CLAIMS

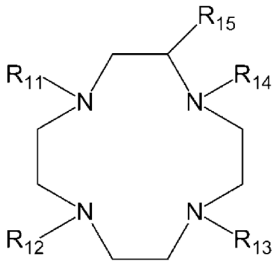
1. A method for producing a radioactive zirconium complex, the method comprising a step of reacting a radioactive zirconium ion and a ligand compound represented by Formula (1) below in a reaction solution to form a radioactive zirconium complex, wherein

the reaction solution has:

an amount of radioactivity of the radioactive zirconium ion of 60 MBq or more at a start of the reaction; and

an amount of radioactivity of the radioactive zirconium ion of 5 MBq or more per 1 nmol of the ligand compound at the start of the reaction, and

the step is performed in presence of an additive represented by Formula (2) below or a salt thereof:



(1)

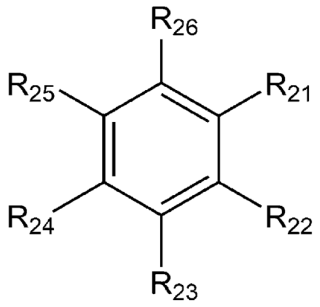
wherein R_{11}, R_{12}, and R_{13} each independently represent a $-(CH_2)_pCOOH$ group, a $-(CH_2)_pC_5H_4N$ group, a $-(CH_2)_pPO_3H_2$ group, or a $-(CH_2)_pCONH_2$ group,

one of R_{14} and R_{15} represents a hydrogen atom, a $-(CH_2)_pCOOH$ group, a $-(CH_2)_pC_5H_4N$ group, a $-(CH_2)_pPO_3H_2$ group, a $-(CH_2)_pCONH_2$ group, or a $-(CHCOOH)(CH_2)_pCOOH$ group, the other one is a $-(CH_2)_pCOOH$ group, a $-(CH_2)_pC_5H_4N$ group, a $-(CH_2)_pPO_3H_2$ group, a $-(CH_2)_pCONH_2$ group, a reactive atomic group to be linked to a targeting agent, or a group linked to the targeting agent,

wherein the targeting agent includes an atomic group containing one or two or more selected from the group consisting of a chain peptide, a cyclic peptide, or a combination thereof, a protein, an antibody or a fragment thereof, a growth factor, Affibody, UniBody, Nanobody, a monosaccharide, a polysaccharide, a vitamin, an antisense nucleic acid, a siRNA, a miRNA, a nucleic acid aptamer, a decoy nucleic acid, a cPG oligonucleic acid, a peptide nucleic acid, a liposome, a micelle, a carbon nanotube, and a nanoparticle,

wherein the reactive atomic group to be linked to the targeting agent includes an azido group, an alkynyl group, a diene or a dienophile, and

p each independently represents an integer of 0 or more and 3 or less;



(2)

wherein R_{21} represents a -COOH group,

1 or more and 3 or less groups of R_{22} to R_{26} represent hydroxy groups, other groups represent hydrogen atoms, and

R_{28} represents a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, or a substituted or unsubstituted alkylaryl.

2. The method for producing a radioactive zirconium complex according to claim 1, wherein the step is performed in a state where a pH of the reaction solution is in an acidic region.

3. The method for producing a radioactive zirconium complex according to claim 2, wherein the step is performed in a state where the pH of the reaction solution is 2.0 or more and 6.0 or less.

4. The method for producing a radioactive zirconium complex according to any one of claims 1 to 3,

wherein the additive or the salt thereof in which one or more and three or less groups among R_{22} to R_{26} are hydroxy groups, and other groups are hydrogen atoms in Formula (2) is used, and

the step is performed in a state where a pH of the reaction solution is 2.0 or more and 6.0 or less.

5. The method for producing a radioactive zirconium complex according to any one of claims 1 to 4,

wherein the additive or the salt thereof in which one or more and three or less

groups among R_{22} to R_{26} are hydroxy groups, and other groups are hydrogen atoms in Formula (2) is used, and

a ratio of a content of the additive to the amount of radioactivity (MBq) of the radioactive zirconium ion at the start of the reaction is 5 nmol/MBq or more.

6. The method for producing a radioactive zirconium complex according to any one of claims 1 to 5,

wherein the additive or the salt thereof in which both of R_{22} and R_{25} represent hydroxy groups, and all of R_{23}, R_{24}, and R_{26} represent hydrogen atoms in Formula (2) is used, and

a ratio of a content of the additive to the amount of radioactivity (MBq) of the radioactive zirconium ion at the start of the reaction is 5 nmol/MBq or more and 125 nmol/MBq or less.

7. The method for producing a radioactive zirconium complex according to any one of claims 1 to 6,

wherein the additive or the salt thereof in which both of R_{22} and R_{25} represent hydroxy groups, and all of R_{23}, R_{24}, and R_{26} represent hydrogen atoms in Formula (2) is used, and

a ratio of a molar amount (nmol) of the additive to a molar amount (nmol) of the ligand compound is 60 or more and 1,500 or less.

8. The method for producing a radioactive zirconium complex according to any one of claims 1 to 7,

wherein the reaction solution further contains water and a water-soluble organic compound, and

the water-soluble organic compound includes at least one of acetic acid and a salt thereof, phosphoric acid and a salt thereof, 2-amino-2-(hydroxymethyl)propane-1,3-diol, 2-[4-(2-hydroxyethyl)-1-piperazinyl)ethanesulfonic acid, tetramethylammonium acetate, and a basic amino acid.

9. The method for producing a radioactive zirconium complex according to claim 8, wherein a concentration of the water-soluble organic compound contained in the reaction solution is 0.01 mol/L or more and 5.0 mol/L or less.

10. The method for producing a radioactive zirconium complex according to claim 8 or 9, wherein the reaction solution contains acetic acid and a salt thereof as the water-soluble organic compound.

11. The method for producing a radioactive zirconium complex according to any one of claims 1 to 10, wherein the reaction solution is heated to 30°C or higher and 100°C or lower to react the radioactive zirconium ion with the ligand compound.

12. The method for producing a radioactive zirconium complex according to any one of claims 1 to 11,

wherein in Formula (1) above, all of R_{11}, R_{12}, and R_{13} represent $-(CH_2)_pCOOH$ groups,

one of R_{14} and R_{15} represents a hydrogen atom or a $-(CH_2)_pCOOH$ group,

the other of R_{14} and R_{15} represents a $-(CH_2)_pCOOH$ group, the reactive atomic group to be linked to the targeting agent, or the group linked to the targeting agent,

R_{15} represents a hydrogen atom in a case where R_{14} represents the reactive atomic group to be linked to the targeting agent or the group linked to the targeting agent, and

R_{14} represents a hydrogen atom in a case where R_{15} represents the reactive atomic group to be linked to the targeting agent or the group linked to the targeting agent.

13. The method for producing a radioactive zirconium complex according to any one of claims 1 to 12,

wherein the radioactive zirconium ion is coordinated to the ligand compound using the ligand compound having the reactive atomic group to be linked to the targeting agent in Formula (1) above, and

the reactive atomic group is then reacted with the targeting agent.