WHAT IS CLAIMED IS:

1. A method for preparing an intermediate of dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 2, as shown in the following Reaction Formula 1, the method comprising:

(Step a) preparing a compound represented by Chemical Formula 6 by ring-opening of epoxide ring using Grinard reagent in a compound represented by Chemical Formula 5;

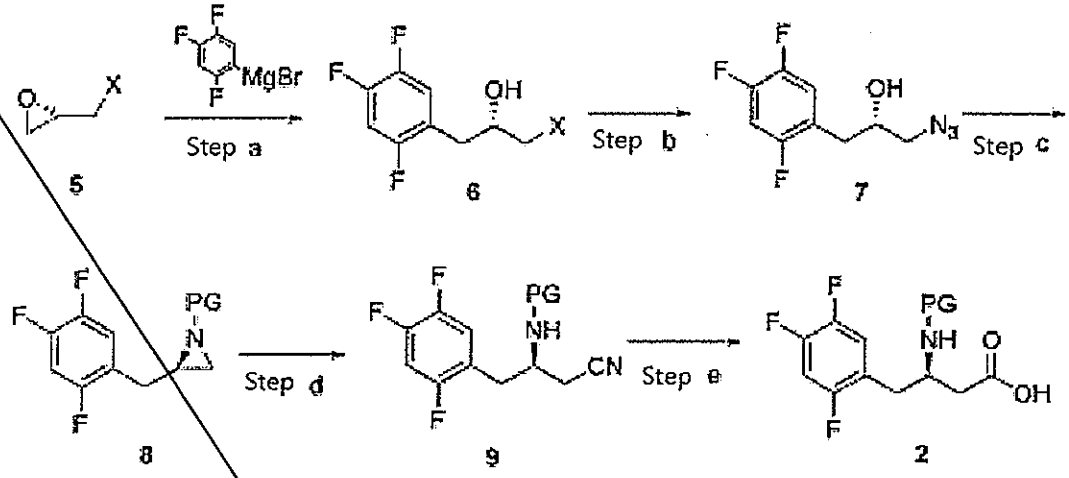
(Step b) preparing a compound represented by Chemical Formula 7 by reacting the compound represented by Chemical Formula 6 with sodium azide;

(Step c) preparing a compound represented by Chemical Formula 8 by reacting the compound represented by Chemical Formula 7 with triphenylphosphine;

(Step d) preparing a compound represented by Chemical Formula 9 by ring-opening of aziridine ring using a cyanogen-based reagent in the compound represented by Chemical Formula 8; and

(Step e) preparing a compound represented by Chemical Formula 2 by hydrolyzing the compound represented by Chemical Formula 9 using a base;

[Reaction Formula 1]

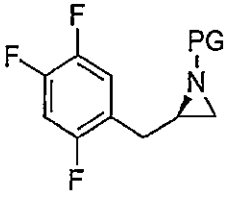


(In the above Reaction Formula 1, X is a halogen and PG is a protecting group.)

2. The method as set forth in claim 1, wherein the amine-protecting group is selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, and tosyl.

3. A derivative represented by the following Chemical Formula 8, wherein the derivative is produced when producing the compound represented by Chemical Formula 2 as set forth in claim 1:

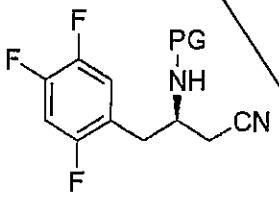
[Chemical Formula 8]



(In the above Chemical Formula 8, PG is a protecting group.)

4. A derivative represented by the following Chemical Formula 9, wherein the derivative is produced when producing the compound represented by Chemical Formula 2 as set forth in claim 1:

[Chemical Formula 9]



(In the above Chemical Formula 9, PG is a protecting group.)

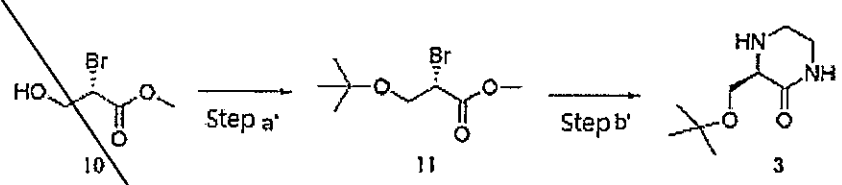
5. A method for preparing an intermediate of dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 3, as shown in the following Reaction Formula 2, the method comprising:

(Step a') preparing a compound represented by Chemical Formula 11 by introducing t-butoxy group to hydroxyl group of a compound represented by Chemical Formula 10; and

(Step b') preparing a compound represented by Chemical Formula 3 by inducing a cyclization by reacting the compound

represented by Chemical Formula 11 with ethylene diamine;

[Reaction Formula 2]

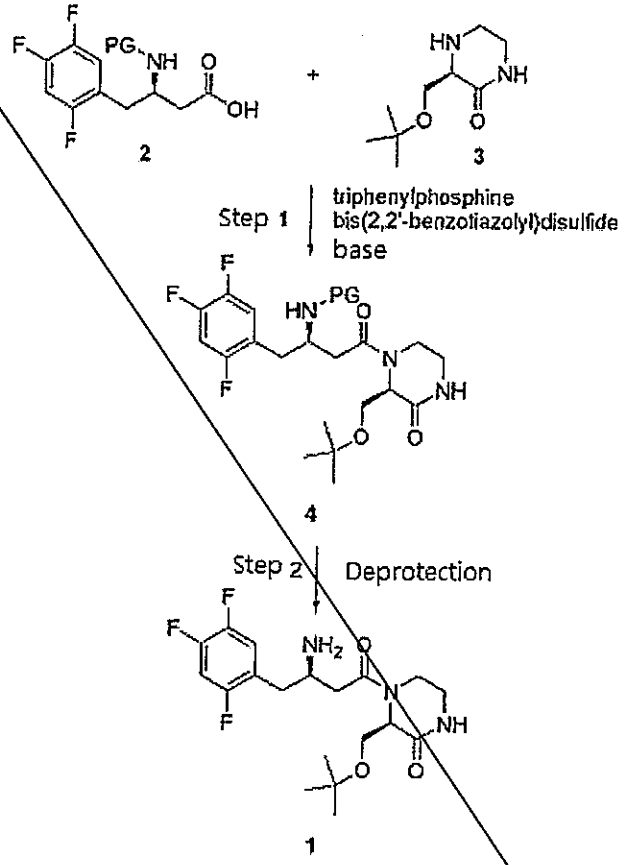


6. An improved method for preparing dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 1, as shown in the following Reaction Formula 3, the method comprising:

(Step 1) preparing a compound represented by Chemical Formula 4 by bonding a compound represented by Chemical Formula 2 and a compound represented by Chemical Formula 3 with peptide bond by reacting them using triphenylphosphine, bis(2,2'-benzothiazolyl)disulfide, and a base in the presence of a reaction solvent; and

(Step 2) preparing a compound represented by Chemical Formula 1 by removing an amine-protecting group of the compound represented by Chemical Formula 4 produced in the above Step 1;

[Reaction Formula 3]



(In the above Reaction Formula 3, PG is a protecting group.)

7. The improved method as set forth in claim 6, wherein the reaction solvent is selected from the group consisting of toluene, tetrahydrofuran, methylene chloride, acetonitrile, and N,N-dimethylformamide.

8. The improved method as set forth in claim 6, wherein the base is more than one selected from the group consisting

of N-methyl morpholine, isopropylethylamine, triethylamine, and pyridine.

9. The improved method as set forth in claim 6, wherein the reaction of the above Step 1 is performed at -20 ℃ to 80 ℃.

10. The improved method as set forth in claim 6, wherein the amine-protecting group is selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, and tosyl.

11. The improved method as set forth in claim 6, wherein in the Step 2, when the amine-protecting group is butoxycarbonyl (Boc), the amine-protecting group is removed by reacting the compound represented by Chemical Formula 4 with trifluoroacetic acid/dichloromethane, ethyl acetate/hydrogen chloride, diethylether/hydrogen chloride, hydrogen chloride/dichloromethane or methanol/hydrogen chloride.

12. The improved method as set forth in claim 6, wherein in the Step 2, when the amine-protecting group is benzyloxycarbonyl (Cbz), the amine-protecting group is removed by reacting the compound represented by Chemical Formula 4 with hydrogen in the presence of palladium/carbon.

What is claimed is

1. A method for preparing an intermediate of dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 2, as shown in the following Reaction Formula 1, the method comprising:

(Step a) preparing a compound represented by Chemical Formula 6 by ring-opening of epoxide ring using Grinard reagent in a compound represented by Chemical Formula 5;

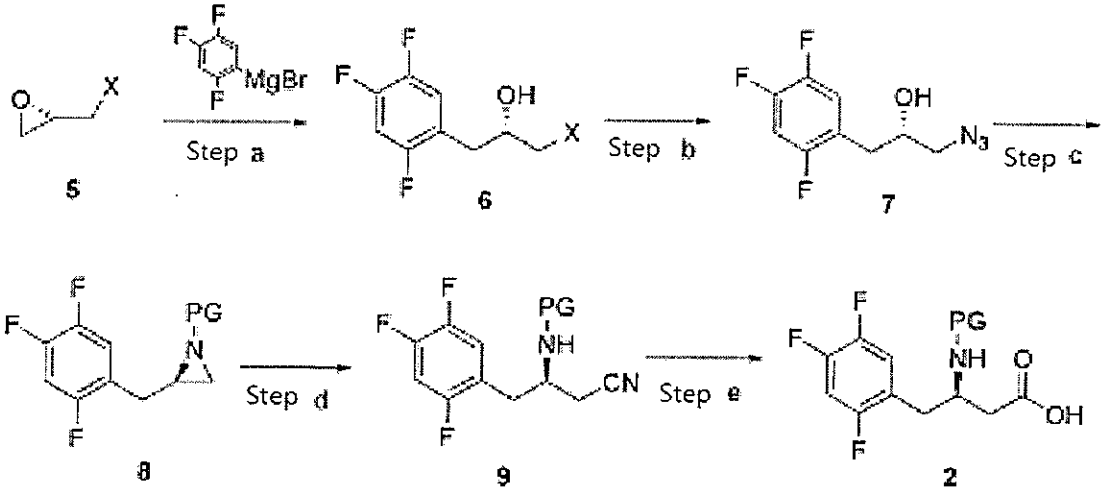
(Step b) preparing a compound represented by Chemical Formula 7 by reacting the compound represented by Chemical Formula 6 with sodium azide;

(Step c) preparing a compound represented by Chemical Formula 8 by reacting the compound represented by Chemical Formula 7 with triphenylphosphine;

(Step d) preparing a compound represented by Chemical Formula 9 by ring-opening of aziridine ring using a cyanogen-based reagent in the compound represented by Chemical Formula 8; and

(Step e) preparing a compound represented by Chemical Formula 2 by hydrolyzing the compound represented by Chemical Formula 9 using a base;

[Reaction Formula 1]

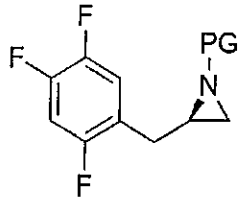


(In the above Reaction Formula 1, X is a halogen and PG is a protecting group.)

2. The method as set forth in claim 1, wherein the amine-protecting group is selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, and tosyl.

3. A derivative represented by the following Chemical Formula 8, wherein the derivative is produced when producing the compound represented by Chemical Formula 2 as set forth in claim 1:

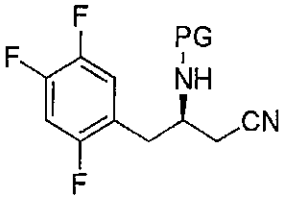
[Chemical Formula 8]



(In the above Chemical Formula 8, PG is a protecting group **selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, or tosyl**).

4. A derivative represented by the following Chemical Formula 9, wherein the derivative is produced when producing the compound represented by Chemical Formula 2 as set forth in claim 1:

[Chemical Formula 9]



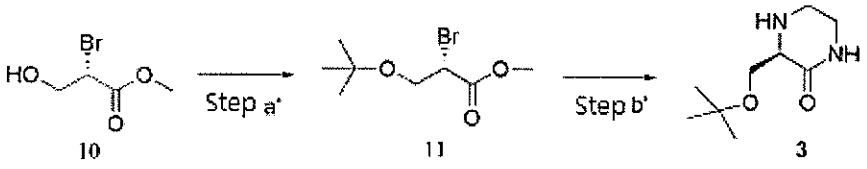
(In the above Chemical Formula 9, PG is a protecting group **selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, or tosyl)**

5. A method for preparing an intermediate of dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 3, as shown in the following Reaction Formula 2, the method comprising:

(Step a') preparing a compound represented by Chemical Formula 11 by introducing t-butoxy group to hydroxyl group of a compound represented by Chemical Formula 10; and

(Step b') preparing a compound represented by Chemical Formula 3 by inducing a cyclization by reacting the compound represented by Chemical Formula 11 with ethylene diamine;

[Reaction Formula 2]



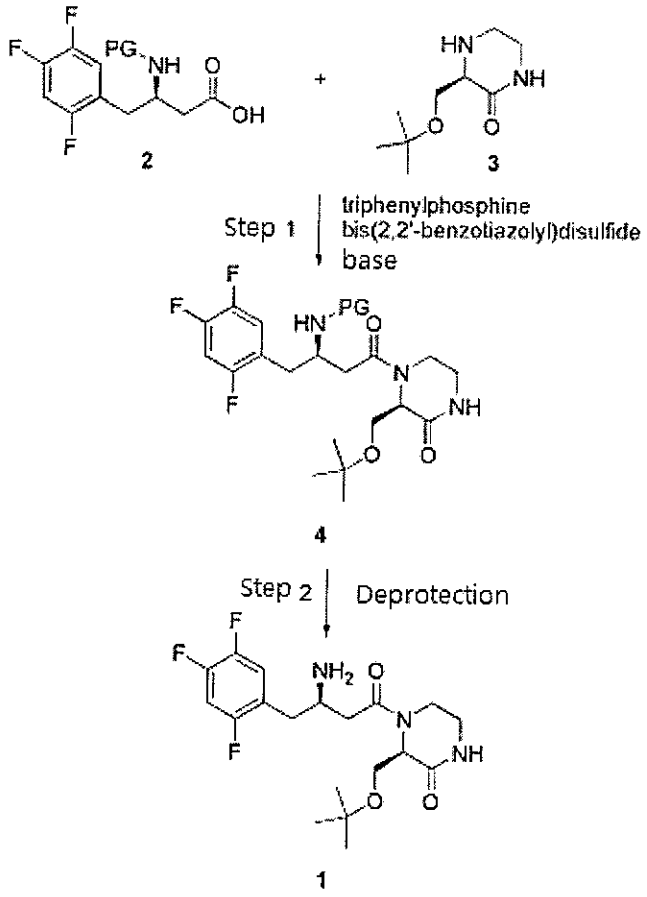
6. An improved method for preparing dipeptidyl peptidase-IV inhibitor represented by Chemical Formula 1, as shown in the following Reaction Formula 3, the method comprising:

(Step 1) preparing a compound represented by Chemical Formula 4 by bonding a compound represented by Chemical Formula 2 and a compound represented by Chemical Formula 3 with peptide bond by reacting them using triphenylphosphine, bis(2,2'-benzothiazolyl)disulfide, and a

base in the presence of a reaction solvent; and

(Step 2) preparing a compound represented by Chemical Formula 1 by removing an amine-protecting group of the compound represented by Chemical Formula 4 produced in the above Step 1;

[Reaction Formula 3]



(In the above Reaction Formula 3, PG is a protecting group.).

7. The improved method as set forth in claim 6, wherein the reaction solvent is selected from the group consisting of toluene, tetrahydrofuran, methylene chloride, acetonitrile, and N,N-dimethylformamide.

8. The improved method as set forth in claim 6, wherein the base is more than one selected from the group consisting of N-methyl morpholine, isopropylethylamine, triethylamine, and pyridine.

9. The improved method as set forth in claim 6, wherein the reaction of the above Step 1 is performed at -20 ℃ to 80 ℃.

10. The improved method as set forth in claim 6, wherein the amine-protecting group is selected from the group consisting of butoxycarbonyl (Boc), benzyloxycarbonyl (Cbz), 9-

fluorenylmethoxycarbonyl (Fmoc), acetyl, benzoyl, and tosyl.

11. The improved method as set forth in claim 6, wherein in the Step 2, when the amine-protecting group is butoxycarbonyl (Boc), the amine-protecting group is removed by reacting the compound represented by Chemical Formula 4 with trifluoroacetic acid/dichloromethane, ethyl acetate/hydrogen chloride, diethylether/hydrogen chloride, hydrogen chloride/dichloromethane or methanol/hydrogen chloride.

12. The improved method as set forth in claim 6, wherein in the Step 2, when the amine-protecting group is benzyloxycarbonyl (Cbz), the amine-protecting group is removed by reacting the compound represented by Chemical Formula 4 with hydrogen in the presence of palladium/carbon.