

trimethylsilanyloxy) propane
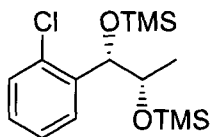
To a stirred solution of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14, 67g, 0.35mol) in CH_2Cl_2 (670ml) was added Et_3N (200mL, 1.43mol) and TMSC1 (113.9mL, 0.89mol) at 0°C under N_2. The reaction mixture was allowed to stir at 0°C for 3hr. The reaction mixture was quenched with H_2O (650mL) at 0°C. The organic layer was separated and collected. The aqueous layer was extracted with CH_2Cl_2 (300mL), dried over MgSC^. Concentration under vacuum provided a crude product. 104. 18g (117.44%).

H NMR(400MHz, $CDCl_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.1 5(d, *J*=5.6Hz, 3H), 3.977-3.91 8(m, 1H), 4.973(d, *J*=6.4Hz, 1H), 7.207~7.165(m,lH), 7.321~7.245(m, 2H), 7.566~7.543(m, 1H)

Preparation Example 70 : Preparation of 1-(2-chlorophenyl)-(R,R)-1,2-(Bis-trimethylsilanyloxy) propane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-chlorophenyl)-(R,R)-1,2-propanediol(Preparation example15)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation exairiple14) to obtain the title compound (8.5g, yield 90-120%).
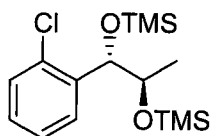
H NMR(400MHz, $CDCl_3$)8-0.053(s, 9H), 0.044(s, 9H), 1.15(d, *J*=5.6Hz, 3H), 3.977~3.918(m, 1H), 4.973(d, *J*=6.4Hz, 1H), 7.21~7.54(m,4H)

Preparation Example 71 : Preparation of 1-(2-chlorophenyl)—1,2-(Bis-trimethylsilanyloxy) propane
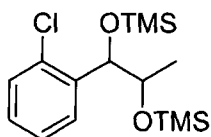
The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)propane-l,2-diol(Preparation example16)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (5.2g, yield 90-120%).

5   **н NMPv**(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.15(d, **J**=5.6Hz, 3H), 3.977~3.918(m, 1H), 4.973(d, **J**6.4Hz, 1H), 7.21~7.54(m,4H)

Preparation Example 72 : Preparation of l-(2-chlorophenyl)-(S,R)-l,2-(Bis-trimethylsilanyloxy) propane
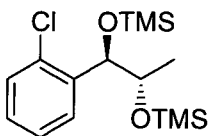

10   The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-(S,R)-l,2-propanediol(Preparation example56)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.4g, yield 90-1 20%).

15   **н NMR**(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.15(d, **J**=5.6Hz, 3H), 3.977~3.918(m, 1H), 4.973(d, **J**=6.4Hz, 1H), 7.21~7.54(m,4H)

Preparation Example 73 : Preparation of l-(2-chlorophenyl)-(R,S)-l,2-(Bis-trimethylsilanyloxy) propane
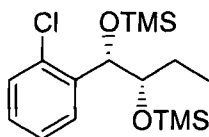

20   The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-(R,S)-l,2-propanediol(Preparation example55)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.2g, yield 90-120%).

25   **н NMR**(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.1 5(d, **J**=5.6Hz, 3H), 3.977~3.918(m, 1H), 4.973(d, **J**=6.4Hz, 1H), 7.21~7.54(m,4H)

Preparation Example 74 : Preparation of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-

trimethylsilanyloxy) butane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-chlorophenyl)-(S,S)-1,2-butanediol(Preparation example 17)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14) to obtain the title compound (3.6g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.01(t, J=7.4Hz, 3H), 1.52~1.65(m, 2H), 3.69~3.75(m, 1H), 5.05(t, J=5.0Hz, 1H), 7.23~7.54(m,4H)
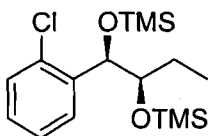
Preparation Example 75 : Preparation of 1-(2-chlorophenyl)-(R,R)-1,2-(Bis-trimethylsilanyloxy) butane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-chlorophenyl)-(R,R)-1,2-butanediol(Preparation example18)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation exampleH) to obtain the title compound (3.5g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.01(t, J=7.4Hz, 3H), 1.52~1.65(m, 2H), 3.69~3.75(m, 1H), 5.05(t, J=5.0Hz, 1H), 7.23-7.54(m,4H)
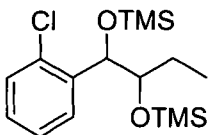
Preparation Example 76 : Preparation of 1-(2-chIorophenyl)-1,2-(Bis-trimethylsilanyloxy) butane
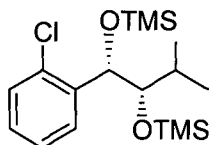
The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-chlorophenyl)-1,2-butanediol(Preparation example 19)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation exampleH) to obtain the title compound (3.0g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.01(t, J=7.4Hz, 3H), 1.52~1.65(m,

2H), 3.69~3.75(m, 1H), 5.05(t, *J*=5.0Hz, 1H), 7.23~7.54(m,4H)

Preparation Example 77 : Preparation of l-(2-chlorophenyl)-3-methyl-(S,S)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-3-methyl-(S,S)-l,2-butanediol(Preparation example20)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title (2.7g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.07(t, *J*=7.2Hz, 6H), 1.83~1.89(m, 1H), 3.53~3.56(m, 1H), 5.22~5.25(m, 1H), 7.23~7.55(m,4H)

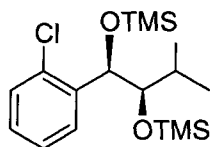**Preparation Example 78 : Preparation of l-(2-chlorophenyl)-3-methyl-(R,R)-l,2-(Bis-trimethylsilanyloxy)-butane**

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-3-methyl-(R,R)-l,2-butanediol(Preparation example21)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.4g, yield 90-1 20%).

^{1}H NMRHOOMHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.07(t, *J*=7.2Hz, 6H), 1.83~1.89(m, 1H), 3.53~3.56(m, 1H), 5.22~5.25(m, 1H), 7.23~7.55(m,4H)

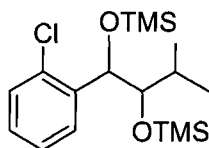**Preparation Example 79 : Preparation of l-(2-chlorophenyI)-3-methyl-l,2-(Bis-trimethylsilanyloxy)-butane**
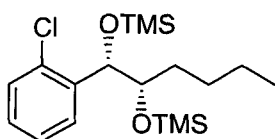

The substantially same method as described in Preparation Example 69 was conducted,

41

except that l-(2-chlorophenyl)-3 -methyl- 1,2-butanediol(Preparati on example22)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.8g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.07(t, J=7.2Hz, 6H),

5   1.83~1.89(m, 1H), 3.53~3.56(m, 1H), 5.22~5.25(m, 1H), 7.23~7.55(m,4H)

Preparation Example 80 : Preparation of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyIoxy)-hexane

10   The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-(S,S)-l,2-hexanediol(Preparation example23)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.1g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.90(t, J=7.2Hz, 3H),

15   1.35~1.65(m, 6H), 3.78~3.83(m, 1H), 5.04(t, J=5.0Hz, 1H), 7.23~7.53(m,4H)

Preparation Example 81 : Preparation of l-(2-chIorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-hexane
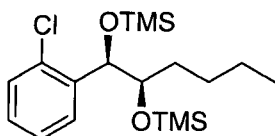
20   The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-(R,R)-l,2-hexanediol(Preparation example24)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.3g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), **0.90(t,** J=7.2Hz, 3H),

25   1.35-1.65(m, 6H), 3.78~3.83(m, 1H), **5.04(t,** J=5.0Hz, 1H), 7.23~7.53(m,4H)

Preparation Example 82 : Preparation of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-hexane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-chlorophenyl)-l,2-hexanediol(Preparation example25)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation examplel4) to obtain the title compound (3.2g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 0.90(t, *J*=7.2Hz, 3H), 1.35~1.65(m, 6H), 3.78~3.83(m, 1H), 5.04(t, *J*=5.0Hz, 1H), 7.23~7.53(m,4H)
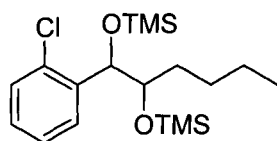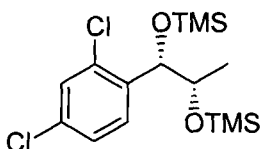

Preparation Example 83 :   Preparation of l-(2,4-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyIoxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-(S,S)-l,2-propanediol(Preparation example26)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation examplel4) to obtain the title compound (2.4g,   yield 90-120%).

H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.22(d, *J*=6.4Hz, 3H), 3.90~3.95(m, 1H), 4.94(t, *J*=5.0Hz, 1H), 7.31(dd, *J*=2.0Hz, *J*=8.0Hz, 1H), 7.40(d, *J*=2.0Hz, 1H), 7.49(d, *J*=8.4Hz, 1H)
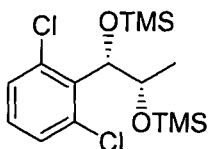

Preparation Example 84 :   Preparation of l-(2,6-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-(S,S)-l,2-propanediol(Preparation example38)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation examplel4) to obtain the title compound (3.4g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.10(d, *J*=6.4Hz, 3H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.13~7.36(m, 3H)

Preparation Example 85 :   Preparation of 1-(2,3-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2,3-dichlorophenyl)-(S,S)-1,2-propanediol(Preparation   example57)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   exampleH) to obtain the title compound (2.2g,   yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.10(d, *J*=6.4Hz, 3H,), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.22(m, 3H)
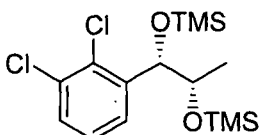

Preparation Example 86 :   Preparation of 1-(2,4-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2,4-dichlorophenyl)-(S,S)-1,2-butanediol(Preparation   example29)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   exampleH)   to   obtain   the   title compound (3.1g,   yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.02(t, *J*=7.4Hz, 3H), 1.54~1.61(m, 2H), 3.65~3.68(m, 1H), 5.01(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)
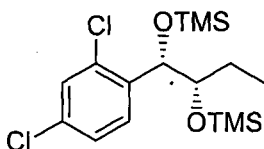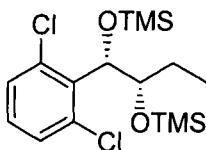
Preparation Example 87 :   Preparation of 1-(2,6-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted,

except that l-(2,6-dichlorophenyl)-(S,S)-l,2-butanediol(Preparation example41)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.8g,   yield 90-120%).

H NMR(400MHz, CDCl$_3$)8-0.053(s, 9H), 0.044(s, 9H), 0.97(t, J=7.6Hz, 3H), 1.26~1.53(m, 2H), 4.22~4.26(m, 1H), 5.26(t, J=8.4Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 88 :   Preparation of l-(2,4-dichlorophenyi)-3-methyl-(S,S)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol(Preparation example32)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.7g,   yield 90- 120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.30~7.53(m, 3H)

Preparation Example 89 :   Preparation of l-(2,6-dichlorophenyl)-3-methyl-(S,S)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol(Preparation example44)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.3g,   yield 90-1 20%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13-4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 90 :   Preparation of l-(2,4-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-hexane
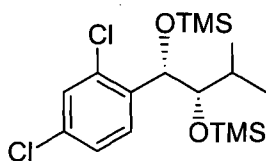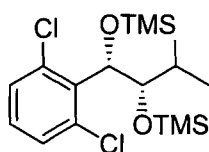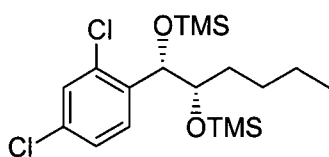
45

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-(S,S)-l,2-hexanediol(Preparation example90)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.6g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H), 1.56~1.6(m, 2H), 3.72~3.77(m, IH), 4.98(t, *J*=4.8Hz, IH), 7.28~7.50(m, 3H)
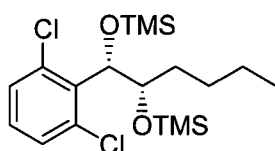
Preparation Example 91 :   Preparation of l-(2,6-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-hexane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-(S,S)-l,2-hexanediol(Preparation example47)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.8g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.85(t, *J*=6.7Hz, 3H), 1.20-1. 3l(m, 4H), 1.45~1.53(m, 2H), 4.28~4.33(m, IH), 5.25(t, *J*=8.4Hz, IH), 7.18~7.35(m, 3H)

Preparation Example 92 :   Preparation of l-(2,4-dichlorophenyl)-(R,R)-l   ,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation example27)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.2g, yield 90-1 20%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), **1.22(d, *J*=6.4Hz, 3H)**, 3.90-3.95 **(m,**

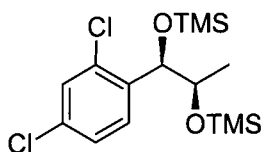1H), 4.94(t, *J*=5.0Hz, 1H), 7.31~7.49(m, 3H)

Preparation Example 93 : Preparation of l-(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation example39)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example14) to obtain the title compound (2.6g, yield 90-120%).

H NMR(400MHz, CDCl₃)δ-0.053(s, 9H), 0.044(s, 9H), 1.10(d, *J*=6.4Hz, 3H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.36(m, 3H)

Preparation Example 94 : Preparation of l-(2,3-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-propane
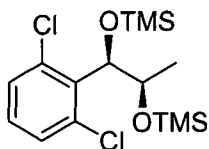

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,3-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation example58)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example14) to obtain the title compound (2.9g, yield 90-120%).

H NMR(400MHz, CDCl₃)δ-0.053(s, 9H), 0.044(s, 9H), 1.10(d, *J*=6.4Hz, 3H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.22(m, 3H)
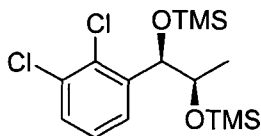
Preparation Example 95 : Preparation of l-(2,4-dichlorophenyi)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted,

except that l-(2,4-dichlorophenyl)-(R,R)-l,2-butanediol(Preparation example30)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.6g,   yield 90~120%).

ᴴ NMR(400MHz, CDCl$_3$)δ-0.053(s, 9H), 0.044(s, 9H), 1.02(t, J=7.4Hz, 3H), 1.54~1.61(m, 2H), 3.65~3.68(m, 1H), 5.01(t, J=5.0Hz, 1H), 7.31~7.49(m, 3H)
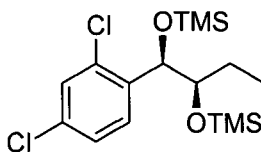

Preparation Example 96 :   Preparation of l-(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-butane
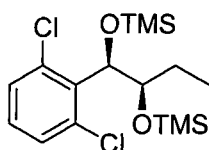

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-(R,R)-l,2-butanediol(Preparation example42)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.3g,   yield 90-120%).

ᴴ NMR(400MHz, CDCl$_3$)δ-0.053(s, 9H), 0.044(s, 9H), 0.97(t, J=7.6Hz, 3H), 1.26~1.53(m, 2H), 4.22~4.26(m, 1H), 5.26(t, J=8.4Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 97 :   Preparation of l-(2,4-dichlorophenyl)-3-methyl-(R,R)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-(R,R)- 1,2-butanediol(Preparation example33)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.5g,   yield 90-120%).

ᴴ NMR(400MHz, CDCl$_3$)δ-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.30~7.53(m, 3H)

Preparation Example 98 :   Preparation of l-(2,6-dichlorophenyl)-3-methyl-(R,R)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-3-methyl-(R,R)-l,2-butanediol(Preparation example45)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example14) to obtain the title compound (3.4g,   yield 90-120%).

н   NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)·
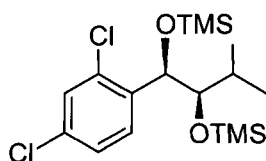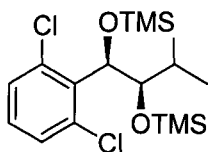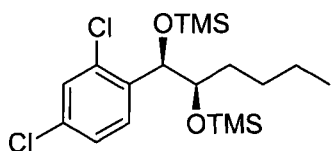
Preparation Example 99 :   Preparation of l-(2,4-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-hexane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-(R,R)-l,2-hexanediol(Preparation example36)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleM) to obtain the title compound (3.6g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H), 1.56~1.62(m, 2H), 3.72~3.77(m, 1H), 4.98(t, J=4.8Hz, 1H), 7.28~7.50(m, 3H)

Preparation Example 100 :   Preparation of l-(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)-hexane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-(R,R)-l,2-hexanediol(Preparation example48)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleM) to obtain the title compound (3.3g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), **0.85(t, *J*=6.7Hz, 3H)**, 1.20-1.31(m, 4H), 1.45~1.53(m, 2H), 4.28~4.33(m, 1H), **5.25(t, *J*=8.4Hz, 1H)**, 7.18~7.35(m, 3H)

Preparation Example 101 : Preparation of l-(2,4-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-l,2-propanediol(Preparation example28)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example14) to obtain the title compound (2.6g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.22(d, *J*=6.4Hz, 3H), 3.90~3.95(**m, 1H**), 4.94(t, *J*=5.0Hz, 1H), 7.31~7.49(**m, 3H**)
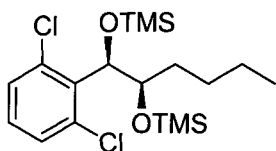

Preparation Example 102 : Preparation of l-(2,6-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-l,2-propanediol(Preparation example40)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example 14) to obtain the title compound (3.1g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.10(d, *J*=6.4Hz, 3H), 4.47~4.54(m, 1H), 5.24(t, *J*=8.8Hz, 1H), 7.18~7.36(m, 3H)
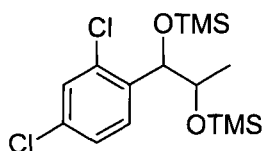

Preparation Example 103 : Preparation of l-(2,3-dichIorophenyi)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,3-dichlorophenyl)-l,2-propanediol(Preparation example59)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.7g, yield 90-120%).

5 H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.10(d, J=6.4Hz, 3H), 4.47~4.54(m, 1H), 5.24(t, J=8.8Hz, 1H), 7.18~7.22(m, 3H)
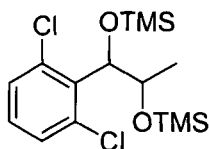

Preparation Example 104 : Preparation of l-(2,4-dichlorophenyl)-l,2-(Bis-trimethyIsilanyloxy)-butane

10 The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-l,2-butanediol(Preparation example31)was used instead of 1-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.9g, yield 90-120%).

15 H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.02(t, J=7.4Hz, 3H), 1.54~1.61(m, 2H), 3.65~3.68(m, 1H), 5.01(t, J=5.0Hz, 1H), 7.31~7.49(m, 3H)
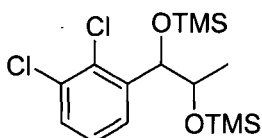

Preparation Example 105 : Preparation of l-(2,6-dichlorophenyl)-l,2-(Bis-trimethylsilanyIoxy)-butane

20 The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-l,2-butanediol(Preparation example43)was used instead of 1-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.1g, yield 90-120%).

25 ^{l}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.97(t, J=7.6Hz, 3H), 1.26~1.53(m, 2H), 4.22~4.26(m, 1H), 5.26(t, J=8.4Hz, 1H), 7.17~7.35(m, 3H)

Preparation Example 106 : Preparation of l-(2,4-dichlorophenyl)-3-methyl-l,2-

(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-l,2-butanediol(Preparation example34)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.7g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.30~7.53(m, 3H)

Preparation Example 107 : Preparation of l-(2,6-dichlorophenyl)-3-methyl-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-3 -methyl- 1,2-butanediol(Preparation example46)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.6g, yield 90-1 20%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.00(d, J=6.8Hz, 6H), 1.60~1.65(m, 1H), 4.13~4.18(m, 1H), 5.36(t, J=7.6Hz, 1H), 7.17~7.35(m, 3H)
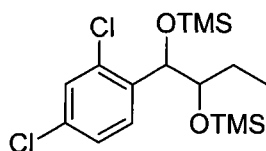

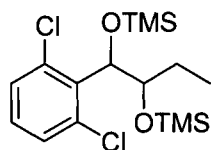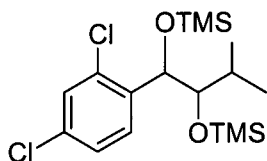**Preparation Example 108 : Preparation of l-(2,4-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)-hexane**

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,4-dichlorophenyl)-l,2-hexanediol(Preparation example37)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.7g, yield 90-120%).

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ʜ NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 0.89~0.93(m, 3H), 1.30~1.39(m, 2H), 1.49~1.52(m, 2H), 1.56~1.62(m, 2H), 3.72~3.77(m, 1H), 4.98(t, *J*=4.8Hz, 1H), 7.28~7.50(m, 3H)
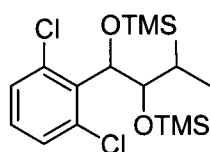
Preparation Example 109 : Preparation of l-(2,6-dichlorophenyi)-l,2-(Bis-trimethylsilanyloxy)-hexane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2,6-dichlorophenyl)-l,2-hexanediol(Preparation example49)was used instead of 1-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (3.2g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 0.85(t, *J*=6.7Hz, 3H), 1.20-1. 3l(m, 4H), 1.45~1.53(m, 2H), 4.28~4.33(m, 1H), 5.25(t, *J*=8.4Hz, 1H), 7.18~7.35(m, 3H)
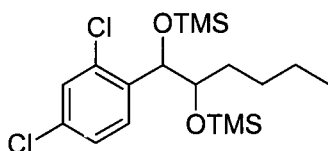
Preparation Example 110 : Preparation of l-(2-fluorophenyi)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-fulorophenyl)-(S,S)-l,2-propanediol(Preparation example61)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation exampleH) to obtain the title compound (2.8g, yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.15(d, *J*=6.4Hz, 3H), 3.90~3.98(m, 1H), 4.78(dd, *J*=4.4, 7.2Hz, 1H), 7.04~7.50(m, 4H)

Preparation Example 111 : Preparation of l-(2-fulorophenyl)-(R,R)-1.2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-fulorophenyl)-(R,R)-1,2-propanediol(Preparation example62)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14) to obtain the title compound (2.5g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.15(d, J=6.4Hz, 3H), 3.90~3.98(m, 1H), 4.78(dd, J=4.4, 7.2Hz, 1H), 7.04~7.50(m, 4H)
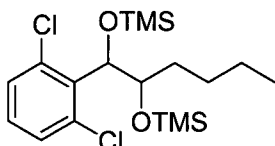
Preparation Example 112 :   Preparation of 1-(2-iodophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-iodophenyl)-(S,S)-1,2-propanediol(Preparation example66)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14) to obtain the title compound (3.1g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.27(d, J=6.4Hz, 3H), 3.99(t, J=6.0Hz, 1H), 4.81(d, J=4.0Hz, 1H), 7.01~7.87(m, 4H)
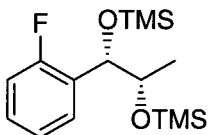
Preparation Example 113 :   Preparation of 1-(2-iodophenyl)-(R,R)-1,2-(Bis-trimethylsilanyloxy)-propane

The substantially same method as described in Preparation Example 69 was conducted, except that 1-(2-iodophenyl)-(R,R)-1,2-propanediol(Preparation example67)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14) to obtain the title compound (2.8g,   yield 90-120%).

^{1}H NMR(400MHz, CDCl$_3$)6-0.053(s, 9H), 0.044(s, 9H), 1.26(d, J=6.4Hz, 3H), 3.98(t, J=6.2Hz,
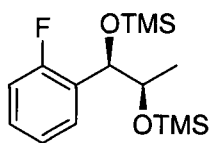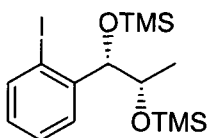
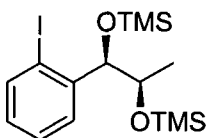1H), 4.88(d, J=4.4Hz, 1H), 7.00~7.87(m, 4H)

Preparation Example 114 : Preparation of l-(2-iodophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)-butane

The substantially same method as described in Preparation Example 69 was conducted, except that l-(2-iodophenyl)-(S,S)-l,2-butanediol(Preparation example68)was used instead of 1-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation examplel4) to obtain the title compound (3.3g, yield 90-120%).

H NMR(400MHz, CDCl$_3$)5-0.053(s, 9H), 0.044(s, 9H), 1.04(t, J=7.6Hz, 3H), 1.60-1. 7 1(m, 2H), 3.71~3.76(m, 1H), 4.87(d, J=4.8Hz, 1H), 7.01~7.87(m, 4H)

Example 1 : Preparation of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(S)-2-carbamate(l)
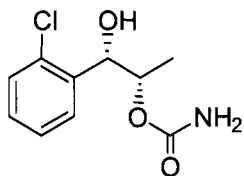
To a stirred solution of crude l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane(preparation example69, 104g, 0.31mol) in toluene (670mL) was added by Chlorosulfonyl isocynate(62.5mL, 0.71mol) at 0°C. The reaction mixture was stirred for 2hr. The reaction mixture was quenched with ice water and then was stirred by additional cold H$_2$0 (500mL) for 2hr. After separation of organic layer, the aqueous was adjusted pH2~3 with sat. NaHCO$_3$(400mL) and extracted with EtOAc (300mL x3). The EtOAc layer was washed with sat. NaHC0$_3$ (500mL) and H$_2$O(500mL). The organic phase was treated with Charcol for . 1.5hr. The organic phase was filtered with Cellite, dreid over MgS0$_4$. Filterion and concentration under vacuum provided the title compound of white solid(yield 85%(71.1g), ee = 99.9% MP = 83~84°C, [α]$_D$=+57.8(c=0.25, MeOH))

H NMR(400MHz, CDC1$_3$) 61.24(d, J-6.4, 3H), 2.91(d, J=4.8, 1H), 4.68(br s, 2H), 5.06~5.09(m, 1H), 5.18~5.21(m, 1H), 7.23~7.39(m, 3H), 7.55(dd, J=1.6, J=7.8, 1H)

^{13}C NMR(100MHz, CDCl₃) 516.4, 73.1, 75.0, 127.0, 128.4, 129.1, 129.5, 132.7, 138.0, 156.6

Example 2 :   Preparation of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(2)
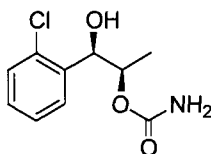
The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example70)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (5.7g,   yield 60~90%).

H NMR(400MHz, CDCl₃) 51.24(d, J=6.4, 3H), 2.91(d, *J*=4.8, IH), 4.68(br s, 2H), 5.06~5.09(m, IH), 5.18~5.21(m, IH), 7.23~7.39(m, 3H), 7.55(dd, *J*=1.6, *J*=7.8, IH)

Example 3 :   Preparation of l-(2-chlorophenyl)-l-hydroxypropyl-2-carbamate(3)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example71)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (3.8g,   yield 60-90%).

^{1}H NMR(400MHz, CDCl₃) 51.24(d, J=6.4, 3H), 2.91(d, *J*=4.8, IH), 4.68(br s, 2H), 5.06~5.09(m, IH), 5.18~5.21(m, IH), 7.23~7.39(m, 3H), 7.55(dd, *J*=1.6, *J*=7.8, IH)

Example 4 :   Preparation of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(R)-2-carbamate(4)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(S,R)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example72)was used

instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.4g, yield 60~90%).

н NMR(400MHz, CDC1₃) 51.24(d, J=6.4, 3H), 2.91(d, *J*=4.8, 1H), 4.68(br s, 2H), 5.06~5.09(m, 1H), 5.18~5.21(m, 1H), 7.23~7.39(m, 3H), 7.55(dd, *J*=1.6, *J*=7.8, 1H)

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Example 5 : Preparation of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(S)-2-carbamate(5)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(R,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example73)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.3g, yield 60-90%).

¹H NMR(400MHz, CDC1₃) 51.24(d, J=6.4, 3H), 2.91(d, *J*=4.8, 1H), 4.68(br s, 2H), 5.06~5.09(m, 1H), 5.18~5.21(m, 1H), 7.23~7.39(m, 3H), 7.55(dd, *J*=1.6, *J*=7.8, 1H)
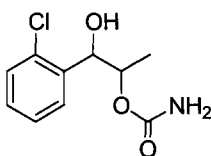
15

Example 6 : Preparation of l-(2-chlorophenyl)-(S)-l-hydroxybutyl-(S)-2-carbamate(6)

The substantially same method as described in Example 1 was conducted, except that l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)butane (Preparation example74)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.6g, yield 60-90%).

н NMR(400MHz, CDC1₃) 80.96(t, *J* = 7.4Hz, 3H), 1.57~1.73(m, 2H), 3.01(d, *J* = 5.6Hz, 1H), 4.74(br s, 2H), 4.95(dt, *J* = 7.2, 8.8Hz, 1H), 5.23(t, *J* = 5.6Hz, 1H), 7.22~7.54(m, 4H)

25

Example 7: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxybtyl-(R)-2-carbamate(7)

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The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(R,R)-1,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 75) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane   (Preparation example69) to obtain the title compound (2.5g,   yield 60-90%).

H   NMR(400MHz,   CDCl$_3$) δ 0.94(t, J=7.4Hz, 3H), 1.53~1.73(m, 2H), 2.92(s, 1H), 4.78(br s, 2H), 4.91~4.96(m, 1H), 5.22(d, J=5.5Hz, 1H), 7.20~7.54(m, 4H)
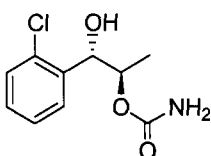

Example 8: Synthesis of 1-(2-chlorophenyl)-1-hydroxybutyl-2-carbamate(8)

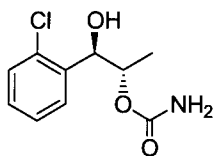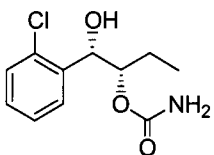
The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-1,2-(Bis-trimethylsilanyloxy)butane   (Preparation   Example   76)   was   used instead   of   1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane   (Preparation example69) to obtain the title compound（1.9g,   yield 60-90%).

H   NMR(400MHz,   CDCl$_3$) δ 0.97(t, J=7Hz, 3H), 1.58-1 .74(m, 2H), 2.94(d, J=6Hz, 1H), 4.69(br s, 2H), 4.94~4.99(m, 1H), 5.24(t, J=6Hz, 1H), 7.23~7.56(m, 4H)

Example 9: Synthesis of 1-(2-chlorophenyl)-(S)-1-hydroxy-3-methyl-butyl-(S)-2-carbamate(9)
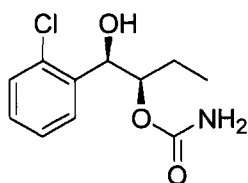

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-3-methyl-(S,S)-1,2-(Bis-trimethylsilanyloxy)butane   (Preparation   Example   77) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound（1.7g,   yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.01(d, J = 6.4Hz, 3H), 1.09(d, *J* = 6.8Hz, 3H), 2.06(m, IH), 2.75(d, *J* = 6.8Hz, IH), 4.58(br s, 2H), 4.85~4.88(m, IH), 5.34~5.37(m, IH), 7.22~7.33(m, 2H), 7.35~7.37(m, IH), 7.51~7.53(m, IH)

Example 10: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxy-3-methyl-butyl-(R)-2-carbamate(lO)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-3-methyl-(R,R)-l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 78) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (1.6g,   yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.01(d, *J* = 6.8Hz, 3H), 1.09(d, *J* = 6.8Hz, 3H), 2.06(m, IH), 2.73(d, *J* = 6.8Hz, IH), 4.57(br s, 2H), 4.85~4.88(m, IH), 5.34~5.37(m, IH), 7.24~7.30(m, 2H), 7.35~7.37(m, IH), 7.51~7.53(m, IH)
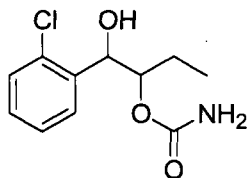
Example 11: Synthesis of l-(2-chlorophenyl)-l-hydroxy-3-methyl-butyl-2-carbamate(ll)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-3 -methyl- l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 79) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (1.7g,   yield 60~90%).

H NMR(400MHz, CDCl$_3$) 51.00(d, *J*=6.4Hz, 3H), 1.09(d, *J*=6.4Hz, 3H), 2.08(m, IH), 2.76(d, *J*=6.0Hz, IH), 4.59(br s, 2H), 4.87(dd, *J*=7.2Hz, 4.4Hz, IH), 5.36(t, *J*=4.6, IH), 7.23~7.54(m, 4H)

Example 12: Synthesis of l-(2-chlorophenyI)-(S)-l-hydroxyhexyl-(S)-2-carbamate(12)

The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)hexane   (Preparation Example 80) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.3g,   yield 60-90%).

H NMR(400MHz, CDC1$_3$) 80.88(t, *J* = 7Hz, 3H), 1.33~1.42(m, 4H), 1.53~1.71(m, 2H), 2.89(d, *J* = 5.6Hz, 1H) 4.64(br s, 2H), 5.04(dt, *J* = 5.0, 9.0Hz, 1H), 5.20(t, *J* = 5.6Hz, 1H), 7.23~7.55(m, 4H)

Example   13:   Synthesis   of   l-(2-chlorophenyl)-(R)-l-hydroxyhexyl-(R)-2-carbamate(13)
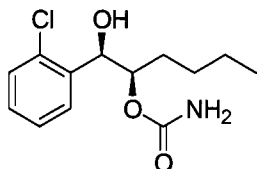
The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)hexane   (Preparation Example 81) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.2g,   yield 60-90%).

H NMR(400MHz, CDC1$_3$) δ 0.89(dd, *J*=5Hz, 3H), 1.28~1.43(m, 4H), 1.52~1.58(m, 1H), 1.65~1.72(m, 1H), 2.90(d, *J*=6Hz, 1H), 4.64(br s, 2H), 5.01~5.06(m, 1H), 5.22(t, *J*=6Hz, 1H), 7.22~7.56(m, 4H)

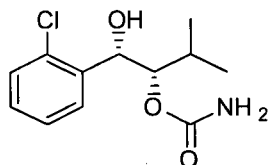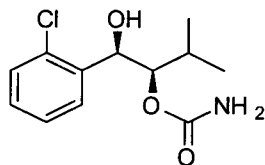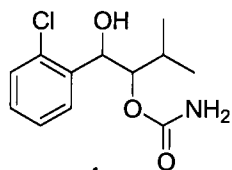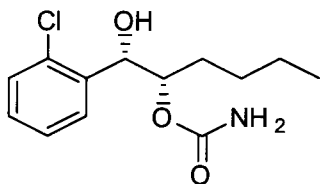**Example 14: Synthesis of l-(2-chlorophenyl)-l-hydroxyhexyl-2-carbamate(14)**
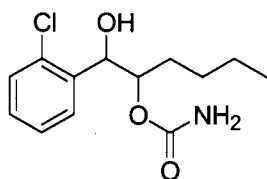
The substantially same method as described in Example 1 was conducted, except that 1-(2-chlorophenyl)-1,2-(Bis-trimethylsilanyloxy)hexane (Preparation Example 82) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.1g, yield 60~90%).

н   NMR(400MHz, CDCl$_3$) δ 0.88(dd, J=5Hz, 3H), 1.31~1.43(m, 4H), 1.63~1.70(m, 1H), 1.52~1.60(m, 1H), 3.06(d, J=6Hz, 1H), 4.75(br s, 2H), 5.00~5.05(m, 1H), 5.21(t, J=6Hz, 1H), 7.22~7.55(m, 4H)

Example 15: Synthesis of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(S)-2-N-methylcarbamate(15)
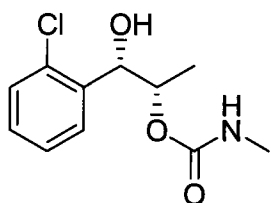
l-(2-chlorophenyl)-(S,S)-l,2-propanediol(2.4g)   obtained in Preparation Example 14, tetrahydrofuran (THF, 12ml), and carbonyldiimidazole (CDI, 3.12g) were put into a flask and stirred at the room temperature.   After approximately 3 hours, methylamine solution(CH$_3$NH$_2$, 4ml(33% in EtOH)) was added thereto.   When the reaction was completed, the obtained product was washed with 1M HCl solution and ethylacetate (EA).   The separated organic layer was dehydrated with anhydrous magnesium sulfate (MgSO$_4$), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography, to obtain the title compound (1.6g, yield 51%).

н   NMR(400MHz, CDCl$_3$) 51.03~1.25(m, 3H), 2.76(s, 3H), 3.34(s, 1H), 4.80(br s 1H), 5.04(t, J=12.5Hz, 1H), 5.14(s, 1H), 7.20~7.53(m, 4H)

Example 16: Synthesis of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(S)-2-N-propylcarbamate(16)
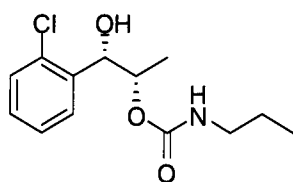
The substantially same method as described in Example 15 was conducted, except that

propylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (0.79g, yield 25%).

H NMR(400MHz, $CDCl_3$) 60.90(t, *J*=6.8Hz, 3H), 1.20(d, *J*=5.96Hz, 3H), 1.49(dd, *J*=14.2Hz, 2H), 3.11(d, *J*=6.28Hz, 2H), 3.34(s, IH), 4.84(br s, IH), 5.05(t, *J*=5.88Hz, IH), 5.14(s, IH), 7.22~7.53(m, 4H)

Example 17: Synthesis of l-(2-ch!orophenyl)-(S)-l-hydroxypropyl-(R)-2-N-isopropylcarbamate(17)

The substantially same method as described in Example 15 was conducted, except that isopropylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (1.5g, yield 41%).

H NMR(400MHz, $CDCl_3$) 61.14(dd, *J*=6.5Hz, 6H), 1.19(d, *J*=6.4Hz, 3H), 3.21(s, IH), 3.73~3.82(m, IH), 4.59(br s, IH), 5.01~5.07(m, IH), 5.14(t, *J*=5.8Hz, IH), 7.20~7.53(m, 4H)

Example 18: Synthesis of l-(2-chlorophenyI)-(S)-l-hydroxypropyl-(R)-2-N-cyclopropylcarbamate(1 8)

The substantially same method as described in Example 15 was conducted, except that cyclopropylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (2.2g, yield 43%).

H NMR(400MHz, $CDCl_3$) 50.50~0.56(m, 2H), 0.74(d, J=7.21Hz, 2H), 1.25(s, 3H), 2.56~2.61(m, IH), 3.72(s, IH), 4.98(br s, IH), 5.05~5.11(m, IH), 7.16(s, IH), 7.23~7.54(m, 4H)

Example 19: Synthesis of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(R)-2-N-cyclohexyl carbamate(19)

The substantially same method as described in Example 15 was conducted, except that cyclohexylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (1.1g, yield 26%).

H NMR(400MHz, $CDCl_3$) 51.06~1.40(m, 7H), 1.56-1.61(m, 2H), 1.69-1.71(m, 2H), 1.87~1.94(m, 2H), 3.19(d, J=4.32Hz, 1H), 3.45(s, 1H), 4.64(br s 1H), 5.02~5.07(m, 1H), 5.14(t, J=6.08Hz, 1H) 7.20~7.53(m, 4H)

Example 20: Synthesis of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(S)-2-N-benzyl carbamate(20)
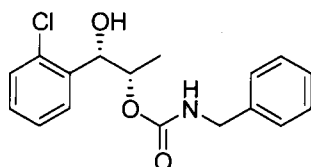
The substantially same method as described in Example 15 was conducted, except that benzylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (1.2g, yield 18%).

H NMR(400MHz, $CDCl_3$) δ 1.27(d, J=10Hz, 3H), 3.12(d, J=5Hz, 1H), 4.37(d, J=6Hz, 2H), 5.12~5.19(m, 3H), 7.15~7.56(m, 9H)

Example 21: Synthesis of l-(2-chlorophenyl)-(S)-l-hydroxypropyl-(S)-2-N-bicyclo[2,2,l]heptanescarbamate(21)
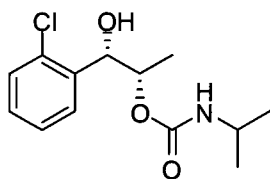

The substantially same method as described in Example 15 was conducted, except that 2-aminonorbomane was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (1.7g, yield 32%).

^{1}H NMR(400MHz, $CDCl_3$) 51.08~1.35(m, 9H), 1.65(br s, 1H), 1.75~1.71(m, 1H),

2.14~2.24(m, IH), 2.27~2.30(m, IH), 3.23~3.29(m, IH), 3.47~3.52(m, IH), 4.67(br s, IH), 5.01~5.09(m, IH), 5.12~5.18(m, IH), 7.22~7.55(m, 4H)

Example 22: Synthesis of l-(2-chlorophenyI)-(R)-l-hydroxypropyl-(R)-2-N-methylcarbamate(22)

The substantially same method as described in Example 15 was conducted, except that l-(2-chlorophenyl)-(R,R)-l,2-propanediol(Preparation   example 15) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (3.36g, yield 60%).

H NMR(400MHz, CDC1$_3$) δ 1.20(d, J=6.8Hz, 3H), 2.80(d, J=4.8Hz, 3H), 3.20(d, J=4.4Hz, IH), 4.75(br s, IH), 5.03~5.09(m, IH), 5.14~5.17(m, IH), 7.22~7.55(m, 4H)
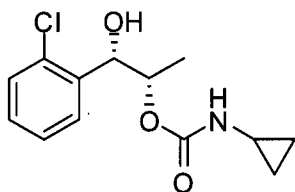
Example 23: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-propylcarbamate(23)

The substantially same method as described in Example 22 was conducted, except that propylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (3.1g, yield 53%).

H NMR(400MHz, CDC1$_3$) 60.92(t, J=7.6Hz, 3H), 1.21(d, J=6.4Hz, 3H), 1.51(m, 2H), 3.09-3. 14(m, 2H), 3.28(d, J=4.4Hz, IH), 4.82(br s, IH), 5.03~5.09(m, IH), 5.14~5.17(m, IH), 7.22~7.55(m. 4H)
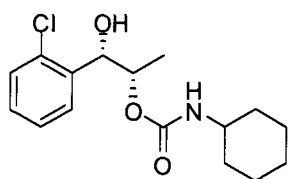
Example 24: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-isopropylcarbamate(24)

The substantially same method as described in Example 22 was conducted, except that isopropylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (0.16g, yield 27%).

H NMR(400MHz, CDC1$_3$) δ0.88-1. 16(m, 6H), 1.19~1.26(m, 3H), 3.34(s, IH), 3.71~3.78(m, IH), 4.62(br s, IH), 5.03(t, *J*=5.8Hz, IH), 5.13(d, *J*=4.9Hz, IH), 7.20~7.53(m, 4H)

Example 25: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-cyclopropylcarbamate(25)

The substantially same method as described in Example 22 was conducted, except that cyclopropylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (3.7g, yield 60%).

H NMR(400MHz, CDC1$_3$) δ0.49~0.54(m, 2H), 0.74(d, J=7.2Hz, 2H), 1.22(s, 3H), 2.55~2.60(m, IH), 3.16(s, IH), 5.00(s, IH), 5.04~5.11(m, IH), 5.16(s, IH), 7.23~7.54(m, 4H)
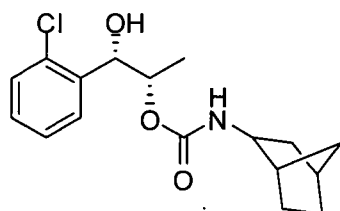
Example 26: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-cyclohexyl carbamate(26)

The substantially same method as described in Example 22 was conducted, except that cyclohexylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (1.9g, yield 28%).

H NMR(400MHz, CDC1$_3$) δ1.05~1.38(m, 8H), 1.58~1.70(m, 3H), 1.85~1.95(m, 2H), 3.39~3.47(m, IH), 3.56(s, IH), 4.79(br s, IH), 5.01~5.07(m, IH), 5.14(t, *J*=5.2Hz, IH),

7.20~7.54(m, 4H)

Example 27: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-benzylcarbamate(27)

The substantially same method as described in Example 22 was conducted, except that benzylamine was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (0.52g, yield 19%).

H NMR(400MHz, CDCl$_3$) 61.25(d, *J*=6Hz, 3H), 1.64(s, 1H), 3.13(d, *J*=4.4Hz, 1H), 4.37(d, *J*=5.6Hz, 2H), 5.12~5.19(m, 2H), 7.23~7.55(m, 9H)

Example 28: Synthesis of l-(2-chlorophenyl)-(R)-l-hydroxypropyl-(R)-2-N-bicyclo[2,2,l]heptanecarbamate(28)
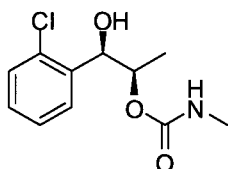

The substantially same method as described in Example 22 was conducted, except that 2-aminonorbornane was used instead of methylamine solution(CH_3NH_2 in EtOH), to obtain the title compound (1.7g, yield 20-50%).

H NMR(400MHz, CDCl$_3$) 61.08~1.35(m, 9H), 1.65(br s, 1H), 1.75~1.71(m, 1H), 2.14~2.24(m, 1H), 2.27~2.30(m, 1H), 3.23~3.29(m, 1H), 3.47~3.52(m, 1H), 4.67(br s, 1H), 5.01~5.09(m, 1H), 5.12-5. 18(m, 1H), 7.22~7.55(m, 4H)
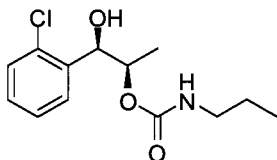
Example 29: Synthesis of l-(2-chlorophenyl)-l-hydroxypropyl-2-N-methylcarbamate(29)

The substantially same method as described in Example 15 was conducted, except that l-(2-chlorophenyl)-l,2-propanediol(Preparation example 16) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example 14), to obtain the title compound (2.6g, yield 45%).

н NMR(400MHz, CDC1$_3$) δ 1.21(d, *J*=6Hz, 3H), 2.81(d, *J*=5Hz, 3H), 3.14(d, *J*=4Hz, IH), 4.72(br s, IH), 5.07(dd, *J*=6Hz, IH), 5.16(t, *J*=6Hz, IH), 7.22~7.56(m, 4H)
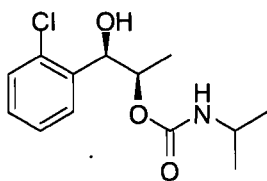
Example 30: Synthesis of l-(2-chlorophenyl)-l-hydroxypropyl-2-N-propylcarbamate(30)

The substantially same method as described in Example 29 was conducted, except that propylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (l.Og, yield 17%).

^{1}H NMR(400MHz, CDC1$_3$) δ 0.92(t, *J*=7Hz, 3H), 1.21(d, *J*=6Hz, 3H), 1.53(dd, *J*=7Hz, 2H), 3.13(dd, *J*=7Hz, 2H), 3.28(d, IH), 4.82(S, IH), 5.06(dd, *J*=7Hz, IH), 5.16(t, *J*=5Hz, IH), 7.21~7.56(m, 4H)
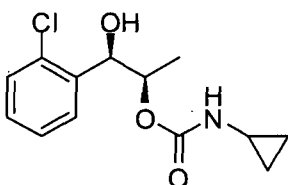
Example 31: Synthesis of l-(2-chlorophenyl)-l-hydroxypropyl-2-N-isopropylcarbamate(31)
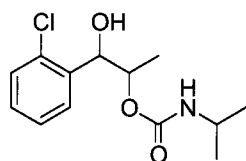
The substantially same method as described in Example 29 was conducted, except that isopropylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (0.54g, yield 16%).

н NMR(400MHz, CDC1$_3$) δ 1.16(dd, *J*=6Hz, 6H), 1.21(d, *J*=6Hz, 3H), 3.23(d, *J*=6Hz, IH), 3.75~3.84(m, IH), 4.61(br s, IH), 5.06(t, *J*=6Hz, IH), 5.16(t, *J*=6Hz, IH), 7.22~7.56(m, 4H)

Example   32:   Synthesis   of   l-(2-chlorophenyl)-l-hydroxypropyl-2-N-cyclopropylcarbamate(32)
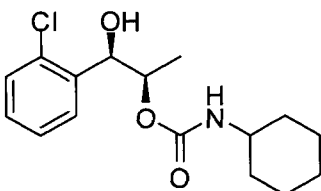

The substantially same method as described in Example 29 was conducted, except that
cyclopropylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the
title compound (l.Og, yield 17%).

ʜ NMR(400MHz, CDC1$_3$) δ 0.50(t, *J*=6Hz, 2H), 0.77(t, *J*=3Hz, 2H), 1.12(d, *J*=7Hz,
3H), 2.53~2.59(m, IH), 3.22(d, *J*=4Hz, IH), 5.08(dd, *J*=6Hz, IH), 5.15(S, IH), 7.22~7.55(m,
4H)

Example   33:   Synthesis   of   l-(2-chlorophenyl)-l-hydroxypropyl-2-N-cyclohexylcarbamate(33)
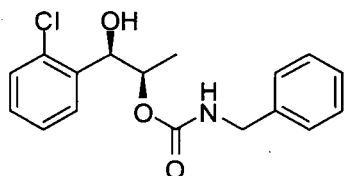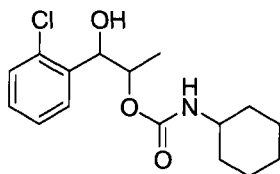

The substantially same method as described in Example 29 was conducted, except that
cyclohexylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title
compound (2.2g, yield 33%).

ʜ NMR(400MHz, CDC1$_3$) δ 1.07-1.17(m, 3H), 1.21(d, *J*=6Hz, 3H), 1.29~1.42(m, 3H),
1.72(dd, *J*=6Hz, 2H), 1.92(dd, *J*=6Hz, 2H), 3.26(d, *J*=4Hz, IH), 3.46(t, *J*=4Hz, IH), 4.68(d,
J=6Hz, IH), 5.07(dd, *J*=6Hz, IH), 5.16(t, *J*=6Hz, IH), 7.22~7.55(m, 4H)

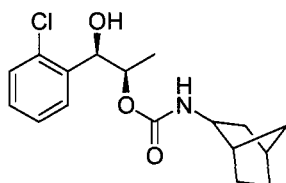**Example   34:   Synthesis   of   l-(2-chlorophenyl)-l-hydroxypropyl-2-N-benzylcarbamate(34)**
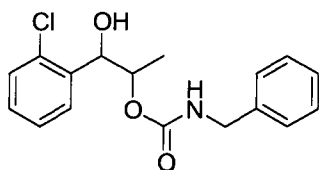
The substantially same method as described in Example 29 was conducted, except that
benzylamine was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title

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compound (1.3g, yield 19%).

H NMR(400MHz, CDCl$_3$) δ 1.25(d, *J*=6Hz, 3H), 3.16(d, *J*=4Hz, 1H), 4.36(d, *J*=6Hz, 2H), 5.14(dd, *J*=6Hz, 3H), 7.23~7.56(m, 9H), yield:19%(1.3g)

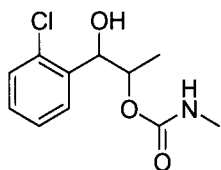**Example 35: Synthesis of l-(2-chlorophenyl)-l-hydroxypropyl-2-N-bicyclo[2,2,l]heptanecarbamate(35)**

The substantially same method as described in Example 29 was conducted, except that 2-aminonorbornane was used instead of methylamine solution(CH$_3$NH$_2$ in EtOH), to obtain the title compound (1.7g, yield 20-50%).

H NMR(400MHz, CDCl$_3$) 61.08~1.35(m, 9H), 1.65(br s, 1H), 1.75~1.71(m, 1H), 2.14~2.24(m, 1H), 2.27~2.30(m, 1H), 3.23~3.29(m, 1H), 3.47~3.52(m, 1H), 4.67(br s, 1H), 5.01~5.09(m, 1H), 5.12~5.18(m, 1H), 7.22~7.55(m, 4H)
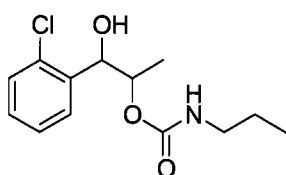
Example 36: Synthesis of l-(2,4-dichlorophenyl)-(S)-l-hydroxypropyl-(S)-2-carbamate(36)
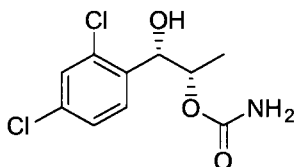
The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)propane (Preparation Example 83) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (1.8g, yield 60~90%).

H NMR(400MHz, CDCl$_3$) 61.22(d, *J* = 6.4Hz, 3H), 4.16(br t, 1H) 4.96(br t, 3H), 5.07(t, *J* = 4.8Hz, 1H), 7.23~7.52(m, 3H)

Example 37: Synthesis of l-(2,6-dichlorophenyl)-(S)-l-hydroxypropyl-(S)-2-carbamate(37)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)propane (Preparation Example 84) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.6g, yield 60-90%)

Example 38 : Synthesis of 1-(2,3-dichlorophenyl)-(S)-1-hydroxypropyl-(S)-2-carbamate(38)
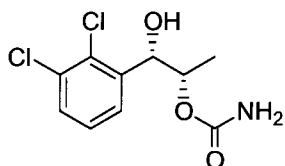
The substantially same method as described in Example 1 was conducted, except that 1-(2,3-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)propane (Preparation Example 85) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound（1.4g, yield 60-90%）

H NMR(400MHz, CDCl$_3$) 61.15(d, J = 6.4Hz, 3H), 3.66(d, J = 9.2Hz, 1H), 4.73(br s, 2H), 5.43(t, J = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 39: Synthesis of 1-(2,4-dichlorophenyl)-(S)-1-hydroxybutyl-(S)-2-carbamate(39)
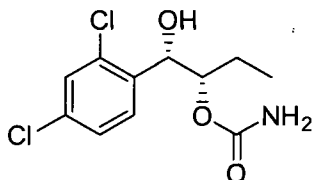
The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 86) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.3g, yield 60-90%).

^{1}H NMR(400MHz, CDCl$_3$) δ0.96(t, *J* = 7.4Hz, 3H), 1.58~1.74(m, 2H), 2.98(d, *J* = 5.6Hz, 1H) 4.68(br s, 2H), 5.59(dt, *J* = 5.2, 8.8Hz, 1H), 5.19(t, *J* = 5.4Hz, 1H), 7.30~7.50(m, 3H)

Example 40: Synthesis of l-(2,6-dichlorophenyl)-(S)-l-hydroxybutyl-(S)-2-carbamate(40)
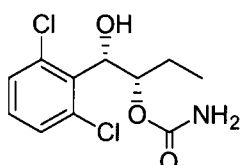
The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 87) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (1.7g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) δ0.92(t, *J* = 7.4Hz, 3H), 1.30~1.38(m, 1H), 1.57~1.64(m, 1H), 3.74(d, *J* = 9.2Hz, 1H), 4.80(br s, 2H), 5.40~5.50(m, 2H), 7.17~7.34(m, 3H)

Example 41: Synthesis of l-(2,4-dichlorophenyl)-(S)-l-hydroxy-3-methyl-butyl-(S)-2-carbamate(41)
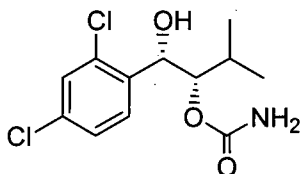
The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-3-methyl-(S,S)- 1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 88) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (1.9g, yield 60~90%).

H NMR(400MHz, CDCl$_3$) δ1.00(t, *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.30~7.50(m, 3H)

Example 42: Synthesis of l-(2,6-dichlorophenyl)-(S)-l-hydroxy-3-methyl-butyl-(S)-2-carbamate(42)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-3-methyl-(S,S)-1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 89) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.4g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 51.00(t, J = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.16~7.33(m, 3H)
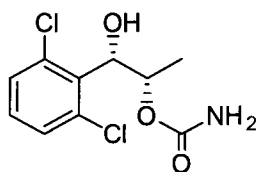
Example 43: Synthesis of 1-(2,4-dich!orophenyl)-(S)-1-hydroxyhexyl-(S)-2-carbamate(43)

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)hexane (Preparation Example 90) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-:trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.2g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 60.89(t, J = 3.6Hz, 3H), 1.28~1.42(m, 4H), 1.52~1.59(m, 1H), 1.64~1.71(m, 1H), 2.98(d, J = 5.6Hz, 1H), 4.67(br s, 2H), 4.96~5.00(m, 1H), 5.17(t, J = 5.6Hz, 1H), 7.30~7.49(m 3H)

Example 44: Synthesis of 1-(2,6-dichIorophenyl)-(S)-1-hydroxyhexyl-(S)-2-carbamate(44)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)hexane (Preparation Example 91) was

used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation

example69) to obtain the title compound (2.1g,   yield 60-90%)

^{1}H NMR(400MHz, CDCl$_3$) 60.84(t, J = 7.0Hz, 3H), 1.20~1.35(m, 4H), 1.36~1.41(m,

1H), 1.59~1.63(m, 1H), 3.71(d, J = 10.0Hz, 1H), 4.74(br s, 2H), 5.40~5.44(m, 1H), 5.52~5.57(m,

1H), 7.17-7.35(m, 3H)

Example 45: Synthesis of l-(2,4-dichlorophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(45)

The substantially same method as described in Example 1 was conducted, except that 1-

(2,4-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 92) was

used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation

example69) to obtain the title compound (1.2g,   yield 60-90%),

H NMR(400MHz, CDCl$_3$) 81.22(d, J = 6.4Hz, 3H), 4.16(br t, 1H) 4.96(br t, 3H), 5.07(t,

J = 4.8Hz, 1H), 7.23~7.52(m, 3H)

Example 46: Synthesis of l-(2,6-dichlorophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(46)

The substantially same method as described in Example 1 was conducted, except that 1-

(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 93) was

used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation

example69) to obtain the title compound (1.7g,   yield 60-90%),

^{l}H NMR(400MHz, CDCl$_3$) 81.15(d, J = 6.4Hz, 3H), 3.66(d, J = 9.2Hz, 1H), 4.73(br s,

2H), 5.43(t, J = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 47: Synthesis of l-(2,3-dichlorophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(47)

The substantially same method as described in Example 1 was conducted, except that 1-(2,3-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 94) was used instead of 1-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.0g,   yield 60-90%)

'H NMR(400MHz, CDCl$_3$) 51.15(d, *J* = 6.4Hz, 3H), 3.66(d, *J* = 9.2Hz, 1H), 4.73(br s, 2H), 5.43(t, *J* = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 48: Synthesis of l-(2,4-dichlorophenyl)-(R)-l-hydroxybutyl-(R)-2-carbamate(48)

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 95) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.3g,   yield 60~90%).

H NMR(400MHz, CDCl$_3$) 60.96(t, *J* = 7.4Hz, 3H), 1.58~1.74(m, 2H), 2.98(d, *J* = 5.6Hz, 1H) 4.68(br s, 2H), 5.59(dt, *J* = 5.2, 8.8Hz, 1H), 5.19(t, *J* = 5.4Hz, 1H), 7.30~7.50(m, 3H)
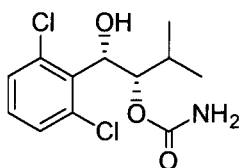
Example 49: Synthesis of l-(2,6-dichlorophenyl)-(R)-l-hydroxybutyl-(R)-2-carbamate(49)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 96) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.5g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 60.92(t, *J* = 7.4Hz, 3H), 1.30~1.38(m, 1H), 1.57~1.64(m, 1H), 3.74(d, *J* = 9.2Hz, 1H), 4.80(br s, 2H), 5.40~5.50(m, 2H), 7.17~7.34(m, 3H)

Example 50: Synthesis of l-(2,4-dichIorophenyl)-(R)-l-hydroxy-3-methyl-butyl-(R)-2-carbamate(50)

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-3-methyl-(R,R)-l ,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 97) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.8g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.00(t, *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.30~7.50(m, 3H)
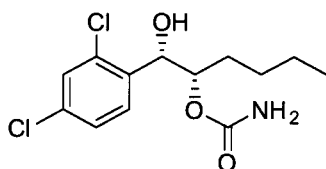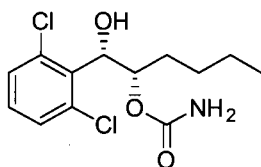

Example 51: Synthesis of l-(2,6-dichlorophenyl)-(R)-l-hydroxy-3-methyl-butyl-(R)-2-carbamate(51)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-3-methyl-(R,R)- 1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 98) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.6g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.00(t, *J* = 7.2Hz, 6H), 1.73-1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.16~7.33(m, 3H)

Example 52: Synthesis of l-(2,4-dichlorophenyl)-(R)-l-hydroxyhexyl-(R)-2-carbamate(52)
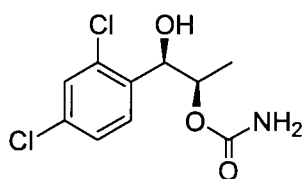

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)hexane   (Preparation Example 99) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.5g,   yield 60-90%).

^{1}H NMR(400MHz, CDCl$_3$) 60.89(t, J = 3.6Hz, 3H), 1.28~1.42(m, 4H), 1.52~1.59(m, 1H), 1.64~1.71(m, 1H), 2.98(d, J = 5.6Hz, 1H), 4.67(br s, 2H), 4.96~5.00(m, 1H), 5.17(t, J = 5.6Hz, 1H), 7.30~7.49(m, 3H)

Example 53: Synthesis of l-(2,6-dichlorophenyl)-(R)-l-hydroxyhexyl-(R)-2-carbamate(53)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)hexane   (Preparation Example 100) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.4g,   yield 60-90%).

^{1}H NMR(400MHz, CDCl$_3$) δ0.84(i, J = 7.0Hz, 3H), 1.20-1.35(m, 4H), 1.36~1.41(m, 1H), 1.59~1.63(m, 1H), 3.71(d, J = 10.0Hz, 1H), 4.74(br s, 2H), 5.40~5.44(m, 1H), 5.52~5.57(m, 1H), 7.17~7.35(m, 3H)
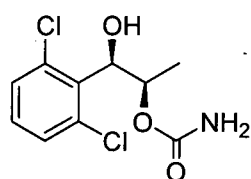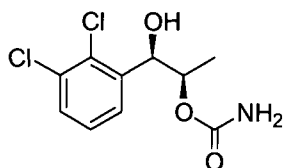
Example 54: Synthesis of l-(2,4-dichlorophenyl)-l-hydroxypropyl-2-carbamate(54)

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-1,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 101) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane (Preparation

5   example69) to obtain the title compound (1.7g,   yield 60-90%).

ᴴ NMR(400MHz, CDCl$_3$) 51.22(d, J = 6.4Hz, 3H), 4.16(br t, 1H) 4.96(br t, 3H), 5.07(t, J = 4.8Hz, 1H), 7.23~7.52(m, 3H)

Example 55: Synthesis of 1-(2,6-dichlorophenyl)-1-hydroxypropyl-2-
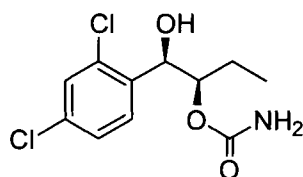
10   **carbamate(55)**

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-1,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 102) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane (Preparation

15   example69) to obtain the title compound (2.4g,   yield 60~90%).

^{1}H NMR(400MHz, CDCl$_3$) 61.15(d, J = 6.4Hz, 3H), 3.66(d, J = 9.2Hz, 1H), 4.73(br s, 2H), 5.43(t, J = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 56: Synthesis of 1-(2,3-dichlorophenyl)-1-hydroxypropyl-2-
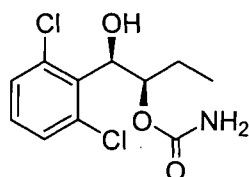
20   **carbamate(56)**

The substantially same method as described in Example 1 was conducted, except that 1-(2,3-dichlorophenyl)-1,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 103) was used instead   of   1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy)   propane   (Preparation

example69) to obtain the title compound (1.6g, yield 60-90%).

^{1}H NMR(400MHz, CDC1$_3$) 61.15(d, **J** = 6.4Hz, 3H), 3.66(d, **J** = 9.2Hz, 1H), 4.73(br s, 2H), 5.43(t, **J** = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 57: Synthesis of l-(2,4-dichlorophenyl)-l-hydroxybutyl-2-carbamate(57)

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 104) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (1.7g, yield 60~90%).

H NMR(400MHz, CDC1$_3$) 60.96(t, **J** = 7.4Hz, 3H), 1.58~1.74(m, 2H), 2.98(d, **J** = 5.6Hz, 1H) 4.68(br s, 2H), 5.59(dt, **J** = 5.2, 8.8Hz, 1H), 5.19(t, **J** = 5.4Hz, 1H), 7.30~7.50(m, 3H)
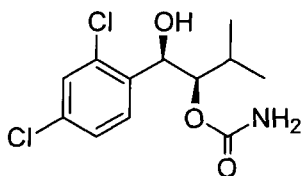
Example 58: Synthesis of l-(2,6-dichlorophenyl)-l-hydroxybutyl-2-carbamate(58)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 105) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.4g, yield 60~90%).

H NMR(400MHz, CDC1$_3$) 60.92(t, **J** = 7.4Hz, 3H), 1.30~1.38(m, 1H), 1.57~1.64(m, 1H), 3.74(d, **J** = 9.2Hz, 1H), 4.80(br s, 2H), 5.40~5.50(m, 2H), 7.17~7.34(m, 3H)

Example 59: Synthesis of l-(2,4-dichlorophenyl)-l-hydroxy-3-methyl-butyl-2-carbamate(59)
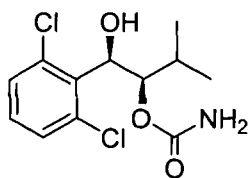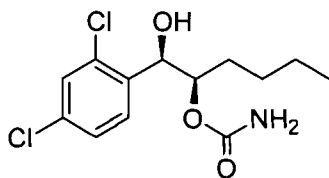
The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-3-methyl-1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 106) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (1.9g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.00(t, J = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.30~7.50(m, 3H)

Example 60: Synthesis of 1-(2,6-dichlorophenyl)-1-hydroxy-3-methyl-butyl-2-carbamate(60)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-3-methyl-1,2-(Bis-trimethylsilanyloxy)butane (Preparation Example 107) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (1.7g, yield 60-90%).

H NMR(400MHz, CDCl$_3$) 61.00(t, J = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.85(br s, 2H), 5.40~5.43(m, 1H), 5.49~5.54(m, 1H), 7.16~7.33(m, 3H)
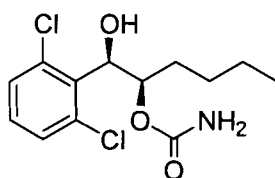
Example 61: Synthesis of 1-(2,4-dichlorophenyl)-1-hydroxyhexyl-2-carbamate(61)
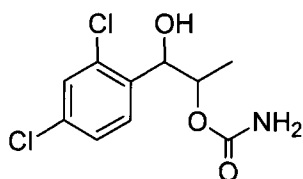

The substantially same method as described in Example 1 was conducted, except that 1-(2,4-dichlorophenyl)-1,2-(Bis-trimethylsilanyloxy)hexane (Preparation Example 108) was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.6g, yield 60-90%).

^{1}H NMR(400MHz, CDCl$_3$) 60.89(t, J = 3.6Hz, 3H), 1.28~1.42(m, 4H), 1.52~1.59(m, 1H), 1.64~1.71(m, 1H), 2.98(d, J = 5.6Hz, 1H), 4.67(br s, 2H), 4.96~5.00(m, 1H), 5.17(t, J = 5.6Hz, 1H), 7.30-7.49(m, 3H)

Example 62: Synthesis of l-(2,6-dichlorophenyl)-l-hydroxyhexyl-2-carbamate(62)

The substantially same method as described in Example 1 was conducted, except that 1-(2,6-dichlorophenyl)-l,2-(Bis-trimethylsilanyloxy)hexane   (Preparation Example 109) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound (2.5g,   yield 60-90%).

^{1}H NMR(400MHz, CDC1$_3$) 60.84(t, **J** = 7.0Hz, 3H), 1.20~1.35(m, 4H), 1.36-1. 4 1(m, 1H), 1.59-1 .63(m, 1H), 3.71(d, **J** = 10.0Hz, 1H), 4.74(br s, 2H), 5.40~5.44(m, 1H), 5.52~5.57(m, 1H), 7.17~7.35(m, 3H)

Example   63:   Synthesis   of   l-(2-fluorophenyl)-(S)-l-hydroxypropyl-(S)-2-carbamate(63)
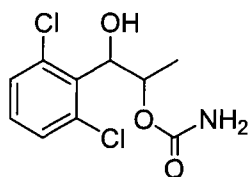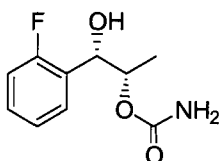

The substantially same method as described in Example 1 was conducted, except that 1-(2-fluorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 110) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane (Preparation example69) to obtain the title compound（1.8g,   yield 60-90%）.

н NMR(400MHz, CDC1$_3$) 61.19(d, **J** =5.2Hz, 3H), 2.93(d, **J**=4.4Hz, 1H), 4.71(br s, 2H), 4.99~5.06(m, H),   7.04~7.48(m, 4H)
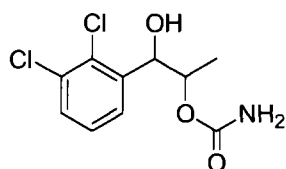
Example   64:   Synthesis   of   l-(2-fluorophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(64)
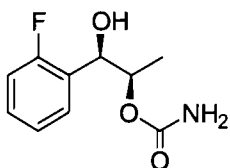
The substantially same method as described in Example 1 was conducted, except that 1-(2-fluorophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 111) was

used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound（1.6g, yield 60~90%）.

H **NMPv**(400MHz, CDC1₃) 51.19(d, **J**=5.2Hz, 3H), 2.93(d, **J**=4.4Hz, 1H), 4.71(br s, 2H), 4.99~5.06(m, H), 7.04~7.48(m, 4H)

Example   65:   Synthesis   of   l-(2-iodophenyl)-(S)-l-hydroxypropyl-(S)-2-carbamate(65)
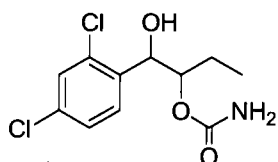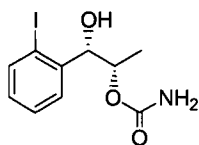

The substantially same method as described in Example 1 was conducted, except that 1-(2-iodophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 112) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound (2.2g, yield 60~90%).

H   NMR(400MHz, CDC1₃) 6l.27(d, **J**=6.4Hz, 3H), 3.09(br s, 1H), 4.83(br s, 2H), 5.00~5.10(m, 2H), 7.00~7.76(m, 4H)
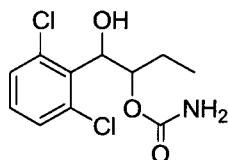
Example   66:   Synthesis   of   l-(2-iodophenyl)-(R)-l-hydroxypropyl-(R)-2-carbamate(66)
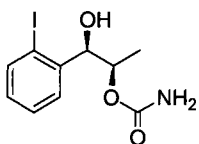
The substantially same method as described in Example 1 was conducted, except that 1-(2-iodophenyl)-(R,R)-l,2-(Bis-trimethylsilanyloxy)propane   (Preparation Example 113) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy) propane (Preparation example69) to obtain the title compound（1.7g, yield 60~90%）.

^{1}H NMR(400MHz, CDC1₃) 51.27(d, **J**=6.4Hz, 3H), 2.95(d, **J**=3.6Hz, 1H), 4.73(br s, 2H), 5.01-5. ll(m, 2H), 7.01~7.86(m, 4H)
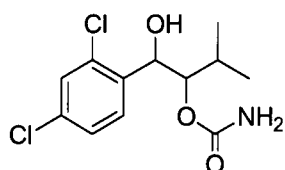
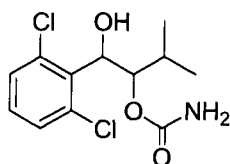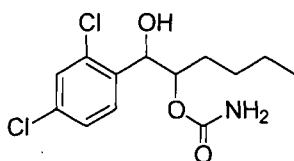**Example   67:   Synthesis   of   l-(2-iodophenyl)-(S)-l-hydroxybutyl-(S)-2-carbamate(67)**
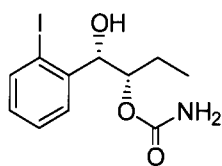
The substantially same method as described in Example 1 was conducted, except that 1-(2-iodophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)butane   (Preparation Example 114) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-(Bis-trimethylsilanyloxy)   propane   (Preparation example69) to obtain the title compound (2.1 g,   yield 60-90%).

H   NMR(400MHz, CDCl$_3$) 61.27(d, J=6.4Hz, 3H), 3.09(br s, 1H), 4.83(br s, 2H), 5.00-5. 10(m, 2H),   7.00~7.76(m, 4H)

Example 68: Synthesis of l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-carbamate(68)
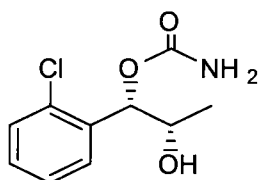
l-(2-chlorophenyl)-(S,S)-l,2-propanediol(2.33g,   Preparation example 14) obtained in Preparation Example 14, tetrahydrofuran (THF, 12ml), and carbonyldiimidazole (CDI, 3.04g) were put into a flask and stirred at the room temperature.   After approximately 3 hours, ammonia solution (NH$_4$OH, 4ml) was added thereto.   When the reaction was completed, the obtained product was washed with 1M HC1 solution and ethylacetate (EA).   The separated organic layer was dehydrated with anhydrous magnesium sulfate (MgSCv), filtrated, and concented under reduced pressure.   The concentrated residue was purified by a silica gel column chromatography, to obtain the title compound (0.28g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 81.24(d, J = 6.8Hz, 3H), 2.13(d, J = 4.4Hz, 1H), 4.12~4.16(m, 1H), 4.85(br s, 2H), 5.98(d, J = 5.6Hz, 1H), 7.24~7.43(m, 4H)

Example 69: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-carbamate(69)
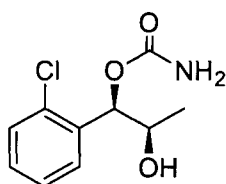
The substantially same method as described in Example 68 was conducted, except that l-(2-chlorophenyl)-(R,R)-l,2-propanediol   (Preparation Example 15) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol   (Preparation example 14) to obtain the title compound (0.77g, yield 16%).

H   NMR(400MHz, CDCl$_3$) 61.24(d, J = 6.4Hz, 3H), 2.04(d, J = 4.8Hz, 1H), 4.11~4.18(m, 1H), 4.74(br s, 2H), 6.00(d, J = 5.6Hz, 1H), 7.24-7 .43(m, 4H)
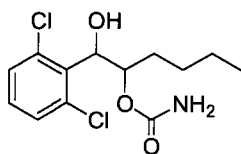

Example 70: Synthesis of l-(2-chlorophenyl)-2-hydroxypropyl-l-carbamate(70)
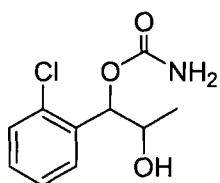
The substantially same method as described in Example 68 was conducted, except that l-(2-chlorophenyl)-(R,R)-l,2-propanediol   (Preparation Example 16) was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol   (Preparation example 14) to obtain the title compound (0.1 6g, yield 10-30%).

H   NMR(400MHz, CDCl$_3$) 61.24(d, J = 6.4Hz, 3H), 2.04(d, J = 4.8Hz, 1H), 4.11~4.18(m, 1H), 4.74(br s, 2H), 6.00(d, J = 5.6Hz, 1H), 7.24-7 .43(m, 4H)

Example   71:   Synthesis   of   l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-N-methylcarbamate(71)
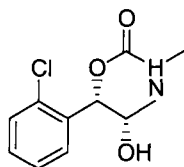
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 15, to obtain the title compound (0.70g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 51.21(d, J=6.4Hz, 3H), 2.80(d, J=4.8Hz, 3H), 3.12(s, 1H),

83

4.09~4.16(m, 1H), 4.86(br s, 1H), 5.99(d, J= 6.0Hz, 1H), 7.23~7.40(m, 4H)

Example 72: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-N-methylcarbamate(72)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 22, to obtain the title compound (0.69g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 51.21(d, J=6.4Hz, 3H), 2.80(d, J=4.8Hz, 3H), 3.12(s, 1H), 4.09~4.16(m, 1H), 4.86(br s, 1H), 5.99(d, J= 6.0Hz, 1H), 7.23~7.40(m, 4H)

Example 73: Synthesis of l-(2-chlorophenyl)-2-hydroxypropyl-l-N-methylcarbamate(73)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 29, to obtain the title compound (0.73g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) δ 1.22(d, J=6Hz, 3H), 2.15(d, J=4Hz, 1H), 2.81(d, J=5Hz, 3H), 4.12(dd, J=6Hz, 1H), 4.83(br s, 1H), 6.00(d, J=6Hz, 1H), 7.23~7.41(m, 4H)

Example 74: Synthesis of l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-N-propylcarbamate(74)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel

column chromatography as described in Example 16, to obtain the title compound (0.15g, yield 10-30%).·

H NMR(400MHz, CDCl$_3$) δ 0.91(t, *J*=7Hz, 3H), 1.22(d, *J*=6Hz, 3H), 1.52(dd, *J*=7Hz, 2H), 2.23(d, *J*=4Hz, 1H), 3.09~3.21(m, 2H), 4.09~4.17(m, 1H), 4.93(s, 1H), 5.99(d, *J*=6Hz, 1H), 7.23~7.47(m, 4H)

Example 75: Synthesis of 1-(2-ch!orophenyl)-(R)-2-hydroxypropyl-(R)-1-N-propylcarbamate(75)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 23, to obtain the title compound (0.04g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) δ 0.91(t, *J*=7Hz, 3H), 1.22(d, *J*=6Hz, 3H), 1.52(dd, *J*=7Hz, 2H), 2.23(d, *J*=4Hz, 1H), 3.09~3.21(m, 2H), 4.09~4.17(m, 1H), 4.93(s, 1H), 5.99(d, *J*=6Hz, 1H), 7.23~7.47(m, 4H)

Example 76: Synthesis of 1-(2-chlorophenyl)-2-hydroxypropyl-1-N-propylcarbamate(76)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 30, to obtain the title compound (0.15g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) δ 0.91(t, *J*=7Hz, 3H), 1.22(d, *J*=6Hz, 3H), 1.52(dd, *J*=7Hz, 2H), 2.23(d, *J*=4Hz, 1H), 3.09~3.21(m, 2H), 4.09~4.17(m, 1H), 4.93(s, 1H), 5.99(d, *J*=6Hz, 1H), 7.23~7.47(m, 4H)

Example 77: Synthesis of 1-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-1-N-

isopropylcarbamate(77)

A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 17, to obtain the title compound (0.42g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 81.10(d, *J*=6.0Hz, 3H), 1.15~1.19(m, 6H), 2.41(s, 1H), 3.76~4.08(m, 1H), 4.34(s, 1H), 4.83(br s 1H), 5.95(d, *J*=5.3Hz, 1H), 7.19~7.39(m, 4H)

Example 78: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-N-isopropylcarbamate(78)
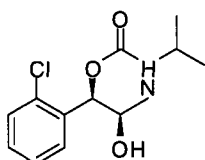
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 24, to obtain the title compound (0.5g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 61.13(d, J=6Hz, 3H), 1.20(dd, J=9.2Hz, 6H), 2.23(s, 1H), 3.77~3.82(m, 1H), 4.10(s, 1H), 4.76(br s, 1H), 5.98(d, J=5.6Hz, 1H), 7.23~7.41(m, 4H)

Example 79: Synthesis of l-(2-chlorophenyl)-2-hydroxypropyl-l-N-isopropylcarbamate(79)
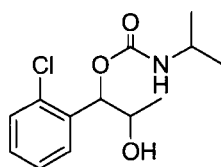
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 31, to obtain the title compound (0.09g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) δ 1.14(d, *J*=6Hz, 3H), 1.21(dd, *J*=6Hz, 6H), 2.16(d, *J*=5Hz, 1H), 3.81(t, *J*=6Hz, 1H), 4.11(d, *J*=5Hz, 1H), 4.73(br s, 1H), 5.98(d, *J*=5Hz, 1H), 7.24-741(m,

4H)

Example 80: Synthesis of l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-N-cyclopropylcarbamate(80)
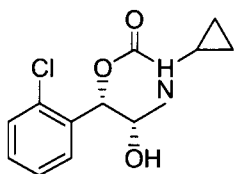
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 18, to obtain the title compound (0.53g, yield 10-30%).

ᴴ NMR(400MHz, CDC1₃) 50.53~0.60(m, 2H), 0.74(s, 2H), 1.21(d, J=6.0Hz, 3H), 2.19(s, 1H), 2.59(s, 1H), 4.11~4.15(m, 1H), 5.13(br s, 1H), 5.99(d, J=5.20Hz, 1H), 7.23~7.40(m, 4H)

Example 81: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-N-cyclopropylcarbamate(81)
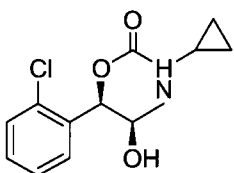
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 25, to obtain the title compound (0.58g, yield 10%).

ᴴ NMR(400MHz, CDC1₃) 50.53~0.60(m, 2H), 0.74(s, 2H), 1.21(d, J=6.0Hz, 3H), 2.19(s, 1H), 2.59(s, 1H), 4.11~4.15(m, 1H), 5.13(br s, 1H), 5.99(d, J=5.20Hz, 1H), 7.23~7.40(m, 4H)

Example 82: Synthesis of l-(2-chlorophenyl)-2-hydroxypropyl-l-N-cyclopropylcarbamate(82)
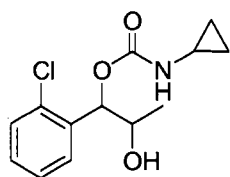
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 32, to obtain the title compound (0.3 8g, yield 14%).

¹H NMR(400MHz, CDCl₃) δ 0.71(s, 2H), 1.1 9(d, *J*=6Hz, 3H), 2.45(S, 1H), 2.57(S, 1H), 4.08~4.12(m, 1H), 5.26(s, 1H), 5.97(d, *J*=4Hz, 1H), 7.22~7.54(m, 4H)

Example 83: Synthesis of l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-N-cyclohexylcarbamate(83)
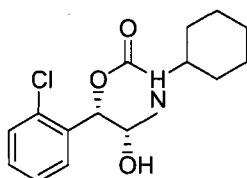
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 19, to obtain the title compound (0.24g, yield 10-30%).

H NMR(400MHz, CDCl₃) 61.10~1.39(m, 7H), 1.61(s, 3H), 1.71~1.74(m, 2H), 1.87(d, *J*=11.2Hz, 1H), 2.48(d, *J*=10.8Hz, 1H), 3.46(t, *J*=4Hz, 1H), 4.10~4.11(m, 1H), 4.80(br s 1H), 5.97(d, *J*=5.6Hz, 1H), 7.23~7.41(m, 4H)

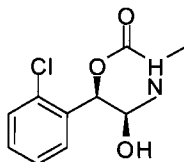**Example 84: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-N-cycIohexyIcarbamate(84)**
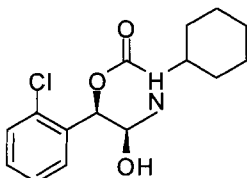
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 26, to obtain the title compound (0.3 5g, yield 10%).

¹H NMR(400MHz, CDCl₃) 61.10~1.39(m, 7H), 1.61(s, 3H), 1.71~1.74(m, 2H), 1.87(d,

88

J=11.2Hz, 1H), 2.48(d, *J*=10.8Hz, 1H), 3.46(t, *J*=4Hz, 1H), 4.10~4.11(m, 1H), 4.80(br s 1H), 5.97(d, *J*=5.6Hz, 1H), 7.23~7.41(m, 4H)
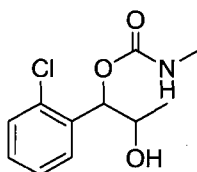
Example 85: Synthesis of l-(2-chlorophenyl)-2-hydroxypropyl-l-N-cyclohexylcarbamate(85)
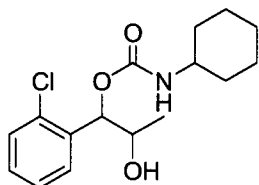
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 33, to obtain the title compound (0.26g, yield 10%).

н NMR(400MHz, CDCl₃) δ 1.12~1.19(m, 3H), 1.22(d, *J*=6Hz, 3H), 1.27~1.37(m, 1H), 1.71(t, J=6Hz, 2H), 1.86~1.88(m, 1H), 1.97~2.00(m, 1H), 2.18(d, *J*=4Hz, 1H), 3.47(S, 1H), 4.12(t, *J*=6Hz, 1H), 4.78(S, 1H), 5.97(d, *J*=6Hz, 1H), 7.23~7.40(m, 4H)
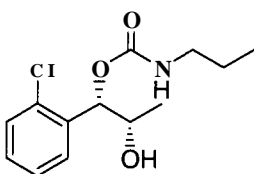
Example 86: Synthesis of l-(2-chlorophenyl)-(S)-2-hydroxypropyl-(S)-l-N-benzylcarbamate(86)
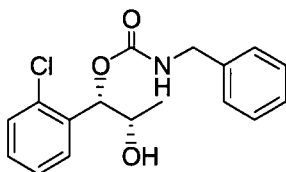
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 20, to obtain the title compound (0.19g, yield 10-30%).

н NMR(400MHz, CDCl₃) δ 1.23(d, *J*=6Hz, 3H), 2.16(d, *J*=4Hz, 1H), 4.12(t, *J*=6Hz, 1H), 4.31~4.44(m, 2H), 5.22(br S, 1H), 6.04(d, *J*=6Hz, 1H), 7.27~7.42(m, 9H)

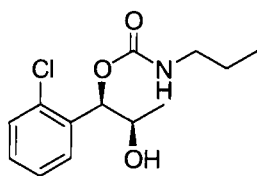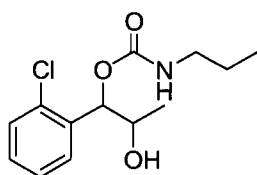**Example 87: Synthesis of l-(2-chlorophenyl)-(R)-2-hydroxypropyl-(R)-l-N-benzylcarbamate(87)**
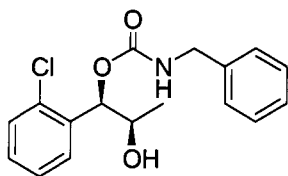
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 27, to obtain the title compound (0.07g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) δ 1.23(d, *J*=6Hz, 3H), 2.16(d, *J*=4Hz, 1H), 4.12(t, *J*=6Hz, 1H), 4.31~4.44(m, 2H), 5.22(br S, 1H), 6.04(d, *J*=6Hz, 1H), 7.27~7.42(m, 9H)
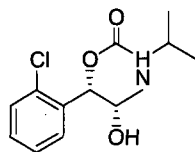

Example   88:   Synthesis   of   l-(2-chlorophenyI)-2-hydroxypropyl-l-N-benzylcarbamate(88)
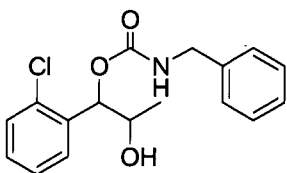
A regioisomer of monocarbamate was separated and purified by conducting the silica gel column chromatography as described in Example 34, to obtain the title compound (0.2 lg, yield 14%).

H NMR(400MHz, CDCl$_3$) δ 1.23(d, *J*=6Hz, 3H), 2.16(d, *J*=4Hz, 1H), 4.12(t, *J*=6Hz, 1H), 4.31~4.44(m, 2H), 5.22(br S, 1H), 6.04(d, *J*=6Hz, 1H), 7.27~7.42(m, 9H)

Example 89: Synthesis of l-(2,4-dichlorophenyl)-(S)-2-hydroxypropyl-(S)-l-carbamate(89)
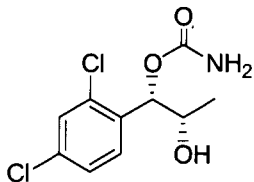
The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 26)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.05g, yield 10-30%).

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ʜ NMR(400MHz, CDС1₃) 61.13(d, *J* = 6.8Hz, 3H), 2.49(d, *J* = 4.0Hz, 1H),

4.66~4.74(m, 1H), 4.76(br s, 2H), 6.20(d, *J* = 8.8Hz, 1H), 7.30(d, J=8.4Hz, 1H), 7.39(d, J=2.0Hz,

2H), 7.50(dd, J=8.4Hz, 2.0Hz, 1H)

Example 90: Synthesis of l-(2,6-dichlorophenyl)-(S)-2-hydroxypropyl-(S)-l-carbamate(90)

The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-(S,S)-l,2-propanediol(Preparation example 38)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example 14), to obtain the title compound (0.07g, yield 24%).

ʜ NMR(400MHz, CDС1₃) 51.13(d, *J* = 6.8Hz, 3H), 2.49(d, *J* = 4.0Hz, 1H),

4.66~4.74(m, 1H), 4.76(br s, 2H), 6.20(d, *J* = 8.8Hz, 1H), 7.25~7.40(m, 3H)

Example 91: Synthesis of l-(2,3-dichlorophenyl)-(S)-2-hydroxypropyl-(S)-l-carbamate(91)

The substantially same method as described in Example 68 was conducted, except that l-(2,3-dichlorophenyl)-(S,S)-l,2-propanediol(Preparation example 57)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example 14), to obtain the title compound (0.08g, yield 10-30%).

ʜ NMR(400MHz, CDCI3) 61.15(d, *J* = 6.4Hz, 3H), 3.66(d, *J* = 9.2Hz, 1H), 4.73(br s,

2H), 5.43(t, *J* = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 92: Synthesis of l-(2,4-dichlorophenyl)-(S)-2-hydroxybutyl-(S)-l-carbamate(92)

The substantially same method as described in Example 68 was conducted, except that 1-(2,4-dichlorophenyl)-(S,S)-1,2-butanediol(Preparation   example 29)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.07g, yield 10-30%).

ʜ NMR(400MHz, CDC1₃) 60.77(t, *J* = 7.4Hz, 3H), 0.92~1.01(m, 1H), 1.18~1.28(m, 1H), 4.06~4.13(m, 1H), 4.96(d, *J* = 6.0Hz, 1H), 5.91(d, *J* = 8.8Hz, 1H), 6.4(br s, 2H), 7.30~7.50(m, 3H)

Example 93:   **Synthesis of l-(2,6-dichlorophenyl)-(S)-2-hydroxybutyl-(S)-l-carbamate(93)**

The substantially same method as described in Example 68 was conducted, except that 1-(2,6-dichlorophenyl)-(S,S)-1,2-butanediol(Preparation   example 41)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.1 lg, yield 29%).

ʜ NMR(400MHz, CDC1₃) 60.77(t, *J* = 7.4Hz, 3H), 0.92~1.01(m, 1H), 1.18~1.28(m, 1H), 4.06~4.13(m, 1H), 4.96(d, *J*=6.0Hz, 1H), 5.91(d, *J*=8.8Hz, 1H), 6.4(br s, 2H), 7.25~7.40(m, 3H)

Example 94: **Synthesis of l-(2 ,4-dichlorophenyl)-(S)-2-hydroxy-3-methyl-butyl-(S)-l-carbamate (94)**

The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-(S,S)-1,2-butanediol(Preparation   example 32)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (O.Olg, yield 10-30%).

^{H} NMR(400MHz, CDCl$_3$) 61.00(t, J = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, J=6.0Hz, 1H), 5.91 (d, J=8.8Hz, 1H), 6.42(br s, 2H), 7.30~7.50(m, 3H)

Example 95: Synthesis of l-(2,6-dichlorophenyl)-(S)-2-hydroxy-3-methyl-butyl-(S)-l-carbamate(95)

The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-3-methyl-(S,S)-l,2-butanediol(Preparation   example 44)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.03g, yield 10-30%).

^{H} NMR(400MHz, CDCl$_3$) 61.00(t, J = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, J=6.0Hz, 1H), 5.91(d, J=8.8Hz, 1H), 6.42(br s, 2H), 7.25~7.40(m, 3H)

Example 96: Synthesis of l-(2,4-dichlorophenyl)-(S)-2-hydroxyhexyl-(S)-l-carbamate(96)

The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-(S,S)-l,2-hexanediol(Preparation   example 35)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.2lg, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 60.85(t, J=7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, J=4.4Hz, IH), 4.45~4.50(m, IH), 4.76(br s, 2H), 6.21(d, J=8.4Hz, IH), 7.30~7.50(m, 3H)

Example 97: Synthesis of l-(2,6-dichlorophenyl)-(S)-2-hydroxyhexyl-(S)-l-carbamate(97)

The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-(S,S)-l,2-hexanediol(Preparation   example 47)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.06g, yield 29%).

H NMR(400MHz, CDCl$_3$) 60.85(t, J = 7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, J = 4.4Hz, IH), 4.45~4.50(m, IH), 4.76(br s, 2H), 6.21(d, J=8.4Hz, IH), 7.16~7.34(m, 3H)

Example 98: Synthesis of l-(2,4-dichlorophenyl)-(R)-2-hydroxypropyl-(R)-l-carbamate(98)

The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation   example 27)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.04g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 61.13(d, J=6.8Hz, 3H), 2.49(d, J=4.0Hz, IH), 4.66~4.74(m, IH), 4.76(br s, 2H), 6.20(d, J=8.8Hz, IH), 7.30~7.50(m, 3H)

Example 99: Synthesis of l-(2,6-dichlorophenyl)-(R)-2-hydroxypropyl-(R)-l-carbamate (99)

The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation   example 39)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.09g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 51.13(d, *J* = 6.8Hz, 3H), 2.49(d, *J* = 4.0Hz, 1H), 4.66~4.74(m, 1H), 4.76(br s, 2H), 6.20(d, *J* = 8.8Hz, 1H), 7.25~7.40(m, 3H)

Example 100: Synthesis of l-(2,3-dichlorophenyl)-(R)-2-hydroxypropyl-(R)-l-carbamate(lOO)

The substantially same method as described in Example 68 was conducted, except that l-(2,3-dichlorophenyl)-(R,R)-l,2-propanediol(Preparation   example 58)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.25g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 61.15(d, *J* = 6.4Hz, 3H), 3.66(d, *J* = 9.2Hz, 1H), 4.73(br s, 2H), 5.43(t, *J* = 9.0Hz, 1H), 5.62~5.69(m, 1H), 7.18~7.22(m, 3H),

Example 101: Synthesis of l-(2,4-dichlorophenyl)-(R)-2-hydroxybutyl-(R)-l-carbamate(lOl)

The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-(R,R)-l,2-butanediol(Preparation   example 30)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   examplel4), to obtain the title compound (0.08g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 60.77(t, *J* = 7.4Hz, 3H), 0.92~1.01(m, 1H), 1.18~1.28(m, 1H), 4.06~4.13(m, 1H), 4.96(d, *J* = 6.0Hz, 1H), 5.91(d, *J* = 8.8Hz, 1H), 6.4(br s, 2H), 7.30~7.50(m, 3H)

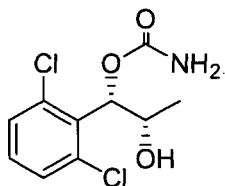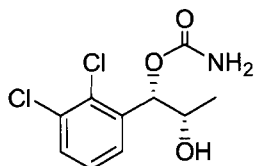**Example 102:   Synthesis of l-(2,6-dichlorophenyl)-(R)-2-hydroxybutyl-(R)-l-carbamate(102)**

The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-(R,R)-l,2-butanediol(Preparation   example 42)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound (0.09g, yield 10-30%).   H NMR(400MHz, CDCl$_3$) 60.77(t, *J* = 7.4Hz, 3H), 0.92~1.01(m, 1H), 1.18~1.28(m, 1H), 4.06~4.13(m, 1H), 4.96(d, *J* = 6.0Hz, 1H), 5.91(d, *J* = 8.8Hz, 1H), 6.4(br s, 2H), 7.25~7.40(m, 3H)

Example 103: Synthesis of l-(2,4-dichlorophenyl)-(R)-2-hydroxy-3-methyl-butyl-(R)-l-carbamate(103)
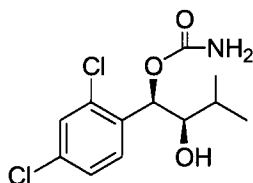
The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-3-methyl-(R,R)-l,2-propanediol(Preparation   example 33)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation   examplel4), to obtain the title compound (0.01g, yield 10-3 0%).

H NMR(400MHz, CDCl$_3$) 6l.00(t, *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, *J*=6.0Hz, 1H), 5.91(d, *J*=8.8Hz, 1H), 6.42(br s, 2H), 7.30~7.50(m, 3H)

Example 104: Synthesis of l-(2,6-dichIorophenyl)-(R)-2-hydroxy-3-methyl-butyl-(R)-l-carbamate(104)
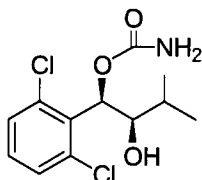
The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-3-methyl-(R,R)-l,2-propanediol(Preparation example 45)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation examplel4), to obtain the title compound (O.Olg, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 6l.00(t, *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, *J*=6.0Hz, 1H), 5.91(d, *J*=8.8Hz, 1H), 6.42(br s, 2H), 7.25~7.40(m, 3H)
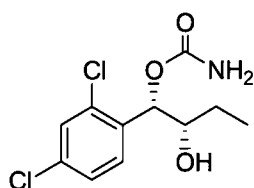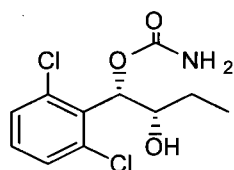
Example 105: Synthesis of l-(2,4-dichlorophenyl)-(R)-2-hydroxyhexyl-(R)-l-carbamate(105)
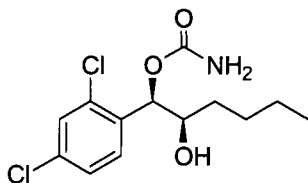
The substantially same method as described in Example 68 was conducted, except that l-(2,4-dichlorophenyl)-(R,R)-l,2-hexanediol(Preparation example 36)was used instead of l-(2-chlorophenyl)-(S,S)-l,2-propanediol(Preparation example 14), to obtain the title compound (0.21g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 50.85(t, *J*=7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, *J*=4.4Hz, 1H), 4.45~4.50(m, 1H), 4.76(br s, 2H), 6.21(d, *J*=8.4Hz, 1H), 7.30~7.50(m, 3H)

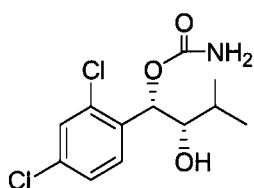**Example 106: Synthesis of l-(2,6-dichlorophenyl)-(R)-2-hydroxyhexyl-(R)-l-carbamate(106)**
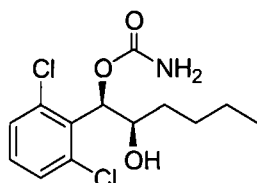
The substantially same method as described in Example 68 was conducted, except that 1-(2,6-dichlorophenyl)-(R,R)-1,2-hexanediol(Preparation   example 48)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.1 2g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 50.85(t, **J** = 7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, **J** = 4.4Hz, 1H), 4.45~4.50(m, 1H), 4.76(br s, 2H), 6.21(d, **J** = 8.4Hz, 1H), 7.16~7.34(m, 3H)

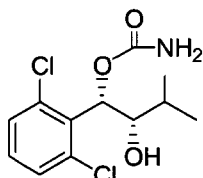**Example 107: Synthesis of l-(2,4-dichlorophenyl)-2-hydroxypropyl-l-carbamate(107)**
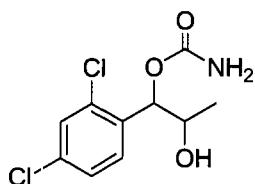
The substantially same method as described in Example 68 was conducted, except that 1-(2,4-dichlorophenyl)- 1,2-propanediol(Preparation example 28)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.05g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 61.13(d, **J**=6.8Hz, 3H), 2.49(d, **J**=4.0Hz, 1H), 4.66~4.74(m, 1H), 4.76(br s, 2H), 6.20(d, **J**=8.8Hz, 1H), 7.30~7.50(m, 3H)

Example 108: Synthesis of l-(2,6-dichlorophenyl)-2-hydroxypropyl-l-carbamate(108)
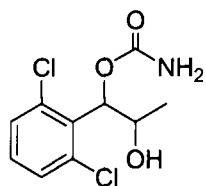
The substantially same method as described in Example 68 was conducted, except that l-(2,6-dichlorophenyl)-l,2-propanediol(Preparation   example 40)was used instead of l-(2-

chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound
(0.06g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 61.13(d, J = 6.8Hz, 3H), 2.49(d, J = 4.0Hz, IH),
4.66~4.74(m, IH), 4.76(br s, 2H), 6.20(d, J = 8.8Hz, IH), 7.25~7.40(m, 3H)

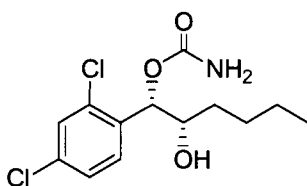**Example 109: Synthesis of l-(2,3-dichlorophenyl)-2-hydroxypropyl-l-carbamate(109)**
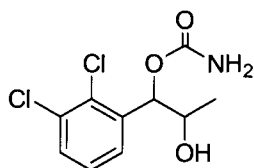
The substantially same method as described in Example 68 was conducted, except that
l-(2,3-dichlorophenyl)-l,2-propanediol(Preparation   example 59)was used instead of l-(2-
chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound
(0.02g, yield 10-30%).

H NMPv(400MHz, CDCl$_3$) 61.l5(d, J = 6.4Hz, 3H), 3.66(d, J = 9.2Hz, IH), 4.73(br s,
2H), 5.43(t, J = 9.0Hz, IH), 5.62~5.69(m, IH), 7.18~7.22(m, 3H),

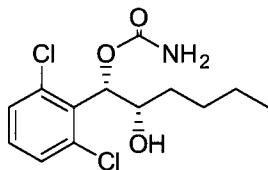**Example 110: Synthesis of l-(2,4-dichlorophenyl)-2-hydroxybutyl-l-carbamate(llO)**
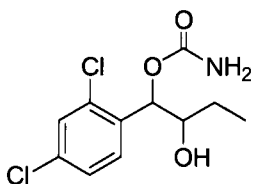
The substantially same method as described in Example 68 was conducted, except that
l-(2,4-dichlorophenyl)-l,2-butanediol(Preparation   example 31)was used instead of l-(2-
chlorophenyl)-(S,S)-l,2-propanediol(Preparation   example 14), to obtain the title compound
(0.07g, yield 10-30%).

^{1}H NMR(400MHz, CDCl$_3$) 60.77(t, J=7.4Hz, 3H), 0.92~1.01(m, IH), 1.18~1.28(m, IH),
4.06~4.13(m, IH), 4.96(d, J=6.0Hz, IH), 5.91(d, J=8.8Hz, IH), 6.4(br s, 2H), 7.30~7.50(m, 3H)

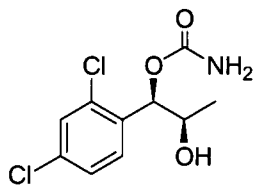**Example 111:   Synthesis of l-(2,6-dichlorophenyl)-2-hydroxybutyl-l-carbamate(lll)**
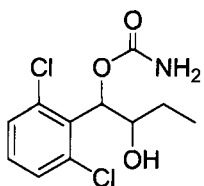
The substantially same method as described in Example 68 was conducted, except that 1-(2,6-dichlorophenyl)-1,2-butanediol(Preparation   example 43)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.1 Og, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 60.77(t, *J* = 7.4Hz, 3H), 0.92~1.01(m, 1H), 1.18~1.28(m, 1H), 4.06~4.13(m, 1H), 4.96(d, *J* = 6.0Hz, 1H), 5.91(d, *J* = 8.8Hz, 1H), 6.4(br s, 2H), 7.25~7.40(m, 3H)

Example 112: Synthesis of 1-(2,4-dichlorophenyl)-2-hydroxy-3-methyl-butyl-1-carbamate(112)
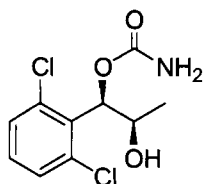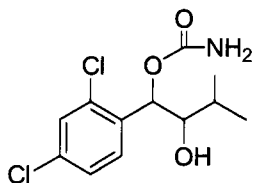

The substantially same method as described in Example 68 was conducted, except that 1-(2,4-dichlorophenyl)-3 -methyl- 1,2-propanediol(Preparation example 34)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation   example 14), to obtain the title compound (0.04g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 51.00(t , *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, *J*=6.0Hz, 1H), 5.91(d, *J*=8.8Hz, 1H), 6.42(br s, 2H), 7.30~7.50(m, 3H)

Example 113: Synthesis of 1-(2,6-dichlorophenyl)-2-hydroxy-3-methyl-butyl-1-carbamate(113)
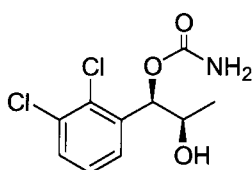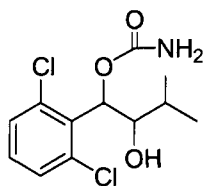

The substantially same method as described in Example 68 was conducted, except that 1-(2,6-dichlorophenyl)-3-methyl-1,2-propanediol(Preparation   example 46)was used instead of 1-

(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example14), to obtain the title compound (O.Olg, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 61.00(t, *J* = 7.2Hz, 6H), 1.73~1.79(m, 1H), 3.67~3.69(m, 1H), 4.96(d, *J*=6.0Hz, 1H), 5.91(d, *J*=8.8Hz, 1H), 6.42(br s, 2H), 7.25~7.40(m, 3H)

Example 114: Synthesis of 1-(2,4-dichlorophenyl)-2-hydroxyhexyl-1-carbamate(114)
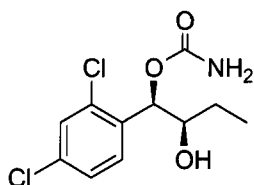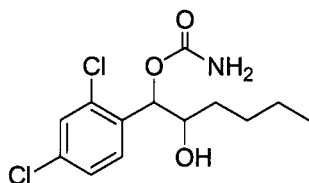

The substantially same method as described in Example 68 was conducted, except that 1-(2,4-dichlorophenyl)-1,2-hexanediol(Preparation example 37)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example 14), to obtain the title compound (0.21g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 50.85(t, *J*=7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, *J*=4.4Hz, 1H), 4.45~4.50(m, 1H), 4.76(br s, 2H), 6.21(d, *J*=8.4Hz, 1H), 7.30~7.50(m, 3H)
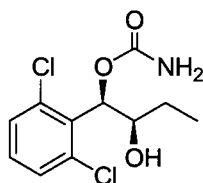
Example 115: Synthesis of 1-(2,6-dichlorophenyl)-2-hydroxyhexyl-1-carbamate(115)
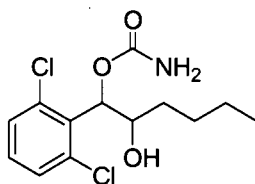
The substantially same method as described in Example 68 was conducted, except that 1-(2,6-dichlorophenyl)-1,2-hexanediol(Preparation example 49)was used instead of 1-(2-chlorophenyl)-(S,S)-1,2-propanediol(Preparation example 14), to obtain the title compound (0.12g, yield 10-30%).

H NMR(400MHz, CDCl$_3$) 60.85(t, *J* = 7.2Hz, 3H), 1.18~1.33(m, 4H), 1.48~1.55(m, 2H), 2.35(d, *J* = 4.4Hz, 1H), 4.45~4.50(m, 1H), 4.76(br s, 2H), 6.21(d, *J* = 8.4Hz, 1H), 7.16~7.34(m, 3H)

Compounds 1 to 115 produced in Examples 1 to 115 were summarized in following

Tables 1 and 2.

(Table 1) Compounds 1 to 67 having the structure of Chemical Formula 1 where 'A' is a

carbamoyl derivative and 'B' is H

No.	X	n (position)	1st Chiral	2nd Chiral	R1	A	B
						A = carbamoyl derivative R2 =	B = H
1	Cl	1(2-)	S	S	Me	H	H
2	Cl	1(2-)	R	R	Me	H	H
3	Cl	1(2-)	Rac.	Rac.	Me	H	H
4	Cl	1(2-)	S	R	Me	H	H
5	Cl	1(2-)	R	S	Me	H	H
6	Cl	1(2-)	S	S	Et	H	H
7	Cl	1(2-)	R	R	Et	H	H
8	Cl	1(2-)	Rac.	Rac.	Et	H	H
9	Cl	1(2-)	S	S	Isopropyl	H	H
10	Cl	1(2-)	R	R	Isopropyl	H	H
11	Cl	1(2-)	Rac.	Rac.	Isopropyl	H	H
12	Cl	1(2-)	S	S	butyl	H	H
13	Cl	1(2-)	R	R	butyl	H	H
14	Cl	1(2-)	Rac.	Rac.	butyl	H	H
15	Cl	1(2-)	S	S	Me	Me	H
16	Cl	1(2-)	S	S	Me	Propyl	H
17	Cl	1(2-)	S	S	Me	Isopropyl	H
18	Cl	1(2-)	S	S	Me	Cyclopropyl	H
19	Cl	1(2-)	S	S	Me	Cyclohexyl	H
20	Cl	1(2-)	S	S	Me	Benzyl	H
21	Cl	1(2-)	S	S	Me	Bicyclo[2.2.1]heptane	H
22	Cl	1(2-)	R	R	Me	Me	H
23	Cl	1(2-)	R	R	Me	Propyl	H
24	Cl	1(2-)	R	R	Me	Isopropyl	H
25	Cl	1(2-)	R	R	Me	Cyclopropyl	H
26	Cl	1(2-)	R	R	Me	Cyclohexyl	H
27	Cl	1(2-)	R	R	Me	Benzyl	H
28	Cl	1(2-)	R	R	Me	Bicyclo[2.2.1]heptane	H
29	Cl	1(2-)	Rac.	Rac.	Me	Me	H
30	Cl	1(2-)	Rac.	Rac.	Me	Propyl	H
31	Cl	1(2-)	Rac.	Rac.	Me	Isopropyl	H
32	Cl	1(2-)	Rac.	Rac.	Me	Cyclopropyl	H
33	Cl	1(2-)	Rac.	Rac.	Me	Cyclohexyl	H
34	Cl	1(2-)	Rac.	Rac.	Me	Benzyl	H
35	Cl	1(2-)	Rac,	Rac.	Me	Bicyclo[2.2.1]heptane	H
36	Cl	2(2,4-)	S	S	Me	H	H
37	Cl	2(2,6-)	S	S	Me	H	H
38	Cl	2(2,3-)	S	S	Me	H	H
39	Cl	2(2,4-)	S	S	Et	H	H
40	Cl	2(2,6-)	S	S	Et	H	H
41	Cl	2(2,4-)	S	S	Isopropyl	H	H
42	Cl	2(2,6-)	S	S	Isopropyl	H	H

43	Cl	2(2,4-)	S	S	butyl	H	H
44	Cl	2(2,6-)	S	S	butyl	H	H
45	Cl	2(2,4-)	R	R	Me	H	H
46	Cl	2(2,6-)	R	R	Me	H	H
47	Cl	2(2,3-)	R	R	Me	H	H
48	Cl	2(2,4-)	R	R	Et	H	H
49	Cl	2(2,6-)	R	R	Et	H	H
50	Cl	2(2,4-)	R	R	Isopropyl	H	H
51	Cl	2(2,6-)	R	R	Isopropyl	H	H
52	Cl	2(2,4-)	R	R	butyl	H	H
53	Cl	2(2,6-)	R	R	butyl	H	H
54	Cl	2(2,4-)	Rac,	Rac.	Me	H	H
55	Cl	2(2,6-)	Rac,	Rac.	Me	H	H
56	Cl	2(2,3-)	Rac,	Rac.	Me	H	H
57	Cl	2(2,4-)	Rac,	Rac.	Et	H	H
58	Cl	2(2,6-)	Rac,	Rac.	Et	H	H
59	Cl	2(2,4-)	Rac,	Rac.	Isopropyl	H	H
60	Cl	2(2,6-)	Rac,	Rac.	Isopropyl	H	H
61	Cl	2(2,4-)	Rac,	Rac.	butyl	H	H
62	Cl	2(2,6-)	Rac,	Rac.	butyl	H	H
63	F	1(2-)	S	S	Me	H	H
64	F	1(2-)	R	R	Me	H	H
65	I	1(2-)	S	S	Me	H	H
66	I	1(2-)	R	R	Me	H	H
67	I	1(2-)	S	S	Et	H	H

(Table 2) Compounds 68 to 115 having the structure of Chemical Formula 1 where 'A' is H and 'B' is a carbamoyl derivative

No.	X	n (position)	1st Chiral	2nd Chiral	R^1	A	B
						A=H	B= carbamoyl derivative R^3=
68	Cl	1(2-)	S	S	Me	H	H
69	Cl	1(2-)	R	R	Me	H	H
70	Cl	1(2-)	Rac.	Rac.	Me	H	H
71	Cl	1(2-)	S	S	Me	H	Me
72	Cl	1(2-)	R	R	Me	H	Me
73	Cl	1(2-)	Rac.	Rac.	Me	H	Me
74	Cl	1(2-)	S	S	Me	H	Propyl
75	Cl	1(2-)	R	R	Me	H	Propyl
76	Cl	1(2-)	Rac.	Rac.	Me	H	Propyl
77	Cl	1(2-)	S	S	Me	H	Isopropyl
78	Cl	1(2-)	R	R	Me	H	Isopropyl
79	Cl	1(2-)	Rac.	Rac.	Me	H	Isopropyl
80	Cl	1(2-)	S	S	Me	H	Cyclopropyl
81	Cl	1(2-)	R	R	Me	H	Cyclopropyl
82	Cl	1(2-)	Rac.	Rac.	Me	H	Cyclopropyl
83	Cl	1(2-)	S	S	Me	H	Cyclohexyl
84	Cl	1(2-)	R	R	Me	H	Cyclohexyl
85	Cl	1(2-)	Rac.	Rac.	Me	H	Cyclohexyl
86	Cl	1(2-)	S	S	Me	H	Benzyl
87	Cl	1(2-)	R	R	Me	H	Benzyl
88	Cl	1(2-)	Rac.	Rac.	Me	H	Benzyl

89	Cl	2(2,4-)	S	S	Me	H	H
90	Cl	2(2,6-)	S	S	Me	H	H .
91	Cl	2(2,3-)	S	S	Me	H	H
92	Cl	2(2,4-)	S	S	Et	H	H
93	Cl	2(2,6-)	S	S	Et	H	H
94	Cl	2(2,4-)	S	S	Isopropyl	H	H
95	Cl	2(2,6-)	S	S	Isopropyl	H	H
96	Cl	2(2,4-)	S	S	Butyl	H	H
97	Cl	2(2,6-)	S	S	Butyl	H	H
98	Cl	2(2,4-)	R	R	Me	H	H
99	Cl	2(2,6-)	R	R	Me	H	H
100	Cl	2(2,3-)	R	R	Me	H	H
101	Cl	2(2,4-)	R	R	Et	H	H
102	Cl	2(2,6-)	R	R	Et	H	H
103	Cl	2(2,4-)	R	R	Isopropyl	H	H
104	Cl	2(2,6-)	R	R	Isopropyl	H	H
105	Cl	2(2,4-)	R	R	Butyl	H	H
106	Cl	2(2,6-)	R	R	Butyl	H	H
107	Cl	2(2,4-)	Rac.	Rac.	Me	H	H
108	Cl	2(2,6-)	Rac.	Rac.	Me	H	H
109	Cl	2(2,3-)	Rac.	Rac.	Me	H	H
110	Cl	2(2,4-)	Rac.	Rac.	Et	H	H
111	Cl	2(2,6-)	Rac.	Rac.	Et	H	H
112	Cl	2(2,4-)	Rac.	Rac.	Isopropyl	H	H
113	Cl	2(2,6-)	Rac.	Rac.	Isopropyl	H	H
114	Cl	2(2,4-)	Rac.	Rac.	Butyl	H	H
115	Cl	2(2,6-)	Rac.	Rac.	Butyl	H	H

Experimental Example 1: Test of Muscle Relaxation Activity

1.1. Animals

For testing, male mice (ICR) were purchased from ORIENT BIO INC. (Korea), divided into several groups with 6 mice in each group, and were adapted for 4-5 days.   The mice having the weight ranging from 19g to 26g were employed for the test. The pharmacological effect of the test compounds on muscle relaxation was evaluated by Rotarod test, grip strength test, and muscular force (wire hang) test.   All mice were adapted to the test environment at one hour before starting the tests.   The pharmacological effects of all the test compounds were evaluated by administration through peritoneal cavity of the mice (10 ul/g, bw).

1.2. Measurement of muscle relaxation activity by endurance time on a rotarod rotating at accelerated speed

At 24 hours before testing, the mice to be tested were preliminarily trained for 5 minutes on a rod rotating at the rate of 6 revolutions per a minute.   The pharmacological effect on muscle relaxation of the test compounds were evaluated by observing the mice on a rod for 5

minutes, where the rod was accelerated from 4 to 40 revolutions per a minute during the test time. The endurance time that each mouse endures on the acceleratedly rotated rod without falling off from the rod was recorded.   As test time for evaluation, a maximum of 5 minutes was applied. In case the mouse does not fall off from the rod for testing time, the endurance time was recorded as 5 minutes.   All the test compounds were intraperitoneally administered (10 ul/g, bw) to the mice at 15 minutes, 30 minutes, 1 hour, and 2 hours prior to the testing, and the median effective concentration (ED50) was determined at the time that the drug exhibits its maximum pharmacological effect.   The obtained results were shown in following Table 1. This experimentation was conducted according to the method described in the reference, 'Monville et al. (2006) Comparison of incremental and accelerating protocol of the rotarod test for the assessment of motor deficits in the 6-OHDA model. J. Neurosci. Meth. 158: 219-223'.

1.3. Measurement of muscle relaxation activity by residence time on a rotarod rotating at a fixed speed

All the mice to be tested were preliminarily trained for 5 minutes on a rod rotating at the rate of 15 revolutions per a minute. The mice that could not remain on the rod without falling off therefrom for a minimum of 2 minutes were excluded from this testing.   After the training, all the mice were allowed to rest for 45-60 minutes. Before the administration of the test compounds, the mice were subjected to a further training for one minute on the rod rotating under the same condition, where the mice falling off from the rod were excluded from this experimentation. All the test compounds were intraperitoneally administered (10 ul/g, bw) to the mice at 15 minutes, 30 minutes, 1 hour, and 2 hours prior to the testing, and the median effective concentration (ED50) was determined at the time(generally 15 min, 30min or 60min) that the compounds exhibit their maximum pharmacological effect. In case a mouse stays on the rod until the test is finished, the time was recorded as 10 minutes.   As test time for evaluation, a maximum of 10 minutes was applied.   The obtained results were shown in following Table 3. This experimentation was conducted according to the method described in the reference, 'Yasuda et al. (2005) Antipyretic, analgesic and muscle relaxant activities of Pueraria isoflavonoids and their metabolites from Pueraria lobata Ohwi - a traditional Chinese drug. Biol. Pharm. Bull. 28: 1224-1228'.

1.4. Measurement of muscle relaxation activity by grip strength

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A grip strength test using the test animals' forelimbs was performed using an instrument equipped with triangle ring and designed so as to easily grip with the forelimbs of experimental animals, manufactured from Ugo Basile Inc.(Ugo Basile, Model47106, Italy). The test was conducted before and after administration of the compounds to evaluate the effects thereof. All the test compounds were intraperitoneally administered (10 ul/g, bw) at 15 minutes, 30 minutes, 1 hour, and 2 hours before test, and the median effective concentration (ED50) was determined at the time(generally 15 min, 30min or 60min) that the compounds exhibits therir maximum pharmacological effect. The mouse was made to grip the rod with its forelimbs, and its tail was pulled, where the force at which the mouse detached from the rod was recorded. The instrument indicated the force in grams. All of the mice were given 3 opportunities for test, and the 3 highest values among the test opportunities were selected and the mean value was used as the test result. The obtained results are shown in Table 3. This experimentation was conducted according to the method described in the reference, 'Nevins et al. (1993) Quantitative grip strength assessment as a means of evaluating muscle relaxation in mice. Psychopharmacol. 110: 92-96'.

1.5. Measurement of muscle relaxation activity by wire hang

This experimentation was conducted using a metal wire of 30cm in length, which was suspended between two pillars at a height of about 40cm from the bottom covered with a soft pad. All the test compounds were administered to the mice through peritoneal cavity (10 ul/g, bw) at 15 minutes, 30 minutes, 1 hour, and 2 hours prior to the testing, and the median effective concentration (ED50) was determined at the time that the compound exhibits the maximum pharmacological effect. Each mouse was made to grip the wire using two forelimbs, and the elapse time before the mouse fell off from the wire to the pad on the bottom was recorded in seconds. Each mouse was given 5 opportunities for this test at an interval of 2 minutes period. The highest 3 records among the test opportunities were selected and the mean value was used as the test result. The obtained results are shown in Table 3. This experimentation was conducted according to the method described in the reference, 'Jacqueline N. Crawley (1999) Behavioral phenotyping of transgenic and knockout mice: experimental design and evaluation of general health, sensory functions, motor abilities, and specific behavioral tests. Brain Res. 835: 18-26'.

[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.

[Results]

The results of muscle relaxation activity of the phenyl carbamate compounds measured in above Experimental Examples 1.2 to 1.4 are shown in following Table 3. In the Table 3, the ED50 was represented by the concentration where the compound shows the 50% of muscle relaxation activity compared to the vehicle only (100%).

[Table 3] Results of the measurements of muscle relaxation activity of the phenyl carbamate compounds

No.	MR test (ED50; mg/kg, bw)				control
	I	II	III	IV	
1	39.7	23.3	40.9	13.3	1
2	66.3	76.5	110.0	43.3	1
3	57.1	47.7	72.6	34.0	1
4	69.3	65.0	124.2	40.0	1
5	66.9	65.5	95.0	52.5	1
6	-	-	70.7	-	1
7	-	-	248.4	-	1
8	50.6	-	69.5	-	1
9	-	-	103.9	-	1
11	102.5	-	126.1	-	1
15	51.4	42.8	83.6	25.4	1
16	48.7	61.6	67.8	16.1	2
17	73.1	66.4	91.5	41.4	2
18	59.2	61.2	87.4	29.5	2
19	95.3	-	109.8	28.5	2
22	25.7	25.1	28.3	22.4	1
23	-	-	73.8	46.0	2
24	38.6	44.3	48.8	17.8	2
25	30.0	18.3	46.1	32.9	1
26	-	-	-	63.8	2
29	30.2	41.0	46.0	38.0	2
30	-	-	65.4	31.7	2
31	-	-	50.4	52.1	1
32	-	-	45.2	36.6	2
33	-	-	-	74.6	2
63			118.3	100^a(84.2%)	1
64			120^a(35.4%)	100^a(30.8%)	1
65		28.0	42.9	23.4	2
66		67.9	46.0	76.3	2
67		30.2	69.1	26.2	2

I = Acc. Rotatod (accelerated rotating rotarod test; Experimental Example 1.2),

11= Fixed 15 r.p.m. Rotarod (constantly rotating rotarod test; Experimental Example 1.3),

III = Grip strength (Experimental Example 1.4),

IV = Wire hang (Experimental Example 1.5)

a = the concentration administered and effect (%) compared to that of control treated with vehicle only

Control 1: administered with vehicle only (Vehicle 1: 30% PEG400(Polyethylene Glycol 400))

Control 2: administered with vehicle only (Vehicle 2: 20% Tween 80)

Experimental Example 2: Observation of biological behavior of ALS transgenic animals

2.1. Animals

All animal experiments were be carried out according to the National Institute of Health (NIH) guidelines for the care and use of laboratory animals, and approved by the State Provincial Office of Southern Finland. Altogether 80 male and female mice expressing mutated human SOD1-G93A transgene (heterozygous TgN-SODl-G93A-lGur; Gurney et al. (1994), Science 264, 1772. 1775) and 15 of their wild type littermates were used for the experiments. Animals were housed at a standard temperature (22 ± 2℃) and in a light controlled environment (lights on from 7AM to 8PM) with libitum access to food and water. PCR was used to genotype the mice before the start of the experiments.

The animals were grouped as follows:

<Non-transgenic male mice>

- Group 1: 15 WT mice treated with vehicle (30%(w/v) polyethyleneclycol 400(PEG400), once a day, p.o.) starting at 60 days of age and continuing until end-point

<Transgenic G93A SOD1 male mice: ALS-transgenic mice>

- Group 2: 20 transgenic mice treated with vehicle (30%(w/v) polyethyleneclycol 400(PEG400), once a day, p.o.) staring at 60 days of age and continuing until end-point

- Group 3: 20 transgenic mice treated with a drug (Compound 1) at dose of 3mg/kg (once a day, p.o.) staring at 60 days of age and continuing until end-

point

- Group 4: 20 transgenic mice treated with Compound 1 at dose of lOmg/kg (once
  a day, p.o.) staring at 60 days of age and continuing until end-point
- Group 5: 20 transgenic mice treated with Compound 1 at dose of 50mg/kg (once
  a day, p.o.) staring at 60 days of age and continuing until end-point

To the animals, various experiments such as measurements of body weight, clinical score, and survival ratio, and open field test were conducted as follows, staring at 60 days of age until end-point (150 days of age).

2.2. Husbandry

All the provided mice were housed in groups of up to max 5 per cage (single sex, males), in a temperature (22 ± 2℃) and humidity (30-70 %) controlled environment with a normal light-dark cycle (lights on from 7AM to 8PM). All mice were housed in cages with woodchip bedding covering the ground that is changed as frequently as needed to provide the animals with dry bedding. This basic environment was enriched with igloo (amber color, certified, transparent, BioServ). Food (Standard Lab Diet) and water were available ad libitum to the mice in their cages. Starting at age of 100 days or when the mouse reaches score 3 (referring to the following Example 2.8) whichever comes first, the transgenic G93A SODl mice received wet powdered food (Standard Lab Diet mixed with water to form a paste) placed inside a cup on the floor of the cages. In addition, water spouts were long enough to allow mice to easily access from floor level.

2.3. Breeding and Weaning

Eighty transgenic G93A SODl mice and 15 WT littermates were bred by Charles River Germany (under Cerebricon license) by mating hemizygous TG males (strain 002726M; B6SJL TG SODl x G93A 1GUR/J, JAX) with WT females (strain 10012, JAX). Pups were weaned from their mothers and segregated to new cages for male, not exceeding 4-5 mice per cage. Tail/ear snips were taken during the weaned process at 3 weeks for genotype as described below.

2.4. Genotyping

The mice were ear-marked at the age of 3 weeks and ear/tail samples were collected at the same time for genotyping with PCR. Genotypes were determined by standard PCR by Charles River under the following conditions.

<Primer>

Primer	5' Label	Sequence 5' → 3'	3' Label	Primer Type
oIMR0113	-	CAT CAG CCC TAA TCC ATC TGA	-	Transgene
OIMR0114	-	CGC GAC TAA CAA TCA AAG TGA	-	Transgene
OIMR7338	-	CTA GGC CAC AGA ATT GAA AGA TCT	-	Internal Positive Control Forward
OIMR7339	-	GTA GGT GGA AAT TCT AGC ATC ATC C	-	Internal Positive Control Reverse

<Reaction component>

Reaction Component	Volume (μĭ)	Final Concentration	Total Volume (μĭ)
ddH20	3.52	-	3.52
10 X AB PCR Bufferll	0.84	0.70 X	0.84
25 mM MgC12	0.48	1.00 mM	0.48
2.5 mM dNTP	0.96	0.20 mM	0.96
20 uM OIMR7338	0.45	0.75 uM	0.45
20 uM OIMR7339	0.45	0.75 uM	0.45
20 uM oIMR0113	0.80	1.33 uM	0.80
20 uM oIMR0114	0.80	1.33 uM	0.80
5 mM DNA Loading Dye	1.66	0.69 mM	1.66
5 U/ul Taq DNA Polymerase	0.04	0.02 U/ul	0.04
DNA	2.00	-	2.00

5   **<Cycling>**

Step #	Temp °C	Time	Note
1	95	3 min	-
2	95	30 sec	-
3	60	30 sec	-

4	72	45 sec	repeat steps 2-4 for 35 cycles
5	72	2 min	-
6	10	-	hold

2.5. Experimental set up of mice

For systematic drug testing, the following best practices were applied:

In setting up groups for testing (i.e., vehicle or drug treated), transgenic mice were randomized based on body weight just before beginning of treatment and also into groups so that whole litters of mice do not end up in a single testing group, to avoid 'litter effect' on the overall results.

Mice were housed in groups of 4-5 (max 5) mice, in case of aggressive behavior occurs, single housing was applied.

Experimentation was conducted in a blinded manner. For instance, the experimenter, dosing mice with the vehicle or the drug was different from the experimenter actually running the phenotype tests.   Alternatively, if the same experimenter does dosing and phenotypic testing, that the experimenter does not have the code for mice receiving drug or vehicle and the vials with vehicle or drug were labeled so as not to allow distinction.

2.6. Drug administration

Treatment with drug (Compound 1) was started at the age of 60 days and continued until the mice reached 150 days of age. The drug was administered p.o. once a day between 8-12 am. The drug solubilized in 30%(w/v) polyethyleneclycol 400(PEG400), and the obtained solution was briefly vortexed and sonicated at RT (room temperature) for 20minutes. Treatment solution of the drug was prepared fresh every day.

2.7. Measurement of body weight and mortality

Since weight loss has proven to correlate well with disease development and is easily scored co-jointly with disease stage, the mice were weighted once-a-week at the age of 60 days to 90 days and three times a week after they reach the age of 91 days (13 weeks).

Mice were monitored twice-a-day by laboratory personnel (8 am to 4 pm) for "survival". It is most optimal to measure "true survival" when mouse has no detectable heartbeat, which is

prevented by IACUC (Institutional Animal Care and Use Committees) restrictions, and thus the "survival" end-point was defined as a 25% or more loss in body weight. For these alternative measures combining these "survival" data (body weight or temperature decrease) with survival of spontaneous death mice (age hound dead in a cage) is suitable. No tissues were collected from the terminated or spontaneously dead mice.

The measured rate (%) of survivor for each group was shown in Figs. 1 and 2 (TG: transgenic G93A SODl). Fig. 1 shows that the survival time is extended by administration of Compound 1 at early stage of ALS, indicating that Compound 1 has a pharmacological effect to increase the survival rate at early stage of ALS. Such pharmacological effect is especially remarkable in the group treated with lOmg/kg of Compound 1. Fig. 2 shows that Compound 1 has an effect to delay the disease onset, and such effect is especially remarkable in the group treated with lOmg/kg of Compound 1. Both increased survival rate and delayed disease onset are very meaningful considering the high mortality of the SODl transgenic mice model.

In addition, the average of the measured body weight for each group was shown in Fig. 3. As shown in Fig. 3, the body weight loss compared with WT group was decrease by administration of the drug in the dose-dependent manner.

2.8. Clinical scoring

In the transgenic G93A SODl mice, early onset of the disease (ALS) (~100 days) and rapid decline with the affected mice reaching the end stage on average within 40 days (typical survival of 130 to 160 days), has been reported.

The mice were carefully examined once a week until age of 90 days and two times a week after they reached the age of 9 1 days.

The earliest clinical signs were tremor and shaking of their limbs when the mice are suspended briefly in the air by their tails. The clinical scoring system is on a scale of 1 to 5; with 1 as the end-point for euthanasia and 5 as healthy with little or no signs of onset of disease. Animals were scored by lifting them gently by the base of their tails and observing them for tremors, stiffness and their ability to extend their limbs.

A more specific breakdown of the scoring system is as follows:

- 5 = healthy
- 4-5 = most healthy, very active, extension of all limbs
- 4 = extension of all limbs, very active

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- 3-4 = with some minor stiffness, very active

- 3 = stiffness of limbs, maybe some minor paralysis, active

- 2-3 = partial paralysis, stiffness, extension of all limbs is labored, active

- 2 = paralysis, somewhat active

- 1-2 = paralysis of hind limbs, no extension of hind limbs, euthanasia may be performed dependent upon the activity of animal and its ability to right itself within 30seconds

- 1 = end-point, animal unable to right itself

Onset of disease for each mouse was recorded when they reach a disease stage 4.

The measured clinical scores were shown in Fig. 4, wherein the term "scoring day" refers to a specific date of the specific age of the test animal that is selected by the experimenter for measuring the clinical signs in the scoring system. As shown in Fig. 4, the clinical scores were increased by administration of the drug in the dose-dependent manner compared to TG vehicle group.

2.9. Open field test

Open field test measurements were performed before the dosing is stated (baseline) and around day 90 (13th age week) and day 110 (16th age week). Mice born within 2-4 days were pooled for open field testing. Activity chambers (Med Associates Inc., St. Albans, VT; 27x27x10.3 cm) were equipped with IR (Infrared Ray) beams. Mice were placed in the center of the chamber and their behaviors were recorded for 10 minutes. The following parameters were recorded: distance moved.

The obtained results were shown in Fig 5. Fig. 5 shows the measured distance moved (traveled). There were some differences between treatments group of transgenic mice.

2.10. Statistical Analysis

All values were presented as mean ± standard deviation (SD) or Standard Error of Mean (SEM), and differences were considered to be statistically significant at the $P<0.05$ level. Statistical analyses were performed using StatsDirect statistical software. Differences between group means were compared with one-way ANOVA followed by Dunnet's post hoc test and within-group differences were assessed by two-way ANOVA followed by Dunnet's post hoc test (comparison to baseline = day 60). Kaplan-Meyer survival curves were provided for disease

stage score and onset and for survival. Non-parametric data were analyzed with Kruskal-Wallis ANOVA (between groups) or Friedman ANIVA (within groups).

Experimental Example 3 : MES(maximal electroshock seizure) test

5   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 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 30% PEG400 prepared by saline solvent applied to oral before

10   the test.   If the test animal stretching their hind limb in a straight line weren't observed in the MES test, the results indicate that the test sample had an anti-epilepsy activity. Three doses of the test sample were administered orally to over 18 mice (6 mice per dose) for evaluating the respective doses at which 50% of the animals are protected from seizure (ED50). The value of ED50 (median effective dose) is calculated by Litchfield and Wicoxon log-probit method which

15   is a dose-response relationship. Then, the test results are shown in following Table 4. Experimental animal, male ICR mice and male SD rats, were purchased from OrientBio or Nara biotech, Korea, and housed 4-5 mice per a cage for 4-5 days. The range of mice body weight was used between 19 and 26 grams and range of rats body weight was used between 100 and 130 grams.

20   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.

[Table 4] : Measurement results of anti-epilepsy activity of compounds in the test

25   animals (Mice and Rats)

Compound No.	MES test(po)	
	ED50(mg/kg)	Peak Time(h)
1	13.0	2
2	51.0	0.25
3	31.4	2
4	82.4	0.5
5	84.1	0.5
6	22.2	1
8	100 [a](100%)	
9	67.1	0.5
12	100 [a](75%)	
13	200 [a](75%)	

14	200 [a](100%)	
15	100 [a](75%)	
16	200 [a](25%)	
18	200 [a](100%)	
23	200 [a](25%)	
25	200 [a](25%)	
29	200 [a](75%)	
30	200 [a](25%)	
31	200 [a](25%)	
32	200 [a](100%)	
36	82.8	
37	25.8	0.25
38	91.4	2
39	41.2	1
40	46.9	
42	35.2	0.5
43	100 [a](25%)	
44	100 [a](75%)	
45	200 [a](0%)	
46	35.2	1
63	50 [a](100%)	
65	50 [a](100%)	
67	100[a](100%)	

\# a: Injection amount(mg/kg), Protection%(4 mice);

b: Injection amount(mg/kg), Protection%(6 Rats);

Biological Experimental Example 4: Measurement of pharmaceutical efficacy duration time through MES

The ED50 values according to time were measured in the test animals (mice and rats) after oral administration of test compound 1 as described in Biological Experimental Example I. The obtained results are shown in following Table 5 and Fig. 1.

[Table 5] Duration of MES test ED50(mg/kg), (po)

No	species	Time								
		0.25h	0.5h	1h	2h	3h	4h	6h	8h	12h
1	Mouse	21.2	22.5	13.3	13.0	14.7	18.7	30.0	49.4	118.8
	Rat	-	5.9	3.3	1.4	-	6.9	-	14.4	36.1

As shown in Table 5 and Fig. 1, the test compound 1 exhibits the efficacy duration time of at least 12 hours in both of the tested rats and mice.

WHAT IS CLAIMED IS:

1.   A pharmaceutical composition for preventing or treating amyotrophic lateral sclerosis (ALS) comprising a phenyl carbamate compound represented by Chemical Formula 1 or a pharmaceutically acceptable salt thereof as an active ingredient:

[Chemical formula 1]

wherein

X is a halogen;

n is an integer from 1 to 5;

R1 is a linear or branched alkyl group of C1-C4;

A is hydrogen or a carbamoyl derivative represented by ;

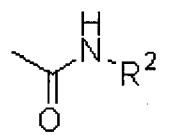B is hydrogen, a carbamoyl derivative represented by , trialkyl silyl groups, trialkylaryl silyl groups (wherein the total number of alkyl and aryl groups is three), or a trialkyl silyl ether group, wherein each alkyl group is independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups, and each aryl group is independently selected from the group consisting of C5-C8 aryl groups ;

A and B are not the carbamoyl derivative at same time; and

R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, a linear or branched alkyl group of C1-C4, a cycloalkyl group of C3-C8, and benzyl group.

2.   The pharmaceutical composition according to Claim 1, wherein

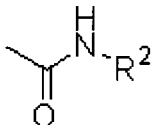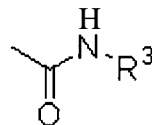X is chlorine, fluorine, iodine, or bromine;

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n is 1 or 2;

R1 is methyl group, ethyl group, isopropyl group, or butyl group;

A is hydrogen or a carbamoyl derivative represented by [structure] ;

B is hydrogen, a carbamoyl derivative represented by [structure], a trimethyl silyl
(TMS) group, a triethyl silyl (TES) group, a triisopropyl silyl (TIPS) group, t-butyl dimethyl silyl
(TBDMS) group, a t-butyl diphenyl silyl (TBDPS) group, or a trialkyl silyl ether group, wherein
each alkyl group is independently selected from the group consisting of linear, branched, or
cyclic C1-C4 alkyl groups;

A and B are not the carbamoyl derivative at same time; and

R2 and R3 are the same as or different from each other, and independently selected from
the group consisting of hydrogen, methyl group, propyl group, isopropyl group, cyclopropyl
group, cyclohexyl group, bicycloheptane group, and benzyl group.

3.   The pharmaceutical composition according to Claim 1, wherein the compound
is selected from the group consisting of:

1-(2-chlorophenyl)-1-hydroxypropyl-2-carbamate,

1-(2-chlorophenyl)-1-hydroxybutyl-2-carbamate,

1-(2-chlorophenyl)-1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2-chlorophenyl)-1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-methylcarbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-propylcarbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-isopropylcarbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-cyclopropylcarbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-cyclohexylcarbamate,

1-(2-chlorophenyl)-1-hydroxypropyl-2-N-benzylcarbamate,

1-(2-chlorophenyl)-l-hydroxypropyl-2-N-bicyclo[2,2,l]heptanecarbamate,

1-(2,4-dichlorophenyl)-1-hydroxypropyl-2-carbamate,

1-(2,6-dichlorophenyl)-1-hydroxypropyl-2-carbamate,

1-(2,4-dichlorophenyl)-1-hydroxybutyl-2-carbamate,

1-(2,6-dichlorophenyl)-1-hydroxybutyl-2-carbamate,

1-(2,4-dichlorophenyl)-1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2,6-dichlorophenyl)-1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2,4-dichlorophenyl)-1-hydroxyhexyl-2-carbamate,

1-(2,6-dichlorophenyl)-1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-methylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-propylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-isopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-cyclopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-cyclohexylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl-1-N-benzylcarbamate,

1-(2,4-dichlorophenyl)-2-hydroxypropyl-1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxypropyl-1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxybutyl-1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxybutyl-1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxy-3-methyl-butyl-1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxy-3-methyl-butyl-1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxyhexyl-1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxyhexyl-1-carbamate,

1-(2-fluorophenyl)-1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)-1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)-1-hydroxybutyl-2-carbamate,

1-(2,3-dichlorophenyl)-1-hydroxypropyl-2-carbamate, and

1-(2,3-dichlorophenyl)-2-hydroxypropyl-1-carbamate.

4.   The pharmaceutical composition according to any one of Claims 1 to 3, wherein the compound is in the form of racemate, enantiomer, diastereomer, a mixture of enantiomer, or a mixture of diastereomer.

5.   A phenyl carbamate compound represented by Chemical Formula 1 or a

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pharmaceutically acceptable salt thereof for use in preventing or treating amyotrophic lateral sclerosis (ALS):
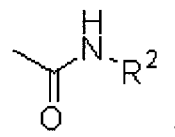
[Chemical formula 1]
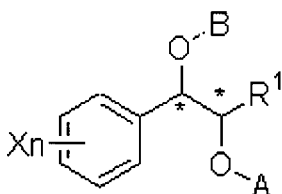
5   wherein

X is a halogen;

n is an integer from 1 to 5;

R1 is a linear or branched alkyl group of C1-C4;
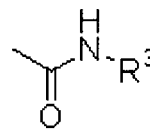
A is hydrogen or a carbamoyl derivative represented by ;

10   B is hydrogen, a carbamoyl derivative represented by , trialkyl silyl groups, trialkylaryl silyl groups (wherein the total number of alkyl and aryl groups is three), or a trialkyl silyl ether group, wherein each alkyl group is independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups, and each aryl group is independently selected from the group consisting of C5-C8 aryl groups;

15   A and B are not carbamoyl derivatives at same time; and

R2 and R3 may be the same as or different from each other, and independently selected from the group consisting of hydrogen, a linear or branched alkyl group of C1-C4, a cycloalkyl group of C3-C8, and benzyl group.
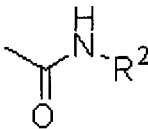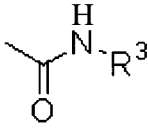
20   6.   The phenyl carbamate compound or a pharmaceutically acceptable salt according to Claim 5, wherein

X is chlorine, fluorine, iodine, or bromine;

n is 1 or 2;

R1 is methyl group, ethyl group, isopropyl group, or butyl group;

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A is hydrogen or a carbamoyl derivative represented by $\underset{O}{\overset{\overset{H}{N}{}^{\backprime}R^2}{\bigvee}}$;

B is hydrogen, a carbamoyl derivative represented by $\underset{O}{\overset{\overset{H}{N}{}^{\backprime}R^3}{\bigvee}}$, a trimethyl silyl

(TMS) group, a triethyl silyl (TES) group, a triisopropyl silyl (TIPS) group, t-butyl dimethyl silyl (TBDMS) group, a t-butyl diphenyl silyl (TBDPS) group, or a trialkyl silyl ether group, wherein each alkyl group is independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups;

A and B are not carbamoyl derivatives at same time; and

R2 and R3 are the same as or different from each other, and independently selected from the group consisting of hydrogen, methyl group, propyl group, isopropyl group, cyclopropyl group, cyclohexyl group, bicycloheptane group, and benzyl group.

7.   The phenyl carbamate compound or a pharmaceutically acceptable salt according to Claim 5, wherein the compound is selected from the group consisting of:

1-(2-chlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-methylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-propylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-isopropyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclopropyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclohexyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-benzylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-bicyclo[2,2, 1Jheptanecarbamate,

1-(2,4-dichlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2,6-dichlorophenyl)-1 -hydroxypropyl-2-carbamate,

1-(2,4-dichlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxybutyl-2-carbamate,

l-(2,4-dichlorophenyl)-l-hydroxy-3-methyl-butyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxy-3-methyl-butyl-2-carbamate,

1-(2,4-dichlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-methylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-propylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-isopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclohexylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-benzylcarbamate,

1-(2,4-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

l-(2,4-dichlorophenyl)-2-hydroxy-3-methyl-butyl-l-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxy-3-methyl-butyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2-fluorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,3-dichlorophenyl)- 1-hydroxypropyl-2-carbamate, and

1-(2,3-dichlorophenyl)-2-hydroxypropyl- 1-carbamate.

8.   The phenyl carbamate compound or a pharmaceutically acceptable salt according to any one of Claims 5 to 7, wherein the compound is in the form of racemate, enantiomer, diastereomer, a mixture of enantiomer, or a mixture of diastereomer.

9.   A use of a phenyl carbamate compound represented by Chemical Formula 1 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for preventing or treating amyotrophic lateral sclerosis (ALS):

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[Chemical formula 1]

wherein

X is a halogen;

n is an integer from 1 to 5;

R1 is a linear or branched alkyl group of C1-C4;
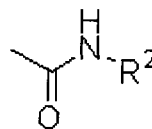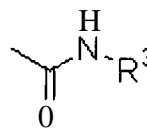
A is hydrogen or a carbamoyl derivative represented by ;

B is hydrogen, a carbamoyl derivative represented by , trialkyl silyl groups, trialkylaryl silyl groups (wherein the total number of alkyl and aryl groups is three), or a trialkyl silyl ether group, wherein each alkyl group is independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups, and each aryl group is independently selected from the group consisting of C5-C8 aryl groups;

A and B are not the carbamoyl derivative at same time; and

R2 and R3 may be the same as or-different from each other, and independently selected from the group consisting of hydrogen, a linear or branched alkyl group of C1-C4, a cycloalkyl group of C3-C8, and benzyl group.
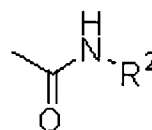
10.   The use according to Claim 9, wherein
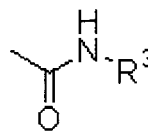
X is chlorine, fluorine, iodine, or bromine;
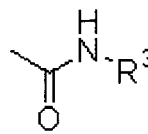
n is 1 or 2;

R1 is methyl group, ethyl group, isopropyl group, or butyl group;

A is hydrogen or a carbamoyl derivative represented by ;

B is hydrogen, a carbamoyl derivative represented by [structure: H-N-R³ with C=O], , a trimethyl silyl (TMS) group, a triethyl silyl (TES) group, a triisopropyl silyl (TIPS) group, t-butyl dimethyl silyl (TBDMS) group, a t-butyl diphenyl silyl (TBDPS) group, or a trialkyl silyl ether group, wherein each alkyl group is independently selected from the group consisting of linear, branched, or cyclic C1-C4 alkyl groups;

A and B are not the carbamoyl derivative at same time; and

R2 and R3 are the same as or different from each other, and independently selected from the group consisting of hydrogen, methyl group, propyl group, isopropyl group, cyclopropyl group, cyclohexyl group, bicycloheptane group, and benzyl group.

11.   The use according to Claim 9, wherein the compound is selected from the group consisting of:

1-(2-chlorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxy-3 -methyl-butyl-2-carbamate,

1-(2-chlorophenyl)-1 -hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-methylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-propyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-isopropylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclopropylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-cyclohexyl carbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-benzylcarbamate,

1-(2-chlorophenyl)- 1-hydroxypropyl-2-N-bicyclo[2,2, 1]heptanecarbamate,

1-(2,4-dichlorophenyl))- 1-hydroxypropyl-2-carbamate,

1-(2,6-dichlorophenyl))- 1-hydroxypropyl-2-carbamate,

1-(2,4-dichlorophenyl))- 1-hydroxybutyl-2-carbamate,

1-(2,6-dichlorophenyl))- 1-hydroxybutyl-2-carbamate,

1-(2,4-dichlorophenyl))- 1-hydroxy-3 -methyl-butyl-2-carbamate,

1-(2,6-dichlorophenyl))- 1-hydroxy-3 -methyl-butyl-2-carbamate,

1-(2,4-dichlorophenyl))- 1-hydroxyhexyl-2-carbamate,

1-(2,6-dichlorophenyl)- 1-hydroxyhexyl-2-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-methylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-propylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-isopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclopropylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-cyclohexylcarbamate,

1-(2-chlorophenyl)-2-hydroxypropyl- 1-N-benzylcarbamate,

1-(2,4-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxypropyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxybutyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxy-3-methyl-butyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxy-3-methyl-butyl- 1-carbamate,

1-(2,4-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2,6-dichlorophenyl)-2-hydroxyhexyl- 1-carbamate,

1-(2-fluorophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxypropyl-2-carbamate,

1-(2-iodophenyl)- 1-hydroxybutyl-2-carbamate,

1-(2,3-dichlorophenyl)- 1-hydroxypropyl-2-carbamate, and

1-(2,3-dichlorophenyl)-2-hydroxypropyl- 1-carbamate.

12.   The use according to any one of Claims 9 to 11, wherein the compound is in the form of racemate, enantiomer, diastereomer, a mixture of enantiomer, or a mixture of diastereomer.
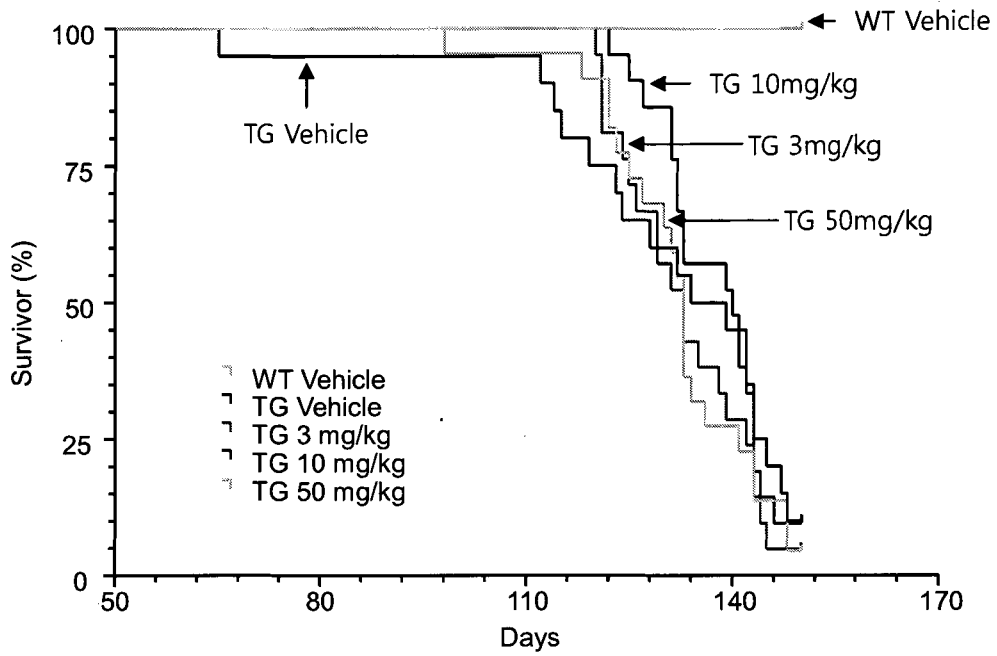
Fig. 1

Compound 1 Survival
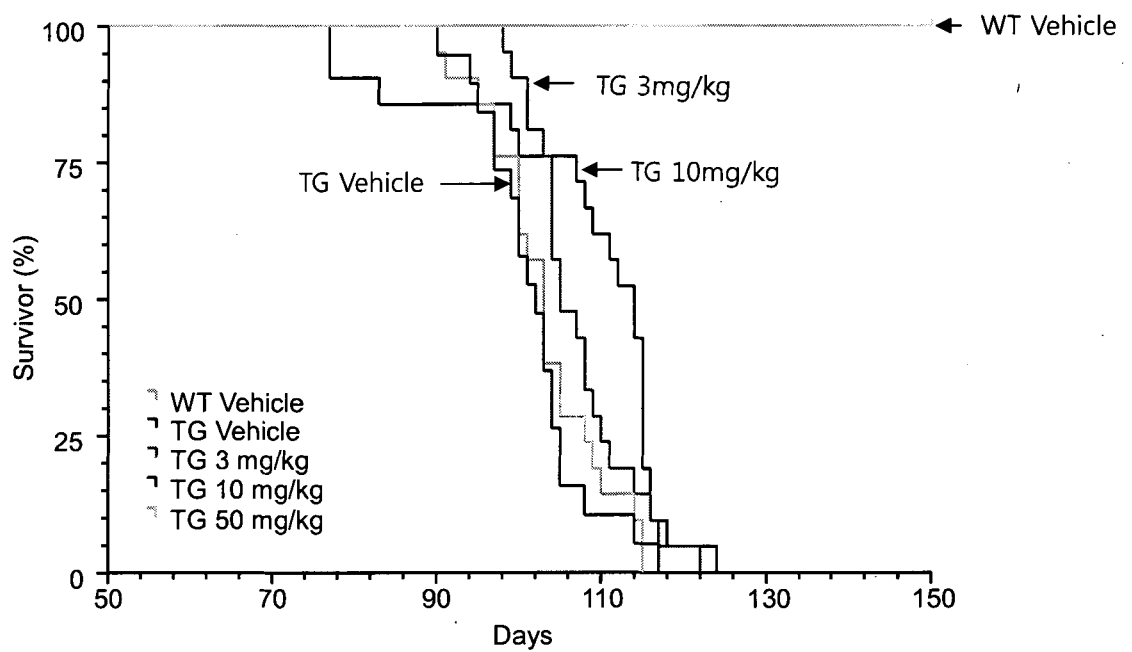

Fig. 2

Compound 1 Disease Onset
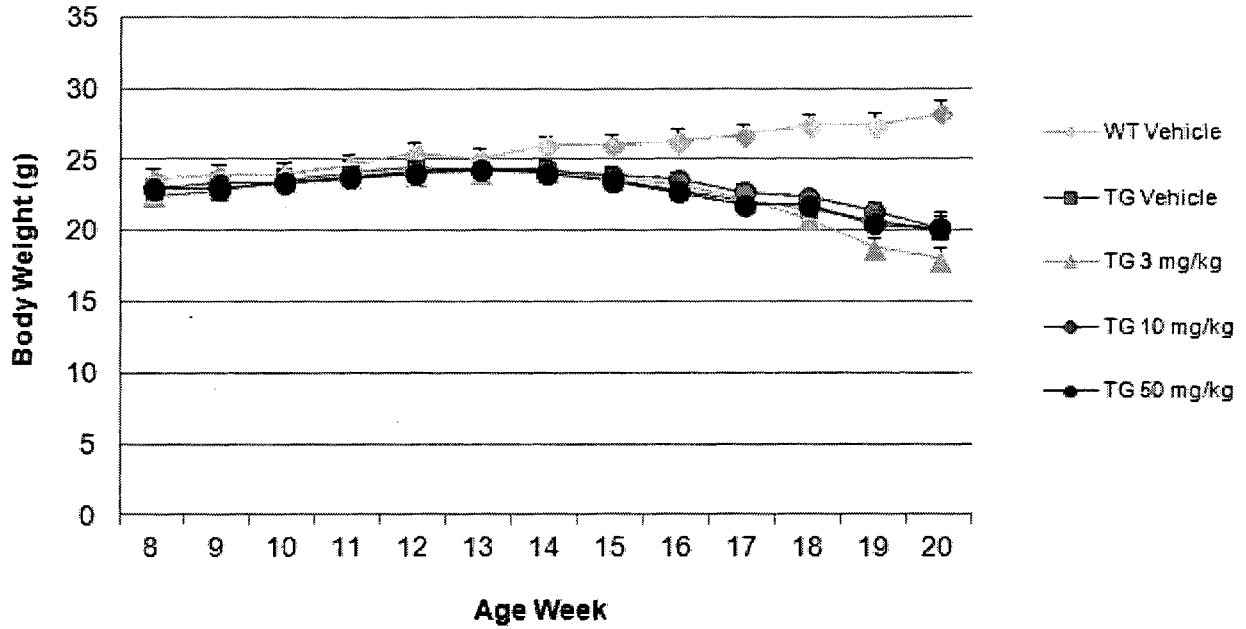
Fig. 3

Compound 1 Body Weight

Fig. 4

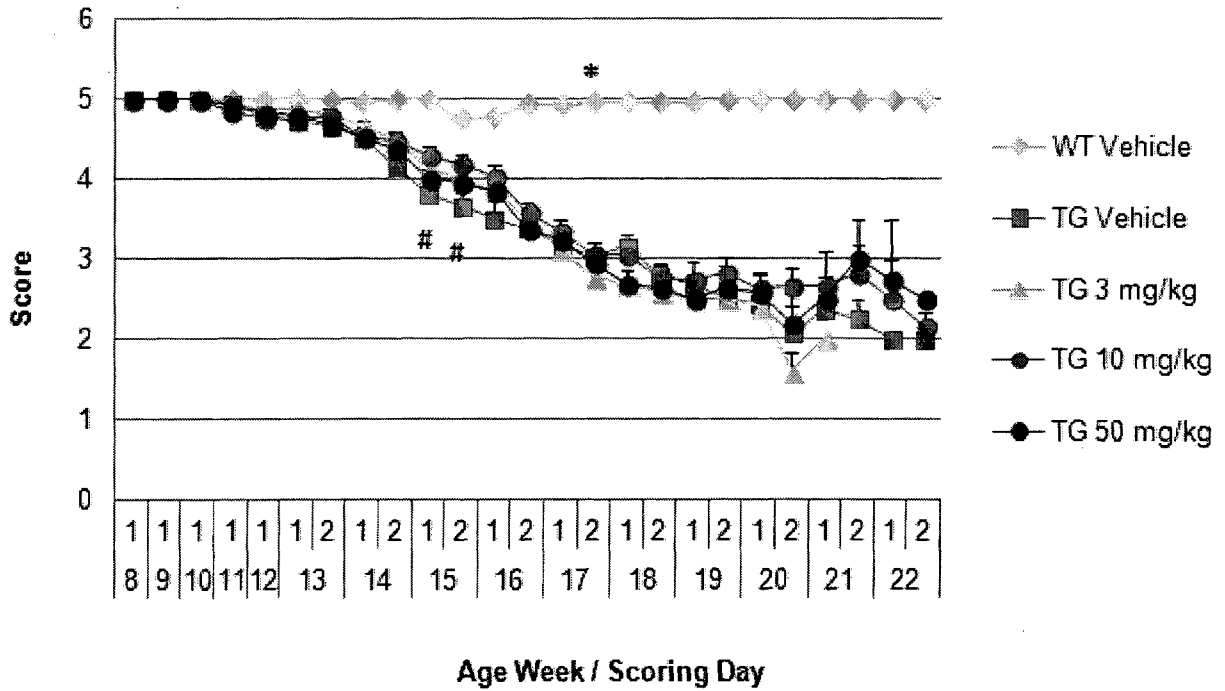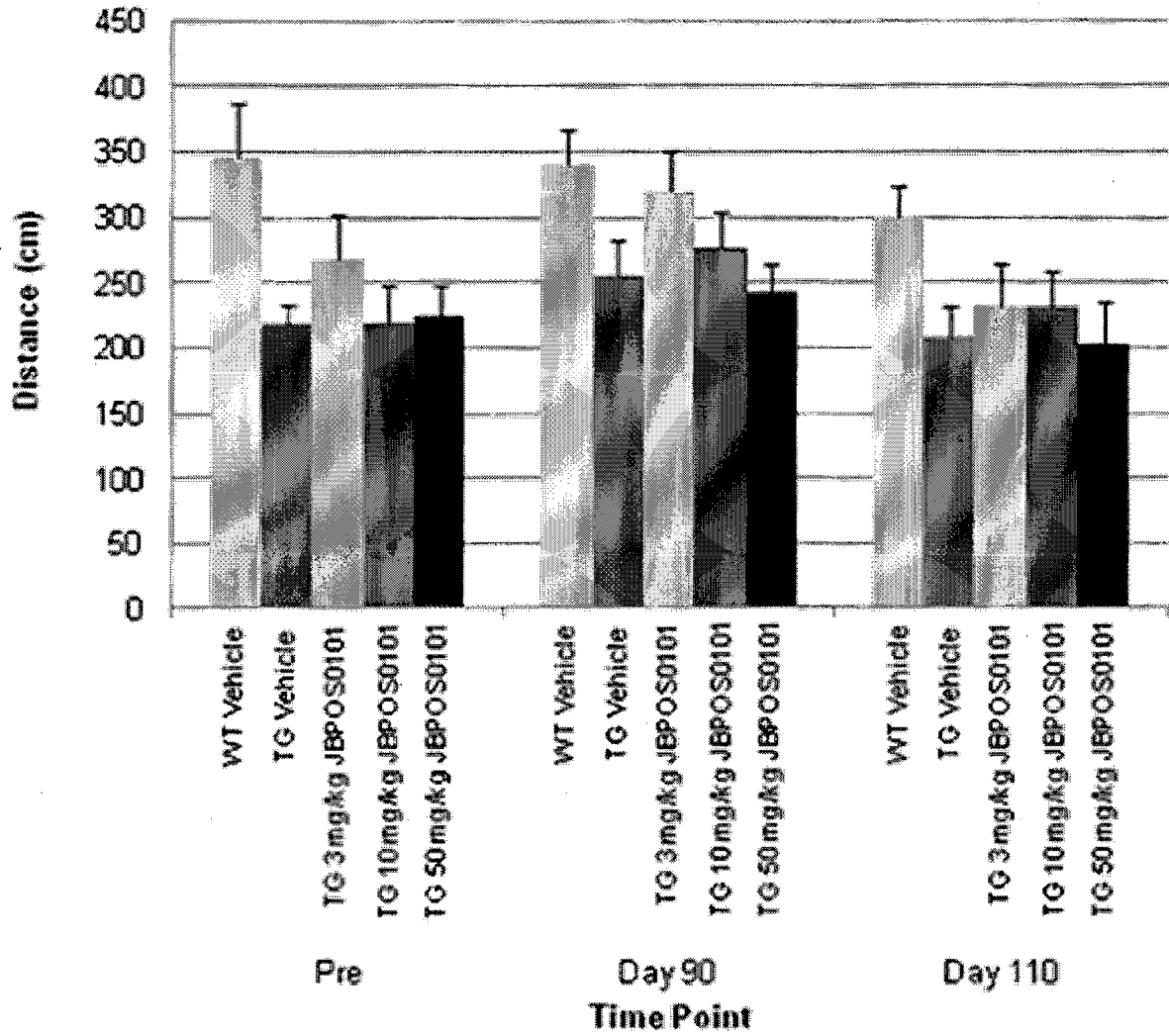**Compound1 Clinical Score**

Fig. 5

Open Field - Distance Traveled

| A. | CLASSIFICATION OF SUBJECT MATTER |

C07C 271/10(2006.01)i, C07C 271/12(2006.01)1, A61K 31/16(2006.01)1, A61P 25/00(2006.01)1

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)
  C07C 271/10; A61K 31/495; C07D 487/00; C07D 401/10; C07D 401/00; C12P 7/22

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: phenyl carbamate, amyotrophic lateral sclerosis, ALS

| C. | DOCUMENTS CONSIDERED TO BE RELEVANT |

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JIAO, P. et al., A Sequential 0-Nitrosoaldol and Grignard Addition Process: An Enantio- and Diastereoselective Entry to Chiral 1,2-Diols, Angewandte Chemie, International Edition (2009), Vol. 48(18), pp. 3333-3336	5,6,8
A	See Table 2, entry 9.	1-4,7,9-12
X	WO 2008-124848 A1 (SGX PHARMACEUTICALS, INC. et al.) 16 October 2008	5,6,8
A	See pages 153-154, step 3.	1-4,7,9-12
X	WO 2008-013213 A1 (EISAI R & D MANAGEMENT CO., LTD. et al.) 31 January 2008	5,8
A	See example 4, paragraph [0198].	1-4,6-7,9-12
X	JP 61-271992 A (CENTRAL GLASS CO., LTD) 02 December 1986	5,6,8
A	See formula [1]; page 509, right column, examples 4-6; and claim.	1-4,7,9-12
X	GIRIJAVALLABHAN, V.M. et al., Synthesis of the antifungal agent SCH 42427(SM 9164), Bioorganic & Medicinal Chemistry Letters (1991), Vol. 1(7), pp. 349-352 See 1-(2,4-difluorophenyl)-1,2-propanediol.	5,6,8

☒ 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 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	Date of mailing of the international search report
19 April 2013 (19.04.2013)	**23 April 2013 (23.04.2013)**

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C (Continuation).   DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A		1-4,7,9-12
A	US 3313699 A (CHARLES D. BOSSINGER et al.) 11 April 1967 See column 1, lines 11-20, 44-70; claims 1-13.	1-12
A	US 3313700 A (CHARLES D. BOSSINGER et al.) 11 April 1967 See column 1, lines 31-36; column 2, lines 9-31; claims 1-13.	1-12

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