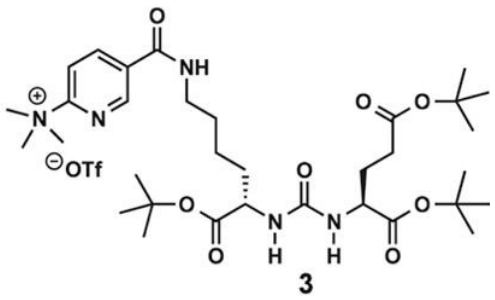
Claims

1. A method of synthesizing 2-(3-{1-carboxy-5-[(6-[^{18}F]fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid ([^{18}F]DCFPyL), the method comprising:

(i) radiofluorinating a DCFPyL precursor comprising ester moiety protecting groups to form a radiofluorinated DCPFPyL precursor, wherein the precursor is



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(compound (3));

(ii) deprotecting the ester moiety protecting groups of the radiofluorinated DCPFPyL precursor of step (i) with phosphoric acid to form [^{18}F]DCFPyL in a reaction mixture; and

(iii) purifying the [^{18}F]DCFPyL from the reaction mixture of step (ii) to provide [^{18}F]DCFPyL.

2. The method of claim 1, wherein step (i) and step (ii) are performed in one reactor.

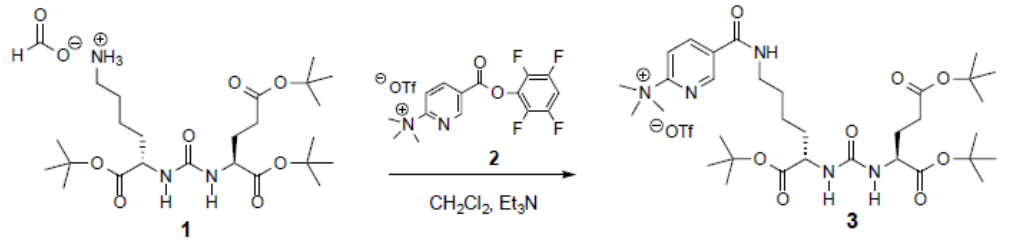
3. The method of claim 1, wherein the synthesizing is automated by use of a radiofluorination module (RFM) comprising a heating block, two syringe pumps, a multi-port cap, and valved reagent addition vials.

4. The method of claim 3, wherein the RFM further comprises a thermal heating cavity.

5. The method of claim 1, wherein the synthesizing is automated by use of an automated radiochemistry synthesizer.

6. The method of claim 3, wherein components of the RFM or the automated radiochemistry synthesizer are free of fluorine.

7. The method of claim 1, wherein the DCFPyL precursor is synthesized according to

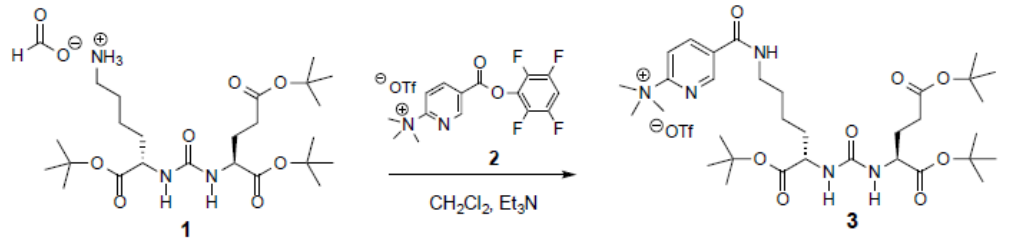


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8. The method of claim 1, wherein the DCFPyL precursor is synthesized by a method comprising:

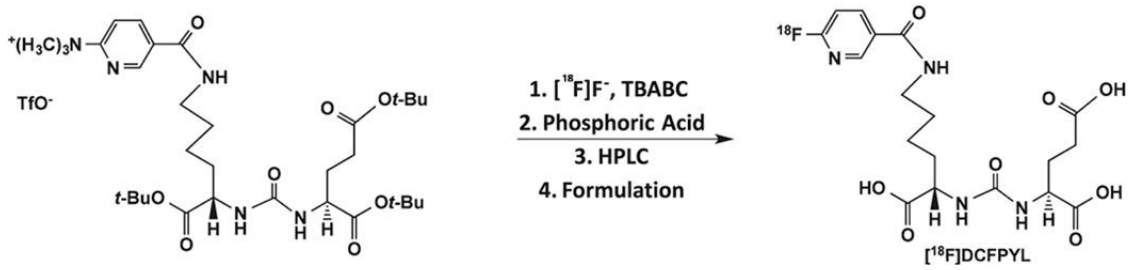
coupling of N,N,N-trimethyl-5-((2,3,5,6-tetrafluorophenoxy)carbonyl)pyridin-2-aminium trifluoromethanesulfonate and 2- {3-[l-t-butylcarboxylate-(5-aminopentyl)]-uriedo]-di-t-butyl pentandioate.

9. The method of claim 1, wherein the method further comprises synthesizing the DCFPyL precursor according to



or by coupling of N,N,N-trimethyl-5-((2,3,5,6-tetrafluorophenoxy)carbonyl)pyridin-2-aminium trifluoromethanesulfonate and 2-[3-[l-t-butylcarboxylate-(5-aminopentyl)]-uriedo]-di-t-butyl pentandioate.

10. The method of claim 1, wherein the radiofluorinating a DCFPyL precursor is performed according to



11. The method of claim 1, wherein the radiofluorinating a DCFPyL precursor comprises:

(a) trapping [18F]fluoride ion in a cartridge;

(b) eluting the cartridge with a solution of tetrabutylammonium base salt to release the [18F]fluoride ion trapped in the cartridge;

(c) drying the eluate comprising the [18F]fluoride ion to form dried [18F]fluoride ion; and

(d) adding a solution of compound (3) to the dried [18F]fluoride ion.

12. The method of claim 11, wherein the cartridge is an anion exchange chromatographic cartridge.

13. The method of claim 11, wherein the radiofluorinating a DCFPyL precursor further comprises heating the combined solution of compound (3) and the dried [18F]fluoride ion.

14. The method of claim 13, wherein the heating is done at a temperature between 30 °C to 70 °C.

15. The method of claim 13 or 14, wherein the heating time is for between 2 min to 10 min.

16. The method of claim 11, wherein the eluate of step (c) comprising the [18F]fluoride ion is dried at a temperature of between 80°C to 150°C.

17. The method of claim 11 or 16, wherein the eluate of step (c) comprising the [18F]fluoride ion is dried under nitrogen flow.

18. The method of claim 11 or 17, wherein the drying is performed for 50 seconds to 300 seconds.

19. The method of claim 11, wherein CH_3CN is added to the dried [18F]fluoride ion for further drying.

20. The method of claim 1, wherein the deprotecting with phosphoric acid is performed at a temperature of between 30°C to 55°C.

21. The method of claim 20, wherein the temperature is maintained for 2 min to 10 min.

22. The method of claim 1, further comprising adjusting the pH of the reaction mixture of step (ii) after the deprotecting with phosphoric acid to a pH of between 2 to 2.5.

23. The method of claim 1, wherein the purifying is performed by liquid chromatography.

24. The method of claim 23, wherein the liquid chromatography involves at least one Cl8 column.

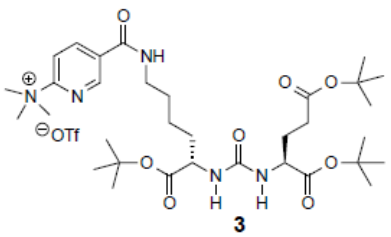
25. A method of radiofluorinating a DCFPyL precursor, which comprises:

(i) trapping [^{18}F]fluoride ion in a cartridge;

(ii) eluting the cartridge with a solution of tetrabutylammonium hydrogen carbonate (TBABC) to release the [^{18}F]fluoride ion trapped in the cartridge,

(iii) drying the eluate comprising the [^{18}F]fluoride ion from step (ii);

(iv) adding a solution of (compound (3))



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to the [^{18}F]fluoride ion from step (iii); and

(v) heating the combined solution of step (iv).

26. The method of claim 25, wherein the heating is at between 30 °C to 70 °C.

27. The method of claim 26, wherein the heating is for between 2 min to 10 min.

28. The method of claim 25, wherein the eluate comprising the [18F]fluoride ion is dried at a temperature of between 80 °C to 150 °C.

29. The method of claim 25 or 28, wherein the eluate comprising the [18F]fluoride ion from step (ii) is dried under nitrogen flow.

30. The method of claim 25 or 29, wherein the drying is performed for between 50 seconds to 300 seconds.

31. The method of claim 25, wherein CH_3CN is added to the dried [18F]fluoride ion for further drying.

32. The method of claim 25, wherein the cartridge is an anion exchange chromatographic cartridge.

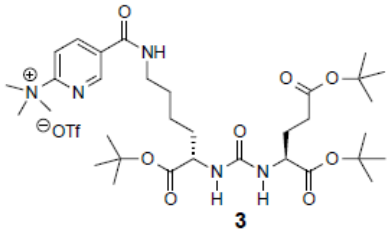
33. The method of claim 25 or 11, wherein the cartridge is preconditioned by washing with high purity water prior to trapping [18F]fluoride ion in the cartridge.

34. A composition comprising [^{18}F]DCFPyL produced by the method of claim 1.

35. A method of imaging comprising (i) contacting cells, organs or tissues with a composition of claim 34, and (ii) imaging the cells, organs or tissues.

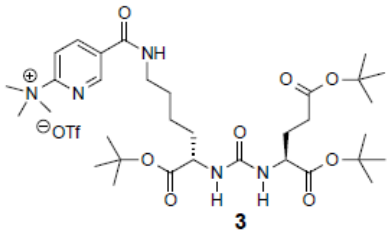
36. The composition of claim 34 for use in imaging, wherein the composition is to be administered to a subject.

37. Use of the composition of claim 34 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to a subject.

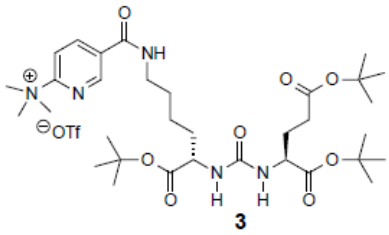
38. A composition comprising a DCFPyL precursor, wherein the precursor is (compound (3))  .

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39. A kit comprising the composition of claim 34.

40. A kit comprising a DCFPyL precursor, wherein the precursor is (compound (3))  , and phosphoric acid.

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41. A kit comprising a DCFPyL precursor, wherein the precursor is (compound (3))  , and tetrabutylammonium hydrogen carbonate.

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