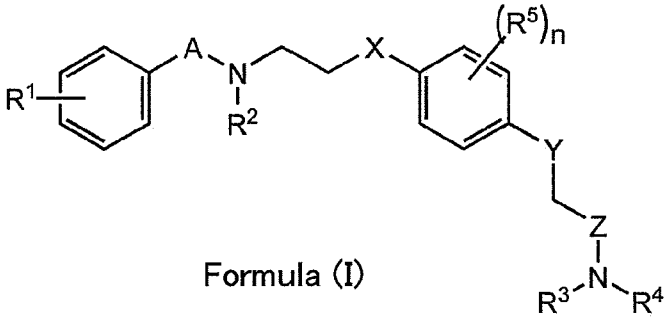
The compound of the present invention can specifically bind to an AMPA receptor and has extremely high brain uptake. In particular, the compound of the present invention can be used as a molecular probe, for example, a PET probe, and can image the AMPA receptor in living organisms in vivo. Further, the compound of the present invention is easily synthesized and can be obtained with a high yield.

SUMMARY

[0007a]

In one aspect, there is provided a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 1]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 , R^3 and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

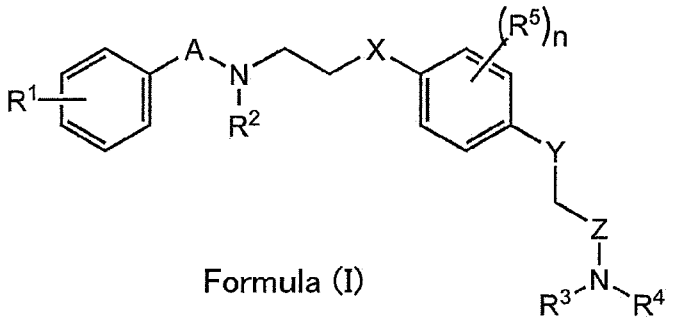
each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.)

[0007b]

In another aspect, there is provided a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 3]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1, R^3 and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo;

n represents an integer of 0 to 4; and

one or more atoms are a radioisotope of the atom or atoms.)

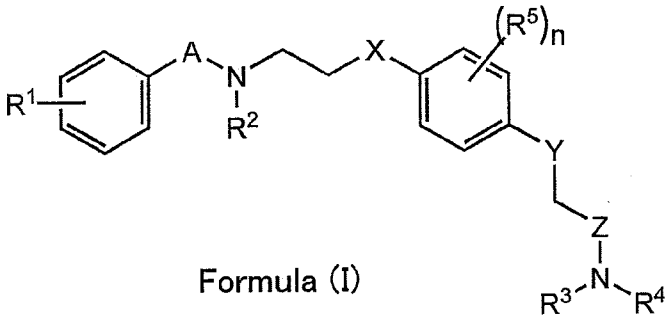
[0007c]

In another aspect, there is provided a composition comprising the compounds described herein, or the pharmaceutically acceptable salt or solvate thereof.

[0007d]

In another aspect, there is provided a composition being used for imaging an α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor in the brain in living organisms, the composition comprising a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 5]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 to R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

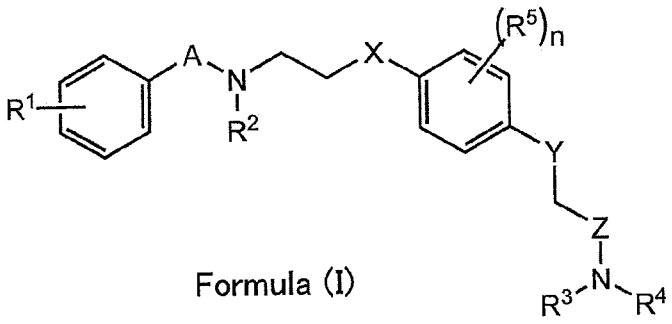
n represents an integer of 0 to 4.)

[0007e]

In another aspect, there is provided a method for producing a compound represented by Formula (I), or a

pharmaceutically acceptable salt or solvate thereof, the producing method comprising reacting a compound represented by Formula (II), or a pharmaceutically acceptable salt or solvate thereof (in the formula, A, X, Y, Z, R^1, R^3, R^4, R^5, and n are the same as defined above) with X^1-R^2 (in the formula, R^2 is the same as defined above and X^1 represents halogen):

[Chem. 6]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

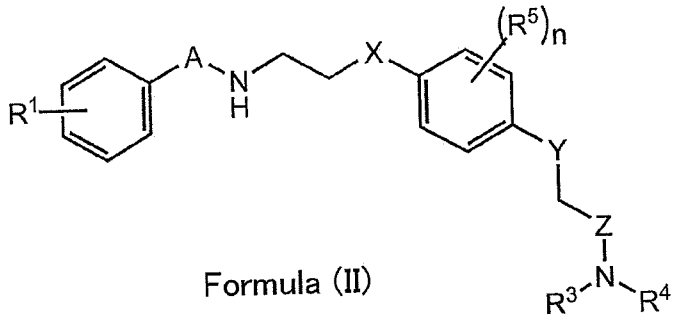
each of R^1, R^3, and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.)

[Chem. 7]

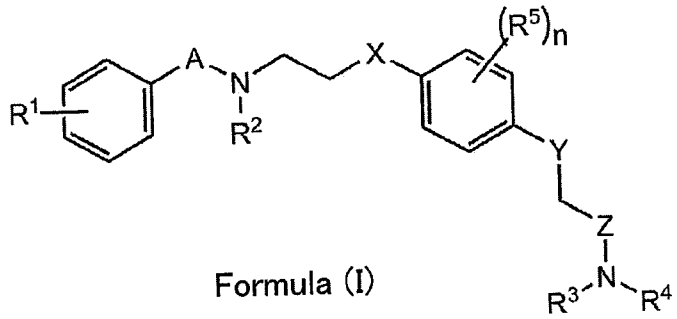


Formula (II)

[0007f]

In another aspect, there is provided a method for imaging an α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor in the brain in living organisms, the method comprising a step of detecting radiation emitted from the brain in living organisms of a subject to which a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof has been administered:

[Chem. 12]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 to R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.; and

one or more atoms are a radioisotope of the atom or atoms.)

BRIEF DESCRIPTION OF THE DRAWINGS

[0008]

Fig. 1 is a graph showing accumulation ratios of various compounds in hippocampal tissues.

Fig. 2 is a graph showing a ratio of an AMPA current to a reference value after administration of PEPA or K-2.

Fig. 3 is a graph showing a change in the amount of an AMPA receptor when K-2 or a vehicle is administered to a living organism. Left diagram: An amount of the AMPA receptor presented on the surface of the cell membrane, Right diagram: A total amount of the AMPA receptor.

Fig. 4 is an in vivo PET image of a rat using radio-labeled K-2. Left diagram: A rat to which a vehicle is administered, Right diagram: A rat which is subjected to blocking by 0.5 mg/kg of non-radio-labeled K-2.

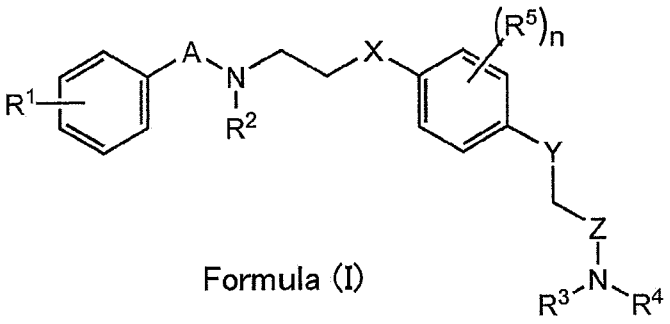
Fig. 5 shows time-activity curves (TAC) of K-2 of the hippocampus and the brain stem of a rat.

(a) Hippocampus after administration of the vehicle, (b) Hippocampus after blocking, (c) Brain stem after

CLAIMS

1. A compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 1]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 , R^3 and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.

2. The compound or a pharmaceutically acceptable salt or solvate according to claim 1, wherein each of A and Z independently represents CO or SO_2.

3. The compound or a pharmaceutically acceptable

salt or solvate according to claims 1 or 2, wherein A represents SO_2 and Z represents CO.

4. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1, 2 or 3, wherein X represents S and Y represents O.

5. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1 to 4, wherein R^2 represents alkyl.

6. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1 to 5, wherein R^1 represents alkyl or halo.

7. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1 to 6, wherein one of R^3 and R^4 represents hydrogen and the other one is alkyl.

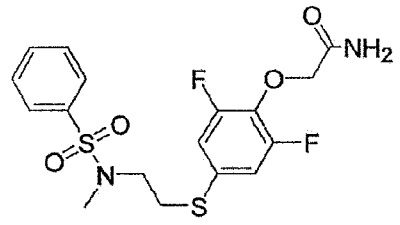
8. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1 to 7, wherein R^5 represents halo.

9. The compound or a pharmaceutically acceptable salt or solvate according to claim 8, wherein the halo is fluoro.

10. The compound or a pharmaceutically acceptable salt or solvate according to any one of claims 1 to 9, wherein n is 2.

11. The compound or a pharmaceutically acceptable salt or solvate is selected from the group consisting of the following:

[Chem. 2]



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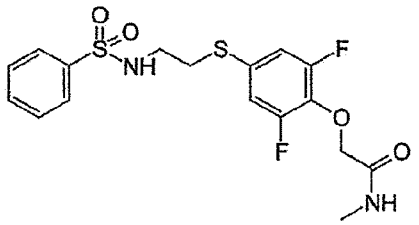

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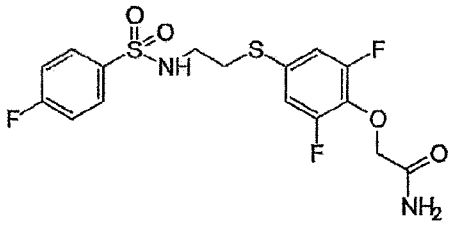
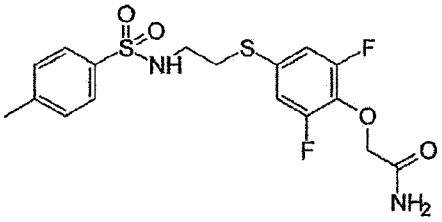
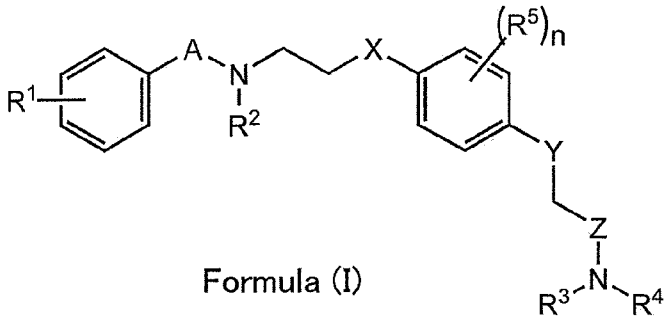


; and



12. A compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 3]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1, R^3 and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo;

n represents an integer of 0 to 4; and

one or more atoms are a radioisotope of the atom or atoms.)

13. The compound according to claim 12, or the pharmaceutically acceptable salt or solvate thereof, wherein the radioisotope is ^{11}C or ^{18}F.

14. The compound according to claim 13, or the pharmaceutically acceptable salt or solvate thereof, wherein a group containing a radioisotope is R^1.

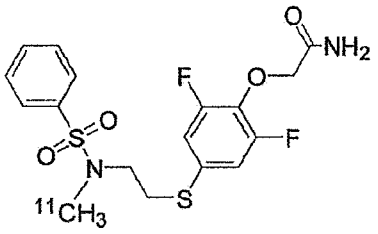
15. The compound according to claim 13, or the pharmaceutically acceptable salt or solvate thereof, wherein a

group containing a radioisotope is R^2.

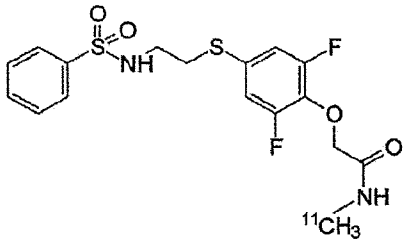
16. The compound according to claim 13, or the pharmaceutically acceptable salt or solvate thereof, wherein a group containing a radioisotope is at least one of R^3 and R^4.

17. The compound or a pharmaceutically acceptable salt or solvate is selected from the group consisting of the following:

[Chem. 4]



;



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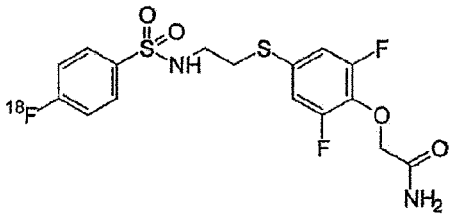
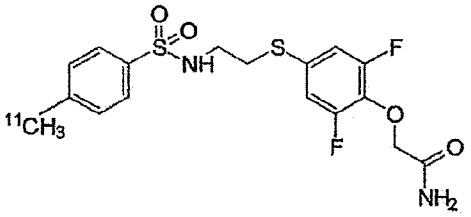


; and

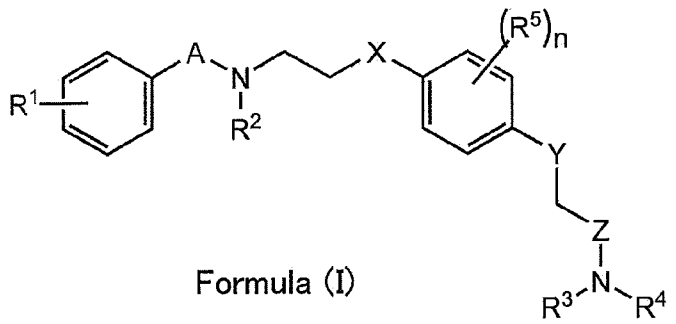


18. A composition comprising the compound according to any one of claims 1 to 17, or the pharmaceutically acceptable salt or solvate thereof.

19. The composition, wherein the composition is used for imaging an α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor in the brain in living subjects,

represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof:

[Chem. 13]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 to R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4; and

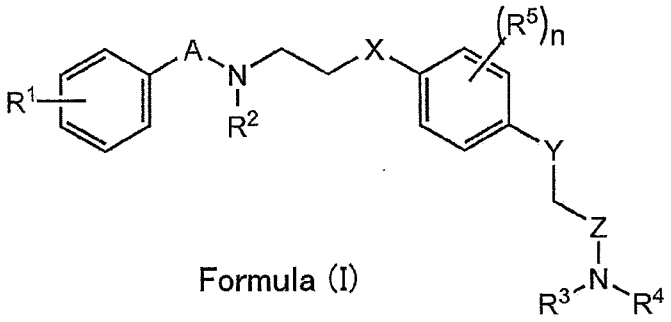
one or more atoms are a radioisotope of the atom or atoms.)

20. The composition according to claim 19, wherein the composition is used for molecular imaging.

21. A composition being used for imaging an α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor in the brain in living subjects, the composition comprising a compound represented by Formula (I), or a

pharmaceutically acceptable salt or solvate thereof:

[Chem. 5]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

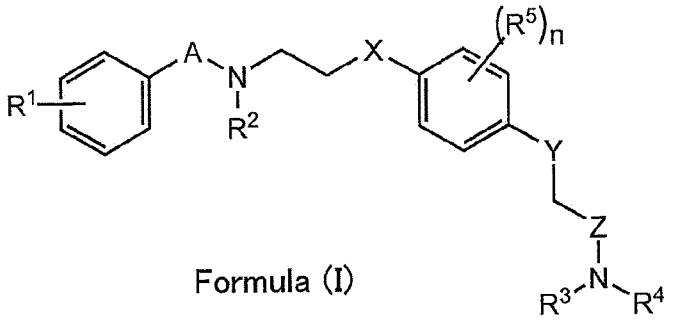
each of R^1 to R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.)

22. A method for producing a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof, the producing method comprising reacting a compound represented by Formula (II), or a pharmaceutically acceptable salt or solvate thereof (in the formula, A, X, Y, Z, R^1, R^3, R^4, R^5, and n are the same as defined above) with X^1-R^2 (in the formula, R^2 is the same as defined above and X^1 represents halogen):

[Chem. 6]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

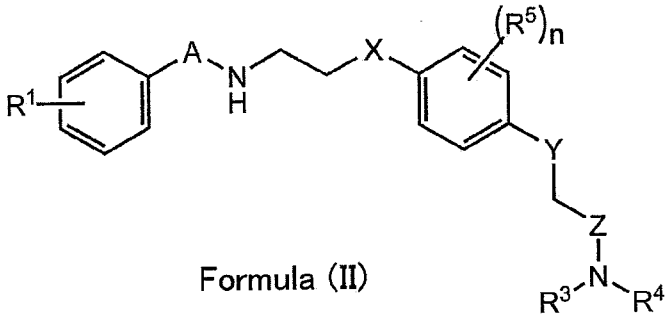
each of R^1, R^3, and R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

R^2 represents alkyl, alkenyl, or alkynyl;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.)

[Chem. 7]

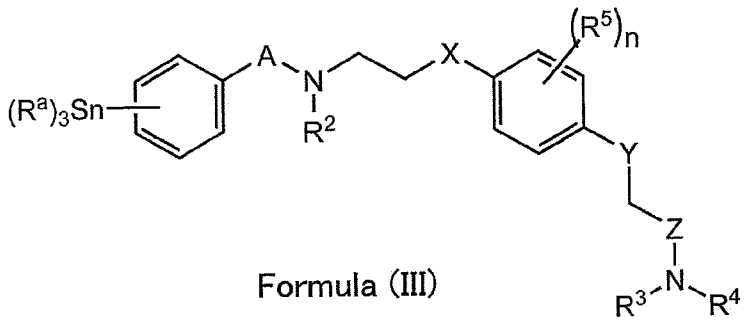


Formula (II)

23. The producing method according to claim 22, wherein the R^2 represents [^{11}C]alkyl.

24. The producing method according to claim 22 or 23, wherein both the R^3 and the R^4 in Formula (I) and Formula (II)

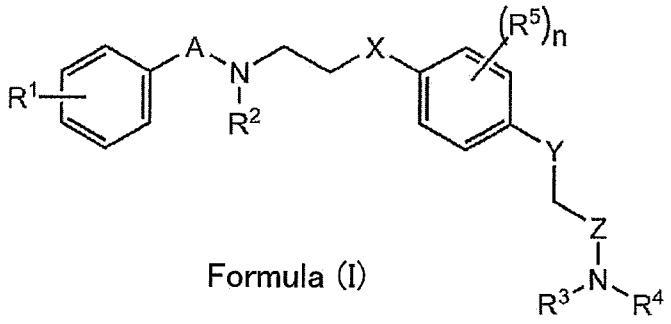
represent hydrogen.



Formula (III)

25. A method for imaging an α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor in the brain in living subjects, the method comprising a step of detecting radiation emitted from the brain in living subjects to which a compound represented by Formula (I), or a pharmaceutically acceptable salt or solvate thereof has been administered:

[Chem. 12]



Formula (I)

(in the formula,

each of A and Z independently represents CO, SO, or SO_2;

each of X and Y independently represents S or O;

each of R^1 to R^4 independently represents hydrogen, alkyl, alkenyl, alkynyl, or halo;

each R^5 independently represents alkyl, alkenyl, alkynyl, or halo; and

n represents an integer of 0 to 4.; and

one or more atoms are a radioisotope of the atom or atoms.)