

[0004] For example, an attempt at performing imaging by using a peptide ligand having an Arg-Gly-Asp (RGD) sequence is reported in Non-Patent Documents 4 and 5 and the like, and an attempt using a non-peptide low-molecular weight compound is reported in Cardiovascular Research, Vol. 78, pp. 395~403, 2008, and the like. In addition, the compound into which ^{18}F of a positron nuclide is introduced (Non-Patent Documents 6 and 7) is used to portray a human tumor (Non-Patent Documents 8 and 9)

Prior Art Documents

Patent Documents

[0005]

Patent Document 1: US6001961A

Patent Document 2: US6130231A

Patent Document 3: US2002/169200A

Patent Document 4: US2001/53853A

Patent Document 5: JP2002-532440A

Patent Document 6: WO2013/048996

Patent Document 7: WO2011/149250A

Non-Patent Documents

[0006]

Non-Patent Document 1: Nature Reviews cancer, Vol. 10, pp. 9-23, 2010

Non-Patent Document 2: Clin. Cancer Res. Vol. 12, pp. 3942-3949, 2006

Non-Patent Document 3: Circulation, Vol. 107, pp. 1046-1052, 2003

Non-Patent Document 4: Cancer Res. Vol. 61, pp. 1781-1785, 2001

Non-Patent Document 5: Cardiovascular Research, Vol. 78, pp. 395-403, 2008

Non-Patent Document 6: Clin. Cancer Res., Vol. 13, pp. 6610-6616, 2007

Non-Patent Document 7: J. Nucl. Med., Vol. 49, pp. 879-886, 2008

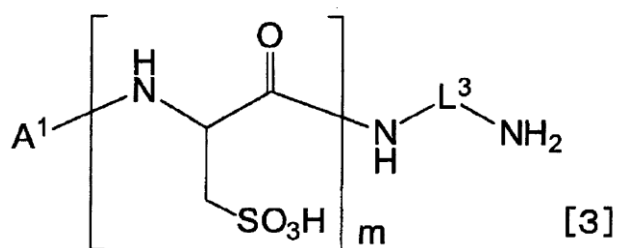
Non-Patent Document 8: Cancer Res., Vol. 62, pp. 6146-6151, 2002

Non-Patent Document 9: Int. J. Cancer., Vol. 123, pp.709-715, 2008

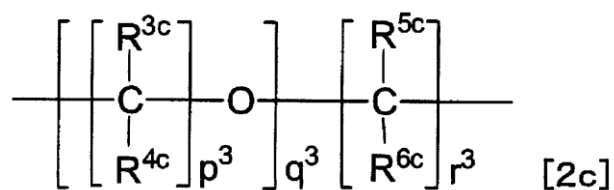
SUMMARY

[0006a] In a first aspect, the present disclosure refers to a compound represented by Formula [3] or a salt thereof

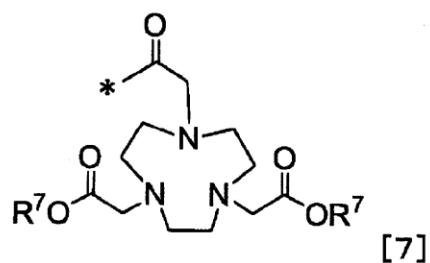
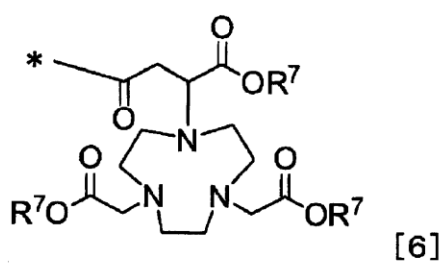
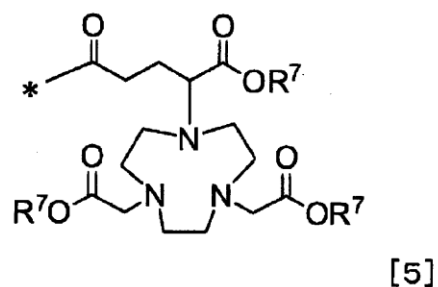
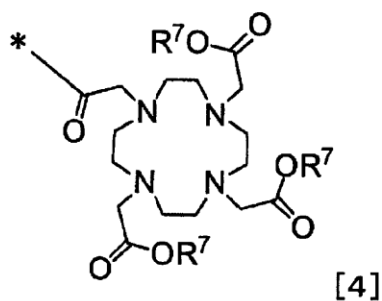
2a



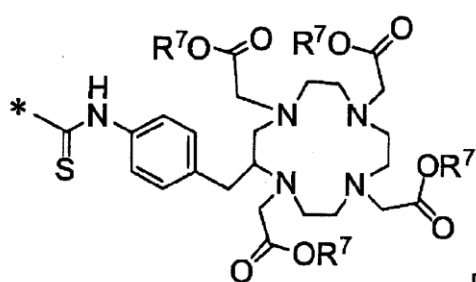
(in the formula, L^3 represents a group represented by Formula [2c])



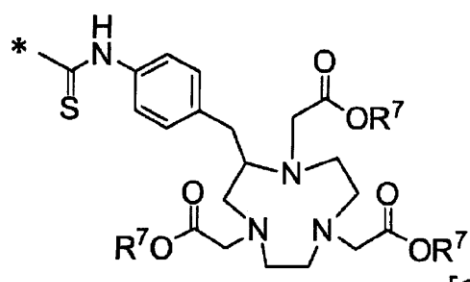
(in the formula, R^{3c} , R^{4c} , R^{5c} , and R^{6c} are the same as or different from each other and represent a hydrogen atom or a C_{1-6} alkyl group; p^3 represents an integer of 1 to 3; q^3 represents an integer of 0 to 3; and r^3 represents an integer of 1 to 6); A^1 represents any one of the groups represented by Formulae [4] to [9]



2b



[8]



[9]

(in the formulae, * represents a binding position; and R^7 represents a carboxyl-protecting group); and m represents an integer of 1 to 3).

[0007] According to the knowledge of the inventors of the present disclosure, a nitrogen-containing compound represented by the following Formula [11] is an excellent integrin-binding compound which exhibits high integrating properties and persistency with

2,2'-(7-((R)-1-carboxy-4-(((R)-1-((2-(4-(4-(N-((S)-1-carboxy-2-(5-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)pentanamide)ethyl)sulfamoyl)-3,5-dimethylphenoxy)pentanamide)ethyl)amino)-1-oxo-3-sulfopropan-2-yl)amino)-4-oxobutyl)-1,4,7-triazonane-1,4-diyl)diacetic acid (hereinafter, referred to as a compound B as well), and the like.

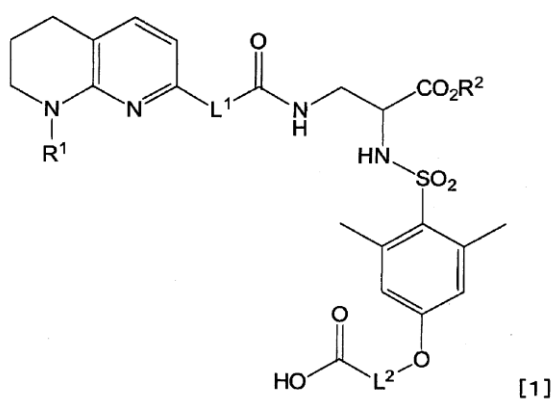
[0018] Objects of the present disclosure are to provide an efficient method for manufacturing a nitrogen-containing compound used for manufacturing a treatment agent for treating integrin-related diseases or a salt thereof and to provide a manufacturing intermediate of the compound or the salt.

[0019] In order to achieve the aforementioned objects, the inventors of the present disclosure repeated thorough research. As a result, they found that, by the following manufacturing method, a nitrogen-containing compound used for manufacturing a treatment agent for treating integrin-related diseases or a salt thereof can be efficiently manufactured. Furthermore, they found that the following manufacturing intermediate is an intermediate advantageous for efficiently manufacturing the nitrogen-containing compound used for manufacturing a treatment agent for treating integrin-related diseases or a salt thereof. Based on what they found, the inventors accomplished the present disclosure.

[0020] That is, the present disclosure provides the following.

<1> A method for manufacturing a compound represented by Formula [11] or a salt thereof, comprising (1) a step of reacting a compound represented by Formula [1] or a salt thereof

[0021]



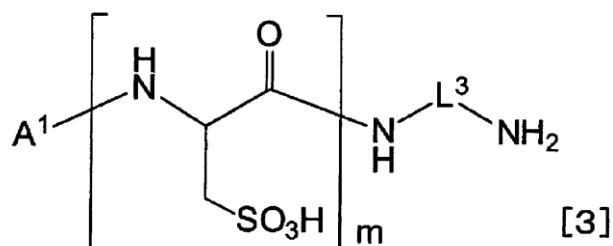
[0022] (in the formula, R¹ represents a hydrogen atom or an amino-protecting group; R² represents a carboxyl-protecting group; L¹ represents a group represented by Formula [2a]

[0023]

<16> The compound described in any one of <10> to <15> or a salt thereof, in which R^7 is a C_{1-6} alkyl group which may be substituted or a benzyl group which may be substituted.

<17> A compound represented by Formula [3] or a salt thereof

[0057]



[0058] (in the formula, L^3 , A^1 , and m have the same definition as L^3 , A^1 , and m described above).

<18> The compound described in <17> or a salt thereof, in which R^7 is a C_{1-6} alkyl group which may be substituted or a benzyl group which may be substituted.

[0059] According to the manufacturing method of the present disclosure, it is possible to industrially obtain a novel nitrogen-containing compound having high optical purity or a salt thereof in a simple manner through short steps.

Furthermore, the manufacturing intermediate of the present disclosure is useful as an intermediate of a novel nitrogen-containing compound or a salt thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0060] Fig. 1 shows results obtained by imaging an integrin expression tumor by PET using [^{64}Cu]- (compound A).

Fig. 2 shows results obtained by imaging an integrin expression tumor by PET using [^{64}Cu]- (compound B).

Fig. 3 shows results obtained by imaging an integrin expression tumor by using a gamma camera.

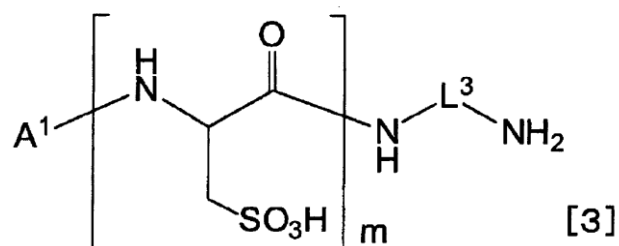
Fig. 4 shows results obtained by imaging an integrin expression tumor in an intracranial tumor model.

Fig. 5 shows a trend of radioactivity concentration in blood of a monkey for which [^{111}In]- (compound A) is used.

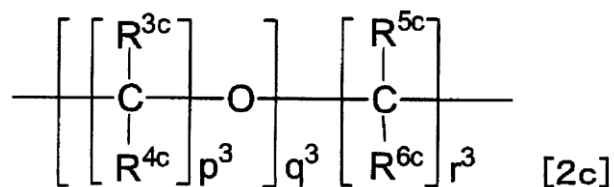
Fig. 6 shows results obtained by temporally performing planar imaging on a monkey

WHAT IS CLAIMED IS:

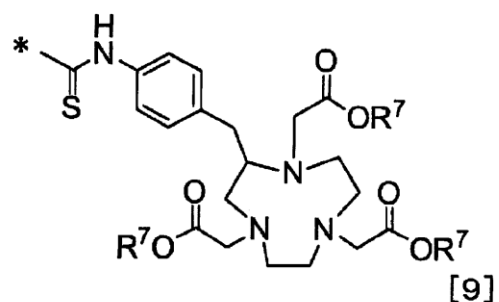
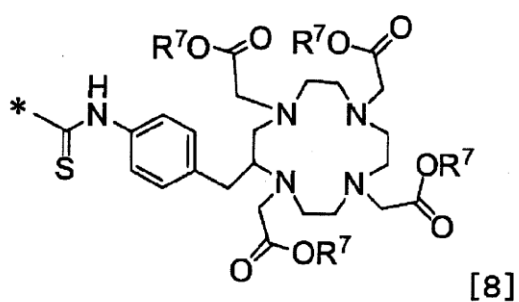
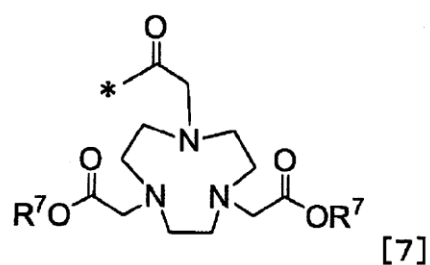
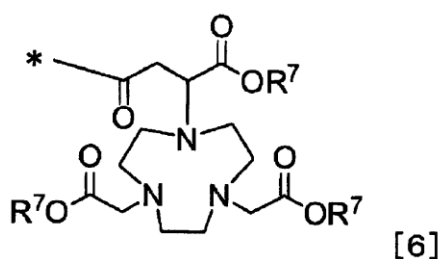
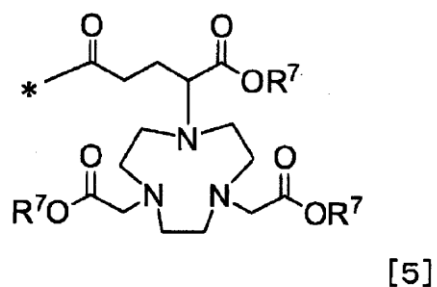
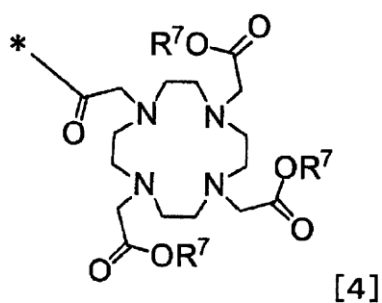
1. A compound represented by Formula [3] or a salt thereof



(in the formula, L^3 represents a group represented by Formula [2c])



(in the formula, R^{3c} , R^{4c} , R^{5c} , and R^{6c} are the same as or different from each other and represent a hydrogen atom or a C_{1-6} alkyl group; p^3 represents an integer of 1 to 3; q^3 represents an integer of 0 to 3; and r^3 represents an integer of 1 to 6); A^1 represents any one of the groups represented by Formulae [4] to [9]



(in the formulae, * represents a binding position; and R^7 represents a carboxyl-protecting group); and m represents an integer of 1 to 3).

2. The compound according to claim 1 or a salt thereof,

wherein R^7 is a C_{1-6} alkyl group which may be substituted or a benzyl group which may be substituted.