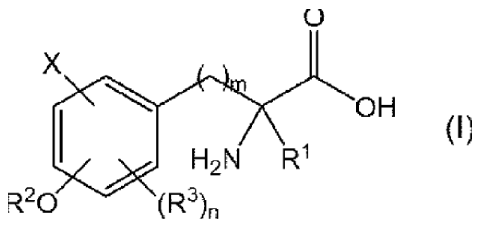
List of patents related to astatine (updated 2024/05/30)

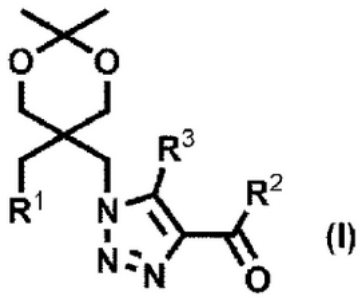
To date 47 patents were found[1–47]

(1) [Radiolabeled compounds and their use] Kaneda, K.; Shirakami, Y.; Kadonaga, Y.; Toyoshima, A.; Fukase, K.; Nagata, H.
Radiolabeled Tyrosine Derivative and Application Thereof.
WO2024063095A1, March 28, 2024.
https://worldwide.espacenet.com/patent/search/family/090454665/publication/WO2024063095A1?q=WO2024063095A1.
The prevent invention provides a radiolabeled tyrosine derivative which has excellent LAT1 selectability, higher retention at a tumor or cancer site, and a degree of clearance that does not cause side effects, and which can be safely manufactured at favorable purity by a safe method suitable for industrial production. The present invention provides a radiolabeled compound represented by formula (I), or a pharmaceutically-acceptable salt thereof. [In the formula, each symbol is as defined in the description.]



(I)

(2) [Radiolabeling method] Tanaka, H.; Uehara, T. Radiolabeled Activated Ester and Precursor Thereof.
WO2024019014A1, January 25, 2024.
https://worldwide.espacenet.com/patent/search/family/089617784/publication/WO2024019014A1?q=WO2024019014A1.
Provided as a precursor of a radioactive halogen-labeled compound is a compound represented by general formula (I) [in the formula, R1 represents a leaving group that can undergo nucleophilic substitution by a halide ion, R2 represents a leaving group in which nucleophilic substitution proceeds by an amino group, and R3 represents a hydrogen atom or a halogen atom.].



(I)

(3) [Radiolabeling method] Fukase, K.; Toyoshima, A.; Shinohara, A.; Shirakami, Y.; Kaneda, K.; Shimoyama, A.; Kadonaga, Y.

Method for Producing Radiolabeled Aryl Compound by Electrolytic Oxidation Reaction.
WO2023171617A1, September 14, 2023.
https://worldwide.espacenet.com/patent/search/family/087935096/publication/WO2023171617A1?q=WO2023171617A1.
[Problem] The present invention addresses the problem of providing a novel method for, under simpler and stabler conditions, labeling a radionuclide such as 211At at a high radiochemical yield. [Solution] Provided is a method for producing an aryl compound labelled with a radionuclide, the method comprising: a step for applying a voltage to a solution A comprising a radionuclide, and electrolytically oxidizing the radionuclide; and a step for mixing the solution A and a solution B comprising a compound S having a halogenated aryl group to replace a halogen atom on the aryl group of the compound S with the radionuclide.

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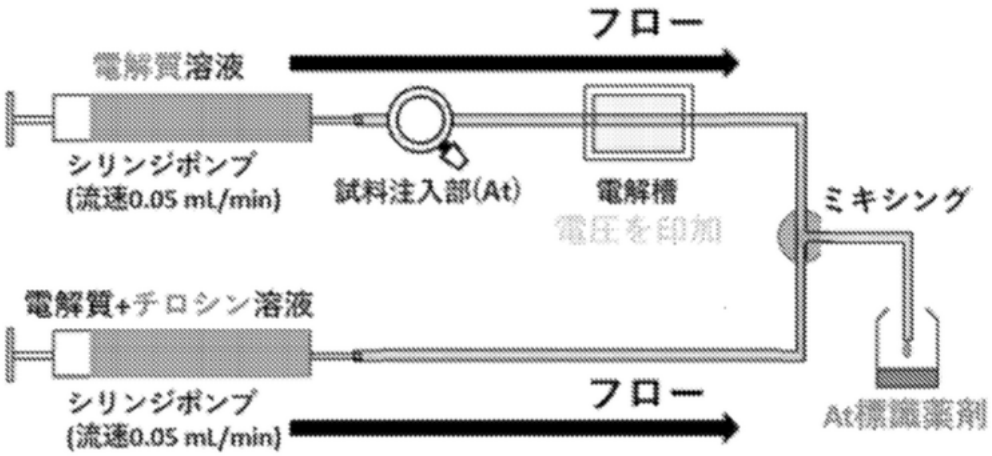
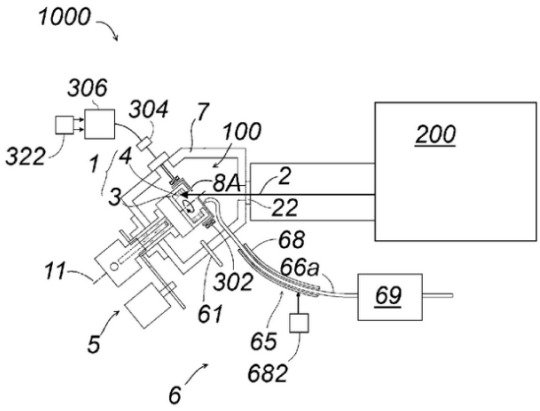
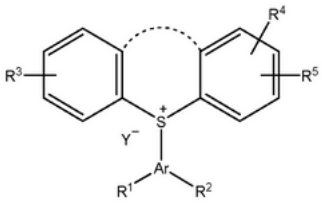


(4) [Astatine-211 production] Arata, H.; Nakamura, S.; Kurihara, T.; Haba, H.
Radionuclide Production Method, Target Holding Device for Quantum Beam Irradiation, System, and Target.
WO2023095818A1, June 1, 2023.
https://worldwide.espacenet.com/patent/search/family/086539525/publication/WO2023095818A1?q=JP2022043283W.
An embodiment of the present disclosure provides a radionuclide production method that includes the stages of setting, irradiation, transport, and collection. In the setting stage, a target material containing a target nuclide is disposed inside a target chamber. In the irradiation stage, at least part of the target material is irradiated with a quantum beam. In the transport stage, a carrier gas is supplied to the inside of the target chamber, and the atmospheric gas surrounding the target material passes through a discharge pipe and is sent to the outside of the target chamber. In the collection stage, a collection device connected to the discharge pipe is in a state that enables collection, from the atmospheric gas, of a radionuclide produced from the target nuclide. In a preferred embodiment of the present disclosure, the target nuclide is bismuth 209, and the radionuclide that is produced is astatine 211. In embodiments of the present disclosure, provided are: a target holding device (100) that is for quantum beam irradiation and that comprises a target material container (3) and a rotation driving mechanism (5); and a quantum beam irradiation system (1000). One example of the target material container (3) is rotatable.



(5) [Radiolabeling method] Guerard, F.; Maingueneau, C.; Eychenne, R.; Gestin, J.-F. Method for Synthesizing Iodo- or Astatoaryl Compounds Using Arylsulfonium Salts. WO2023222909A1, November 23, 2023. https://worldwide.espacenet.com/patent/search/family/082308166/publication/WO2023222909A1?q=EP2023063526W.

The inventors have now succeeded in developing arylsulfonium salts, in particular triarylsulfonium salts and dibenzothiophenium salts and a new use of said arylsulfonium salts. These compounds have the advantage of having a thioaryl group as leaving group, which allows all side products to be separated from the radiolabelled product. Said compounds are therefore useful tools in a method for synthesizing iodo- or astatoarryl compounds, in particular radioiodo- or radioastatoaryl compounds. The present invention relates to a method for synthesizing iodo- or astatoaryl compounds comprising the reaction of an arylsulfonium compound with an iodide or astatide salt, respectively. The invention also relates to arylsulfonium compounds as such. The invention also concerns a method of synthesizing an iodo- or astatolabelled biomolecule and/or vector using said iodo- or astatoraryl compound

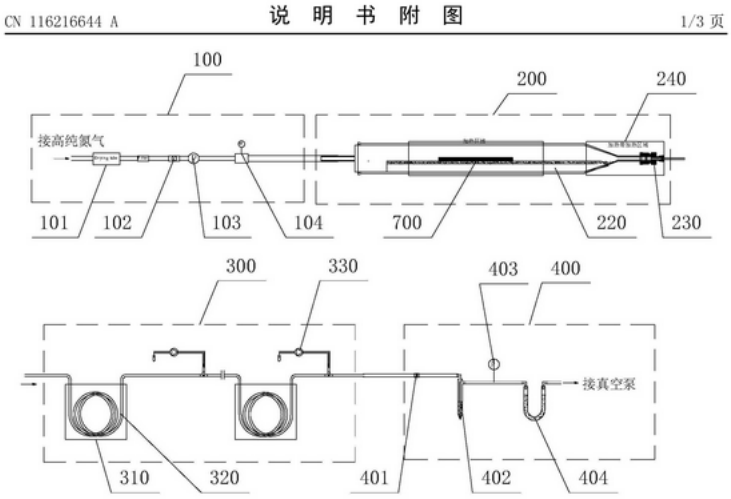


. (I),

(6) [Astatine Extraction/purification method] Li, F.; Qin, Y.; Liao, J.; Yang, Y.; Liu, N.; Lan, T.; Ye, T. Low-Vacuum-Degree High-Purity At-211 Dry Distillation Production System and Production Method Thereof. CN116216644A, June 6, 2023. https://worldwide.espacenet.com/patent/search/family/086575085/publication/CN116216644A?q=CN116216644A.

The invention discloses a low-vacuum-degree high-purity At-211 dry distillation production system and a production method thereof.The system adopts dried and filtered inert gas to drive gasified At-211 to move, adopts a variable-diameter quartz tube to install a bombarded Bi target, adopts a six-stage variable-temperature cold trap to collect products, and is provided with a tail gas treatment unit and a radiation shielding unit; when the system runs, only hundred-Pa-level vacuum degree is needed, and the requirement for material of system components is lowered; target scraping operation is not needed; the inert gas loaded into the system by the gas control unit can bring the gasified At-211 into a product collecting pipe in the time-controllable multi-stage variable-temperature cold trap for enrichment, and after the enrichment is completed, a high-purity At-211 product is leached by using

proper leacheate, so that the product is small in size, low in loss and high in purity. The system and the method are suitable for various types of At-211-based experimental research work.



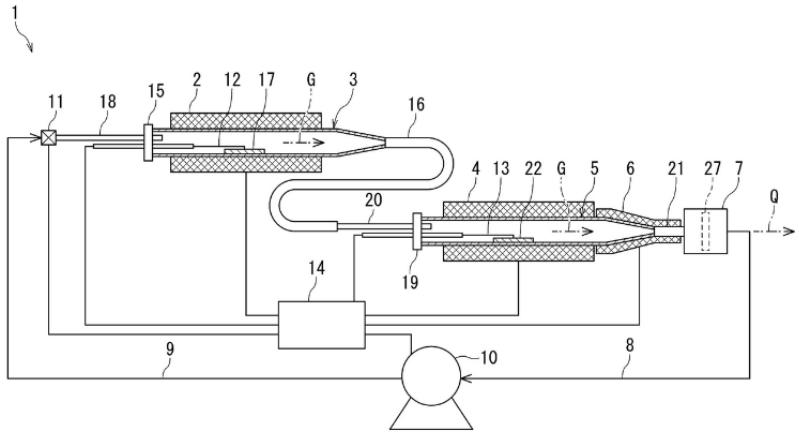
(7) [Astatine Extraction/purification method] Miyamoto, M.; Yuhara, M.; Omori, T.; Wada, R.; Miyadera, H.; Tezuka, M.

Device and Method for Producing Astatine Isotope.

JP2023000409A, January 4, 2023.

https://worldwide.espacenet.com/patent/search/family/084687168/publication/JP2023000409A?q=JP2023000409A.

To provide a technique for producing astatine isotopes that can efficiently produce the astatine isotopes. SOLUTION: A device for producing an astatine isotope 1 has: an aerosol generator 2 that generates aerosol; an astatine separator 4 that separates an astatine isotope from a target material 22 that has generated the astatine isotope by irradiation with alpha rays α; an adhesion preventive heater 6 that heats at least a part of a member forming a channel downstream from the astatine separator 4 and prevents the adhesion of aerosol to the inner surface of the member; and a collector 7 that catches aerosol contained in a gas flow G from a separation chamber 5 and collects the astatine isotope contained in the caught aerosol.SELECTED DRAWING: Figure 1



(8) [Astatine purification method] Tereshatov, E. E.; Burns, J. D.; Mcintosh, L. a; Tabacaru, G. C.; Yennello, S. J.

Systems and Methods for Automated Separation and Recovery of Astatine.
WO2023113774A1, June 22, 2023.
https://worldwide.espacenet.com/patent/search/family/086773213/publication/WO2023113774A1?q=WO2023113774A1.
Systems and methods for automated separation and recovery of compounds from solution are disclosed herein. In some embodiments, the system can use a pump in fluid/air communication with a chromatography column to dissolve and recover astatine from a solution containing astatine, bismuth, and nitric acid. The system can be in communication with a controller that can automate and/or remotely signal each component of the system to execute the recovery without manual user inputs.

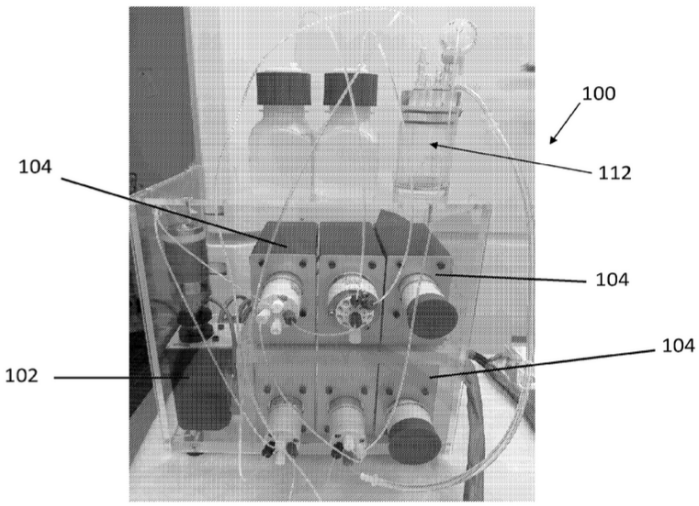
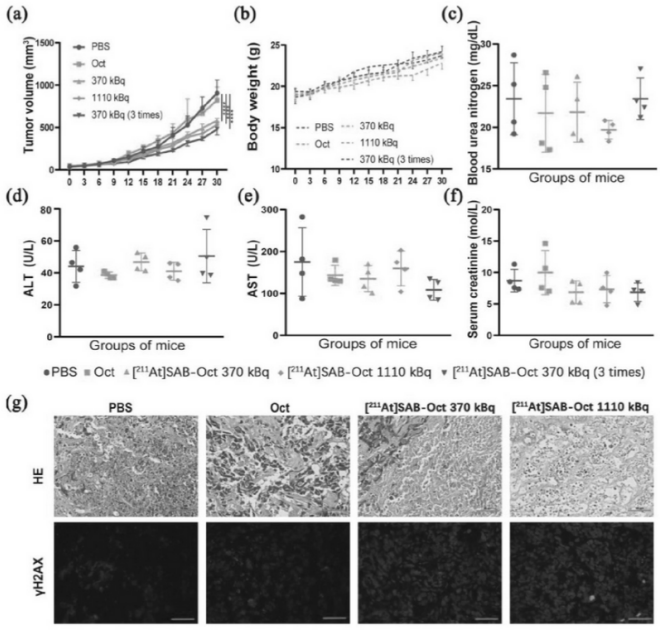


FIG. 1A

(9) [Radiolabeled compounds and their use] Yu, F.; Qin, S.; Zhang, J.; Zhang, H.; Zhang, S.
Astatine 211 Labeled
Octreotide Compound as Well as Preparation Method and Application Thereof.
CN115991735A, April 21, 2023.
https://worldwide.espacenet.com/patent/search/family/085995172/publication/CN115991735A?q=CN115991735A.
The invention discloses a preparation method of a 211At labeled octreotide compound, which comprises the following steps: dissolving octreotide with the concentration of 5 mg/mL in a phosphate buffer solution with the concentration of 0.1 mol/L and the pH value of 7.6, and combining with N-succinimide-3-tri-n-butyltin-benzoate with the concentration of 26 mmol/L dissolved in dimethyl sulfoxide to obtain a mixture; incubating the mixture at room temperature for 30 minutes; the method comprises the following steps: separating Oct-m-MeATE from PBS (Phosphate Buffer Solution) by using a sephadex column G-10, and adjusting the pH value to 5.5 by adding acetic acid before 211At labeling; the method comprises the following steps: adding Oct-m-MeATE and 20 L of 20 mg/mL N-chlorosuccinimide solution dissolved in methanol into about 370 MBq Na211At solution, and incubating the reaction mixture at room temperature for 5 minutes; and adding 20 [mu] L of a 40 mg/mL sodium pyrosulfite aqueous solution, terminating the labeling reaction, and separating the 211At labeled octreotide compound from PBS by using a sephadex column G-10. The invention also provides application of the compound in tumor treatment. According to the invention, the cell death rate of unit absorbed dose is obviously improved, the bone marrow toxicity is reduced, and the limitation of hypoxia of a tumor microenvironment on traditional radiotherapy and chemotherapy is overcome.



(10) [Astatine-211 production] [Astatine Extraction/purification method] Feng, Y.; Zarutsky, M.; Ma, B.
Eluting Solution and Preparation Method of Radionuclide Astatine-211 for Targeted Nuclide Drug. CN114249301A, March 29, 2022.
https://worldwide.espacenet.com/patent/search/family/080790739/publication/CN114249301A?q=CN114249301A.
The invention discloses an eluent and a preparation method of radionuclide astatine-211 for a targeted nuclide drug, the eluent is prepared by dissolving an eluent in an organic solvent, and the eluent is at least one of N-chlorosuccinimide, hydrogen peroxide, N-bromosuccinimide, chloramine-T and acetic acid. The preparation method comprises the following steps: adopting a bismuth-aluminum composite target material as an inner target, weighing the inner target, embedding the inner target into an accelerator inner target station, operating an accelerator, and closing the accelerator after operating for 1-6 hours; exiting the inner target station, taking out the inner target, and cleaning the surface of the metal bismuth layer of the inner target by using a cleaning agent; drying the inner target, placing the dried inner target in a dry distillation cooling device, introducing inert gas, and carrying out dry distillation cooling to obtain solid astatine-211; extracting solid astatine-211 from the eluted solution to obtain a solution containing the astatine-211; according to the elution solution, the stability of the solution can be improved, free radicals and ionization by-products are reduced, and the yield is increased; the preparation method can improve the production yield of astatine-211 and shorten the preparation time.

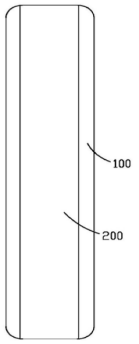
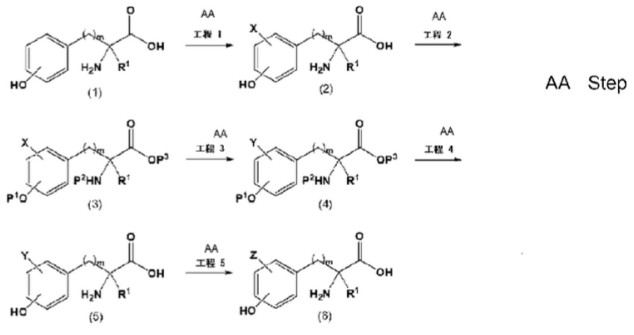


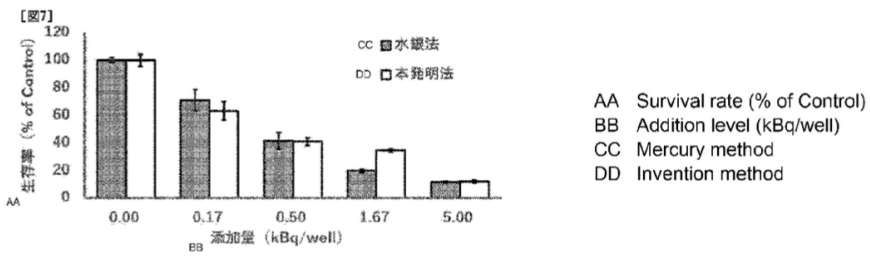
图1

(11) [Radiolabeling method] Janiszewska, Ł.; Koźmiński, P.; Pruszyński, M.; Majkowska, A.; Bilewicz, A.
Therapeutic Radiopharmaceutical Based on Gold Nanoparticles Marked with Astatine-211 and Method for Producing It.
PL239724B1, January 3, 2022.
https://worldwide.espacenet.com/patent/search/family/056617456/publication/PL239724B1?q=PL239724B1.
Automatic translation from polish : A therapeutic radiopharmaceutical based on the radionuclide asthma, it is characterized by being an astat-211 radionuclide embedded on gold nanoparticles, possibly attached to biologically active molecules selected from a group comprising biologically active peptides, monoclonal antibodies or their fragments. The method of producing a therapeutic radiopharmaceutical based on the radionuclide astat, using the adsorption process, is that gold nanoparticles are used to adsorb the astat-211 radionuclide at room temperature. Then, in order to separate the marked nanoparticles from the solution, nanoparticles are centrifuged, washed with distilled water and dispersed, preferably using ultrasonic waves.

No drawing available

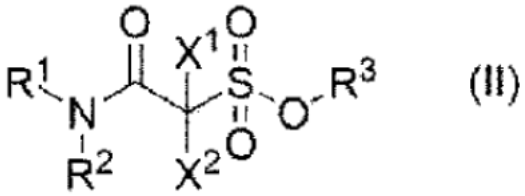
(12) [Radiolabeling method] [Radiolabeled compounds and their use] Shirakami, Y.; Kaneda, K.; Kadonaga, Y.; Watabe, T.; Toyoshima, A.; Fukase, K.; Shinohara, A.; Yamanaka, T.; Kondoh, Y.
Boronic Acid Compound and Method for Producing Same.
WO2022202956A1, September 29, 2022.
https://worldwide.espacenet.com/patent/search/family/083397467/publication/WO2022202956A1?q=WO2022202956A1.
Provided is a method by which a stably radiolabeled tyrosine derivative having a good purity can be produced in a safe manner suitable for the industrial production of pharmaceuticals. The present invention pertains to a method for producing compound (5) and radiolabeled compound (6). [In the formulae, each symbol is as defined in the description.]





(13) [Radiolabeling method] Tanaka, H.; Takahashi, K.; Suzuki, M.
Radioactive Halogen-Labeled Precursor Compound.

WO2022158442A1, July 28, 2022.
https://worldwide.espacenet.com/patent/search/family/082549450/publication/WO2022158442A1?q=JP2022110777A.
The present invention provides, as a radioactive halogen-labeled precursor compound that is highly stable and reactive, a compound represented by general formula (II) [in the formula, R1 and R2 each independently represent an alkyl group having 5-20 carbon atoms, X1 and X2 each independently represent a halogen atom, and R3 represents a monovalent group derived from a sugar].



(II)

(14) [Radiolabeling method] Wilbur, D. S.; Chyan, M.-K.; Hamlin, D. K.
Reagents and Methods for Labeling Molecules with Astatine Isotopes in Higher Oxidation States.
US2022354974A1, November 10, 2022.
https://worldwide.espacenet.com/patent/search/family/083901025/publication/US2022354974A1?q=US2022354974A1.
Reagents and methods for labeling biomolecules with astatine isotopes in higher oxidation states. The reagents and methods allow for efficient labeling of biomolecules, such as antibodies, without the formation of high molecular weight by products that arise due to 211At-promoted dimerization and higher aggregation of the conjugated biomolecules, and diminish cellular retention of astatine caused by cellular oxidization of the bonded astatine atom in vivo.

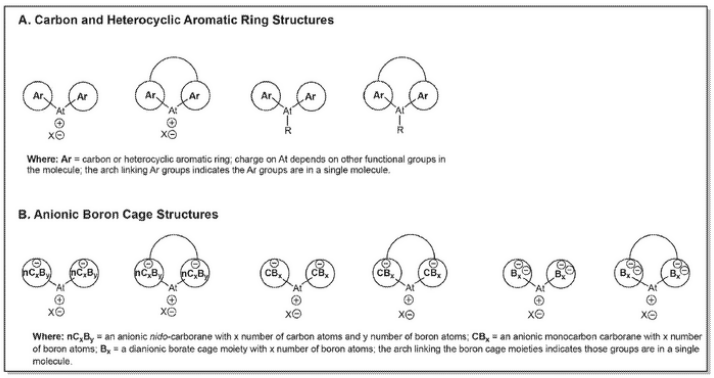
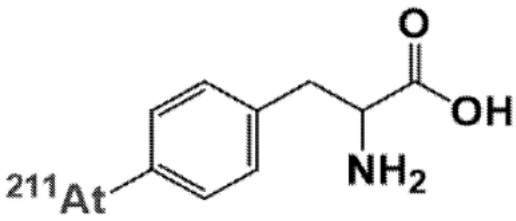


FIG. 10

(15) [Radiolabeled compounds and their use] Yan, E.; Wheatcroft, M. P.; Gaschet, J.; Chérel, M.; Gestin, J.-F.; Guerard, F.; Eychenne, R.
Methods of Treatment.
WO2022016231A1, January 27, 2022.
https://worldwide.espacenet.com/patent/search/family/079729502/publication/WO2022016231A1?q=WO2022016231A1.
The present invention is directed to methods of treating or preventing multiple myeloma in a patient in need thereof by administering 4-[211At]Astato-L-phenylalanine (4-[211At]APA) or a pharmaceutical derivative thereof to said patient.



(16) [Astatine Extraction/purification method] Burns, J. D.; Tereshatov, E. E.; Mcintosh, L. a; Tabacaru, G. C.; Yennello, S. J.
Astatine Purification Method.
WO2021202718 (A1), October 7, 2021.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20211007&DB=EPODOC&locale=en_EP&CC=WO&NR=2021202718A1&KC=A1&ND=4 (accessed 2021-10-18).
A process for isolating astatine includes (a) contacting a composition comprising astatine and bismuth with nitric acid to form a first solution comprising astatine, bismuth, and nitric acid; (b) contacting a resin with the first solution so that astatine partitions out of the first solution and into the resin; and (c) eluting astatine from the resin. A composition comprising astatine may be of the formula AtO+X-, wherein X- is a counterion.

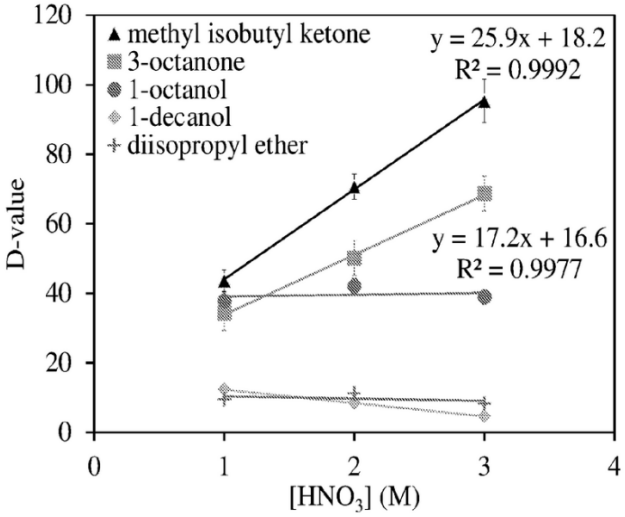
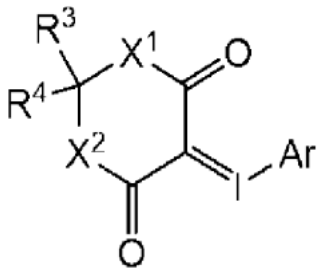


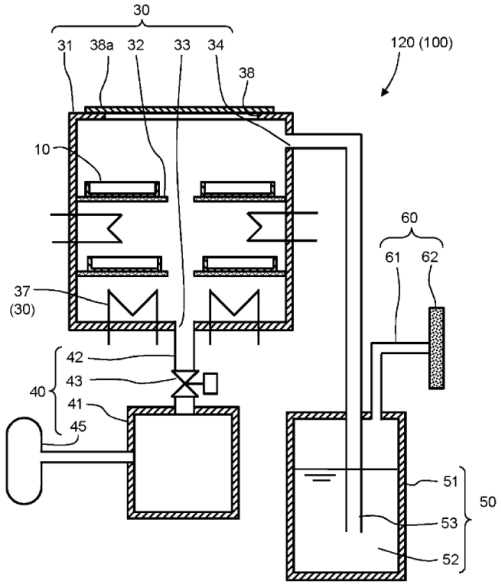
Fig 1

(17) [Radiolabeling method] Matsunaga, S.; Yoshino, T.; Matsuoka, K.; Ogawa, M. Method for Producing Aromatic Astatine Compound.
WO2021167008 (A1), August 26, 2021.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20210826&DB=EPODOC&locale=en_EP&CC=WO&NR=2021167008A1&KC=A1&ND=4 (accessed 2021-09-06).
This method for producing an aromatic astatine compound comprises reacting aromatic iodonium ylide with astatine to produce an aromatic astatine compound.



(1)

(18) [Astatine Extraction/purification method] Miyamoto, M.; Yuhara, M.; Wada, R.; Miyadera, H.; Nakada, K.; Tezuka, M.
Producing Method and Device for Astatine Isotope, and Separation/Recovery Method and Device for Astatine Isotope.
JP2021092483A, June 17, 2021.
https://worldwide.espacenet.com/patent/search/family/076312178/publication/JP2021092483A?q=JP2021092483A.
To provide a method for efficiently and quickly separating an astatine isotope.SOLUTION: A method for producing an astatine isotope includes: an irradiation step S30 of irradiating an irradiation sample containing bismuth that is an element to be irradiated with helium accelerated by an accelerator; and recovery steps S40 to S60 of recovering an astatine isotope produced in the irradiation step. The recovery steps includes a step of transferring a gaseous astatine isotope using aerosol.SELECTED DRAWING: Figure 3



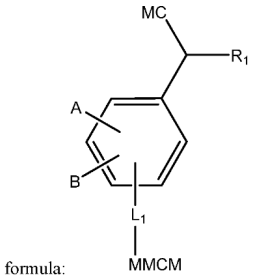
(19) [Astatine Extraction/purification method] Tanaka, H.; Takahashi, K.; Suzuki, M.
Simple Astatine Concentration Method.
WO2021225147A1, November 11, 2021.
https://worldwide.espacenet.com/patent/search/family/078468033/publication/WO2021225147A1?q=WO2021225147A1.
For the purpose of producing astatine-211 free from chloride ions with high yield, an astatine-211 production method is provided, the method being characterized by comprising: (1) a step for irradiating bismuth with an α ray to produce astatine-211; (2) a step for heating the astatine-211 produced in step (1) to vaporize the astatine-211; (3) a step for cooling the astatine-211 vaporized in step (2) and collecting the astatine-211 with a volatile and polar solvent to produce an astatine-211

solution; (4) a step for adding a weak acid salt to the astatine-211 solution produced in step (3) to produce an astatine-211 solution containing the weak acid salt; and (5) a step for removing the solvent from the astatine-211 solution containing the weak acid salt which is produced in step (4).

No drawing available

(20) [Radiolabeled compounds and their use] Zhu, R.; Shi, X.; Zhang, M.; Wang, F.; Li, Q.; Wang, G.; Zhang, C.; Zhang, L.
Astatine 211 Labeled Semiconductor Polymer Nanoparticles as Well as Preparation Method and Application Thereof.
CN112451686A, March 9, 2021.
https://worldwide.espacenet.com/patent/search/family/074799929/publication/CN112451686A?q=CN112451686A.
The invention relates to the technical field of radionuclide labeling, The invention provides an astatine 211 labeled semiconductor polymer nanoparticles as well as a preparation method and application thereof. The preparation method comprises the following steps: respectively dissolving a reaction product of gastric inhibitory polypeptide and Mal-PEG12-DSPE and PCPDTBT in tetrahydrofuran, respectively dissolving MeATE and NH2-PEG45-DSPE in dimethyl sulfoxide, performing reactions and uniform mixing, and pumping the mixture in water for self-assembly to obtain a MeATE-SPN aqueous solution; andreacting 211At, NCS and the MeATE-SPN aqueous solution to obtain the 211At labeled semiconductor polymer nanoparticles. The 211At labeled semiconductor polymer nanoparticles have excellent activity,can be used for effectively inhibiting tumors, have durable killing effect on tumor cells and have small toxic and side effects under the treatment dosage.

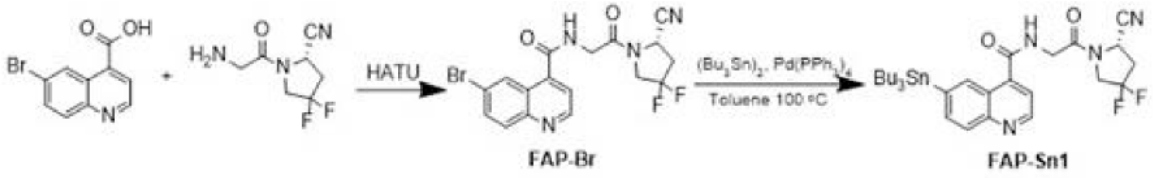
(21) [Radiolabeled compounds and their use] Zalutsky, M. R.; Vaidyanathan, G.; Mcdougald, D. L.
Radiohalogen Prosthetic Moieties and Radiolabeled Biomolecules.
WO2021096968A1, May 20, 2021.
https://worldwide.espacenet.com/patent/search/family/073790210/publication/WO2021096968A1?q=WO2021096968A1. (22) Berdal, M.; Faivre-Chauvet, A.; Gestin, J.-F.; Guerard, F. Method for Radioiodination or Radioastatination of a Biomolecule. WO2020221744A1, November 5, 2020. https://worldwide.espacenet.com/patent/search/family/066647350/publication/WO2020221744A1?q=WO2020221744A1.
The application is drawn to radiohalogen prosthetic moieties and precursors thereof and to radiolabeled biomolecules comprising such radiohalogen prosthetic moieties. The biomolecules have an affinity for particular types of cells and may specifically bind a certain cell, such as a cancer cell. Relevant biomolecules include antibodies, monoclonal antibodies, antibody fragments, peptides, other proteins, nanoparticles, aptamers, and pharamacological moieties used to target prostate-specific membrane antigen (PSMA)



formula:

(23) [Radiolabeled compounds and their use] Liu, Z.; Zhang, H.; Liu, J.; Wang, H.; Chen, D.

Tin-Based Derivative of Fibroblast Activation Protein Inhibitor for Marking Nuclide 211At as Well as Preparation Method and Application of Tin-Based Derivative.
CN112023064A, December 4, 2020.
https://worldwide.espacenet.com/patent/search/family/073573195/publication/CN112023064A?q=CN112023064A.
The invention belongs to the technical field of medicines, and particularly relates to a tin-based derivative of a fibroblast activation protein inhibitor for marking radionuclide 211At as well as a preparation method and application of the tin-based derivative. The tin-based derivative obtained by modifying the FAP inhibitor can be used as a key precursor for marking the radionuclide 211At, and amaterial basis is provided for 211At-based radiopharmaceutical synthesis of targeted FAP.



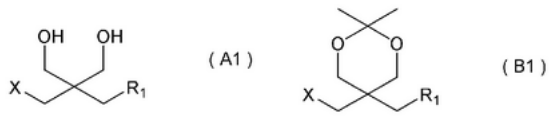
(24) [Radiolabeling method] Arano, Y.; Uehara, T.; Suzuki, H.; Tanaka, H.; Ishioka, N.; Watanabe, S.

Radioactive Pharmaceutical. WO2019151384 (A1),

August 8, 2019.

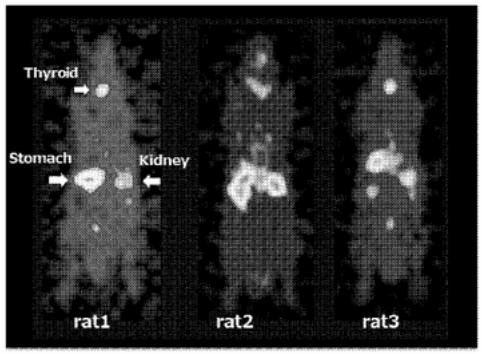
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20190808&DB=EPODOC&locale=en_EP&CC=WO&NR=2019151384A1&KC=A1&ND=5

One embodiment of the present invention relates to novel substances, etc., which are: [1] a compound, etc., represented by formula (A1) or formula (B1); [2] a compound, etc., represented by formula (A2) or formula (B2); [3] a compound, etc., represented by formula (A3) or formula (B3); [4] a compound, etc., represented by formula (A4) or formula (B4); [5] a radioactive pharmaceutical including the compound. etc., described in [1] or [2]; [6] a radiotherapeutic agent including the compound, etc., described in [1] or [2]; [7] a radiographic imaging diagnostic agent including the compound, etc., described in [1] or [2]; [8] a use of the compound, etc., described in [1] or [2], for production of radioactive pharmaceuticals; and [9] a medical agent, etc., for preparation of radioactive pharmaceuticals, including the compound, etc., described in [1] or [2].



(25) [Radiolabeled compounds and their use] Fukase, K.; Shinohara, A.; Kanai, Y.; Kabayama, K.; Kaneda, K.; Zhang, Z.; Hatazawa, J.; Shirakami, Y.; Shimoyama, A.; Manabe, Y.
Pharmaceutical Composition Containing 211at-Labeled Amino Acid Derivative, and Method for Producing Said Pharmaceutical Composition.
WO2019176505A1, September 19, 2019.
https://worldwide.espacenet.com/patent/search/family/067908155/publication/WO2019176505A1?q=WO2019176505A1.
[Problem] To develop a compound which exhibits high accumulation in cancer cells and can emit α rays, and to provide a pharmaceutical composition for cancer treatment that contains said compound.

[Solution] A pharmaceutical composition for cancer treatment that contains a compound having a structure in which 211At has been introduced as a substituent into an amino acid derivative having an affinity for amino acid transporter LAT1, or contains a pharmacologically acceptable salt thereof.



(26) [Astatine Extraction/purification method] Shirakami, Y.; Watabe, T.; Kaneda, K.; Shimosegawa, E.; Shinohara, A.; Hatazawa, J.
Astatine Solution and Method for Producing Same.
WO2019131998A1, July 4, 2019.
https://worldwide.espacenet.com/patent/search/family/067063794/publication/WO2019131998A1?q=WO2019131998A1.
The present invention addresses the problem of providing an astatine solution that can be used in radionuclide therapy for the treatment of thyroid disease or the like, and a method for producing the same. The present invention provides: a method for producing a solution including 211At- (astatinide ion) using 211At obtained by nuclear reaction as a raw material, wherein the method for producing a solution including 211At- (astatinide ion) at high radiochemical purity includes a step for adding a reducing agent to a solution including impurities derived from 211At; and a solution including 211At- (astatinide ion) at a radiochemical purity of 30% or higher.

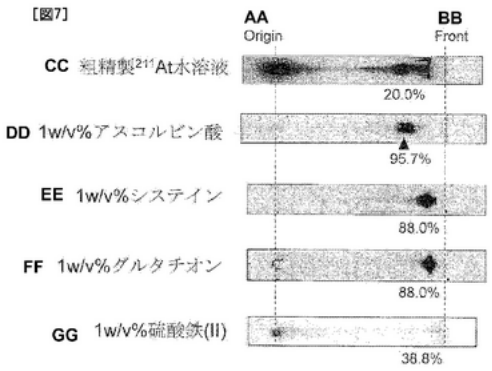
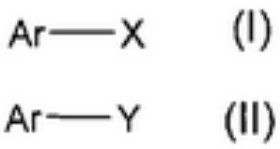


FIG. 7:
AA Origin
BB Front
CC Crudely purified 211At aqueous solution
DD 1 w/v% ascorbic acid
EE 1 w/v% cysteine
FF 1 w/v% glutathione
GG 1 w/v% iron(II) sulfate

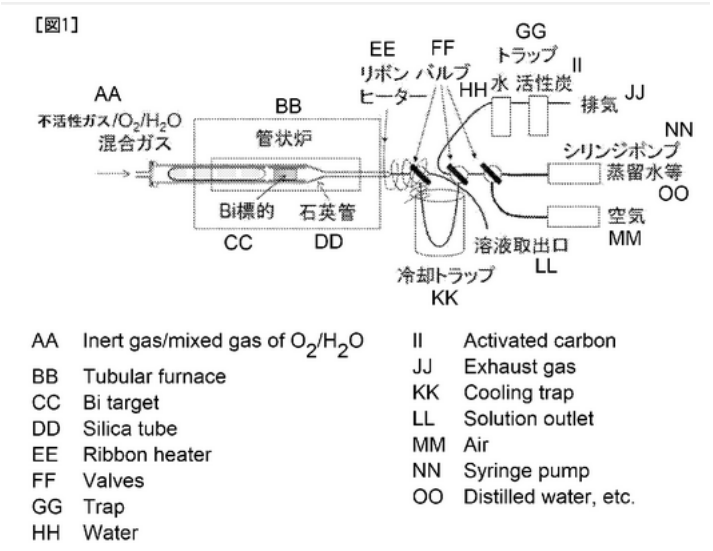
(27) [Radiolabeling method] Shirakami, Y.; Ikeda, H.; Kanai, Y.; Shimosegawa, E.; Hatazawa, J.; Watabe, T.; Kaneda, K.
Production Method for Radiolabeled Aryl Compound.
WO2019027059 (A1), February 7, 2019.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20190207&DB=EPODOC&locale=en_EP&CC=WO&NR=2019027059A1&KC=A1&ND=4

The purpose of the present invention is to produce a radiolabeled aryl compound by a simple method in which labeling can be carried out in a short time in high radiochemical yield and which renders the radiolabeled aryl compound usable in formulation immediately after the labeling. The present

invention relates to a production method for a radiolabeled aryl compound (I), characterized by reacting an arylboronic acid compound (II) with a radioactive nuclide selected from among 211At, 210At, 123I, 124I, 125I, and 131I in water in the presence of an oxidant selected from among alkali metal iodides, alkali metal bromides, N-bromosuccinimide, N-chlorosuccinimide, and hydrogen peroxide. (In the formulae, the symbols are as defined in the description.)



(28) [Astatine Extraction/purification method] Shinohara, A.; Toyoshima, A.; Yoshimura, T.; Kanda, A. Method for Producing Astatine.
WO2019112034A1, June 13, 2019.
https://worldwide.espacenet.com/patent/search/family/066750219/publication/WO2019112034A1?q=WO2019112034A1.
Provided is a method in which astatine-211 can be isolated/purified at high yield and dissolved in a solution. This method for producing astatine-211 includes: a step for irradiating bismuth with α rays to generate astatine-211 in the bismuth; and a step for distilling, using an inert gas and a carrier gas including O2 and H2O, the bismuth irradiated with the α rays to isolate/purify the astatine-211, and for dissolving the astatine-211 in a solution.



(29) [Astatine Extraction/purification method] O'hara, M. J.
System and Process for Purification of Astatine-211 from Target Materials.
WO2018194760A1, October 25, 2018.
https://worldwide.espacenet.com/patent/search/family/063852779/publication/WO2018194760A1?q=WO2018194760A1.
A new column-based purification system and approach are described for rapid separation and purification of the alpha-emitting therapeutic radioisotope 211At from dissolved cyclotron targets that provide highly reproducible product results with excellent 211At species distributions and high antibody labeling yields compared with prior art manual extraction results of the prior art that can be expected to enable enhanced production of purified 211At isotope products suitable for therapeutic medical applications such as treatment of cancer in human patients.

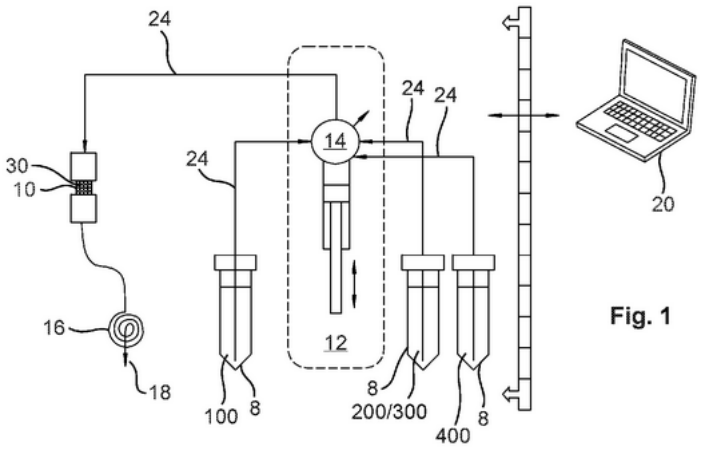


Fig. 1

(30) [Astatine-211 production] HENRIKSEN, G.; MÜLLER, J. C.; SIEM, S.; GÖRGEN, A.; SCHOULTZ, B. W.
Method of Producing Radionuclides and Apparatus Therefore.
WO2018007643 (A1), January 11, 2018.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20180111&DB=EPODOC&locale=en_EP&CC=WO&NR=2018007643A1&KC=A1&ND=4
The present disclosure provides a method and an apparatus for producing astatine-211 from alpha-particle bombardment of bismuth-209. The disclosure also relates to a method and apparatus of producing other radionuclides from target nuclides. The apparatus comprises a plate having a recessed portion. The recessed portion has a generally inert surface of ceramic or metal, preferably aluminium oxide that does not react with molten bismuth. A bismuth target is placed in the recessed portion and held therein by a foil cover. The foil has a melting temperature greater than target nuclide (i.e. for bismuth, >271 °C). The foil and target nuclide are held in the recessed portion by a cover that is fastened over the foil. The cover has an aperture to allow a beam of radiation, such as alpha particles, from a cyclotron or other accelerator to pass through the cover to the foil and target nuclide. The apparatus can be used with any orientation of beam of radiation.

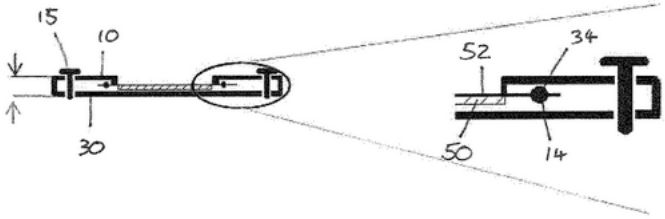
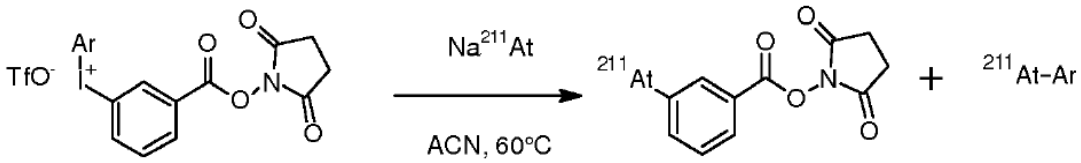


Fig. 6

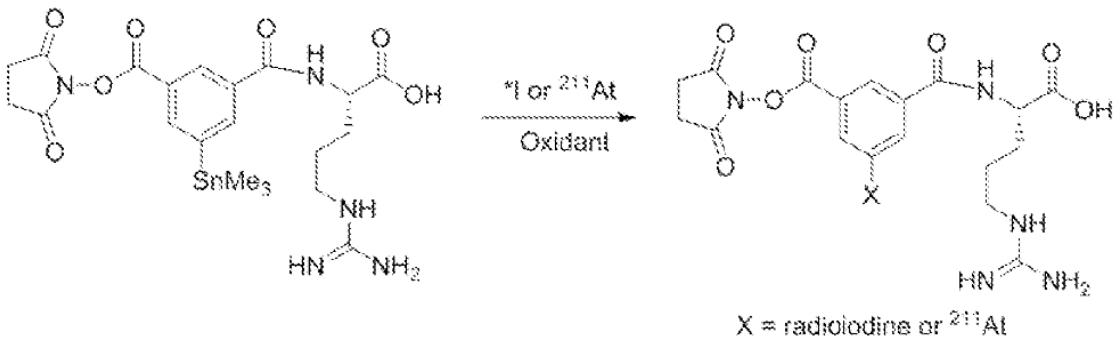
(31) [Radiolabeling method] GUERARD, F.; GESTIN, J.-F.; BRECHBIEL, M. W.; LEE, Y.-S.
Method for Synthesizing Iodo- or Astatoarenes Using Diaryliodonium Salts.
WO2017089492 (A1), June 1, 2017.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20170601&DB=EPODOC&locale=en_EP&CC=WO&NR=2017089492A1&KC=A1&ND=4
The present invention concerns a method of synthesizing a iodo- or astatoarene comprising the reaction of a diaryliodonium compound with a iodide or astatide salt, respectively. The invention also

relates to said iodo- or astatoarene and diaryliodonium compound as such. The invention also concerns a method of synthesizing a iodo- or astatolabelled biomolecule and/or vector using said iodo- or astatoarene.

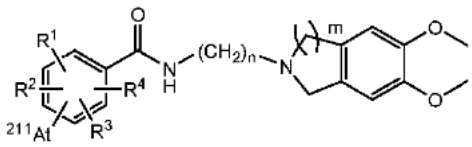


(32) [Radiolabeled compounds and their use] ZALUTSKY, M. R.; VAIDYANATHAN, G. Radiolabeled Biomolecules and Their Use. WO2018178936 (A1), October 4, 2018. https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20181004&DB=EPODOC&locale=en_EP&CC=WO&NR=2018178936A1&KC=A1&ND=4

The application is drawn to radiolabeled biomolecules and methods for radiolabeling biomolecules with radioactive halogen atoms that minimizes loss of the radioactive halogen due to dehalogenation in vivo, preserves the biological activity of the biomolecule, maximizes retention of radioactivity in cancer cells, and minimizes the retention of radioactivity in normal tissues after in vivo administration. Some such radiolabeled biomolecules comprise a radioactive metal atom in place of, or in addition to the radioactive halogen. The biomolecules have an affinity for particular types of cells and may specifically bind a certain cell, such as cancer cells. Relevant biomolecules include antibodies, monoclonal antibodies, antibody fragments, peptides, other proteins, nanoparticles and aptamers.



(33) [Radiolabeled compounds and their use] Pryma, D. a; Lieberman, B. P.; Makvandi, M.; Mach, R. H.
211-Astatine Containing Radiotherapeutics for the Treatment of Cancer.
WO2016178852A1, November 10, 2016.
https://worldwide.espacenet.com/patent/search/family/057218257/publication/WO2016178852A1?q=WO2016178852A1.
Described herein is an alpha-emitting radionuclide, 211At, which has been incorporated into a selective sigma-2 ligand moiety to provide cytotoxic capabilities to a chemical compound. As described herein, a compound of formula (I), wherein R1-R4, m, and n are defined herein, was prepared and utilized in in vitro and in vivo tumor targeting of alpha-emitting sigma-2 ligand in a breast cancer model. In one embodiment, the compound is 5-(211At)-N-(4-(6,7-dimethoxy-3,4- dihydroisoquinolin-2(lH)-yl)butyl)-2,3-dimethoxybenzamide.



(I)

(34) [Astatine Extraction/purification method] Wilbur, D. S.; Chyan, M.-K.; Hamlin, D. K.; Gagnon, K.; Watanabe, S.
PROCESS FOR ISOLATION AND PURIFICATION OF ASTATINE-211.
US20160053345, 2016.
https://worldwide.espacenet.com/patent/search/family/055347793/publication/US2016053345A1?q=20160053345
This disclosure relates to methods for purifying and isolating astatine-211 from bismuth metal. Also disclosed are automated methods for purifying and isolating astatine-211 from bismuth metal.

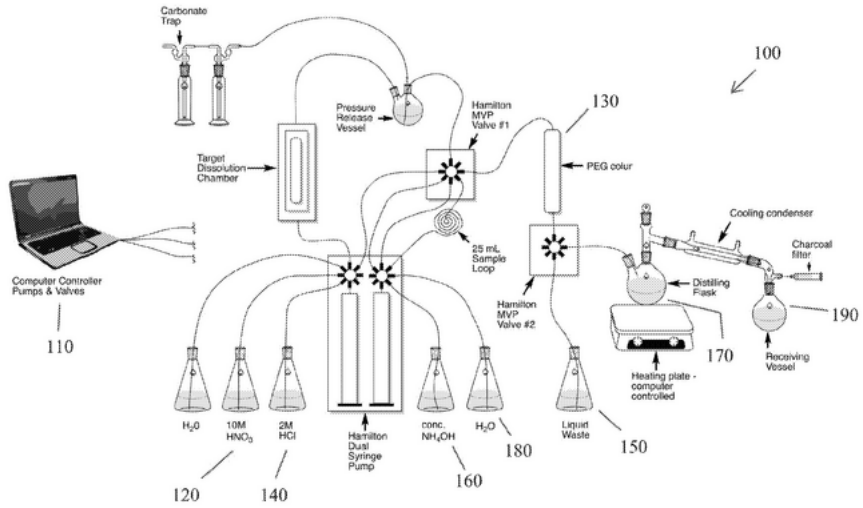
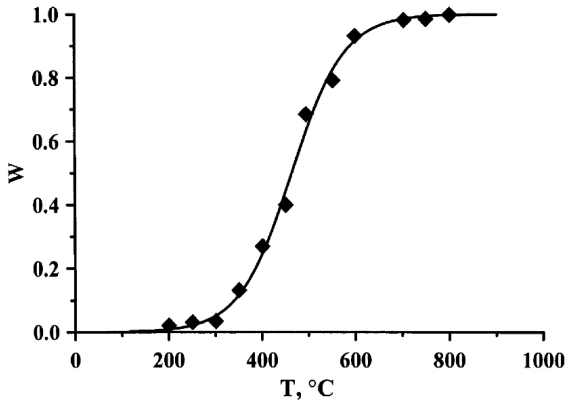


FIGURE 1

(35) [Astatine Extraction/purification method] Yuminov, O. A.; Drozdov, V. A.; Eremenko, D. O.; Platonov, S. Y.; Fotina, O. V. Method of Producing Radiopharmaceutical Preparation “Astatine-211.” RU2593017C1, July 27, 2016. https://worldwide.espacenet.com/patent/search/family/056557179/publication/RU2593017C1?q=RU2593017C1.

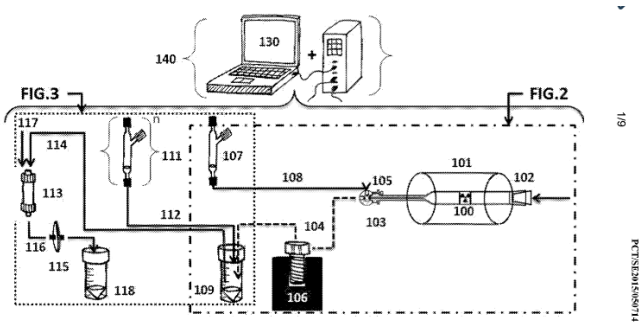
FIELD: chemistry; medicine.SUBSTANCE: present invention relates to conversion of chemical elements and radiation sources for medical purposes, particularly to a method of producing radiopharmaceutical preparation “Astatine-211” from an irradiated target, which includes subliming radionuclide at temperature 700÷850 °C for 4÷6 minutes, with its deposition in low-alkali buffer saline solution with pH 7.5-9, where target is Bi of natural isotopic composition that is irradiated by αparticles with energy 29÷31 MeV.EFFECT: invention provides considerable reduction of time for obtaining stable forms ofAt, trophic to thyroid gland, reduction of radiation exposures on personnel, involved in manufacturing of preparation, and increased efficiency of synthesis of preparation.1 cl, 1 dwg, 5 ex



(36) [Radiolabeling method] Legoupy, S.; Faye, D.; Gestin, J.-F.; Rajerison, H.; Faivre-Chauvet, A.; Boeda, F.
Ionic Liquid Supported Organotin Reagents for the Manufacturing of Radiopharmaceuticals Compounds.
WO/2015/104300, July 17, 2015.
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2015104300&recNum=19&docAn=EP2015050180&queryString=FP:(EN_ALL:NMR%20AND%20PA:(Centre%20national%20de%20la%20recherche%20scientifique))&maxRec=1227.
The present invention relates to an ionic liquid supported organotin reagent of formula (I). The invention further relates to a process for manufacturing the ionic liquid supported organotin reagent of formula (I) and to a process for manufacturing an halogenated or radio-halogenated compound using compound of formula (I). The invention also relates to a device for implementing the halogenating process of the invention and to a kit comprising the compound of formula (I).

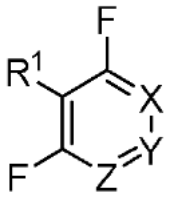
(37) [Astatine Extraction/purification method] [Radiolabeling method] Lindegren, S.; Aneheim, E. AUTOMATIC PROCESS PLATFORM FOR THE PRODUCTION OF ASTATINE-211 [At-211]-RADIOPHARMACEUTICALS. WO2015195042A1, December 23, 2015. https://worldwide.espacenet.com/patent/search/family/054935878/publication/WO2015195042A1?q=WO2015195042A1.

A system and method for automatic production of astatine-211labeled molecules is described. The invention represents a significant advantage in the preparation of At-211 radiopharmaceuticals including better reproducibility, reduced production time and increased radiation safety. The invention also enables routine automatic synthesis of radiopharmaceuticals in a clinical setting, in conjunction or at short distance from a cyclotron unit capable of producing the radionuclide.



(38) [Radiolabeling method] [Radiolabeled compounds and their use] Dimagno, S. Stabilization of Radioiodinated and Astatinated Pharmaceutials and Imaging Agents.

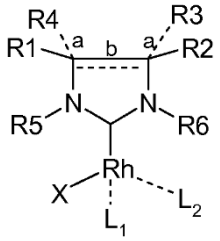
WO2014152431A1, September 25, 2014.
https://worldwide.espacenet.com/patent/search/family/051530140/publication/WO2014152431A1?q=US20140275539A1.
Provided herein are stabilized radioiodinated and astatinated compounds, and to methods for their preparation.



Formula (I).

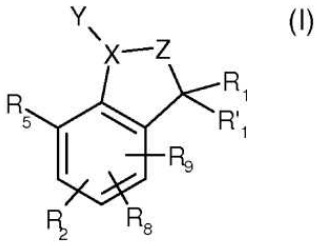
(39) [Radiolabeling method] [Radiolabeled compounds and their use] Faivre-Chauvet, A.; Rajerison, H.; Gestin, J.-F.
Radioactive Rhodium Complexes, Preparation Methods and Uses Thereof. WO2013171224 (A1), November 21, 2013.
https://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20131121&DB=EPODOC&locale=en_EP&CC=WO&NR=2013171224A1&KC=A1&ND=4.

The present invention concerns radioactive rhodium complexes, their preparation methods, and their use for the radiolabelling of biomolecules, especially monoclonal antibodies.



(I)

(40) [Radiolabeling method] [Radiolabeled compounds and their use] Gestin, J.-F.; Guerard, F.; Faivre-Chauvet, A.
Hypervalent Radioactive Astatine or Iodine Compounds, and Preparation Methods Thereof.
WO2011095517 (A1), August 11, 2011.
http://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20110811&DB=EPODOC&locale=en_EP&CC=WO&NR=2011095517A1&KC=A1&ND=4
The present invention relates to a compound having formula (I): wherein: - X is in particular 125I Or 211At; - R1 and R'1 are independently from each other chosen preferably from the group consisting of electron-withdrawing groups and alkyl groups; - R2 is chosen from the group consisting of : H, alkyl groups, functional groups being able to bind a vector, and functional groups having targeting properties which make the compound of the invention a vector itself; - Z is a heteroatom, - R5, R8 and R9 are preferably H; - Y is preferably an electron withdrawing group.



(I)

(41) [Radiolabeling method] Yuanyou, Y.; Ning, L.; Jiali, L.
Coupling Agent for Preparing Radiotherapy Marker, 211At Marker Prepared Thereby and Preparation. CN101486726A, July 22, 2009.
https://worldwide.espacenet.com/patent/search/family/040889803/publication/CN101486726A?q=CN101486726A.
The invention discloses a coupling agent 2, 3, 5, 6-4-tetrafluorophenol 3-propionate TCP which can be used for preparing a radiotherapy marker, a radiotherapy marker At-TCP-BSA which is prepared from the 2, 3, 5, 6-4-tetrafluorophenol 3-propionate TCP, as well as preparation methods of the coupling agent TCP and the marker At-TCP-BSA. The marker At-TCP-BSA prepared by the preparation method is used for radiotherapy, the marking rate can be up to 60 percent, and the radiochemical purity is higher than 98 percent and has no significant change after the marker are placed at room temperature for 24 hours. Compared with free At and At-ATE-BSA (ATE is 3-n-butyltin N-succinimide benzoate), the marker At-TCP-BSA has relatively high stability both in vivo and in vitro; and the TCP is a good intermediate for marking protein by radioactive astatine and lays a good function for the targeted cancer therapy of At-TCP-BSA in the next stage.

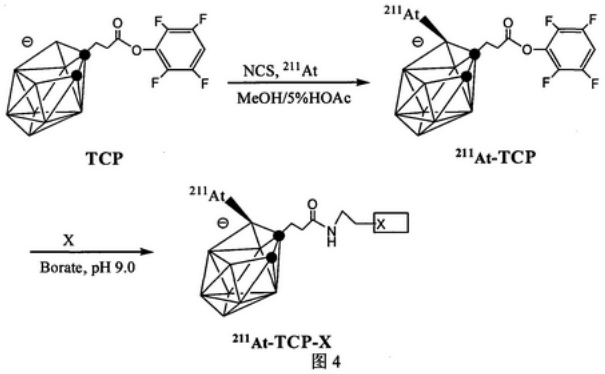


图 4

(42) [Radiolabeling method] [Radiolabeled compounds and their use] Miles, S.; Norseev, J. V.; Sjuch, Z.
Method of Preparing Monoclonal Antibodies Labeled by Astatine-211. SU1695757A1, May 10, 1995.
https://worldwide.espacenet.com/patent/search/family/060532228/publication/SU1695757A1?q=SU1695757A1.
FIELD: radiochemistry, radiotherapy. SUBSTANCE: on final step of isolation and purification astatine-211 is directly distilled into solution of diethyltriamine pentacetic acid (DTPA) having concentration α mol/l. Said solution contains sodium persulfate having concentration 0.05 mol/l as oxidizing agent. Total volume of mixture is not more 10 a. After distillation mixture is heated within 5 min on water bath and then it is cooled to temperature not higher 37 C. Solution of monoclonal antibodies having concentration 1 mg/ml (its quantity being 200 10моль/л) is added into solution of complex compound astatine-DTPA. Thus prepared mixture is allowed to stand within 10 min at 37,0± 0,5C . Duration of labelling monoclonal antibodies by astatine thus decreases 6 times. EFFECT: decreases labelling time.

No drawing available

(43) [Astatine Extraction/purification method] Wilbur, D. S.; Hadley, S. W.
Process for Isolation and Radiolabeling of Pharmaceuticals with Isotopes of Astatine.
WO9109626A1, July 11, 1991.
https://worldwide.espacenet.com/patent/search/family/023823278/publication/WO9109626A1?q=WO9109626A1.
A process for recovering At-211 from a target and simultaneously producing an At-211-labeled radiopharmaceutical agent involves introducing volatilized At-211, produced by dry distillation of an irradiated Bi-209 target, into a solution containing a compound that binds the At-211 to form an At-211-labeled radiopharmaceutical agent. The radiopharmaceutical agent may have therapeutic use as is, or may be attached to a targeting protein such as an antibody prior to administration to a patient.

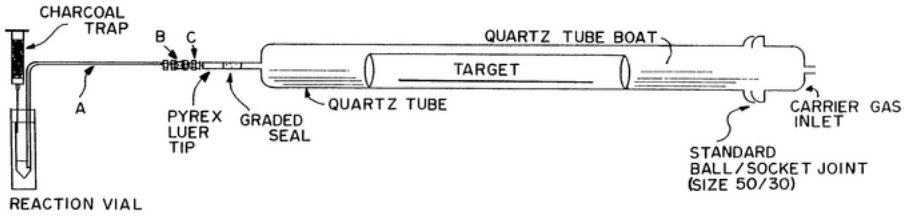
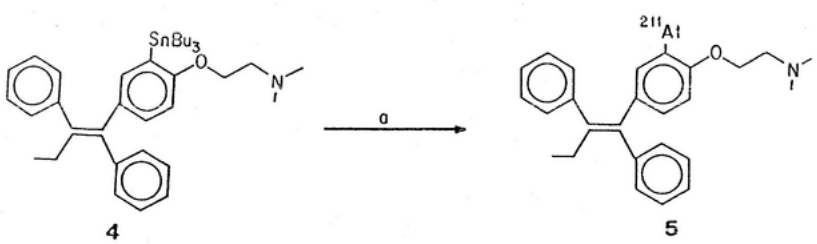


FIG. I

(44) [Radiolabeling method] Milius, R. a; Lambrecht, R. M.; Bloomer, W. D.
Astatinated Organic Compounds.
US4826672A, May 2, 1989.
https://worldwide.espacenet.com/patent/search/family/024983897/publication/US4826672A?q=US4826672A.
Methods and kits for incorporating a radioactive astatine isotope (particularly 211At) into an organic compound by electrophilic astatodestannylation of organostannanes.



(45) [Astatine Extraction/purification method] Mirzadeh, S.; Lambrecht, R. M.
Process for Producing Astatine-211 for Radiopharmaceutical Use.
US4681727A, July 21, 1987.
https://worldwide.espacenet.com/patent/search/family/024396312/publication/US4681727A?q=US4681727A.

A process for reliably and consistently producing astatine-211 in small controlled volumes of a solution, which is selected from a choice of solvents that are useful in selected radiopharmaceutical procedures in which the At-211 activities are to be applied

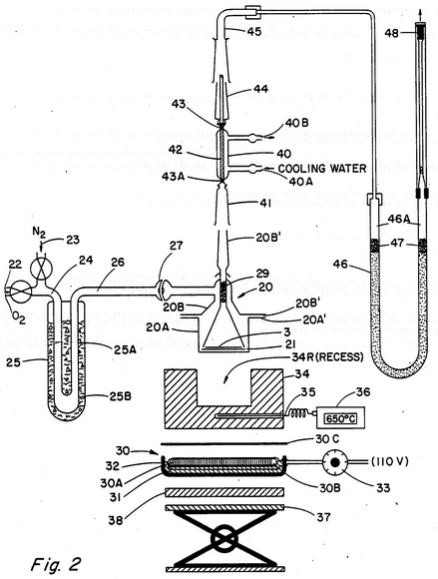


Fig. 2

(46) [Radiolabeling method] Wunderlich, G.; Dreyer, R.; Fischer, S.
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No Abstract found

No drawing available

(47) [Astatine Extraction/purification method] Laslo, V.; Rolf, D.; Milka, M.; Norseev, Y. V.; Khalkin, V. A.
Method for Preparing Astatine Solutions. SU947025A1, July 30, 1982.
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Claim: A method for producing astatine solutions, including distillation at 450-500 ° C of astatine adsorbed on a platinum foil and its condensation, characterized in that, in order to increase the yield of astatine, the condensation is carried out into water. Or into aqueous solutions of alkalis, acids, salts.

No drawing available

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